MULTISCALE MODELING OF OSSEOUS TISSUES

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The paper presents a methodology of the multiscale bone modeling in which the task of identification of material parameters plays the crucial role. A two-scale analysis of the bone is considered and the problem of identification, formulated as an inverse problem, is examined as an important stage of the modelling process. The human femur bone, built form cancellous and cortical bone, is taken as an example of an osseous tissue, and the computational multiscale approach is considered. The methodology presented in the paper allows one to analyze the two-scale model with the use of computational homogenization. The representative volume element (RVE) is created for the microstructure of the basis of micro-CT scans. The macro and micro model analyses are performed by using the finite element method. The identification of trabeculae material parameters on the micro-level is considered as the minimization problem which is solved using evolutionary computing.

Key words: multiscale modeling of bone, computational homogenization, identification of material parameters

1. Introduction

The bone is a kind of connective tissue which is the basic constituent of the skeleton. The osseous tissue consists of cells and the intercellular substance. The bone is a relatively hard and lightweight composite material. These exceptional mechanical properties of bone are mainly due to its specific hierarchical

microstructure. From the macroscale down to the nanometer one, it is possible to distinguish: cancellous and cortical tissues, Haversian systems and osteons, lamellae, collagen fibres, collagen fibrils, and elementary constituents (collagen, mineral, water, etc.).

The modeling of biological tissues has long history. Almost always, the traditional models are focused on single biological scales. But in order to model a bone, it is important to consider the hierarchical structure and to study how the properties at each scale are governed by the material organization at the lower levels (Sansalone *et al.*, 2009).

The main intention of the modelling of cancellous bone is to decrease the extent of necessary laboratory tests. Applications of multiscale approaches, based e.g. on the finite element method (FEM), enable modeling of the representative volume element (RVE) and calculation of the effective material parameters, including analysis of their change with respect to increasing porosity (Ilic *et al.*, 2010). The hierarchical multiscale modeling method for the analysis of the cortical bone consists of two boundary value problems, one for the macroscale and another for the microscale. The coupling between these scales is done using the computational homogenization scheme. In this approach, virtually there is no limitation on the geometry and material model of the RVE and constituents, so it can be applied to any kind of nanostructured material. In addition to the determination of the global behavior and properties of bone, the microstructural results such as stress distribution in the constituents are also available. By considering various RVE's regarding the microstructure of bone in various locations of the macroscopic piece of bone, it is possible to simulate the real behavior of the bone (Ghanbari and Naghdabadi, 2009). The multiscale analysis can be also performed with use of the bridging techniques described in Burczyński *et al.* (2010) on the levels of nano and micrometers.

The multiscale analysis of remodeling with the use of an artificial microstructure of the cancellous bone can be found in Kowalczyk (2010). The multiscale approach to the modeling of the cortical bone is considered in Hamed *et al.* (2010). The paper by Agić *et al.* (2006) describes analytical calculations of cancellous bone material coefficients on the basis of experiments.

The goal of the present paper is to present a methodology of the multiscale bone modeling in which the task of identification of material parameters plays the crucial role. The two scale analysis of the bone is considered and the problem of identification, formulated as an inverse problem, is considered as an important stage of the modeling process. The human femur bone is taken as an example of the osseous tissue and the computational multiscale approach is considered. The femur bone is build form cancellous and cortical bone. The

cortical bone is very stiff. The cancellous (trabecular) bone is a porous structure built from trabeculae. The head of the femur contains cancellous bone with high density. The methodology presented in the paper allows one to analyze the two-scale model taking into account the cancellous bone structure. The representative volume element geometry (RVE) is created for microstructure on the basis of micro-CT scans. The computational homogenization method (Terada and Kikuchi, 2001; Kouznetsova, 2002) is used to obtain averaged material properties of the microstructure. The macro and micro model analyses are performed by using the finite element method (FEM) (Zienkiewicz *et al.*, 2005). The identification of trabeculae material parameters on the micro-level is considered as the minimization problem which is solved using evolutionary computing.

