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Prestress in ”balls and springs” model

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Abstract

Fibres in living cells carry the pre-existing tension (so-called prestress) even without external loading. By changing the prestress, cells are able to control actively their overall mechanical response; it is therefore an important element in cell elasticity. To capture this feature, we propose the hyperelastic model of living tissues composed of balls and springs. The prestress in fibres is maintained due to the assumption of the constant volume of cells (it does not allow the springs to relax). Even if the structure is simple, the determination of reference configuration leads to non-unique solutions and bifurcations.

Keywords: prestress, volume regulation, living tissue, Young's modulus

1. Introduction

Every eukaryotic cell is reinforced by the network of protein polymer chains, the so-called cytoskeleton. It is composed mainly of the three kinds of fibres: actin, intermediate filaments, and microtubules. It pierces the whole cell and has the similar function as the skeleton in human body. Among the others, it prevents cell from collapsing, it transmits mechanical forces and is therefore responsible for the mechanical response of the whole cell. There are experimental evidences that cytoskeleton carries the pre-existing tension even in natural state (state with no external loading), see [4] for details. This so-called prestress consequently plays an important role in cell mechanics. For example the prestress-induced stiffening was experimentally observed in living cells (see [3]), i.e. the cell stiffness increases with increasing prestress in fibres. Since the level of prestress in natural state can be actively controlled by cells (by changing the rest lengths of fibres), it becomes an important mechanism of cells how to control their mechanical properties; by changing the prestress, the cell ”switches” its stiffness. It seems therefore very challenging to capture such a feature in mechanical models of living cells or living tissues.

When trying to understand and model the problem, the crucial question is how the prestress is balanced in the natural state of a cell. The possible explanation is given by the idea of ”tensegrity” (see [4]). There the tension in actin fibres (modelled by cables) is balanced by the compression in microtubules (modelled by struts). Tensegrity models of living cells are therefore complex structures of tensioned cables and compressed struts joined together.

We propose the different approach taking into account another natural feature of a cell, the constant volume. It is known that cells employ both short- and long-term strategies to maintain a constant volume (see [2]). This fact is used as an assumption in our model where the constant volume plays exactly the same role as the struts in tensegrity models. It does not allow fibres to take their rest lengths and thus it balances the prestress.

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The aim of this paper is to propose the hyperelastic model of a living tissue with the level of prestress characterized by some additional microstructural parameter. And via this parameter to control the behaviour of the model at macroscale.

2. Balls and springs model

2.1. Unprestressed natural state

In this model, the soft tissue is assumed to be a continuum Ω, where each continuum point $\mathbf{X}$ is matched with the representative volume element (RVE) as depicted in the fig. 1. Each RVE represents the living cell and the surrounding extracellular matrix. The living cell is modelled by incompressible "ball" with dimensions c_i reinforced by the linear springs k_{c_i} which represent cytoskeleton. Here the assumption of the cell constant volume is taken into account since the ball is incompressible with the volume

$$V_c = c_1 c_2 c_3 = const. \tag{1}$$

The living tissue is assumed to have a periodic structure, so that each cell neighbours with six another cells in main directions. The space between them has the dimensions Δ_i and the interactions are represented by the linear springs k_{Δ_i}.

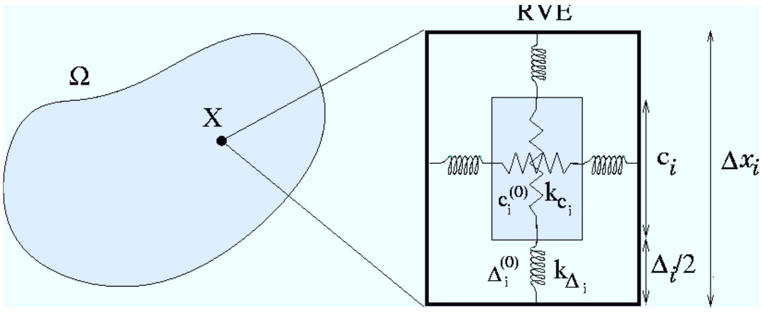

Fig. 1. Reference configuration of the "balls and springs" model. Each continuum point is matched with the RVE that represents the microstructure of a living tissue.

