

A Bone Remodelling Constitutive Model using Mathematical Programming

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1. Abstract

Bone tissue is a porous, heterogeneous and anisotropic material and can grow, modify shape (external remodelling or modelling), self-repair when fractured (fracture healing) and continuously renew by internal remodelling. This evaluative behaviour of the bone is normally known as bone remodelling. Generally, bone remodelling simulations fail into two categories; those which assume global optimality of the structure, and those which the processes of local regulation assumed to be at a cellular and micro structural level. The present work uses the second approach and put forward a specific mathematical formulation which is motivated by successfully modelled in plasticity and damage mechanics (Thermodynamics of Internal Variables). The internal variables are associated with both local loss and gain of stiffness. According to experimental results, strains in bone during physiological activities are very small. In that case the Helmholtz free energy is assumed to be a function of elastic strain tensor and internal variables and may consist of two parts: one mainly related to elastic strain but affected by loss and gain of stiffness, and other is the energy exclusively related to them. The state laws define the “forces” associated with the state variables (stresses and thermodynamical forces). A dissipation potential related to entropy production rate is expressed in terms of this loss and gain of strength conjugate forces. The rate of structural rearrangement is assumed entirely determined by the thermodynamical forces associated with that rearrangement. A finite region in force space within which no remodelling process occurs for any loading path can be defined and the existence of remodelling criterion in the spaces of the thermodynamic conjugated forces can be assumed. The flow equations are derived from thermodynamics pseudo-potentials of associated forces, whereas the concept of “generalized standard materials” is employed. The constitutive relationships and evolution equations define a nonlinear differential problem, which is written in variational form and solved with non-linear mathematical programming algorithms.

2. Keywords: Constitutive Equations, Bone Remodelling, Thermodynamics pseudo-potentials, Mathematical Programming, Convex Analysis

3. Introduction

Bone tissue is one of the materials that form the musculo-skeletal system. It is a living, dynamic, mineralized, connective, highly vascular tissue, which is characterized by its hardness, resilience and growth mechanisms, and its ability to remodel and repair itself[1]. Simply, bone is a natural composite multi-phase material made up of cells embedded in a matrix composed of both organic (collagen fibers, proteins, lipids, peptides, polysaccharides and citrates) and inorganic (calcium-phosphates, carbonates, sodium, magnesium and fluoride salts) elements. Moreover, bone is not purely a structural tissue, but is also responsible for maintaining mineral homeostasis and providing a source of stem cells: bone acts as a mineral (notably calcium) and blood cell reservoir for the rest of the body[2]. Consequently, bone is involved in a constant cycle of the resorbing and forming bone actions, undergoing continual chemical exchange and structural remodeling, due to both internal hormonal regulation and external mechanical demands.

Following Prendergast's ideas [3], it is assumed that there are two adaptation processes that participate of construction of skeleton form: phylogenic process acting over millions of years (Mother Nature's engineering problem [4]) and ontogenic process acting over the life of individual. There are two main approaches to investigating these problems: searching for the optimality of skeletal elements and searching for “mechano-regulation rules” to predict bone adaptation. The first one attempts to discover how a particular bone has achieved some kind of optimal performance while the other one, try to discover “rules” for the response of bone tissues to mechanical forces. The present work uses the second approach and put forward a specific mathematical formulation which is motivated by successfully modelled in plasticity and damage mechanics.