2. The multiscale structure of proximal femur bone

The proximal femur bone is shown in Fig. 1. The cancellous and cortical tissues are the two main components of the bone. The cancellous tissue is a porous structure with complicated geometry (Fig. 1).
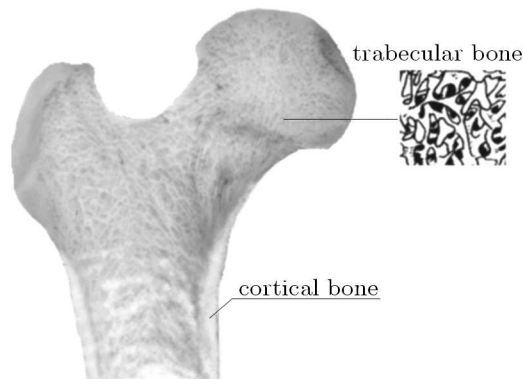

Fig. 1. The proximal femur bone geometry and microstructure

The geometry of the cancellous bone changes in different locations of the femur bone. The experimental tests of single trabeculae revealed isotropic material behavior (Tsubota *et al.*, 2003), however the material properties of the cancellous tissue are no longer isotropic.

The most common model of the material used for the trabecular bone modeling is transversely isotropic and orthotropic. The cortical bone has also hierarchical structure as shown in Hamed *et al.* (2010).

The material properties depend on the structure of tissues and change depending on the location in the femur bone. They can be obtained on the basis of density obtained from CT scans in many papers (Writz *et al.*, 2000). The one-scale analysis takes into account average material properties. The computational homogenization allows one to perform an analysis in which the material properties depend on the microstructure of the trabecular bone.

3. Computational homogenization of osseous tissue

The multiscale modeling allows one to take into account the dependences between two or more scales (Fig. 2). One of the methods used in the multiscale modeling is computational homogenization (Madej *et al.*, 2008). A heterogeneous material is replaced with a homogenous one (Fig. 3). The homogenization is useful when the microstructure is periodic. The influence between scales in the computational homogenization is obtained on the basis of a numerical solution to the boundary value problem performed in each scale.
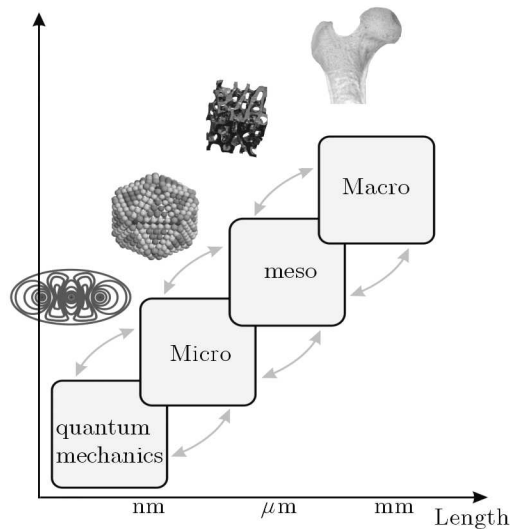