The living tissue itself is assumed to be incompressible. It means that the RVE has got the constant volume

$$V_{RVE} = \Delta x_1 \Delta x_2 \Delta x_3 = const. \,, \quad \Delta x_i = c_i + \Delta_i \,. \tag{2}$$

The natural state is a state with no external loading. It is unprestressed if all the springs are allowed to take their rest lengths. To fulfill this, it must be

$$V_c = c_1^{(0)} c_2^{(0)} c_3^{(0)} \,, \quad V_{RVE} = (c_1^{(0)} + \Delta_1^{(0)})(c_2^{(0)} + \Delta_2^{(0)})(c_3^{(0)} + \Delta_3^{(0)}) \,, \tag{3}$$

where $c_i^{(0)}$ and $\Delta_i^{(0)}$ are rest lengths of inner and outer springs, respectively. For such particular choice of cell volume and RVE volume, the natural state is unprestressed (all the springs are relaxed) and can be chosen as the reference configuration

$$c_i = c_i^{(0)} \,, \quad \Delta x_i = c_i^{(0)} + \Delta_i^{(0)} \,. \tag{4}$$

This case is studied in detail in [1]. There the formula for the stored strain energy function $w(\mathbf{F})$ is derived. Thus the hyperelastic model of a living tissue with no prestress in natural state is completed.

2.2. Prestressed natural state

As mentioned above, the prestress in natural state is in our approach balanced by the constant volume of a living cell. In the proposed model, it means to choose such a volume of the inner ball, that does not allow inner springs to relax. This is fulfilled for an arbitrary volume V_c undergoing the condition

$$V_c \neq c_1^{(0)} c_2^{(0)} c_3^{(0)} \ . \tag{5}$$

The task is now to determine the natural state (the reference configuration), which is much more complicated than in the unprestressed case. The inner springs are in tension (compression), so the elastic energy does not vanish.

The transverse isotropy is assumed (the common assumption when modelling the soft tissues), so the notation can be introduced as follows (see fig. 4a):

$$\begin{aligned} &k_{c_1} = k_d \ , \quad k_{c_2} = k_{c_3} = k_c \ , \quad k_{\Delta_1} = k_\Delta \ , \quad k_{\Delta_2} = k_{\Delta_3} = k_\delta \ , \\ &c_1 = d \ , \quad c_2 = c_3 = c \ , \quad \Delta_1 = \Delta \ , \quad \Delta_2 = \Delta_3 = \delta \ , \\ &\Delta x_1 = \Delta x \ , \quad \Delta x_2 = \Delta x_3 = \Delta y \ . \end{aligned} \tag{6}$$

The elastic energy, which is given only by deformation of the springs, can be written as

$$W = k_c (c - c^{(0)})^2 + \frac{k_d}{2}(d - d^{(0)})^2 + k_\delta (\delta - \delta^{(0)})^2 + \frac{k_\Delta}{2}(\Delta - \Delta^{(0)})^2 \ . \tag{7}$$

It is possible to eliminate Δ, δ, and express the energy in the from

$$W = \bar{K}_c (c - g_c)^2 + \frac{\bar{K}_d}{2}(d - g_d)^2 + W_{net} \ , \tag{8}$$

where

$$\begin{aligned} &\bar{K}_c = k_c + k_\delta \ , \quad \bar{K}_d = k_d + k_\Delta \ , \\ &g_c = \bar{K}_c^{-1} \left[k_c c^{(0)} + k_\delta (\Delta y - \delta^{(0)}) \right] \ , \quad g_d = \bar{K}_d^{-1} \left[k_d d^{(0)} + k_\Delta (\Delta x - \Delta^{(0)}) \right] \ , \\ &W_{net} = -\bar{K}_c g_c^2 - \bar{K}_d/2 \ g_d^2 + k_\delta (\Delta y - \delta^{(0)})^2 + k_\Delta/2 \ (\Delta x - \Delta^{(0)})^2 + \\ &+ k_c (c^{(0)})^2 + k_d/2 \ (d^{(0)})^2 \ . \end{aligned} \tag{9}$$

The natural state (the reference configuration) is the state with minimal elastic energy (but nonzero). The energy minimizing problem is

$$W^{ref} = \min_{\substack{c,d,\Delta x,\Delta y \\ c^2 d = V_c \\ (\Delta y)^2 \Delta x = V_{RVE}}} W \ . \tag{10}$$

