

# Computational model for anisotropic microstructure remodelling of cancellous bone

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## Abstract

A computational model of adaptive bone remodelling is formulated as an optimization problem of instantaneous changes in microstructure that minimize a functional describing the structure quality rate. Microstructure is locally described by a set of scalar geometric parameters. Macroscopic (continuum) elastic properties are assumed anisotropic and expressed as known functions of the geometric parameters. Strain energy is considered as the quality measure of bone at given load conditions. Rate of geometric parameters is postulated to minimize the rate of the quality functional. An optimization problem is formulated in the continuum description and then it is discretized both in space and time, taking finally a form of a system of nonlinear algebraic equations on unknown microstructure parameter increments, repeatedly solved in subsequent time instants.

*Keywords: adaptive remodelling, anisotropy, finite element method, optimization*

## 1. Introduction

Bone remodelling plays an important role in formation, maintenance and repair processes of bone tissues. It determines to a large extent the internal micro-structure of bone and has an essential impact on its strength and mechanical properties. The complete biochemical mechanism of remodelling is not yet known. There is, however, a justified hypothesis that it is mainly driven by mechanical factors. Its consequence is e.g. a very good (and probably optimum) distribution of mechanical loads and internal forces within the bone microstructure. Its performance is also crucial to the long-term success of endoprosthetics.

Several investigations related to the issue of numerical simulation of bone remodelling were reported in the literature. They assumed either isotropic material properties of bone, or anisotropic but with a simplified description in which bone density is the only “design” variable [7, 1]. Only isotropic bone growth or resorption was thus possible to simulate, with no anisotropic rearrangements in bone microstructure allowed.

This paper presents a numerical model that allows to simulate the process of anisotropic remodelling of cancellous bone. The bone is treated as continuum with linear elastic anisotropic mechanical properties. Elastic constants and relative density are explicitly known functions of certain geometric parameters of microstructure. The parameters are nonuniformly distributed in the bone volume and subject to changes in time according to a certain remodelling rule. This rule has a form of an optimization problem in which the “cost” functional is a time rate of a certain global measure of bone quality at a given load state. The instantaneous rate of the parameters’ field is postulated to ensure the minimum value of this functional. Time integration of the optimization problem solution results in determination of the microstructure evolution in time. In particular, it allows to track changes in distribution of density and elastic properties.

## 2. Continuum problem formulation

### 2.1. Constitutive relations

Cancellous bone is a macroscopically continuous medium that exhibits orthotropic elastic properties within the physiologi-

cal range of small deformations. At the micro-level, it has a microstructure formed by trabecular bars and/or plates. Macroscopic mechanical properties are directly related to the microstructural geometry and mechanical properties of tissue building up trabeculae. It is commonly accepted that macroscopic anisotropy of cancellous bone is only due to geometric anisotropy of microstructure [2].

Let us describe the microstructural geometry by a number of parameters  $\boldsymbol{\mu} = \{\mu_p\}$  ( $p = 1, \dots, N_\mu$ ) that quantify such features like spacing and cross-section geometry of trabeculae, directionality of their layout, etc. Components of the elastic stiffness tensor  $D_{ijkl}$  appearing in the constitutive equation

$$\sigma_{ij} = D_{ijkl} \varepsilon_{kl} \quad (1)$$

are assumed known functions of the parameters,  $D_{ijkl}(\boldsymbol{\mu})$ . Such relations have been determined for cellular models of cancellous bone e.g. in [3, 4] (see Section 4 for details). Analogously, the parameters determine the relative density (volume fraction)  $\rho(\boldsymbol{\mu})$ .

### 2.2. Remodelling law

Adaptive bone remodelling is postulated as evolution of its microstructure within the occupied domain  $\Omega$  in a way ensuring the fastest possible improvement of bone quality at the given loading conditions and at certain limitations resulting from bone physiology. Within the frame of the introduced definitions and notation, this means evolution in time of the spatial parameter fields,  $\boldsymbol{\mu}(\mathbf{x}, \tau)$ , in a way ensuring the fastest decrease of a certain scalar functional  $G[\mathbf{u}, \boldsymbol{\mu}]$  at the above mentioned conditions and limitations (with  $\mathbf{u}(\mathbf{x}, \tau)$  standing for the displacement field). In other words, evolution of the parameter fields at each time instant  $\tau = t$ ,  $\dot{\boldsymbol{\mu}}(\mathbf{x}, t)$ , is supposed to minimize the instantaneous rate  $\Psi = \dot{G}(t)$ .

