INŽENÝRSKÁ MECHANIKA 2005
NÁRODNÍ KONFERENCE
s mezinárodní účastí
Svratka, Česká republika, 9. - 12. května 2005

COMPUTATIONAL MODELLING OF SMOOTH MUSCLE CELLS

J. BURŠA, P. JANÍČEK, R. LEBIŠ[1]

Summary: *The paper deals with problems related to computational modelling of stress-strain states in vascular smooth muscle cells (SMCs). Problems of their structure, geometry, constitutive models, initial (stress-free) state, mechanical couplings to each other and to the extracellular matrix are analyzed. Results of a computational simulation of tension test of a SMC are presented. Perspectives, assumptions and limitations of computational modelling of SMCs under physiological load are discussed.*

1. Introduction

Use of various artificial replacements of organs (i.e. prostheses) has been getting more and more frequent in many medical fields. Especially last decades of the 20th century brought an enormous development of much more sophisticated prostheses used in musculo-skeletal system, and many quite new types of prostheses occurred (e.g. big joint endoprostheses). Since the sixties, artificial replacements began to be used in cardio-vascular surgery as well; artificial heart and artificial vascular graft represent examples of replacements of functional elements of the cardio-vascular system. Furthermore, various supports in cardio-vascular system are used more frequently (ventricular assist devices, arterial stents etc.). Also some sorts of surgical treatment based on mechanical principle bring similar, i.e. among others also mechanical problems (e.g. angioplasty, resection of parts of arteries).

A frequent use of these procedures requires a thorough knowledge on properties of all tissues and other materials in question; it is important for a successful treatment that the properties of prostheses are comparable with those of the replaced biological organs. Possibilities of creation of materials showing properties similar to a biological tissue are very limited till now; moreover, a negative biochemical reaction of the living tissues on the strange material can occur and should be avoided. On the other hand, a complex (mechanical, biochemical, physiological or pathophysiological) response of tissues occurs as a consequence of the changed load of individual parts of the system caused by a disease, treatment, or, e.g. by changes in lifestyle. This remodelation of tissues, i.e. adaptation of their structure to the changed conditions, is a typical response of the tissues on the changed mechanical load; this process tends to re-establish the original physiological state. Change in

[1] Ing. Jiří Burša, Ph.D., Prof. Ing. Přemysl Janíček, DrSc., Ing. Radek Lebiš, Inst.. of Solid Mechanics, Mechatronics and Biomechanics, Brno University of Technology, Technická 2, 616 69, Brno, bursa/janicek@fme.vutbr.cz, r.lebis@post.cz.

blood pressure or any invasive treatment such as angioplasty or stent positioning can represent such stimuli for the arterial wall. These processes start at the cellular level; therefore it is very important to study the cell mechanics to understand their fundamentals. An interdisciplinar approach, comprehending biology, biochemistry, biomechanics and various branches of medicine is necessary to contribute to this effort.

2. Basic information on animal cells

Cell is an autonomous functional unit. It is a system (opened in the thermodynamic sense, naturally) created by the following basic elements (see fig.1):

Cell membrane: it separates the space inside the cell (intracellular space) from its surroundings (extracellular space). It is a rather complex structure with thickness of about 7 nm, created mostly by phospholipids and cholesterol. It ensures the integrity of the cell, and, on the other hand, proteins in the membrane ensure a communication (exchange of energy, mass and information) with the surroundings. Its structure is described in the following paragraph in more detail.

Cytoplasm: the mass in the intracellular space allocated by the cell membrane. It comprehends basic mass, organelles (differenced parts with special functions), cytoskeleton (fibrous reinforcement) and cytoplasmic inclusions.

Nucleus: it is composed of nucleus matrix, nucleus membrane, chromatin and nucleolus. It must not absent in any cells able to reproduce themselves, because it contains all the necessary information for cell reproduction in the form of DNA in chromosomes.

Legend:

1. cell (plasmatic) membrane
2. nucleus, covered by porous membrane
3. nucleolus (containing RNA)
4. agranular endoplasmatic reticulum
5. granular endoplasmatic reticulum
6. mitochondrii
7. desmodom
8. cinocilii
9. secrectional granulom or lysosom
10. Golgi apparatus
11. cytoplasmic inclusions
12. centrosom with two centriols
13. cell membrane, with glycocalyx on its surface
14. microvilluses
15. pinocytosis – infolding of the membrane inside the cell