Notice that in the unprestressed case (when the condition (3) holds), this minimization problem has the solution (4) for which the elastic energy vanish. In general, the minimization problem (10) is equivalent to solution of the set of two nonlinear equations for the variables c, Δy

$$\begin{aligned} \bar{K}_c . c^6 - \bar{K}_c g_c . c^5 + \bar{K}_d V_c g_d . c^2 - \bar{K}_d V_c^2 &= 0 \\ k_\delta . (\Delta y)^6 - k_\delta (c + \delta^{(0)}) . (\Delta y)^5 + k_\Delta (d + \Delta^{(0)}) V_{RVE} . (\Delta y)^2 - k_\Delta V_{RVE}^2 &= 0 \ , \end{aligned} \tag{11}$$

which fully determine the reference configuration.

2.3. Numerical simulations in MATLAB

Since the set of equations (11) determining the reference configuration cannot be solved analytically, numerical calculations in MATLAB were performed. The most simple isotropic case is chosen, so that

$$k_{c_i} = k_c \ , \quad k_{\Delta_i} = k_\Delta \ ,$$
$$c_i^{(0)} = c^{(0)} \ , \quad \Delta_i^{(0)} = \Delta^{(0)} \ . \tag{12}$$

Moreover, it is assumed that the prestress occurs only in the inner ball, so that the springs k_Δ always take their rest lengths in the reference configuration. To ensure this, the additional assumption is

$$\Delta x_i = c_i + \Delta^{(0)} \ , \tag{13}$$

see fig. 2.

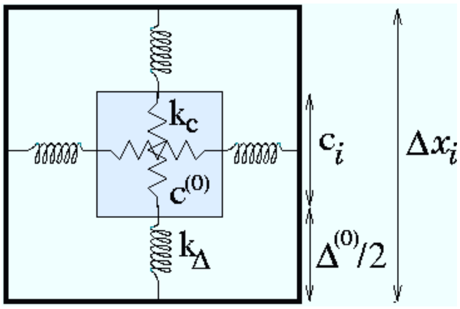

Fig. 2. Reference state of the "balls and springs" model - isotropic case. The prestress is only in the inner springs of the ball, so that $\Delta_i = \Delta^{(0)}$ holds in reference configuration.

Concretely, it was chosen

$$k_c = 1 \ , \quad k_\Delta = 1 \ , \quad \Delta^{(0)} = 1 \ , \quad V_c = 1 \ . \tag{14}$$

The prestress in reference configuration is given by the variable $c^{(0)}$. For $c^{(0)} = \sqrt[3]{V_c} = 1$, there is no prestress because the constant volume $V_c = 1$ allows inner springs to take their rest lengths. With decreasing value of $c^{(0)}$ for $c^{(0)} < \sqrt[3]{V_c}$, the prestress increases, because the springs must be under tension to fill the constant volume. With increasing value of $c^{(0)}$ for $c^{(0)} > \sqrt[3]{V_c}$, the prestress increases again but in the sense of compression.

As mentioned above, this is the isotropic case, so one would expect the symmetric structure in prestressed reference state

$$c_i = c = \sqrt[3]{V_c} \ , \quad \Delta x_i = \Delta x = c + \Delta^{(0)} \ , \tag{15}$$

as depicted in the fig. 2. This holds for the case $c^{(0)} < \sqrt[3]{V_c}$, when the inner springs are under tension (see fig. 3a). When compressed ($c^{(0)} > \sqrt[3]{V_c}$), the structure remains symmetric until the bifurcation point and then collapses. The collapse means flattening of the inner ball with two sides equal and the third side much smaller (see fig. 3b). It is not possible to determine in which direction the flattening is going to happen (those states are energetically equivalent).

In what follows, the prestress is assumed in the sense of tension in inner fibres (which is observed for living cells - see [4]). This corresponds to the domain $c^{(0)} < \sqrt[3]{V_c} = 1$ and thus the problem with bifurcations is avoided.