The functional  $G$  is assumed in the form [6]

$$G[\mathbf{u}, \boldsymbol{\mu}] = \int_{\Omega} \frac{1}{2} u_{i,j} D_{ijkl}(\boldsymbol{\mu}) u_{k,l} \, d\Omega \quad (2)$$

so that

$$\begin{aligned} \Psi[\mathbf{u}, \dot{\mathbf{u}}, \boldsymbol{\mu}, \dot{\boldsymbol{\mu}}] &= \dot{G} = \\ &= \int_{\Omega} \left[ \frac{1}{2} u_{i,j} \left( \frac{dD_{ijkl}}{d\boldsymbol{\mu}} \dot{\boldsymbol{\mu}} \right) u_{k,l} + u_{i,j} D_{ijkl}(\boldsymbol{\mu}) \dot{u}_{k,l} \right] d\Omega. \end{aligned} \quad (3)$$

### 2.3. Constraints

Evolution of microstructure is subject to numerous constraints. The first of them is the static equilibrium, expressed in the variational form as the virtual work equation

$$\int_{\Omega} u_{i,j} D_{ijkl}(\boldsymbol{\mu}) \delta u_{k,l} d\Omega = \int_{\Omega} \hat{b}_i \delta u_i d\Omega + \int_{\Gamma_{\sigma}} \hat{t}_i \delta u_i d\Gamma. \quad (4)$$

given also in the rate form as

$$\int_{\Omega} \left[ u_{i,j} \left( \frac{dD_{ijkl}}{d\boldsymbol{\mu}} \dot{\boldsymbol{\mu}} \right) \delta u_{k,l} + \dot{u}_{i,j} D_{ijkl}(\boldsymbol{\mu}) \delta u_{k,l} \right] d\Omega = \int_{\Omega} \dot{\hat{b}}_i \delta u_i d\Omega + \int_{\Gamma_{\sigma}} \dot{\hat{t}}_i \delta u_i d\Gamma \quad (5)$$

where  $\hat{b}_i$  and  $\hat{t}_i$  are external volume and surface forces, and the displacement variation field  $\delta u_i(\mathbf{x})$  is arbitrary.

Next, constraints on  $\boldsymbol{\mu}$  have to be enforced. They basically result from physiology. All the parameters  $\mu_p$  and their rates  $\dot{\mu}_p$  have lower and upper bounds,

$$\begin{aligned} \mu_p \min \leq \mu_p \leq \mu_p \max, \quad p = 1, \dots, N_{\mu}, \\ \dot{\mu}_p \min \leq \dot{\mu}_p \leq \dot{\mu}_p \max, \quad p = 1, \dots, N_{\mu}. \end{aligned} \quad (6)$$

Further, limitations may exist for relative density and its rate,

$$\begin{aligned} \rho_{\min} \leq \rho(\boldsymbol{\mu}) \leq \rho_{\max}, \\ \dot{\rho}_{\min} \leq \dot{\rho}(\boldsymbol{\mu}, \dot{\boldsymbol{\mu}}) \leq \dot{\rho}_{\max}. \end{aligned} \quad (7)$$

Finally, physiological constraint on the total mass rate has to be included,

$$\int_{\Omega} \dot{\rho} d\Omega = \dot{M}(t) \quad (8)$$

in which the arbitrarily imposed function  $\dot{M}(\tau)$  may e.g. take the constant value of zero (constant bone mass) or negative values (advance of osteoporosis).

### 2.4. Optimization problem

Finally, the optimization problem is formulated as follows.

At an arbitrary time instant  $\tau = t$ , given the fields  $\mathbf{u}(\mathbf{x}, t)$  and  $\boldsymbol{\mu}(\mathbf{x}, t)$  that fulfill the equilibrium equation (4), find the fields  $\dot{\mathbf{u}}(\mathbf{x}, t)$ ,  $\dot{\boldsymbol{\mu}}(\mathbf{x}, t)$  that minimize the functional (3) subject to constraints (5)–(8). Time integration of the solution of this problem yields the desired evolution  $\boldsymbol{\mu}(\mathbf{x}, \tau)$  along with the related evolution  $\mathbf{u}(\mathbf{x}, \tau)$ .