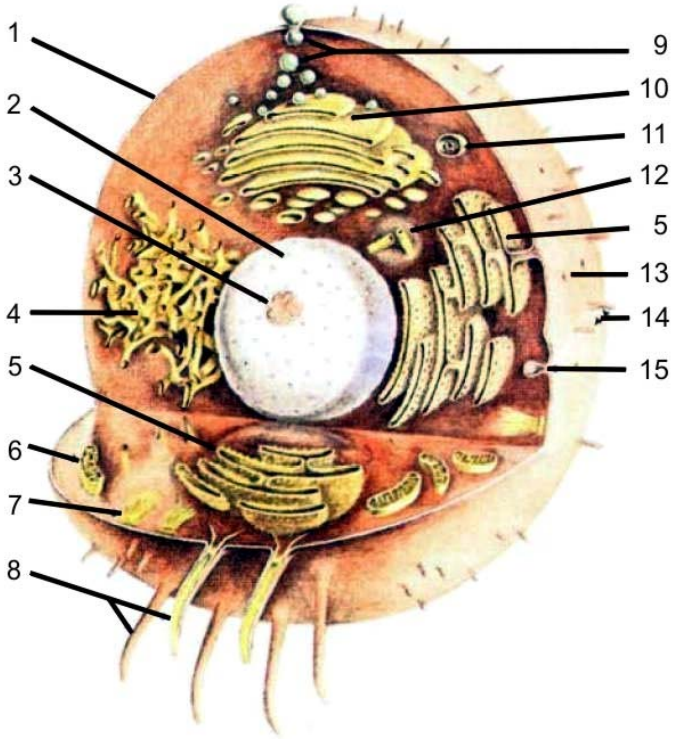

Fig. 1: Structure of an animal cell (from Čihák (2001))

Mechanical properties of the individual organelles can differ substantially from each other and from the properties of cytoplasm. In SMCs, **cytoskeleton** is probably the most important mechanical component. It is a structural lattice comprehending two basic parts: **endoskeleton** (deep cytoskeleton) and **membrane skeleton** (cortex of cell). Endoskeleton is a supporting structure created by a system of filamentous proteins located inside the cell in the cytoplasm while the membrane skeleton stiffens the membrane from its inner side and enables the endoskeleton and contractile apparatus to be anchored to the cell surface. A similar (but passive only) stiffening grid in the extracellular space is called **exoskeleton**. It is connected with the cytoskeleton via integral membrane proteins (see fig.2), i.e. proteins penetrating the cell membrane; integrin is the most important among them from the mechanical viewpoint. The exoskeleton is a network created mostly of elastin and collagen fibres and proteoglycans.

2.1 Structure of the cell membrane

Each molecule of phospholipids, as a main structural component of the cell membrane, consists of two chains of fatty acids (lipid tails – see fig.2), bound by a bipolar phosphate head. The cell membrane consists of two layers of these molecules, both of them with the phosphate heads oriented toward the (inner or outer) membrane surface (see fig.2). The phospholipid chains are hydrophobic (water-repellent) while the phosphate heads are hydrophilic (water-receptive). Owing to the hydrophobic layer, the membrane ensures a chemical separation of the intracellular and extracellular spaces. The mechanical properties (stiffness, strength) of the phospholipid bilayer are, however, very poor and it cannot ensure a sufficient mechanical resistance of the cell, especially in the case of cells with important mechanical function undergoing high loads (e.g. muscle cells).

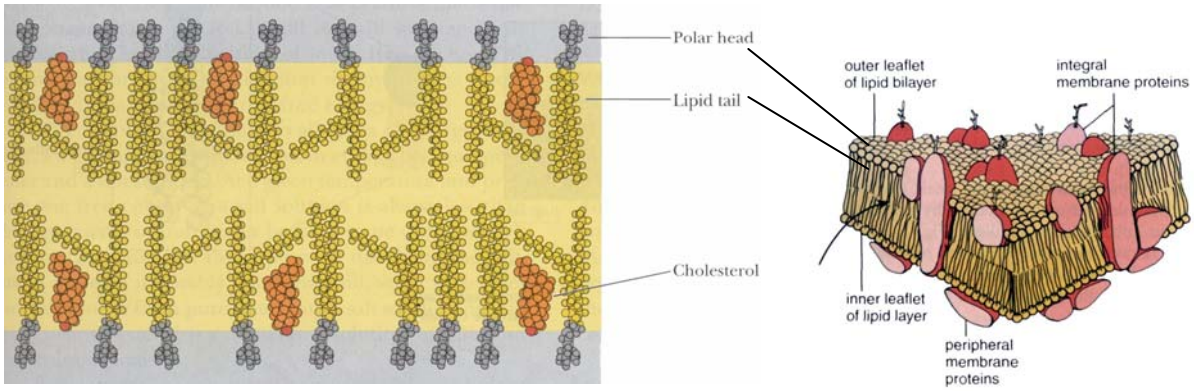

Fig. 2: Structure of cell membrane (from Voet, Voetová (2000))