Fig. 2. Mulsticale modeling

The two-scale analysis of the bone system is shown in Fig. 4. The boundary value problem for RVE should be solved for each Gauss integration point. The strain values are transferred to the micromodel during the localization stage. The traction, displacements or periodic boundary conditions are applied to the
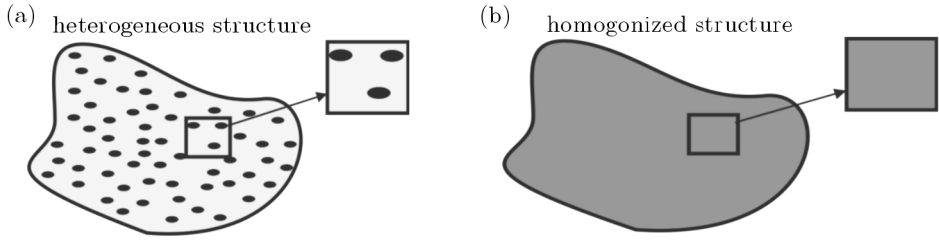
Fig. 3. Homogenization of material, (a) heterogeneous structure, (b) structure after homogenization
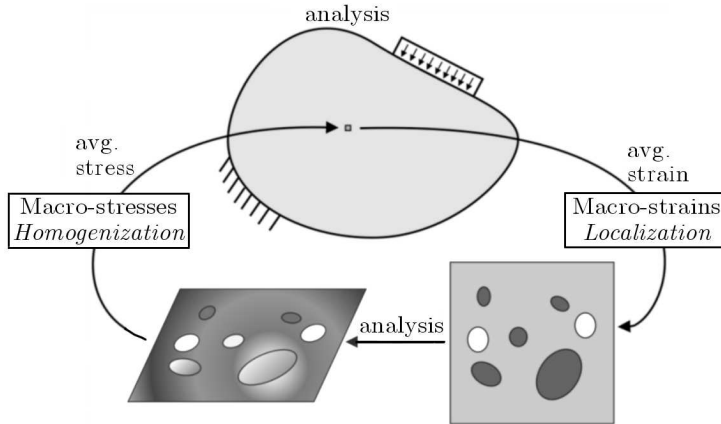

Fig. 4. Two-scale computational homogenization

microstructure. The stresses obtained after boundary value problem analysis are used to obtain homogenized average values which are transferred after the homogenized stage to the higher scale.

The relationship between stresses and strains for an orthotropic elastic material are expressed as follows

$$\boldsymbol{\sigma} = \mathbf{C}\boldsymbol{\varepsilon} \qquad \text{or} \qquad \boldsymbol{\varepsilon} = \mathbf{S}\boldsymbol{\sigma} \qquad (3.1)$$

where

$$\boldsymbol{\sigma} = \left[\sigma_{11}, \sigma_{22}, \sigma_{33}, \sigma_{12}, \sigma_{13}, \sigma_{23}\right]^{\top}$$
$$\boldsymbol{\varepsilon} = \left[\varepsilon_{11}, \varepsilon_{22}, \varepsilon_{33}, \varepsilon_{12}, \varepsilon_{13}, \varepsilon_{23}\right]^{\top} \qquad (3.2)$$

are vectors of stresses and strains.

$\mathbf{C}$ and $\mathbf{S}$ are the stiffness and compliance matrices, of the orthotropic linear elastic material, respectively. They can be written as

$$\mathbf{C} = \begin{bmatrix} c_{11} & c_{12} & c_{13} & 0 & 0 & 0 \\ & c_{22} & c_{23} & 0 & 0 & 0 \\ & & c_{33} & 0 & 0 & 0 \\ & sym. & & c_{44} & 0 & 0 \\ & & & & c_{55} & 0 \\ & & & & & c_{66} \end{bmatrix}$$

(3.3)

$$\mathbf{S} = \mathbf{C}^{-1} = \begin{bmatrix} s_{11} & s_{12} & s_{13} & 0 & 0 & 0 \\ & s_{22} & s_{23} & 0 & 0 & 0 \\ & & s_{33} & 0 & 0 & 0 \\ & sym. & & s_{44} & 0 & 0 \\ & & & & s_{55} & 0 \\ & & & & & s_{66} \end{bmatrix}$$

where

$$
\begin{aligned}
s_{11} &= \frac{1}{E_1} & s_{22} &= \frac{1}{E_2} & s_{33} &= \frac{1}{E_3} \\
s_{44} &= \frac{1}{G_{12}} & s_{55} &= \frac{1}{G_{23}} & s_{66} &= \frac{1}{G_{13}} \\
s_{12} &= \frac{-\nu_{21}}{E_2} & s_{13} &= \frac{-\nu_{31}}{E_3} & s_{21} &= \frac{-\nu_{12}}{E_1} \\
s_{23} &= \frac{-\nu_{32}}{E_3} & s_{31} &= \frac{-\nu_{13}}{E_1} & s_{32} &= \frac{-\nu_{23}}{E_2}
\end{aligned}
$$

(3.4)

where E_i is Young's modulus along the axis i, G_{ij} is the shear modulus in the direction j on the plane whose normal is in the direction i, and ν_{kl} is Poisson's ratio that corresponds to contraction in the direction j when an extension is applied in the direction k.