## 3. Computational model

### 3.1. Space and time discretization

Equations of the problem are subject to space and time discretization. Let us introduce the displacement field approximation, typical of the finite element analysis [8],

$$u_i(\mathbf{x}, \tau) = \sum_{\alpha=1}^{N_N} \Phi_{\alpha}(\mathbf{x}) q_{i\alpha}(\tau), \quad i = 1, 2, 3, \quad (9)$$

where  $N_N$  – number of nodes in the f.e. mesh and  $\mathbf{q} = [q_{i\alpha}]$  – array of time-dependent nodal parameters. Let us also approximate the integration over  $\Omega$  with the Gauss formula

$$\int_{\Omega} a(\mathbf{x}) d\Omega \approx \sum_{\gamma=1}^{N_G} w_{\gamma} a(\mathbf{x}_{\gamma}),$$

with  $\mathbf{x}_{\gamma}$  being the integration points' coordinates and  $w_{\gamma}$  – weights associated with the points. Besides, let us introduce a set of discrete time instants  $\tau = t_0, t_1, t_2, \dots$  at which the optimization problem will be solved with respect to finite increments rather than rates of the unknown fields.

### 3.2. Discretized optimization problem

Substituting the above relations to the continuum optimization problem, we obtain after transformation the formulation in which the fields  $\mathbf{u}(\mathbf{x}, \tau)$  and  $\boldsymbol{\mu}(\mathbf{x}, \tau)$  have been replaced with discrete arrays  $\mathbf{q}_n = \{\mathbf{q}_k(t_n)\}$  ( $k = 1, \dots, 3N_N$ ), and  $\mathbf{m}_n = \{\mu_{p\gamma}(t_n)\}$  ( $p = 1, \dots, N_{\mu}, \gamma = 1, \dots, N_G$ ), with the index  $n = 0, 1, 2, \dots$  referring in both cases to the discrete time instants. The discrete formulation of the problem at a typical time interval  $[t_n, t_{n+1}]$  is as follows.

Given the arrays  $\mathbf{q}_n, \mathbf{m}_n$  that fulfill the equilibrium equation

$$\mathbf{K}(\mathbf{m}_n) \mathbf{q}_n = \mathbf{f}_n, \quad (10)$$

find the arrays  $\mathbf{q}_{n+1}, \mathbf{m}_{n+1}$  (and corresponding increments  $\Delta \mathbf{q} = \mathbf{q}_{n+1} - \mathbf{q}_n, \Delta \mathbf{m} = \mathbf{m}_{n+1} - \mathbf{m}_n$ ) that minimize the functional

$$\begin{aligned} \Psi(\mathbf{q}_n, \Delta \mathbf{q}, \mathbf{m}_n, \Delta \mathbf{m}) = \Delta G = \\ = \frac{1}{2} \mathbf{q}_{n+1}^T \mathbf{K}(\mathbf{m}_{n+1}) \mathbf{q}_{n+1} - \frac{1}{2} \mathbf{q}_n^T \mathbf{K}(\mathbf{m}_n) \mathbf{q}_n. \end{aligned} \quad (11)$$

under the following equality- and inequality-type constraints,

$$\mathbf{K}(\mathbf{m}_{n+1}) \mathbf{q}_{n+1} = \mathbf{f}_{n+1}, \quad (12)$$

$$\begin{aligned} \mu_p \min \leq \mu_{p\gamma n+1} \leq \mu_p \max \\ \Delta t \dot{\mu}_p \min \leq \Delta \mu_{p\gamma} \leq \dot{\mu}_p \max \Delta t \quad \gamma = 1, \dots, N_G, \\ \rho_{\min} \leq \rho_{\gamma n+1} \leq \rho_{\max} \quad p = 1, \dots, N_{\mu}, \end{aligned} \quad (13)$$

$$\Delta t \dot{\rho}_{\min} \leq \Delta \rho_{\gamma} \leq \dot{\rho}_{\max} \Delta t$$

$$\sum_{\gamma=1}^{N_G} w_{\gamma} \Delta \rho_{\gamma} = \dot{M} \Delta t, \quad (14)$$

with  $\mathbf{K}$  and  $\mathbf{f}$  denoting the FE stiffness matrix and load vector, respectively, and

$$\rho_{\gamma n+1} = \rho(\mu_{p\gamma n+1}), \quad \Delta \rho_{\gamma} = \rho_{\gamma n+1} - \rho_{\gamma n}.$$