Between the phospholipid molecules of the membrane some protein molecules are located (see fig.2). Some of them penetrate all the membrane thickness (integral membrane proteins), while others are incorporated from the outer or inner side of the membrane only (peripheral membrane proteins). The membrane proteins serve for several functions, e.g., they insure mass transport across the membrane via ion canals, and they act as antigens and receptors (they can bind neurotransmitters and hormones). Their mechanical function is to create mechanical couplings between cells.

3. Hierarchical structure of muscle

According to system approach, muscles should be investigated with regard to their structure, from the viewpoint of anatomical, physiological, pathological, as well as biomechanical analyses. The following particular hierarchical levels of structure result from the anatomical and histological structure of the muscle tissue and the titles correspond to dimensions of characteristic elements of the individual hierarchical levels:

Level 1: Basic elements at this structural level are actin (thin) and myosin (thick) filaments and Z-discs (transversal protein plates for fixing of filaments, defining the length of sarcomere as the basic functional unit of the muscle). The muscle contraction is a consequence (summation) of microcontractions of individual sarcomeres. Both the above filaments are created of elements with dimensions on the order of nanometers (e.g. diameter of actin filaments is about 6 nm). Therefore this level is denoted as **nanostructure of muscle**.

Level 2: This level is given by myofibrils (diameter about 1 μm). Each myofibril consists of a set of actin and myosin filaments.

Level 3: A muscle fibre (diameter 10 to 100 μm - it is identical with a muscle cell) can represent this structural level. Structural elements of a muscle fibre are myofibrils. The 2nd and 3rd levels are denoted as **microstructure of muscle**.

Level 4: A certain number of muscle fibres (10 to 100) are connected together and coated by a thin layer of connective tissue; they create a bundle (lemniscus - having diameter of 0,1 to 1 mm). In the case of bigger muscles, these primary bundles are mutually connected and create higher order bundles. This is denoted as **mezzostructure of muscle**.

Level 5: This level corresponds to the muscle as an anatomical unit characterized by its shape, couplings and functions. The muscle surface is covered with a continuous connective layer (fascia). It is the highest level in the hierarchy, **macrostructure of muscle**.

These structural levels correspond to the transversally stripped muscles, while the structure of smooth muscles is rather different. The actin and myosin filaments are not arranged in sarcomeres or myofibrils and the individual muscle cells (not fibres but spindle-shaped cells) do not create lemniscuses but they are arranged directly into the smooth muscle tissue. It can be stated that only the levels 1 (nanostructure), 3 (microstructure) and 5 (macrostructure) are valid for smooth muscle tissue. It would be optimal to model this structure at all these levels but it is not possible till now to measure mechanical properties of the elements smaller than muscle cells. Therefore our model will begin at the level of a smooth muscle cell, with an effort to respect its structure as much as possible. This structure is described below in detail.

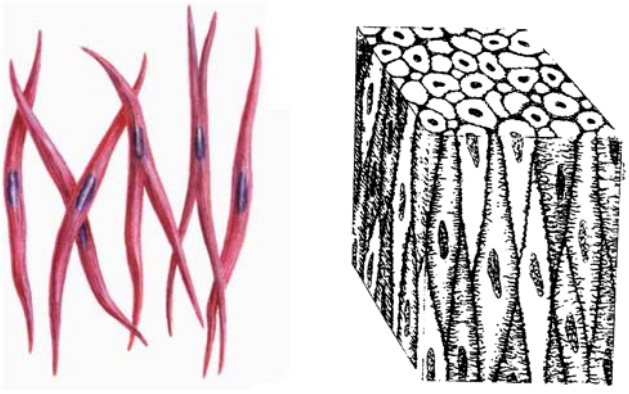

Fig. 3: Typical shape of smooth muscle cells and smooth muscle tissue (from Ross (2002))

4. Structure of smooth muscle cell

Human body counts a large number of various types of cells with different functional specialization. Mechanical properties of the cells have not been

investigated in detail till the last years, with an only exception of red blood cells. In the last decade, however, some attempts occur with the aim to describe mechanical properties of cells, especially of the muscle cells. In particular, SMCs play an important role in vascular wall mechanics, especially at the arteries of muscular type; they increase or decrease the artery lumen by their active contraction or relaxation and change the blood flow in different parts of the body in this way. The contraction mechanism of a transversally stripped muscle has been described very thoroughly in Ganong (1993), while in the case of SMCs, detailed information on geometry and topology of actin and myosin filaments in the cell are not commonly published. In this chapter therefore attention is paid to the basic properties of SMCs, especially to the features of SMC elements important from the mechanical point of view.