Due to symmetry of the stiffness and compliance matrices, the 9 variables are independent in the fully orthotropic elastic material (Bąk and Burczyński, 2009; Schneider *et al.*, 2009). The trabecular tissue is often modeled with the use of 5 parameters, assuming $E_1 = E_2$ and $\nu_{23} = \nu_{31}$.

The material coefficients in the case of linear problems can be obtained once for each microstructure. The six analyses should be performed for each microstructure to obtain the 9 independent orthotropic material coefficients.

The average strains and stresses for RVE are defined as follows

$$\varepsilon_{avg} = \frac{1}{|\Omega_{RVE}|} \int\limits_{\Omega_{RVE}} \varepsilon \, d\Omega_{RVE} \qquad \sigma_{avg} = \frac{1}{|\Omega_{RVE}|} \int\limits_{\Omega_{RVE}} \sigma \, d\Omega_{RVE} \quad (3.5)$$

where Ω_{RVE} is the area of RVE.

The constitutive relation between them has the form

$$\boldsymbol{\sigma}_{avg} = \mathbf{C}^h \boldsymbol{\varepsilon}_{avg} \qquad (3.6)$$

where $\mathbf{C}^h$ is the stiffness tensor of the equivalent homogenous material that fulfils the elastic deformation characteristic for the heterogeneous material. A detailed description of the algorithm of computational homogenization is presented in Fig. 5.
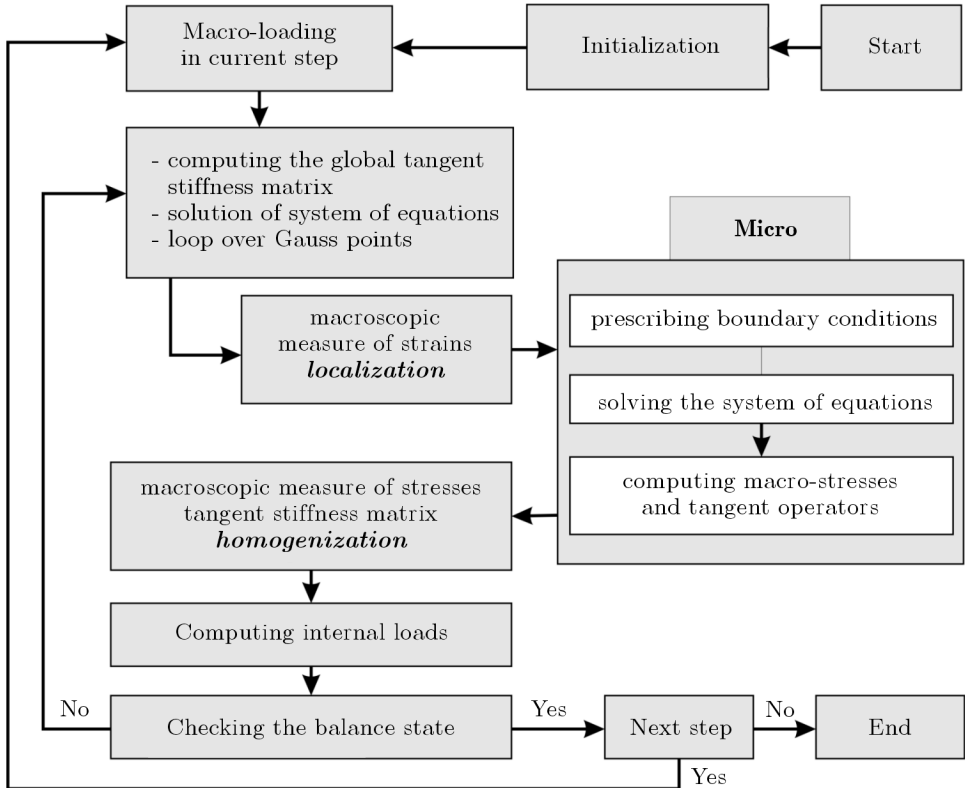

Fig. 5. Computational homogenization algorithm

4. Identification

One of the most important stages of the modeling process is the identification of geometrical and material parameters of the real system. Problems of multiscale modeling need a special kind of identification procedures (Burczyński and Kuś, 2009).