3.1. Some fundamentals of bone remodeling.

Bone matrix, bone cells, bone marrow and its associated vascular network are the elementary level components involved in the bone remodeling. The bone matrix is composed by the organic collagen fibres and the inorganic bone mineral crystals and provides mechanical strength and acts as the body's mineral. There are many cells associated with bone but three of them are of special interest: the osteoblast, osteocyte and osteoclast, which are responsible for the production, maintenance, and resorption of bone, respectively. In bone remodeling, osteoclasts resorb old bone and osteoblasts lay down osteoid that calcifies to form new bone. Bone serves as the major reservoir of total body calcium, and it operates under hormonal control, principally of parathyroid hormone (PTH). PTH mobilizes calcium from bone by activation of osteoclasts, resulting in the resorption of bone. In bone remodeling, osteoclasts and osteoblasts differentiate from less mature precursors, which line bone surfaces in an inactive state. PTH stimulates differentiation of mesenchymal stem cells to preosteoblasts, and through an indirect process, preosteoclasts to osteoclasts. Preosteoblasts differentiate further to form osteoblasts. After osteoblasts have laid down their protein-based matrix, known as osteoid, they bury themselves in the bony matrix, becoming osteocytes, or revert to an inactive cell form and line the bone surfaces as

surface osteocytes or resting osteoblasts. Bone remodeling involves many different factors, such as transforming growth factors (TGF), attachment of osteoclast surface through integrins, possibly release of osteoblast-stimulating factors from the resorption of bone matrix such as IGF-1, IGF-2 or TGF. Multiple biochemical messengers serve to regulate bone remodeling. Osteoclastic stimulation requires the presence of osteoblasts, thus osteoblast and osteoblast precursor responsiveness to hormones and paracrine messengers regulate, at least in part, the responsiveness of pre-osteoclasts and osteoclasts. Also, the availability of nutrients come from high vascularity (oxygen in the surrounding environment) is necessary for the growth and nutrition of healthy bone [2]. Mature bone is composed of two types of tissue: cortical and trabecular bones. The first is relatively dense, while the other consists of a network of struts or trabeculae surrounding interconnected spaces. Bone surfaces consist of cortical bone, and the thickness of this protective skin increases in mechanically demanding regions such as the shafts of long bones, while trabecular bone is found in the interior of bones, such as within the femoral head. This variation in structure of two kinds of bones leads to considerable variation in its toughness, strength and stiffness. The microstructure of cortical bone makes it highly anisotropic, although its density is relatively consistent. The mechanical properties of trabecular bone are highly dependent upon porosity and architecture, both of which vary widely with site and age and its anisotropic structure due to the orientation of major trabeculae along lines of principle stress[5].

3.2. Mathematical models of bone remodelling process

It is well accepted that mechanical loading is one of the factors that influence bone morphology and histology and there are various mathematical continuum formulations of this. These mathematical models use different stimulus (strain, stress, alteration in mineral solubility due to stress, piezoelectric potentials, extracellular fluid pressure, and other ones) to simulate the ignition and evolution of the bone remodelling process. Generally, this process is described with a generic mathematical expression, using apparent density to characterize a bone adaptation to load. In some recent works, which take into account the mechanical and biological point of view of bone remodelling, relate the process not only like a structural adaptation to load, but also regarding the need of removing micro damage and micro cracks from bone structure [6]. The damage, conventionally, is defined as the gradual deterioration of materials induced by nucleation, growth and coalescence of certain microscopic cavities (micro cracks). Frost [7] was the first to propose that remodelling would occur to repair micro damage in bone [8]. The works of Martin & Burr [9], Burr [10], Martin[11], Lee *et al.* [6] and Lee *et al.*[12] also shown that micro damage in cortical bone is associated with increasing activation of bone remodelling. Prendergast and Taylor [13], Prendergast and Huiskes [14] use micro structural finite element analysis to explore the relationship between damage formation and local strain. Garcia *et al.* [15], Doblaré & Garcia[16], Doblaré *et al.* [17], have proposed a model, which combines an anisotropic internal remodelling rule based on continuum “damage-repair” theory. More recently, Ramtani and Zidi [18] have considered a scalar damage state variable and have proposed that bone remodelling stimulus are both damage and strain [19]. Which are the mechanisms throughout the living cells use to initiate the remodelling process still remaining not clear, and it is assumed that damage in bone is one of them. For possible repair, using mass transference as the result of a biochemical reaction as also the energy and entropy can be transferred outwards or inward the matrix structure, by these chemical reactions. Therefore, an inelastic path-dependent mathematical model (initial/boundary value problem) is necessary to simulate such mechanism. Experimental evidences [20] corroborate the need to validate the use of the infinitesimal theory, since in general; the physiological activities induce small deformations in the bones. Also it is commonly point out, the use of adiabatic processes.