### 3.3. Extended cost functional

There are several ways of solution of the above minimization problem. One of them is the formulation with an extended cost functional, in which the constraints are included with appropriate Lagrange multipliers. Let us first replace all the inequality constraints with equalities, which can be done by means of the *slack fields*  $\beta(\mathbf{x})$  (represented in the space-discrete formulation by their values at the integration points,  $\beta_{\gamma}$ ). E.g., the inequality  $A \geq 0$  is equivalent to  $A = \beta^2$  where  $\beta$  is an unknown quantity that assumes the zero value when the constraint is active and non-zero otherwise. The constraints (13) can thus be expressed as

$$\begin{aligned} \mu_{p\gamma n+1} - \mu_p \min &= \beta_{1p\gamma}^2, \\ \mu_p \max - \mu_{p\gamma n+1} &= \beta_{2p\gamma}^2, \\ \Delta \mu_{p\gamma} - \Delta t \dot{\mu}_p \min &= \beta_{3p\gamma}^2, \\ \dot{\mu}_p \max \Delta t - \Delta \mu_{p\gamma} &= \beta_{4p\gamma}^2, \\ \rho_{\gamma n+1} - \rho_{\min} &= \beta_{5\gamma}^2, \\ \rho_{\max} - \rho_{\gamma n+1} &= \beta_{6\gamma}^2, \\ \Delta \rho_{\gamma} - \Delta t \dot{\rho}_{\min} &= \beta_{7\gamma}^2, \\ \dot{\rho}_{\max} \Delta t - \Delta \rho_{\gamma} &= \beta_{8\gamma}^2, \end{aligned} \quad (15)$$

where an additional array of unknowns  $\mathbf{b} = \{\beta_{k\gamma}\}$  ( $k = 1, \dots, 4(N_{\mu}+1), \gamma = 1, \dots, N_G$ ) appears.

Introducing now  $1 + 3N_N + 4(N_{\mu}+1)N_G$  discrete Lagrange multipliers denoted by  $\lambda, \mathbf{q}^a$ , and  $\mathbf{h} = \{\eta_{k\gamma}\}$ , we can

replace the original optimization problem (10)–(14) with the following problem of minimization of an *extended cost functional*  $\mathcal{L}$ , constructed as the functional  $\Psi$  (11) decreased by all the equality constraints weighted by Lagrange multipliers.

Given the arrays  $\mathbf{q}_n, \mathbf{m}_n$  that fulfill the equilibrium equation

$$\mathbf{K}(\mathbf{m}_n) \mathbf{q}_n = \mathbf{f}_n, \quad (16)$$

find the arrays  $\Delta \mathbf{q}$ ,  $\Delta \mathbf{m}$ , and the slack and Lagrange multiplier arrays  $\mathbf{b}$ ,  $\lambda$ ,  $\mathbf{q}^a$ ,  $\mathbf{h}$ , that minimize the functional