One should evaluate some material parameters of structures in one scale having measured information in another scale. In the considered problem, one should identify Young's modulus E and Poisson's ratio ν of the single trabeculae having information about measured material parameters c_{ij} in the macroscale. The material properties in macroscale can be obtained by performing an identification task on the basis of e.g. strains or displacements measured for the macromodel. The material properties can be also obtained by using the ultrasonic velocity measurement or mechanical tests for microspecimens.

The problem can be formulated as a minimization task

$$\min_{E,\nu} F \tag{4.1}$$

where the objective function is formulated as follows

$$F = \sum_{i=1}^{n} |a_i - \widehat{a}_i| \tag{4.2}$$

where a_i are computed homogenized RVE material properties and $\widehat{a}_i$ are RVE homogenized material properties from the macromodel.

For the homogenized orthotropic material

$$n = 9 \qquad \text{and} \qquad a_i = \{c_{11}, c_{22}, c_{33}, c_{12}, c_{13}, c_{23}, c_{44}, c_{55}, c_{66}\}$$

The objective function is multimodal in most cases and the optimization should be performed with the use of an algorithm which is resistant to local minima. The wide range of bioinspired algorithms allow one to solve global optimization problems. The minimization problem can be solved using the distributed parallel evolutionary algorithm (Burczyński, 2010). The searched material parameters – Young's modulus E and Poisson's ratio ν of the single trabeculae create a chromosome

$$\boldsymbol{ch} = [g_1, g_2] \tag{4.3}$$

where g_i $(i = 1, 2)$ are genes: g_1 – Young's modulus E, g_2 – Poisson's ratio ν.

Evolutionary algorithms are methods which search through the space of solutions basing on an analogy to the biological evolution of species. They operate on populations of individuals (chromosomes) which can be considered as a set of problem solutions. Chromosomes consist of genes which play the role of design variables in a minimization problem. In the proposed evolutionary computation, the floating-point representation is applied. It means

that genes are real numbers. The fitness function is represented by the objective function F. In a typical sequential evolutionary algorithm, the number of fitness function evaluations during the optimization problem amounts to thousands or more. Because the fitness function evaluation for the considered problem takes a lot of time, a distributed and parallel version of the evolutionary algorithm has been proposed. The distributed evolutionary algorithm works similarly to many evolutionary algorithms simultaneously operating on subpopulations, and during the migration phase the chromosomes are exchanged between subpopulations. The parallel evolutionary algorithm evaluates fitness function values in a parallel way. More information about such a generalization of evolutionary computing can be found in Burczyński (2010). A flowchart of the distributed parallel evolutionary algorithm is presented in Fig. 6. The random starting subpopulations are created on the beginning. The evolutionary operators change gene values similarly as in the biological phenomena. The fitness function is calculated for every modified chromosome in the parallel way. The objective function is computed on the basis of FEM analysis for the microstructure. The exchange of chromosomes occurs in the migration phase. The best chromosomes migrate between subpopulations. The migration is performed every a few iterations. The immigrated chromosomes are joined with the subpopulation and take part in the selection. The selection process creates an offspring population of chromosomes. The selection is conducted on the basis of fitness function values. The better fitted chromosomes have the highest probability being in the offspring subpopulation. Then stop optimization condition is checked, and the algorithm iterates in the case when it is not fulfilled.