3.3. Inelastic behavior modeling

The inelastic behavior of materials and its numerical solution have been successfully modeled in plasticity and damage theory. Plasticity theory is used in the modeling of ductile metals, and has also been applied to quasi-brittle materials. It is based on the concept of the sum elastic and plastic strains, the latter one only occurs once a criterion (yield function) is satisfied. A rate constitutive relation (flow rule) was proposed such that it defines the mapping between the stress space and the plastic strain rate space. The flow rule given by rate equation is the most familiar version, where the plastic strain rate is expressed in term of a convex function in stress space (yield function). The flow rule is called associated, when the plastic potential coincides with the yield function. When the material has non-associated flow rule, the plastic potential is given by another function. The gradient of the potential provides the direction of the plastic flow and the plastic multiplier its magnitude. The Karush-Kuhn-Tucker or complementary conditions, (also known as the Kuhn-Tucker or the KKT conditions) what relate plastic flows and stresses, complete the characterization of the plastic behavior. The second version of flow rule uses the principle of maximum dissipation (Hill’s principle) to obtain the normality rule. However, for non-associated models, Hill’s inequality does not hold. It can be written in a variational statement and the principal advantage of this strategy is to state the achievement of the solution in an easier and clearer way. The third version uses thermodynamic principles and convex analysis. It consists of defining a set of internal variables that take into account the micro-structural transformations. By properly choosing the number and the kind of the internal variables, several plastic models can be accommodated within the same formal context. For generalized standard materials, the evolution law can be derived from a convex potential, imposing a normality rule. The flow rule is replaced by the evolution law, which relates the rate of change of internal variables, referred to the conjugated forces. Making use of convex analysis tools, Moreau [21] introduced the concept of pseudo-potential as a proper extension of the potential notion to multivalued mechanical laws. Subdifferentials, differential inclusions and Fenchel’s inequality are basic tools of this approach linked to the theory of Convex Analysis [22] which provides an elegant framework where the dissipative laws can be accommodated. As a result, the complete flow rule takes the form of a differential inclusion, in which the plastic strain rate is expressed as the subgradient of the convex complementary pseudo-potential. This formulation gives flow rules of plasticity in a rigorous mathematical meaning and this compact formulation can be used to visualize some tips that allow choosing efficient forms of solution. In this way, the stress is then expressed as the subgradient of the pseudo-potential of dissipation, which coincides with the rate of dissipation. Both functions are convex and related by the Fenchel inequality. Making use of convex analysis, it is possible to include non-smooth phenomena within the class of generalized standard materials, by taking the dissipation potential as convex, but not necessarily differentiable ([23,24,25], [26], [27], [28], [29]). Another important observation coming out is the possibility to solve, within the concept of a generalized standard material, phenomena such as non-associated plasticity and friction with a non-constant normal force [30]. Generally, approximate solution

procedures in the finite element framework are available; some of them are based in the context of a displacement method, on a weak form of the equilibrium and have two main ingredients: one is the numerical integration of the rate constitutive relations over a generic time step (local stage) and the other is the iterative algorithm to solve the nonlinear equilibrium equations (global stage). The local stage of solution can be solved in efficient way with the use of algorithms of the Mathematical Programming [31]. The global stage can be solved using a Quasi-Newton Method. These approaches can generate to an efficient algorithm of solution of elastic-plastic problems.