$$\begin{aligned} \mathcal{L}(\mathbf{q}_n, \Delta \mathbf{q}, \mathbf{m}_n, \Delta \mathbf{m}, \lambda, \mathbf{b}, \mathbf{h}, \mathbf{q}^a) = & \\ = \frac{1}{2} & \left[ \mathbf{q}_{n+1}^T \mathbf{K}(\mathbf{m}_{n+1}) \mathbf{q}_{n+1} - \mathbf{q}_n^T \mathbf{K}(\mathbf{m}_n) \mathbf{q}_n \right] \\ & - \mathbf{q}^{aT} \left[ \mathbf{K}(\mathbf{m}_{n+1}) \mathbf{q}_{n+1} - \mathbf{f}_{n+1} \right] \\ & - \lambda \left( \sum_{\gamma=1}^{N_G} w_\gamma \Delta \rho_\gamma - \Delta M \right) \\ & - \sum_{\gamma=1}^{N_G} \left\{ \eta_{1p\gamma} \left[ \mu_{p\gamma n+1} - \mu_{p\min} - \beta_{1p\gamma}^2 \right] \right. \\ & + \eta_{2p\gamma} \left[ \mu_{p\max} - \mu_{p\gamma n+1} - \beta_{2p\gamma}^2 \right] \\ & + \eta_{3p\gamma} \left[ \Delta \mu_{p\gamma} - \Delta t \dot{\mu}_{p\min} - \beta_{3p\gamma}^2 \right] \\ & + \eta_{4p\gamma} \left[ \dot{\mu}_{p\max} \Delta t - \Delta \mu_{p\gamma} - \beta_{4p\gamma}^2 \right] \\ & + \eta_{5\gamma} \left[ \rho_{\gamma n+1} - \rho_{\min} - \beta_{5\gamma}^2 \right] \\ & + \eta_{6\gamma} \left[ \rho_{\max} - \rho_{\gamma n+1} - \beta_{6\gamma}^2 \right] \\ & + \eta_{7\gamma} \left[ \Delta \rho_\gamma - \Delta t \dot{\rho}_{\min} - \beta_{7\gamma}^2 \right] \\ & \left. + \eta_{8\gamma} \left[ \dot{\rho}_{\max} \Delta t - \Delta \rho_\gamma - \beta_{8\gamma}^2 \right] \right\}. \quad (17) \end{aligned}$$

Taking variation of  $\mathcal{L}$  and requiring  $\delta \mathcal{L} = 0$  we obtain a set of nonlinear equations for the unknown arrays, corresponding to vanishing terms at variations of particular unknown array coefficients. The set consists of the constraints (12), (14), (15) (the terms at  $\delta \mathbf{q}^a$ ,  $\delta \lambda$  and  $\delta \mathbf{h}$ , respectively), equations

$$\eta_{k\gamma} \beta_{k\gamma} = 0, \quad \begin{array}{l} k = 1, \dots, 4(N_\mu + 1), \\ \gamma = 1, \dots, N_G \\ \text{no summation,} \end{array} \quad (18)$$

$$\mathbf{q}^a = \mathbf{q}_{n+1} \quad (19)$$

(the terms at  $\delta \mathbf{b}$  and  $\delta \Delta \mathbf{q}$ , respectively) and the following  $N_G \cdot N_\mu$  equations corresponding to the terms at  $\delta \Delta \mathbf{m}$ ,

$$\begin{aligned} \frac{1}{2} \mathbf{q}_{n+1}^T \frac{\partial \mathbf{K}}{\partial \mu_{p\gamma}} \Big|_{n+1} \mathbf{q}_{n+1} + \lambda w_\gamma \frac{\partial \rho}{\partial \mu_p} \Big|_{\gamma n+1} \\ + \eta_{1p\gamma} - \eta_{2p\gamma} + \eta_{3p\gamma} - \eta_{4p\gamma} \\ + (\eta_{5\gamma} - \eta_{6\gamma} + \eta_{7\gamma} - \eta_{8\gamma}) \frac{\partial \rho}{\partial \mu_p} \Big|_{\gamma n+1} = 0, \quad (20) \end{aligned}$$

(in which Eq. (19) has already been utilized). After straightforward elimination of Eq. (19) and the unknown  $\mathbf{q}^a$ , the total number of equations becomes  $3N_N + 1 + (5N_\mu + 4)N_G$  and is equal to the total number of unknown array coefficients.

Solving repeatedly the system of equations for  $n = 0, 1, 2, \dots$  and updating the bone state to subsequent time instants  $\tau = t_1, t_2, \dots$  allows to determine step-by-step the evolution of the microstructure parameters in a given cancellous bone model.

**Remark.** Associating elements of the arrays  $\mathbf{m}$ ,  $\mathbf{b}$ ,  $\mathbf{h}$  with Gauss integration points of the finite element discretization may make their sizes (and the number of unknowns in the problem) excessively large. A modification to the above formulation may be easily introduced in which the parameters  $\mu$  are constant in certain sub-areas of the bone, each containing a set of different integration points (e.g. finite elements, or groups of finite elements).

In such a case,  $N_G$  in all the above formulae denotes rather the number of such sub-areas, and corresponding weights  $w_\gamma$  should obviously be lumped over Gauss points of sub-areas  $\gamma$ .

