Selected Problems of Modeling in Bone Biomechanics

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Abstract

Three classes of problems are discussed briefly in the present paper. The first one concerns a mathematical and computational modeling of bone functional adaptation. In the second class the problems of optimal design of implants taking into account the effects of bone remodeling are considered. Problems devoted to investigation and modeling of mutual interactions between bone tissue and bone-substitute bio-resorbable materials fall into the last of discussed here classes.

Introduction

Bones are attractive objects of biomechanical research because of their important functions in the organisms. Among the most important biological functions one can mention the following: bones function as a reservoir of minerals, mostly calcium and phosphorus; they play an important role in blood production; they work as a fat storage and different grow factors storage; they contribute in detoxification of organism, control phosphate metabolism and buffer the blood against excessive pH. In addition to their biological functions several important mechanical should be also mentioned namely, they protect internal organs, they enable keeping shape of the body and its movement, they also contribute in sound transduction. Not only they fulfill several important functions but also, or may be because of that, they have a unique ability of self repairing, regeneration and adaptation to variable in time biomechanical conditions by a continuous evolution of a shape and micro-structure. It follows from the complexity of their functions that biomechanical research on bones requires a multidisciplinary approach what makes it even more attractive but also more difficult.

Three classes of problems are discussed briefly in the present paper. The first one concerns a mathematical and computational modeling of bone functional adaptation. In the second class the problems of optimal design of implants taking into account the effects of bone remodeling are considered. Problems devoted to investigation and modeling of mutual interactions between bone tissue and bone-substitute bio-resorbable materials fall into the last of discussed here classes. From a big variety of problems that might be rated among the mentioned classes several examples were chosen that have some links with the optimization methods. Concerning the first class – a big number of theoretical models reflecting adaptation abilities of bones were proposed during last decades, however in the present discussion we focus our attention on the original approach based on the hypothesis of optimal response of bones. In a discussion concerning the second class of problems an example of application of structural optimization methods in a design of optimal endoprosthesis is included. To illustrate the last classes a presentation of an attempt of a description of a set of complex mechanisms present after implantation of grafts from bio-resorbable material in bones is included. It follows from the theoretical considerations and the computational simulations that different scenarios of interactions tissue/graft are possible depending of loading conditions, micro-structure of graft material and different biomechanical factors. It leads to the conclusion that in order to guarantee good integration of a graft in a bone an optimization should be performed to determine the best values of the parameters characterizing graft micro-structure and implantation conditions.

Modeling of Functional Adaptation of Bones

The ability of bones to adapt their external and internal shapes and their micro-structure to variable mechanical loadings is a subject of scientific research for over a hundred years. It is commonly accepted idea that orientation and distribution of material characteristics in bone are associated with the principal stress directions for typical loading conditions. During last decades many theoretical models have been proposed, see e.g. Cowin (2001). In a majority of cases the phenomenological models are proposed on a basis of an explicit postulation of mathematical formulas (called in the following considerations "remodeling formulas" or "adaptation law") describing the effect of applied mechanical load on time evolution of bone topology or distribution of material characteristics. In contrast to such approach the problem formulation based on the hypothesis of optimal response of bone, proposed by Lekszycki (1999, 2002), is briefly discussed in the present section. This formulation enables formal derivation of different remodeling formulas and sometimes leads to the relations that can be considered as a generalization of the postulated ones.

<u>Hypothesis of optimal response of bone:</u> For a given comparison functional the actual structure of bone does not represent an optimal solution. However bone reaction to variable in time physical and biological conditions and constraints guarantees temporary extremum of rate of changes of a comparison functional. If the comparison functional represents quality of a bone its velocity achieves maximum and for the functional representing cost - its velocity is minimal within admissible domain defined by all of the mechanical, structural and biological constraints.

This hypothesis has direct links with a problem formulation making use of calculus of variations. The term "comparison functional" used in the hypothesis represents a functional selected for comparison of different configurations of bones. For example, if one decided that a strength is an important factor characterizing bone quality then the comparison functional should represent a measure of bone strength. For a weight representing a "cost" of a bone the comparison functional represents a total weight of a bone, e.t.c. In the following discussion the detailed derivation of remodeling formulas is not included for the lack of space and due to the fact that many different models can be obtained depending on the effects we are interested in and included in the formulation. Instead, the fundamental elements of the approach are discussed in this section and some examples of the results of the numerical simulations performed with use of implemented specific remodeling formulas are presented.