3.4 Objectives:

The present work presents a damage-remodeling bone problem and is based on generalized thermodynamics [32], in which internal variables are introduced in the thermodynamic constitutive relationships to describe the inelastic processes at the current material state. The internal variables describe both local loss or degradation and gain of stiffness. Like plasticity and damage theory where the plastic behavior and damage variable are completely specified by the flow rule and the loading and unloading conditions, it will be assumed that in the damage-remodeling bone theory, the remodeling process is completely specified by the flow rule and the dissipative (microcracks, microdamage, bone resorption and other one) and gain energy (healing) rules. A scalar-valued variable is introduced in the constitutive equations. According to experimental results, strains in bone during physiological activities are very small. In that case the Helmholtz free energy is assumed to be a function of elastic strain tensor and internal variables and may consist of two parts: one mainly related to elastic strain but affected by loss or degradation and gain of stiffness, and another representing the energy exclusively related to these stiffness variations. The state laws define the “forces” associated with the state variables (stresses and thermodynamical forces). A dissipation potential related to entropy production rate is expressed in terms of this loss and gain of strength conjugate forces. The rate of structural rearrangement is assumed entirely determined by the thermodynamical forces associated with that rearrangement. It is assumed that a finite region in force space exists, within which no remodeling process occurs for any loading path. That is, the existence of a remodeling criterion in the space of the thermodynamic forces is assumed. The flow equations are then derived from thermodynamics pseudo-potentials of associated forces, whereas the concept of “generalized standard materials” is employed ([33], [34]). The constitutive relationships and evolution equations define a nonlinear differential problem, which is written in variational form and solved with non-linear mathematical programming algorithms [31]. This material behavior formulation is specially suited to be combined with a finite element method spatial discretization. Then, the evolution equations are integrated by means of a backward Euler approximation, thus leading to stable numerical procedures for the incremental analysis. This framework allows reproduction of other constitutive models found in the literature, by an appropriate choice of internal variables and constitutive potentials [18]. Further, an effective strength configuration is introduced, in which the body is considered without discontinuities. In order to describe the internal variable evolution, different dissipation potentials for damage and healing are introduced. Supported by experimental observations, and in the context of convex analysis [22], we derive different limit damage thresholds and healing domains. One basic assumption of the model, motivated by experimental observations, is that the healing agent acts when a sufficiently large microcracks density affects the material. In the model this occurs when the degradation of strength domain reaches the critical surface and at the same time the healing thermodynamical forces reach the boundary of the healing domain. An example is given to illustrate the proposed approach, showing an application to damage-remodelling bone.

4. Thermodynamical aspects in damage-remodelling constitutive model

The ability to model bone remodelling as a continuum rests on the development of constitutive relationships that relate stress to deformation variables to the long of the time. This work present a thermomechanical approach where the material behaviour is first described in terms of two thermodynamical potentials. Constitutive relations and the underlying balance equations are then derived directly from the first and second laws of thermodynamics using these potentials. A great number of papers have used this approach to develop models of material behaviour, especially in plasticity and damage. The formulation used in this paper is based on generalized thermodynamics [32], in which internal variables are introduced in the thermodynamic constitutive relationships to describe the inelastic processes at the current material state.

Bone tissue is a living material that changes the mechanical properties with the time and is directly related to bone apparent density and orientation of the microstructure. Bone can vary its density by changing its porosity. The cortical bone (that makes up the outer shells of our bones) has typically 5% porosity. This can increase under conditions of disuse or disease, forming osteoporotic bone; further increases in porosity give rise to a spongy, open structure known as trabecular bone, which is found at the interior of long bones. In this paper, the variable used to describe the porosity is the bulk density ρ_t at present time t . Bulk density can be defined as the mass of bone matrix divided by the volume they occupy. The volume includes bone matrix and the space between particles as well as the space inside the pores of individual particles.