The fitness function is computed on the basis of results obtained from FEM analysis. The MSC.Nastran was used in the numerical example. The isotropic material parameters were coded into the MSC.Nastran format and stored in a text file. Solutions to direct problems for RVE were performed next. The homogenized orthotropic material properties were calculated on the basis of results of FEM analyses. The fitness function value was calculated on the basis of experimental and numerical orthotropic properties of the RVE model.

5. Numerical example of multiscale modeling of the bone

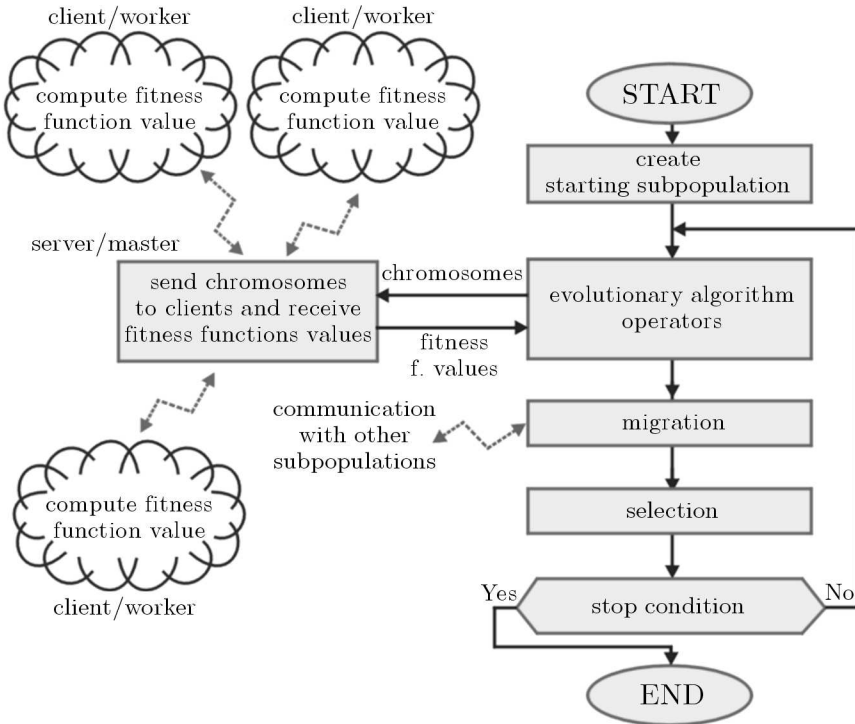Two multiscale modeling problems of the proximal femur bone are considered: analysis and identification.

Fig. 6. The distributed parallel evolutionary algorithm

5.1. Analysis of the multiscale model of bone

The geometry of microstructure is created on the basis of micro CT scans. A single trabeculae is considered to be isotropic and its material properties are presented in Table 1. The material properties of the trabecular bone in the macromodel are orthotropic and obtained on the basis of FEM analysis of RVE micromodels. The cortical tissue properties are based on the properties given in Wirtz *et al.* (2000) and are shown in Table 2.

Table 1. Material properties of single trabeculae used in RVE microstructures analysis

Material parameter	Young's modulus [MPa]	Poisson's ratio
Value	3300.0	0.33

The geometry of the proximal femur bone and loading conditions are shown in Fig. 7. The femur bone is loaded by a force of 1300 N. The discrete model consists of tetrahedron finite elements and has 98000 DOF (degrees of fre-

Table 2. Material properties of cortical tissue

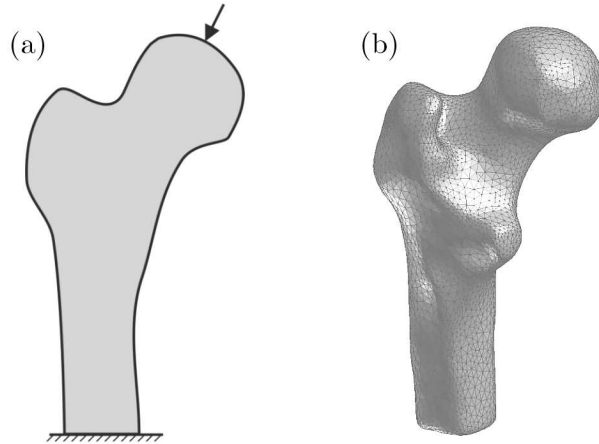| Material parameter	Young's modulus [MPa]	Poisson's ratio
Value	12000.0	0.3