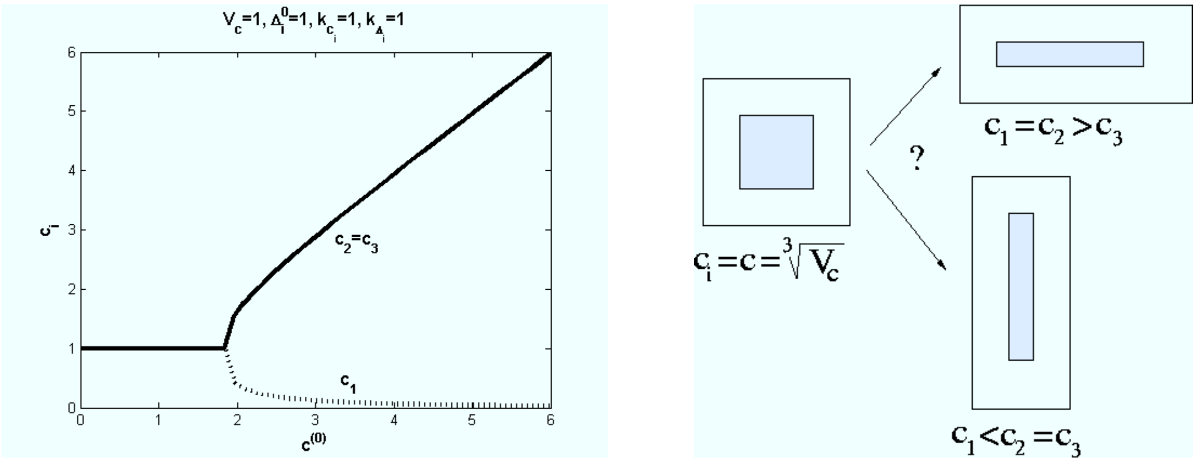

Fig. 3. a) The dependence of the sizes of inner ball on the rest length of inner springs. $c^{(0)} < \sqrt[3]{V_c} = 1$ means tension and $c^{(0)} > \sqrt[3]{V_c} = 1$ compression in inner springs. Bifurcation occurs in compression domain corresponding to the collapse of the inner ball; b) The collapse of the inner ball in the reference state is undeterminable.

3. Young's modulus

3.1. Approximative formula

Once the reference configuration is determined, the Young's modulus can be calculated. We assume again the transverse isotropy, so the notation of variables and parameters is the same as in (6) and the reference configuration is depicted in the fig. 4a.

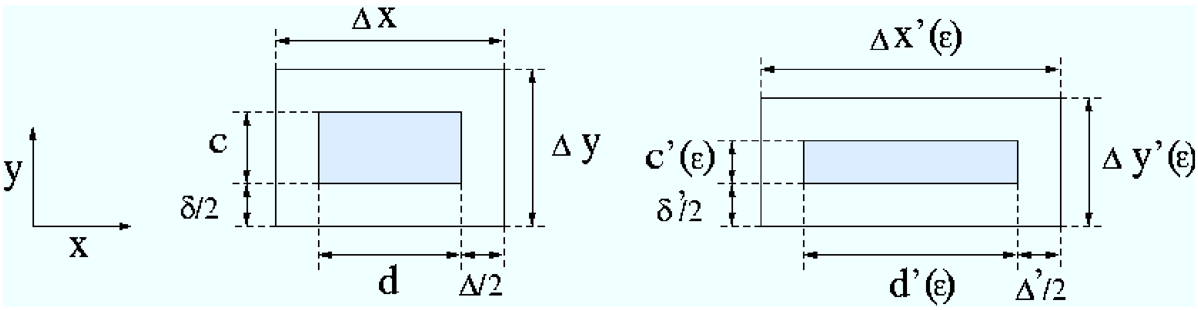

Fig. 4. a) The reference configuration of the "balls and springs" model. Transverse isotropy is assumed, xy plane is depicted; b) The small deformation ε in x direction causes the deformation of inner ball.

When subjected to a small deformation ε in x direction, the new configuration is (see fig. 4b)

$$\Delta x'(\varepsilon) = \Delta x.(1+\varepsilon)\,, \quad \Delta y'(\varepsilon) = \Delta y.(1+\varepsilon)^{-1/2}\,. \tag{16}$$

This deformation of RVE causes the deformation of the inner ball so its new shape is described with $c'(\varepsilon)$ and $d'(\varepsilon)$. This shape is unknown and can be determined as follows.