4.1 State variables

Let consider thermodynamic deformation of a solid (bone) that suffer gradual degradation and healing by rearrangement of the internal structure of the material. Assume that local loss or degradation and gain of stiffness are developed within the solid in relation to the current state. The local state of the material is assumed to be completely defined, for the isothermal case, by knowledge of (a) strain tensor $\boldsymbol{\varepsilon}$ (observable variable), (b) a set of an arbitrary number N of internal scalar variables $\{\alpha_1, \alpha_2, \alpha_3, \dots, \alpha_N\}$ which characterize the internal restructuring when the irreversible (remodelling) process occurs. Some of them, that will be called $\{\alpha_d\}_i$, are used to describe the degradation of stiffness processes (micro-cracking opening, bone loss), while the others one $\{\alpha_h\}_j$ are used to describe the gain of stiffness processes (healing, bone gain).

Different degradation and healing mechanisms must be considered in the model. For example, the types of microcracking observed in bone loaded in tension or in compression are quite different [35,36] and can be treated with different internal variables $\{\alpha_d\}_i$. Also,

the internal variables $\{\alpha_h\}_j$ must be capable of include other biological consideration like parathyroid hormone (PTH) influence. It is considered in this paper that bone is a material which is degraded by the development of distributed microscopic cracks and other mechanisms and leads to the final fracture by their coalescence without significant inelastic deformation. The chemical effects related to the loss and gain bone process are only introduced from a mesoscopic point of view by means of internal variables without considering any diffusion process.

The bulk density ρ_t at present time t is affected of degradation and healing mechanisms, so

$$\rho_t = \rho_t(\{\alpha_d\}_i, \{\alpha_h\}_j) \quad (1)$$

The actual thermodynamic state can be described by the Helmholtz density free energy ψ , which is a proper, strictly convex function of both observable and internal variables

$$\psi = \psi(\boldsymbol{\varepsilon}, \{\alpha_d\}_i, \{\alpha_h\}_j) \quad (2)$$

with $\boldsymbol{\varepsilon}$ being the admissible strain set (without significant inelastic deformation) and $\{\alpha_d\}_i, \{\alpha_h\}_j$ the internal variables used to describe degradation and gain of stiffness. For elastic linear material, the Helmholtz density free energy ψ is

$$\psi(\boldsymbol{\varepsilon}, \{\alpha_d\}_i, \{\alpha_h\}_j) = \frac{1}{2\rho_t} \mathbf{D}(\{\alpha_d\}_i, \{\alpha_h\}_j) \boldsymbol{\varepsilon} \cdot \boldsymbol{\varepsilon} \quad (3)$$

where $\mathbf{D}(\{\alpha_d\}_i, \{\alpha_h\}_j)$ is a fourth order tensor called the elastic tensor, that incorporates the effect of loss and gain of stiffness. The dual state variables, stresses $\boldsymbol{\sigma}$ and the sets of thermodynamic forces $\{A^d\}_i, \{A^h\}_j$ associated with the sets of internal state variables $\{\alpha_d\}_i, \{\alpha_h\}_j$ are derived from the free energy ψ according to the state laws

$$\boldsymbol{\sigma}(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) = \rho(\alpha_d, \alpha_h) \frac{\partial \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)}{\partial \boldsymbol{\varepsilon}} = \mathbf{D}(\alpha_d, \alpha_h) \boldsymbol{\varepsilon} \quad (4)$$

$$A^d(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) = \rho(\alpha_d, \alpha_h) \frac{\partial \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)}{\partial \alpha_d} = \frac{1}{2} \left[\frac{\partial \mathbf{D}(\alpha_d, \alpha_h)}{\partial \alpha_d} - \frac{1}{\rho(\alpha_d, \alpha_h)} \frac{\partial \rho(\alpha_d, \alpha_h)}{\partial \alpha_d} \mathbf{D}(\alpha_d, \alpha_h) \right] \boldsymbol{\varepsilon} \cdot \boldsymbol{\varepsilon} \quad (5)$$