Fig. 7. The macrostructure – proximal femur bone, (a) boundary conditions,
(b) geometry and mesh

edom). The geometry of microstructure of the trabecular bone is presented in
Fig. 8 and Fig. 9. The discrete model consists of tetrahedron finite elements
and has 66000 DOF.

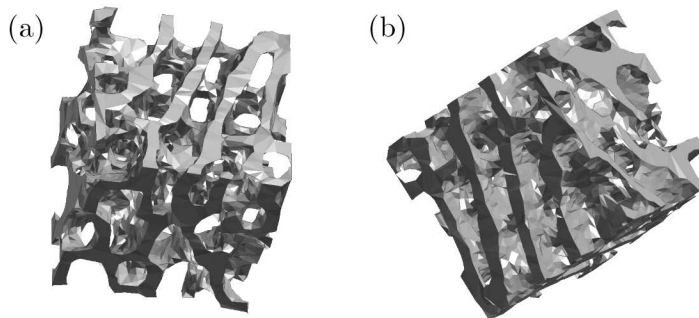The displacement boundary conditions were applied in the microstructures
analysis of RVE.

Fig. 8. The microstructure of the trabecular bone from femur head

The homogenized material properties of the bone obtained from the RVE
microstrucutre are presented in Table 3. The RVE is representative only near
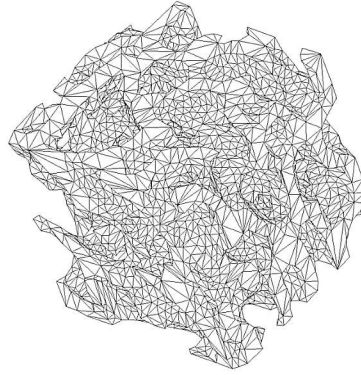
Fig. 9. The mesh of RVE microstructure

the area where the sample of the trabecular bone is extracted from the real bone. To extend the applicability of the obtained material parameters, they should be scaled on the basis of the bone density. This procedure can be applied only for bone areas with the similar geometrical structure. The model can be significantly improved when RVEs are created for characteristic geometries in many areas of the bone. To prepare such RVEs, many samples for CT scanning have to be extracted from the real bone.

Table 3. Material properties of bone derived from RVE micro-model

Material parameter	c_{11}	c_{12}	c_{13}	c_{22}	c_{23}	c_{33}	c_{44}	c_{55}	c_{66}
Value [MPa]	1002.0	321.0	239.0	902.0	239.0	604.0	633.0	457.0	457.0

The Henckey-von Mises-Huber stresses distribution for the applied load and for the macromodel of the bone are shown in Fig. 10.

5.2. Identification of isotropic material properties of a single trabeculae

The isotropic material properties for trabeculae can be found on the basis of known orthotropic material properties of the microstructure model. The orthotropic parameters for the microscale can be obtained by performing a tensile test on a trabeculae specimen or on the basis of ultrasonic velocity measurements (Trębacz and Gawda, 2001). The orthotropic material properties in the microscale can be also acquired by performing identification on the level of macro model.