In addition to their well known contractile function, SMCs can response on their changed load by changing their phenotype from the contractile to the synthetic one. In agreement with the phenotype title, the main function of **contractile smooth muscle cells** is mechanical, i.e. smooth muscle contraction, while the **cells of synthetic phenotype** chiefly synthesize components of extracellular matrix, especially elastin and collagen. These processes can induce changes in geometry and in mechanical properties of arterial wall.

All these processes stimulated by mechanical invasions in vascular system are controlled at the cellular level in a complex physiological-biochemical-mechanical way. To understand the role of mechanical factors in these processes, the properties and behaviour of individual cells need to be investigated and modelled. This could enable us to incorporate the cell response in a global mathematical description of tissue behaviour, e.g. by a model respecting the tissue non-homogeneity at the microstructure level.

4.1 Structure of cytoskeleton in SMCs

As the stiffness and strength of the cell membrane and cytoplasm (here called sarcolemma and sarcoplasm, respectively) themselves are very low, the cytoskeleton is the most substantial structure inside the SMC from the mechanical viewpoint. It maintains the shape of the cell, the location of cellular organelles, ensures the mass transport inside the cell, as well as the mutual interconnections among the cells and their fixation to the extracellular matrix. On the other hand, it enables substantial changes in the cell shape as well, namely by changing its structure in response to the mechanical load. Cytoskeleton can be divided in two morphological parts, endoskeleton (deep cytoskeleton) and membrane skeleton (cortex of cell). It is necessary to distinguish it from the exoskeleton (filamentous network in the extracellular space).

At the most general level, the endoskeleton is created by a number of various protein filaments distributed in the sarcoplasm. It maintains the shape of the cell and the location of cellular organelles, and it ensures the mass transport inside the cell. The basic elements of cytoskeleton are **microtubuluses**, **microfilaments** and **intermediate filaments**.

Mikrotubuluses are long and compliant tubes (wall thickness of 5 nm, diameter of 15 nm) made of protein molecules called tubulin. They create a set of pathways enabling the cell elements (capsules, organelles etc.) to be transported inside

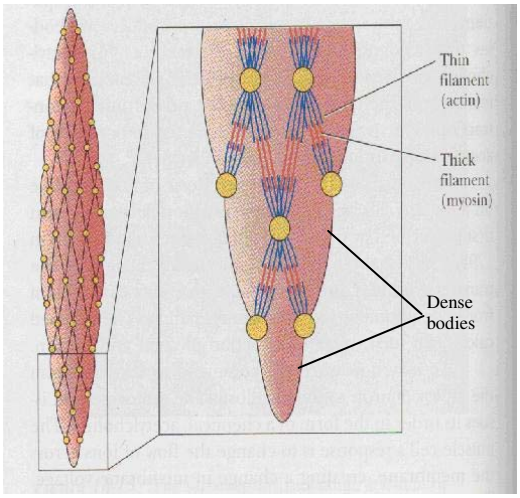

Fig. 4 : Structure of actin and myosin filaments in SMC (from Ross (2002)).

the cell, while their role in cell stiffness is mostly supposed to be lower. Their central point near the nucleus is called centrosome and is created by two centrioles.

Microfilaments create various specialized systems of fibres in sarcoplasm. The basic protein in microfilaments is actin; its molecule is created from 375 amino acids and can be found in two forms in animal cells. About one half of actin is not polymerized and it is denoted as G-actin while the form of long filamentous molecules is called F-actin. Microfilaments show a bi-helical shape with strong interactions between both helical parts and with an electric polarization as well. There are numerous proteins associated with microfilaments and bound to actin. These proteins create entities with various functions. The most important of them from the mechanical viewpoint are:

- Protein ***tropomyosin*** is bound on an actin fibre and contributes to the contraction of muscle.
- Protein ***filamin*** creates crosslinks between the crossing fibres, namely in the cortex of cell close to the cell membrane.
- Protein ***gelsolin*** articulates the fibres into shorter parts and increases the liquidity in this way.
- Motor protein ***myosin*****-**I moves along the microfilament as a molecule motor.

Small and Gimona (1998) suggest that actin filaments are bound to the cytoskeleton (near the dense bodies) and to the longitudinal rib-like reinforcements of the membrane skeleton. Membrane skeleton is bound to other cells and to the extracellular matrix through the "fixing points" (gap junctions – see fig.7) in the cell membrane.