The energy of the new deformed configuration can be written by analogy with the expression (8) as

$$W' = \bar{K}_c(c' - g_c')^2 + \frac{\bar{K}_d}{2}(d' - g_d')^2 + W_{net}'\,. \tag{17}$$

Here g_c', g_d', and W_{net}' are formally the same functions as in (8), where Δx and Δy are substituted with $\Delta x'$ and $\Delta y'$. The inner ball takes such a shape which minimizes the deformation energy.

Thus the problem is to find the minimum

$$W(\varepsilon) = \min_{\substack{c',d' \\ (c')^2 d' = V_c}} W' \,, \tag{18}$$

which is equivalent to solving the set of three nonlinear equations

$$\frac{\partial W'}{\partial c'} = 0 \,, \quad \frac{\partial W'}{\partial d'} = 0 \,, \quad (c')^2 d' = V_c \,. \tag{19}$$

It is not possible to solve these equations analytically, so the linearization comes to the process. The crucial assumption is

$$\begin{aligned} c' &= g'_c + e_c \,, \quad e_c << g'_c \,, \\ d' &= g'_d + e_d \,, \quad e_d << g'_d \,. \end{aligned} \tag{20}$$

After substituting (20) into (19) and neglecting the higher orders of e_c and e_d, the set of linear equations for variables e_c and e_d is obtained. The solution is

$$e_c = \frac{g'_c g'_d}{\bar{K}_c} \frac{\delta V'}{R'} \,, \quad e_d = \frac{(g'_c)^2}{\bar{K}_d} \frac{\delta V'}{R'} \,, \tag{21}$$

where

$$\delta V' = V_c - (g'_c)^2 g'_d \,, \quad R' = 2\frac{(g'_c)^2 (g'_d)^2}{\bar{K}_c} + \frac{(g'_c)^4}{\bar{K}_d} \,. \tag{22}$$

Substituting (21) into (20) gives the shape of inner ball $c'(\varepsilon)$, $d'(\varepsilon)$ in the deformed configuration. Thus the deformation energy is given as a function of one single parameter ε (according to the relation (18)).

It is now possible to determine the Young's modulus of the model which is defined as

$$E = \frac{1}{V_{RVE}} \left. \frac{d^2 W(\varepsilon)}{d\varepsilon^2} \right|_{\varepsilon=0} \,. \tag{23}$$

Calculating the second derivative is quite complicated and yields

$$\begin{aligned} E \;=\; & \frac{k_\delta^2}{\bar{K}_c^{\,2} R \Delta x} \left[3 g_c g_d^2 + \frac{7}{2} \frac{\bar{K}_c}{\bar{K}_d} g_c^3 \right] .\varepsilon_c - 2 \frac{k_\Delta k_\delta}{\bar{K}_c \bar{K}_d R \Delta y} \left[4 g_c^2 g_d + \frac{\bar{K}_c}{\bar{K}_d} \frac{g_c^4}{g_d} \right] .\varepsilon_c + \\ & + 8 \frac{k_\Delta^2 \Delta x}{\bar{K}_d^{\,2} R (\Delta y)^2} g_c^3 .\varepsilon_c - \frac{3}{2} \frac{k_\delta}{\Delta x \Delta y} .\varepsilon_c + \frac{k_\delta^2}{\bar{K}_c^{\,2} R \Delta x} \left[2 \frac{\bar{K}_c^{\,2} R}{k_\delta} - \frac{\bar{K}_c}{\bar{K}_d} \frac{g_c^4}{2} \right] - \\ & - 2 \frac{k_\delta k_\Delta}{\bar{K}_c \bar{K}_d R \Delta y} g_c^3 g_d + \frac{k_\Delta^2 \Delta x}{\bar{K}_d^{\,2} R (\Delta y)^2} \left[\frac{\bar{K}_d^{\,2} R}{k_\Delta} - 2 \frac{\bar{K}_d}{\bar{K}_c} g_c^2 g_d^2 \right] - \frac{3}{2} k_\delta \Delta y (g_c + \delta^{(0)}) \,. \end{aligned} \tag{24}$$

Here

$$\varepsilon_c = e_c|_{\varepsilon=0} \,, \quad R = R'|_{\varepsilon=0} \,, \tag{25}$$

and the formula (24) is derived from (23) with neglecting the higher orders of ε_c.