$$A^h(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) = -\rho(\alpha_d, \alpha_h) \frac{\partial \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)}{\partial \alpha_h} = -\frac{1}{2} \left[\frac{\partial \mathbf{D}(\alpha_d, \alpha_h)}{\partial \alpha_h} - \frac{1}{\rho(\alpha_d, \alpha_h)} \frac{\partial \rho(\alpha_d, \alpha_h)}{\partial \alpha_h} \mathbf{D}(\alpha_d, \alpha_h) \right] \boldsymbol{\varepsilon} \cdot \boldsymbol{\varepsilon} \quad (6)$$

where, to simplify the notation, is used α_d and α_h to represent the sets $\{\alpha_d\}_i, \{\alpha_h\}_j$ and A^d, A^h to represent the sets $\{A^d\}_i, \{A^h\}_j$.

The dual convex function or conjugated function ψ_c of ψ is obtained by Legendre-Fenchel transform

$$\rho(\alpha_d, \alpha_h) \psi_c(\boldsymbol{\sigma}, A^d, A^h) = \sup_{\boldsymbol{\varepsilon}, \alpha_d, \alpha_h} [\boldsymbol{\sigma} \cdot \boldsymbol{\varepsilon} + A^d \cdot \alpha_d - A^h \cdot \alpha_h - \rho(\alpha_d, \alpha_h) \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)] \quad (7)$$

and may be used in order to write the state laws in an equivalent way

$$\boldsymbol{\varepsilon} = \frac{1}{\rho(\alpha_d, \alpha_h)} \frac{\partial \psi_c(\boldsymbol{\sigma}, A^d, A^h)}{\partial \boldsymbol{\sigma}} \quad (8)$$

$$\alpha_d = \frac{1}{\rho(\alpha_d, \alpha_h)} \frac{\partial \psi_c(\boldsymbol{\sigma}, A^d, A^h)}{\partial A^d} \quad (9)$$

$$\alpha_h = \frac{1}{\rho(\alpha_d, \alpha_h)} \frac{\partial \psi_c(\boldsymbol{\sigma}, A^d, A^h)}{\partial A^h} \quad (10)$$

to get the strain $\boldsymbol{\varepsilon}$ and α_d, α_h the sets of internal variables used to describe degradation and gain of stiffness.

4.2 Laws of evolution

To complete the constitutive equations, the laws of evolution of the internal variables (degradation and gain of stiffness) must be added to the state laws. The theory of the thermodynamics of irreversible processes gives a guideline and some restrictions to get the evolution laws such that the second principle of thermodynamics must be satisfied for any evolution of the material, that is, such that the dissipation is non-negative [Chaboche, 1993]. In analogous way to the plasticity theory, two models can be constructed. The first one, that it is used in this paper, deals with an "associated" law where the normality rule is valid. The second one, with a "non-associated" law, implies in the construction of a double potential function of two variables, biconvex and that it satisfies an inequality generalized of Fenchel whose proposal is found for the theory of the plasticity in the works of Géry de Saxcé and collaborators [37,38,39 and others].

In this work, the laws of evolution of the internal variables will be done in the framework of convex analysis [22,28]. The theorem below is the result that will be used to formulate the evolution law in two equivalent forms (see, for example, Han & Reddy, [28] for details):

Theorem. Let X be a reflexive Banach space, and let the $g: X \rightarrow \mathbb{R}$ be a proper, convex and weakly lower semi-continuous function.

Given $x \in X$ and $x^* \in X^*$, then

$$x^* \in \partial g(x) \leftrightarrow x \in \partial g_C(x^*) \quad (11)$$

where g_C is the function conjugated to g .