Intermediate filaments are of various types (e.g. ceratin, vimentin, desmin and skeletin filaments) and they are characterized by the middle thickness of 10-12 nm. In addition to the basic proteins there are other so called associated proteins incorporated in their structure. They play an important role in force transmission and in conservation of the cell shape.

4.2 Cytoskeleton remodelation in SMCs

The cytoskeleton is re-organized permanently in response on the cell load. The principle of the process is based on the effect of cytoskeleton decomposition if the cell is not under load and of its re-arrangement in response to the external load. This effect is extremely important for modelling of the cell mechanical behaviour. SMCs are harvested and investigated in two basic shapes: while the cells in the vascular wall tissue are spindle-shaped (fig.3), the cells cultivated in vitro are nearly spherical. If the stiffness of the cell was given by a "normal" mechanical structure, both of these cell shapes could not be stress-free. As the difference between both shapes of the cell is very pronounced it would have to induce very high (residual) stress levels in the load-bearing parts of the cell, i.e. especially in the cytoskeleton. As a consequence of the re-arrangement, the cytoskeleton can be expected to be in a stress-free state at the beginning of any loading process. The re-arrangement appears to be confirmed by the fact discovered experimentally by Seow et al. (2000) that the dependence of the cell stiffness on the load rate is inverse to the behaviour of most macromolecular substances. Macromolecular substances show often viscoelastic properties what can demonstrate by means of a higher complex elasticity modulus (higher stiffness) under a higher load rate. On the contrary, the cytoskeleton is stiffer under a lower load rate. This effect can be explained by the fact that the slower loading process offers more time for the re-arrangement of the cytoskeleton. The new cytoskeleton structure is created in the optimal way and it can be supposed to minimize the cell stresses and strains under the acting load.

5. Possible levels of computational models

5.1 Computational models of the vascular wall

Computational models of mechanical behaviour of normal arterial wall can be (and have been) created at various levels of their structure; the same level should be used in all steps of computational modelling (incl. evaluation of residual stresses):

- Homogeneous wall – the simplest model without accounting the multilayer structure of the wall (see e.g. Burša (1999)).
- Wall composed of two (or more) basic homogeneous layers, corresponding to adventitia, media and intima (as the least important layer from the mechanical viewpoint, intima is often neglected or joined with media - see e.g. Burša (1999)).
- A single layer decomposed into lower elements of structure, e.g. elastic and muscular membranes (sublayers) in the case of arterial media (see e.g. Matsumoto et al. (2004)).
- Each sublayer decomposed into its elements, i.e. cells and various types of fibres.

Under changed load conditions, an arterial wall remodels itself. In the case of a diseased artery, not only changes in the properties of the above layers occur, but also some new (e.g. fatty) layers with different mechanical properties can occur in the structure of the artery in question. All these processes are controlled at the level of individual cells and are supposed to be affected by the stress-strain states of the cells (especially SMCs in the case of arterial wall). Therefore a model of stress-strain states in individual SMCs is necessary for better understanding of these relationships.

The above remodelation mechanism could be described in more detail as follows: the intracellular actin filaments of the cytoskeleton are connected with the collagen fibres in the extracellular space by means of integrin connections and the load is transferred across the cellular membrane in this way. A changed tissue load, e.g. a higher blood pressure in the case of the media tissue in an arterial wall, is transmitted to the cytoskeleton via integrins from the extracellular space. Therefore it can be supposed that an excessive load of actin filaments of the cytoskeleton can evoke a response in the form of an increased procollagen creation in the cell (accompanied by a change in cell phenotype). This procollagen can pass through the cellular membrane, and collagen fibres are created from it in the extracellular space. The global tissue resistance against the load increases in this way until the normal load of the cell (i.e. normal stress-strain state of its structural elements) is achieved.

5.2 Computational models of smooth muscle cells

In the stress-strain and failure analyses of technical materials, two basic approaches are used. The phenomenological approach is based on very simplified (homogenized) models (homogeneous isotropic material, homogeneous anisotropic material in the case of fibre composites etc.) and it does not deal with the details of material structure at the level of molecules or crystals. The physical approach, in opposite, describes the material behaviour on the base of its structure. The most difficult problem is to unify both these approaches into a general theory, based on detailed knowledge of material structure and valid for its global description.