3.2. Prestress-induced stiffening

To show clearly the dependence of stiffness of the model on the level of prestress in reference configuration, let us consider again the most simple isotropic case. It means, that the parameters and variables are denoted as in (12). The prestress is also assumed only in the inner ball, so that the condition (13) holds (see fig. 2). Moreover, the prestress is assumed to be realized only by tension (not compression) in the inner springs. Thus no bifurcation occurs in the reference configuration which is then given by the relation (15).

For this isotropic case, it is possible to introduce the single parameter describing the prestress as

$$P = 1 - \frac{c^{(0)}}{c} \,, \quad P \in (0; 1) \,. \tag{26}$$

$P = 0$ means $c^{(0)} = c = \sqrt[3]{V_c}$, so there is no prestress in the reference configuration. $P = 1$ means $c^{(0)} = 0$, so there is the maximal prestress (the spring must be elongated from the zero rest length to take the length $c = \sqrt[3]{V_c}$).

When taking all these assumptions into account, the formula (24) determining the Young's modulus reduces into

$$E = E_0 + \frac{1}{2}\frac{k_\delta^2}{\bar{K}_c \Delta x}\left[\frac{1}{\left(1 - \frac{k_c}{\bar{K}_c} P\right)^3} - 1\right] , \tag{27}$$

where

$$E_0 = \frac{3}{2}\frac{k_\delta}{\Delta x}\left[1 - \frac{k_\delta}{\bar{K}_c}\right] \tag{28}$$

is the Young's modulus of unprestressed structure. The dependence of the Young's modulus on the prestress is depicted in the fig. 5. The model exhibits the prestress-induced stiffening (the stiffness increases with the increasing prestress), which is observed for living cells.

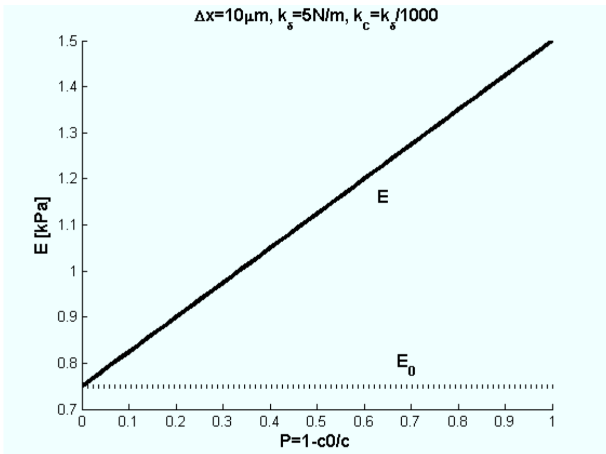

Fig. 5. The dependence of the Young's modulus of the "balls and springs" model on the prestress. The isotropic case is considered.

Since the expression (27) is only approximative, it is important to keep in mind under which conditions is this approximation accurate. The crucial assumption (20) reduces here (for $\varepsilon \to 0$) to the condition

$$c \approx g_c \,. \tag{29}$$

Since the variable g_c can be expressed for this case as

$$g_c = c\left(1 - \frac{k_c}{k_c + k_\delta}P\right) , \tag{30}$$

the condition (29) is equivalent to the condition

$$\frac{k_c}{k_c + k_\delta}P \approx 0 . \tag{31}$$

This means, that the approximation is accurate for the small prestress P or for the rigidity of inner springs k_c much smaller than the rigidity of extracellular springs k_δ.

4. Conclusion

The ”balls and springs” model is proposed for describing the behaviour of living tissues. It is the hyperelastic model which enables to include some microstructural features (such as prestress) into continuum description. Unlike tensegrity models, there are no additional struts, since the prestress is balanced by the constant volume of the ball that represents a living cell. Even if the structure is composed from very simple mechanical elements (linear springs, incompressible ball), the behaviour is nontrivial and leads to bifurcations and non-unique solutions of the reference configuration. However, for the prestress given only by tension within the inner ball in the isotropic case, this problem disappears and the reference configuration is given uniquely. The approximative formula for the Young's modulus is derived and a clear dependence on the prestress for the isotropic case is shown. The prestress-induced stiffening is observed which is in agreement with the behaviour of living cells. The aim for the future is to derive the analytical formula for the stored strain energy as a function dependent on the prestress. It means to complete the hyperelastic model of a living tissue with the behaviour controlled by the prestress at microscopic level.

Acknowledgements

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