The identification of material parameters E and ν of the single trabeculae on the micro level has been performed as minimization of the objective func-
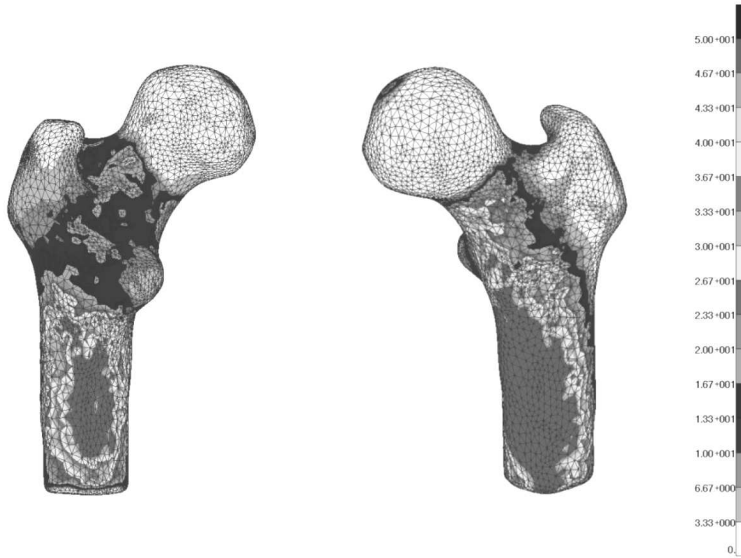
Fig. 10. HMH stresses in the macromodel of the bone

tion F given by (4.2), through the distributed parallel evolutionary algorithm with the following data:

- number of subpopulations – 2
- number of chromosomes in each subpopulation – 15
- number of genes – 2
- evolutionary operators:

    - uniform mutation (10%)
    - simple crossover + Gaussian mutation (90%)
    - ranking selection

- migration of the best chromosome – every 2 generations
- number of iterations – 35
- number of processors used during test – 4
- computations time – 14h

The microstructure model shown in Section 5.1 was used for computations.

The numerical results of identification are presented in Table 4.

The history of the objective function F changing during the optimization for two populations is presented in Fig. 11. Improvements of objective function values in subpopulations after the migration phase can be observed.

Table 4. Actual and found material parameters of trabecular bone in micro-scale

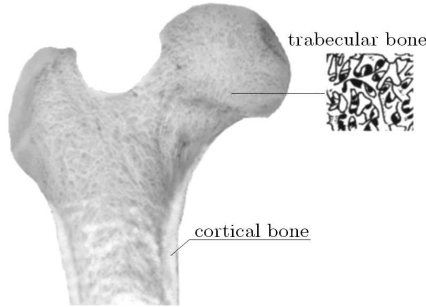| Material parameters	Actual	Found	Error [%]
E [MPa]	3300.0	3305.5	0.16
ν	0.330	0.329	0.30

Fig. 11. History of the objective function for two subpopulations

A very good agreement can be seen between the actual and found material parameters. The identification problem in the multiscale modeling belongs to the newly emerging methodology which is very useful in the determination of some material parameters in the microscale having information about some measurements from the macroscale.

6. Conclusions

The methodology of multiscale modeling of the bone tissue was presented. Two problems of the multiscale modeling were considered for the proximal femur bone: analysis and identification. The studied problem was solved using FEM and computational homogenization for the fully orthotropic elastic material with 9 independent material parameters. The model of the trabecular bone microstructure was prepared on the base of micro-CT scans and used during multiscale computation. The hierarchical structure of the cortical bone could be taken into account in the similar way. The identification problem was considered which enabled determination of material parameters of the isotropic single trabeculae on the microscale having information about orthotropic parameters in the macroscale. This problem was solved as the minimization task using evolutionary computing.

The presented methodology can be used in analysis and identification problems of different kinds of bone tissues. The multiscale approach implemented to the analysis of osseous tissue is very challenging and opens new possibilities to the modeling of processes which take place in biological tissues with hierarchical structures.

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Modelowanie wieloskalowe tkanki kostnej

Streszczenie

W artykule przedstawiono metodologię wieloskalowego modelowania thanki kostnej, w której zagadnienie identyfikacji parametrów materiałowych odgrywa kluczową rolę. Rozpatrzono analizę dwuskalową kości, a problem identyfikacji sformułowano jako zagadnienie odwrotne, będące ważnym etapem procesu modelowania. Jako przykład tkanki kostnej rozważono kość udową zbudowaną z kości gąbczastej i korowej.