#### 4. Geometric model of bone microstructure

To apply the above model in numerical computations, a geometric model of bone microstructure is necessary, in which the parameters  $\mu$  would be defined and their influence on material constants  $D_{ijkl}$  and density  $\rho$  given. In this study, the bone microstructure model proposed by the author in [4] will be adapted. In it, the cancellous bone is modelled as repeatable microstructure whose representative volume element (cell), presented in Fig. 1, is parameterized by four dimensionless geometric parameters. The first three of them,  $t_c, t_h, t_v$ , define proportions between trabecular plate widths and thickness in different directions, while  $t_e$  (not mentioned in the figure) is a scaling factor of the entire cell in the  $x'_1$  direction. The microstructure is orthotropic, and for the particular setting  $t_e = 1$  — transversely isotropic.

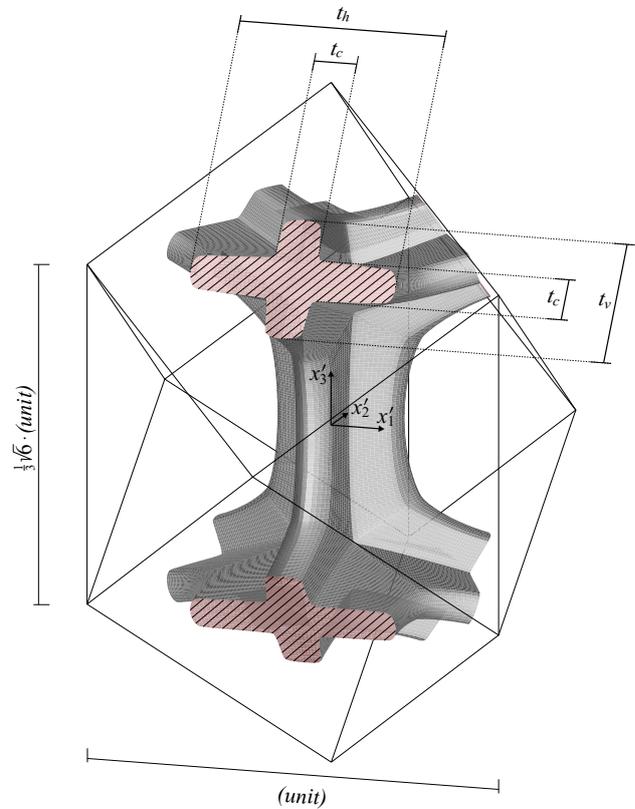


Figure 1: Geometric model of the representative bone cell, based on a space-filling 14-walled polyhedron

Different values of the parameters allow to mimic at a good approximation different types of cancellous bone microstructures encountered in real bones. Figure 2 presents a few examples in which a bar structure (a), a plate structure with spacer bars (b), a honeycomb pipe (c) and a fenestrated polyhedral cell cluster (d) are generated. Setting all parameters approximately equal to 1 may be considered as modelling of a compact bone (note, however, that the model is then isotropic).

Relations between macroscopic density  $\rho$  and orthotropic material constants  $D_{ijkl}$  and the microstructure parameters  $t_c, t_h, t_v, t_e$  have been determined numerically with the finite element method [4] and are available in a tabularized form at the author's web site [5].