<u>The main elements of the formulation</u>

- Fundamental assumptions, choice of the control variables defining bone shape or/and micro-structure of tissue, choice of the effects under consideration and their mathematical description. Many options are possible here. For example if we are interested in a distribution of a density of bone tissue, the density and associated mechanical parameters characterizing material can be selected as control variables. If one is interested in anisotropic characteristics of a tissue probably the components of a fabric tensor could be one of the choices. In case we are interested in trabecular structure, the lengths, cross section areas and orientations of trabeculas may be selected for control variables, e.t.c.

- Choice of the comparison functional (quality or cost). This is an important step which to bei extent determines the final remodeling formulas. In the simplest approach the global measure of bone compliance represented by the functional proportional to the potential energy is often selected.

- Hypothesis of optimal response. Application of the hypothesis of optimal response leads to the objective functional which is represented by a time derivative of the comparison functional.

- Objective functional (rate of changes of the comparison functional). In order to derive remodeling formulas the necessary conditions for the extremum of this functional should be derived. But before doing this, the constraints should be defined and added to the objective functional.

- Global and local constraints. This constraints may define any mechanical, biological and geometrical conditions that should be satisfied. This is an important step because various effects of a different nature can be added in this way to the formulation.

- Lagrangean (extended functional constructed with use of Lagrange multipliers).

- A set of mathematical relations resulting from the stationarity condition of the objective functional (among them - the adaptation law).

As a result of this approach a set of relations - algebraic, differential and integral equations and inequalities is derived. Among them the relations between the rates (time derivatives) of the control variables and the mechanical state (stress and strain fields) resulting from the applied load and boundary conditions are present. They can be interpreted as the adaptation law.

This general approach has been used to derive specific remodeling formulas. This formulas were implemented then into the computer programs to perform numerical simulations of different situations as for example remodeling and adaptation of bone after endoprosthesis implantation, development of changes in bone caused by osteoporosis, remodeling of a tissue at the interface with a metallic implant surface of which has a specific micro-structure and others. Let us quote two interesting examples. In the first example an effect of implantation of three different endoprostheses was investigated. Trabecular model of bone adaptation was used and stiffnesses of trabeculas were selected as control variables, the comparison functional represented a global measure of bone compliance which was subjected minimization and one of the constraints defined constant total bone mass. In Figure 1 the effect of numerical simulations is displayed. The distribution of trabeculas in a femur before and after implantation of three endoprosteses of different shape. The initial and final topologies of bone were generated as a result of external load applied to the head and greater trochanter.

Figure 1. Effect of different endoprostheses implantation.

The next example illustrates an application of remodeling formulas derived with an assumption that actor cells (osteoblasts and osteoclasts) responsible for tissue synthesis and resorption receive a signal (stimulus) from the sensor cells (osteocytes). The stimulus is proportional to the density of the strain energy in the domain where osteocyte is located and is decaying with a distance between sensor cell and actor cell. In addition the effect of osteoporosis was examined. In Figure 2 the result of numerical calculations is presented. The square element of bone tissue 4mm x 4mm was considered. In the upper line the development of trabecular micro-structure after application of a uniform external pressure to initially homogeneous sample is presented. The sequence of time steps are presented then in the lower line with the effect of osteoporosis included.

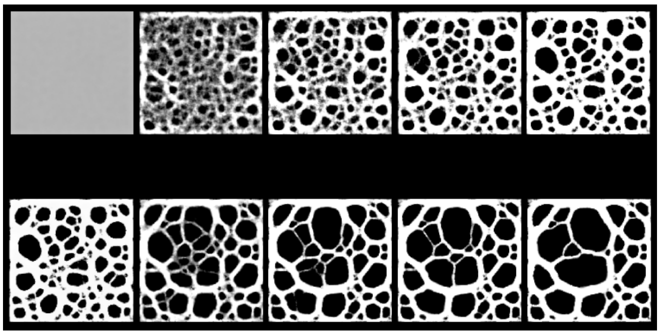

Figure 2. Formation of trabecular bone (upper line) and development of osteoporosis (lower line).