A similar situation occurs in the case of biological materials. The phenomenological approach on one side, describing the overall material behaviour (e.g. of arterial wall or of one of the basic wall layers), should be completed by an approach based on the basic structural

elements. The smallest elements accessible to actual methods of mechanical testing are cells (dimensions of SMCs are on the order of 10^1 μm). Therefore the computational modelling can be carried out at the level of individual SMCs.

The first step in computational modelling of mechanical behaviour of smooth muscle cells is an identification of their stress-strain relations. The complex structure of a SMC can be modelled at various levels:

- Cell modelled as a homogeneous isotropic hyperelastic continuum.
- Cell model created of a relatively stiff shell (sarcolemma and cortex of cell) and of a much more compliant mass (sarcoplasm) inside.
- More complex model based on the above knowledge on the cell structure with the following basic structural parts:
    1. Sarcolemma and cortex of cell modelled as a shell of a homogeneous material, hyperelastic, isotropic or orthotropic (with principal material directions determined by the orientation of filaments in cortex structure or optionally with stiffening rod-like elements).
    2. Sarcoplasm modelled as a highly compliant (hyperelastic, viscoelastic or liquid, i.e. volume-preserving) mass.
    3. Deep cytoskeleton, modelled as a network of rod-like (link) elements, with the structure given by the above histological knowledge.

Naturally, further models at more detailed structural levels could be created. However, the higher resolution of the model, the more complex is the geometry and topology and the more mechanical tests are required for unambiguous identification of its material characteristics. Therefore the level of the appropriate computational model is limited by number and by types of material tests at our disposal.

6. The computational model solved

As the first step in computational modelling of smooth muscle cell, a very simple model was solved. The aim of the solution was a more sophisticated evaluation of tension tests of SMCs. These tests have been published by Miyazaki et al. (2002) as dependencies between cell elongation and reaction force in a micropipette glued to the cell. The cells were cultured “in vitro”, and their initial shape was nearly spherical, so that it was not possible to evaluate stresses and strains using any simple analytic formulas. According to Miyazaki et al. (2002), the cell undergoes large strain and the measured curves are nearly independent from the load direction. Therefore the cell material was supposed to be homogeneous with hyperelastic isotropic behaviour. The computational model enabled us to evaluate the stress-strain curves of this material and to identify the parameters of the chosen constitutive model in this way. Finally, we used Mooney-Rivlin five-parameter constitutive relation, describing the strain energy density function by the following formula:

$$W = a_1(i_1 - 3) + a_2(i_2 - 3) + a_3(i_1 - 3)^2 + a_4(i_1 - 3)(i_2 - 3) + a_5(i_2 - 3)^2 + \frac{\kappa}{2}(i_3 - 1)^2, \qquad (1)$$

where i_i are modified invariants of the right Cauchy-Green deformation tensor, κ denotes the bulk modulus and a_i are other material parameters (Mooney-Rivlin constants).

The parameters of the constitutive model were evaluated using an iterative approach. In the first step, a constitutive σ-ε curve was estimated by a simple calculation (fig.6) from the experimental force-elongation curve published by Miyazaki et al. (2002); the stress was estimated through dividing the force by the maximal cell cross section and the strain through dividing the elongation by the cell diameter. The parameters of the constitutive model were evaluated from this curve. After the first step, i.e. the computation of the force-elongation curve of the cell using the first estimation of its stress-strain dependence, the force-elongation curve obtained by computation was compared with the experimental one. Then the material parameters were modified with the aim to achieve a better agreement between both the computed and experimental curves. When the global difference (in the sense of the least square method) decreases in the following step, the parameter modification is accepted. If the global difference between both curves is lower than the chosen limit, the iteration is finished.