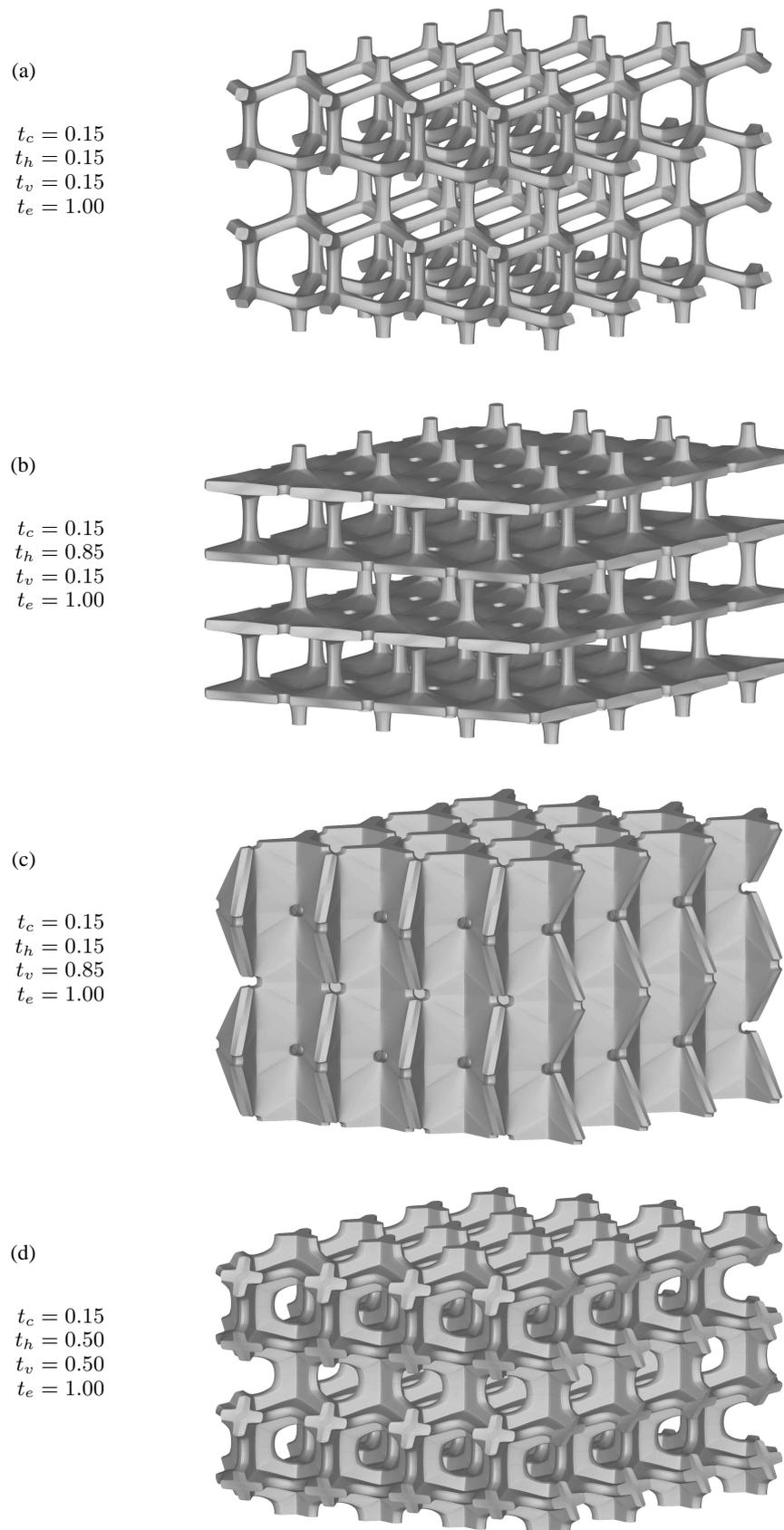


Figure 2: Examples of typical microstructures generated with a representative cell for different values of geometric parameters

Referring now to the constitutive model, Section 2.1, we can consider the geometric parameters  $t_c, t_h, t_v, t_e$  to be the parameters  $\mu_p \in \boldsymbol{\mu}$ . Since orientation of the equivalent microstructure in the real bone space is arbitrary, one has to complete the set  $\boldsymbol{\mu}$  with three Euler angles,  $\alpha_{\text{prec}}, \alpha_{\text{nut}}, \alpha_{\text{rot}}$ , defining the rotation between  $\{x_i\}$  and  $\{x'_i\}$ ,

$$\boldsymbol{\mu} = \{\mu_p\} = \{t_c, t_h, t_v, t_e, \alpha_{\text{prec}}, \alpha_{\text{nut}}, \alpha_{\text{rot}}\}, \quad (21)$$

i.e.  $N_\mu = 7$ . In the case of transverse isotropy,  $t_e$  and  $\alpha_{\text{rot}}$  become obsolete and  $N_\mu$  is reduced to 5,

$$\boldsymbol{\mu} = \{\mu_p\} = \{t_c, t_h, t_v, \alpha_{\text{prec}}, \alpha_{\text{nut}}\}. \quad (22)$$

## 5. Conclusion

The complete numerical model for space-time simulation of cancellous bone remodelling process in continuum approach has been presented. Numerical implementation of the above model is a tedious task and has not been completed yet. The code under development is expected to allow to numerically predict anisotropic bone remodelling in e.g. bones with endoprostheses including, among others, conditions of osteoporosis. These issues have great practical importance in medical applications.

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