Shape optimization of endoprosthesis including effects of bone functional adaptation.

Usually endoprostheses were optimized assuming an arbitrary distribution of bone tissue properties, often adequate to the state immediately after the implantation. However such an approach does not account for the possible changes of bone structure and its shape caused by the functional adaptation. Therefore endoprosthesis should be designed in order to satisfy conditions for the best interaction with the bone at the final (remodeled) state. On the other hand, the design of endoprosthesis (shape, and possibly the distribution of the stiffness) affects the remodeling process which is dependent on the actual stress and strain distributions. Since the remodeling is the path-dependent process, at the time of surgical intervention the final stage is not known. Taking into account this observations the optimization approach that reflects more realistic formulation including fundamental effects of bone functional adaptation was proposed, see (Lekszycki and Piekarski, 2003). The objective functional is defined at the final (remodeled) state, in terms of the design variables defined at the initial moment immediately after surgical operation. The remodeling process for trabecular bone is described using the rule derived on the basis of the hypothesis of optimal response. As the remodeling is an irreversible process, the sensitivity analysis constitutes an additional boundary value problem that has to be solved at each time step of computations.

Similarly as in (Lekszycki, 1999), to define the analysis problem of bone adaptation – in addition to the state equations - the following remodeling formulas for the rate of Young modulus $\dot{E}(\boldsymbol{x},t)=dE(\boldsymbol{x},t)/dt$ were derived assuming the global stiffness as a comparison functional,

$$\int_V \dot{E}(\boldsymbol{x},t)\,dV=A_0(t) \quad , \quad \int_V \dot{E}(\boldsymbol{x},t)\,dV=B_0 \tag{1}$$

$$\frac{dC_{ijkl}}{dE}\epsilon_{ij}\epsilon_{kl}+\beta_1+\beta_2\dot{E}=0 \tag{2}$$

where $\beta_{1,}\,\beta_2$ denote Lagrange multipliers associated with two integral constraints (1). In formulation of optimization problem it was assumed that the domain V with the boundary S is composed of two sub-domains $V_1, V_2 : V=V_1\ U\ V_2$, separated by the interface surface S_i. The sub-domain V_1 is occupied by the bone subjected to functional remodeling, therefore the material has time-dependent mechanical properties, while the sub-domain V_2 is occupied by the implant with linearly elastic material, see Figure 3. The aim of the work was to determine the best shape of the implant, i.e. the optimal shape of the separating surface S_i parametrized with use of a set of parameters b_m, for the final configuration of remodeled bone.

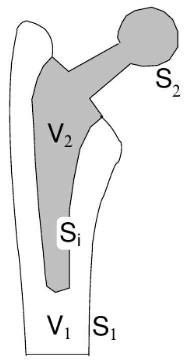

Figure 3. Schematic picture of the implant in a bone.

In order to derive a set of formulas necessary in iterative optimization process the generalized material derivative approach introduced by Dems and Mróz (1998) for the optimization of interfaces in heat conduction problems was used. The numerical calculations leading to the optimal shape of the implant were conducted using iterative procedure.

Modeling of interactions between bone tissue and bone-substitute bio-resorbable material