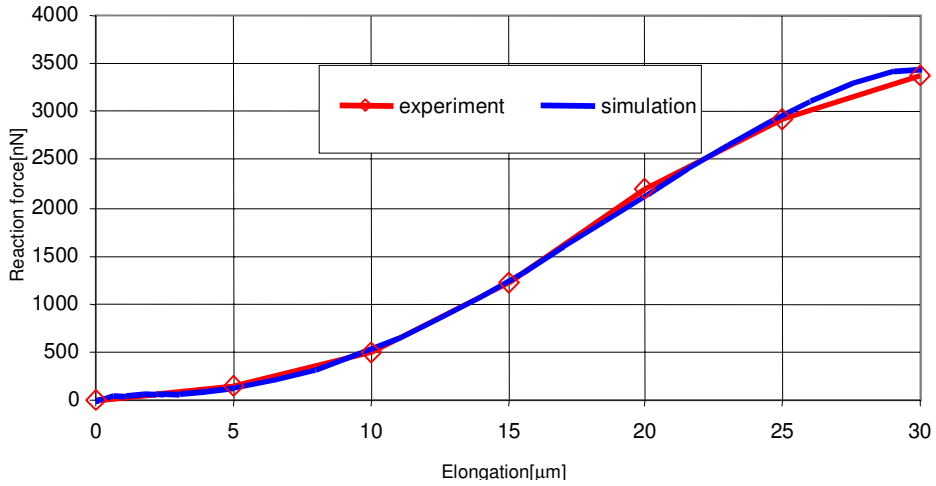

Fig.5: Comparison of measured and simulated curves

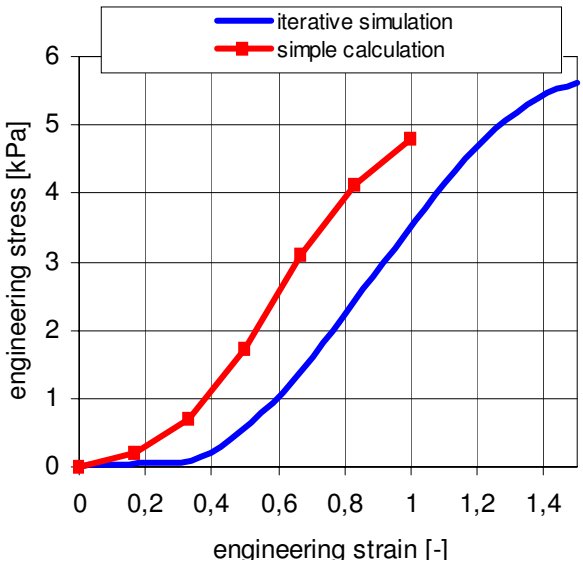

Fig.6: Comparison of initial and simulated curves

The comparison of the experimental and the final computed curve is in fig.5; the difference between them corresponds to the usual difference between hyperelastic constitutive models and reality. The resulting stress-strain curve (i.e. the curve used in the final step of the iterative computation) representing the properties of the homogeneous hyperelastic isotropic cell material is in fig. 6. More details about the procedure see Lebiš et al. (2004).

7. Assumptions of more sophisticated models

The model presented above is a very simple model of the cell structure; it can be accepted only as the first step in a more sophisticated modelling of the SMC behaviour. The constitutive parameters of the model were identified only from one type of experiments published by Miyazaki et al. (2002). Subsequently, an attempt has been carried out to create a more complex model, consisting of a shell (corresponding to the sarcolemma and cortex of cell) on the cell surface and a hyperelastic material (homogeneous isotropic sarcoplasm) inside this shell. The deep cytoskeleton was not taken into account in this model. As only the same experiment (SMC tension test) was used for computational simulation, this model required too many unknown parameters and their identification was not unique. Therefore the stress-strain curve identified in chapter 6 was used for the modelling of sarcoplasm properties, however with stress values divided by 10. This manipulation was based on the assumption that the sarcoplasm is very compliant and that the sarcolemma (together with the cortex of cell) is substantial for the cell stiffness. Then only the parameters of the shell constitutive relation were identified. However, this approach was not successful and we have not managed to approximate the deformed cell shape under any constitutive parameters of the shell. A possible explanation is that the structure of the model without endoskeleton fibres is too compliant and it is not able to bear the load causing excessive distortions of the shell.

This failed attempt showed that a more complex model of smooth muscle cell is necessary to approximate the SMC behaviour. The model should be based on the above structure of the cell and comprehend its structural parts substantial from the mechanical viewpoint, e.g. the following ones:

- ***Cortex of cell*** (membrane skeleton) i. e. the stiffening layer under the compliant and mechanically not significant phospholipid cell membrane, modelled e.g. as a shell on the cell outer surface.
- ***Deep cytoskeleton,*** i.e. a network of fibres (intermediate, actin and other filaments) connecting various structural elements of the cell, with geometry and topology based on the thorough histological information.
- Central part of the cell (***nucleus*** and adjacent organelles) modelled as a hyperelastic continuum.
- Peripheral parts of ***sarcoplasm*** (except for nucleus and its surroundings) modelled as a very compliant continuum (hyperelastic solid, viscoelastic or liquid).

Naturally, this more complex model counts more material parameters to be identified and it requires more material tests for an unambiguous identification. Recently, results of more methods of mechanical testing of cells have been published what offers better possibilities for identification of the constitutive parameters. In addition to the tensile test, micropipette aspiration method, indentation test and compression test with microplates appear to be reasonable for computational modelling and identification of material parameters of the individual constitutive models. The sequence of computational simulations could be as follows:

- **Micropipette aspiration method** (Sato et al. (1987)) is based on aspiration of the cell into a micropipette (with inner diameter of several micrometers, i.e. smaller than SMC dimensions). It can be supposed that the aspiration is influenced mostly by the stiffness of

the membrane with the cortex of cell, modelled together by shell elements. The shell parameters could be identified from this test with the other model components neglected.

- **Indentation tests** (Hayashi (2004)) have shown different stiffness in various parts of the cell. The central part (probably nucleus and its surroundings) is stiffer than peripheral parts of the cell. As the global shape of the cell does not change substantially during the test, the influence of deep cytoskeleton seems to be negligible and this difference is supposed to be caused by different properties of sarcoplasm in central and peripheral parts of the SMC. Under assumption of known properties of the cortex, sarcoplasm constitutive model parameters in both parts of the model could be identified using computational simulation of these tests.
- **Tensile tests** (Miyazaki et al. (2002)) and **compression tests** with microplates (Thoumine and Ott (1997)) induce substantial global changes in the cell shape. As the endoskeleton appears to be the most important load-bearing structure of the cell in this case, it is possible (when the cortex properties are known) to identify the constitutive parameters of this structure with known geometry and topology (created in accordance with the fibrous structure described e.g. in fig.4).

Using results of these tests, it should be possible to identify the constitutive parameters of the above structures. In the end, naturally, all the results must be used in a comprehensive model of all the tests to verify the above assumptions. This approach means that we need results of all the above tests carried out with the same type of cells (under comparable conditions). Unfortunately we have not yet collected such a set of experimental data. We hope to manage it in near future and to be able to identify some of the more complex model of SMC.

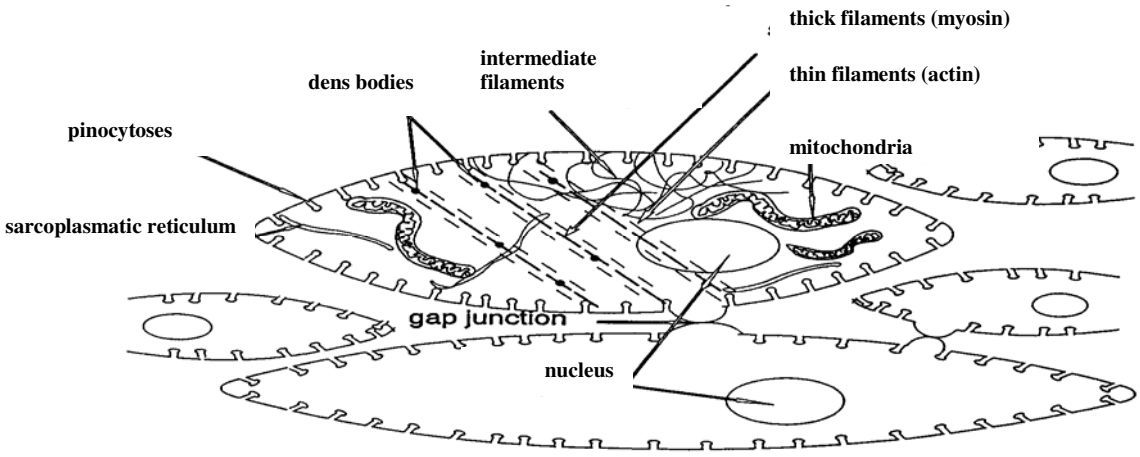

Fig. 7: Structure and junctions of smooth muscle cells (from Ross (2002))

8. Conclusion

An analysis of structure of SMCs is presented in the paper. Based on this knowledge of cell structure, possible levels of computational models of mechanical behaviour of SMCs are reviewed. The more complex is the created model, the more experimental data are necessary for an unambiguous identification of its constitutive parameters. Results of identification of constitutive parameters of the simplest model, based on the assumption of SMC as a

homogeneous isotropic hyperelastic continuum, are presented in the paper. An iterative simulation of SMC behaviour during a tension test enabled us to identify the constitutive parameters of the model. A successful identification of parameters of a more complex and realistic model would create a basis for computational modelling of a syncytium (group of cells-fig.7) or of a more complex structure of an individual muscular layer in the media of arterial wall (accounting interaction between SMCs and fibres of exoskeleton). These results should contribute to understanding the influence of mechanical factors on remodelation processes in the arterial wall as well as on pathological processes accompanying atherosclerotic changes in arterial wall.

9. Acknowledgement

The research has been supported by MSMT of the CR, Research Project No. CEZ:322/98:262100001.

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