Application of bone substitute materials becomes an everyday practice in orthopedic, jaw and skull surgery. There are many bio-compatible materials of different chemical composition, form, macro- and micro-structure, mechanical and biochemical characteristics actually available in the market. Most of them can be categorized as bio-degradable, bio-resorbable or a composition of these two. The materials for application in surgery should satisfy several requirements. One of them is a mechanical strength as the implanted graft serves after surgery as a supporting element. The other important factor is an ability of a graft to integrate with a natural tissue. It is driven by biochemical characteristics, however mechanical factors and micro-structure of a material can also promote or make difficult integration. Appropriate porosity of a material is necessary to enable cells migration. The size of the pores defines also condition for development of vascular system necessary for survival of bone cells. Since natural tissue is usually better compared to an artificial graft it can be expected that the best scenario after graft implantation is its gradual replacement by a natural bone tissue. In such a process different effects are present, among them bone and graft resorption and new tissue formation. These three simultaneous processes are dependent of each other and their individual contribution in the remodeling affects actual topology changes and resulting variations of mechanical state of a bone. Mechanical state controls activities of cells responsible for resorption and formation of intracellular matrix what then determines a final effect of bone recovery. After graft implantation similar effects are present as observed during bone fracture healing. After initial inflammation state and clot formation the callus is created to make a bridge connecting and stabilizing broken fragments of bone. After initial satisfaction of mechanical integrity and mechanical strength the process of remodeling starts to enable formation of fully functional bone tissue. At this stage a graft is surrounded by a new tissue. Generally speaking two basic scenarios are possible next. According to the first, the micro-structure of a graft and surrounding tissue does not enable migration of actor cells into a graft deep from the interface with tissue, or does not enable development of vascular system necessary for cells survival inside a graft. In such a situation the remodeling in a graft is possible only very close to the interface with a tissue. Therefore the majority of graft mass remains unchanged or changed very little and represents a kind of inclusion in a natural tissue. According to the second scenario the actor cells can propagate into a domain occupied by a graft and can survive there. The control signals from osteocytes located in a tissue can also reach the cells in a graft so these cells can normally operate. Depending on activities of osteoblasts and osteoclasts the pores in a graft can be filled with a new tissue or the graft material can be resorbed and possibly replaced later by a natural tissue. All of these complex and related with each other effects are dependent of many factors. But this final process of bone remodeling and integration with a graft is very important and determines the final state of a bone and its quality.

A mathematical description of an interaction of a bone tissue with a bio-resorbable graft was proposed under the following assumptions. A) Osteoblasts and osteoclasts activities are proportional to the stimulus from the osteocytes. B) Sensor cells - osteocytes produce the signal proportional to the density of strain energy in a region where they are located. C) The signal send from osteocytes to the actor cells decreases with the distance between actor cell and sensor cell. D) The actor cells integrate signals send by surrounding sensor cells. E) The sensor cells can be located only in a real living tissue. F) The tissue can be resorbed of synthetized but the graft material can be only resorbed. G) The number of the actor cells in a given place depends on a porosity of a mixture of both materials, graft and tissue. Simple academic, 1-D numerical example was solved to examine different possible scenarios, see (Lekszycki and dell'Isola, 2010). An example of the results obtained after numerical calculations is displayed in Figure4. In this example a bar composed initially of two elements, tissue (red) and bio-material (blue) was subjected to uniform stress. The pictures represent an evolution of distribution of both materials during remodeling process and an intensity of colors is proportional to the desities of both materials..

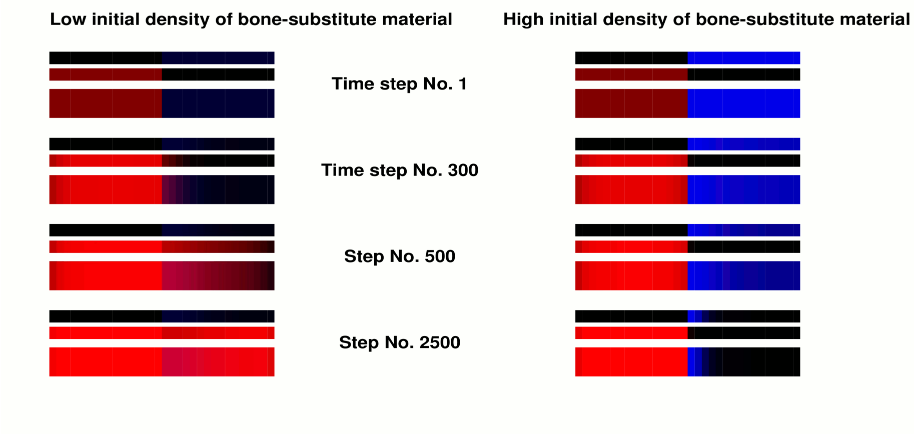

Figure 4. Evolution in time of density of tissue (red) and bio-material (blue) in a rod.

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