Let:

$$P_A = \left\{ \left\{ \{A^d\}_j, \{A^h\}_j \right\} / f(\{A^d\}_j, \{A^h\}_j) \leq 0 \right\} \quad (12)$$

be the region of admissible forces thermodynamics, which is assumed to be a closed, convex and nonempty set. The function $f(A)$ is called the yield function (using the same name as plasticity theory). There is a “dead zone” where neither degradation strength nor gain of strength elastic could happen and this behaviour takes place when $f(A) < 0$; whereas, the loss and gain behaviour takes place when $f(A) = 0$. Let χ be the support function of P_A :

$$\chi(\dot{\alpha}) = \sup_{A^* \in P_A} \left\{ A^* \bullet \dot{\alpha} \right\} \quad (13)$$

where in the context of elasto-plasticity, χ is the dissipation function and in this work, it is the energy dissipated or introduced in the system. It is conjugate to the indicator function of P_A and has the following properties: convex, positively homogenous, lower semi-continuous, $\chi(\dot{\alpha}) \geq 0$ and containing the origin $\chi(0) = 0$. Therefore, from the Theorem above:

$$\dot{\alpha} \in \partial Ind_{P_A} \leftrightarrow A \in \partial \chi(\dot{\alpha}) \quad (14)$$

The expression in (14) yields two equivalent forms of the evolution law. The Lemma presented below completes the theory once it allows to write the evolution law using a multiplier λ .

Lemma. Let a function $f(A)$ be nonnegative and convex, with $f(0) = 0$ and the thermodynamic forces A^* be a point in the interior of $dom(f)$ such that $f(A^*) > 0$. Set $P = \{A / f(A) \leq f(A^*)\}$. Then $\dot{\alpha} \in \partial Ind_C$ if and only if there exists $\lambda \geq 0$ such that $\dot{\alpha} \in \lambda \partial f(A^*)$. The function f can be the canonical “yield” function:

$$f(A) = g_P(A) - 1 \quad (15)$$

Where the gauge function is:

$$g_P(A) = \inf \{ \mu > 0 / A \in \mu P \} \quad (16)$$

or f can be an “yield” function under any other form.

Then, from the Lemma presented above, it is possible to obtain:

$$\dot{\alpha} \in \partial Ind_{P_A} \leftrightarrow \exists \lambda \geq 0, \text{ such that } \dot{\alpha} \in \lambda \partial f(A) \quad (17)$$

Equation (17) represents a generalization of the normality law.

The definition of the convex region of the admissible thermodynamic forces must be made experimentally, therefore the boundary of the region limits from that value of the thermodynamic forces (or a composition of them), will have altered in the strength (loss, gain or simultaneously a loss and a gain of strength).

4.3 Rate formulations for damage-remodelling constitutive equations

In the present work, the rate formulations proposed by Hecke [26] to elastic-plastic model are adapted for damage-remodelling constitutive model. Introducing the potentials:

$$\begin{aligned} j_C(\dot{\sigma}, \dot{A}^d, \dot{A}^h) &= \nabla_{\dot{\sigma}} \left(\frac{\psi_C(\dot{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{\sigma} \bullet \dot{\sigma} + \nabla_{\dot{\alpha}^d} \left(\frac{\psi_C(\dot{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{\sigma} \bullet \dot{A}^d + \\ &+ \nabla_{\dot{\alpha}^h} \left(\frac{\psi_C(\dot{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{\sigma} \bullet \dot{A}^h + \nabla_{A^d A^d} \left(\frac{\psi_C(\dot{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{A}^d \bullet \dot{A}^d + \\ &+ \nabla_{A^d A^h} \left(\frac{\psi_C(\dot{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{A}^d \bullet \dot{A}^h \end{aligned} \quad (18)$$

and the conjugated form

$$j(\dot{\varepsilon}, \dot{\alpha}_d, \dot{\alpha}_h) = \sup_{\dot{\sigma}, \dot{A}^d, \dot{A}^h} \left[\dot{\sigma} \bullet \dot{\varepsilon} + \dot{A}^d \bullet \dot{\alpha}_d + \dot{A}^h \bullet \dot{\alpha}_h - j_C(\dot{\sigma}, \dot{A}^d, \dot{A}^h) \right] \quad (19)$$

of such form that

$$\dot{\varepsilon} = \nabla_{\dot{\sigma}} j_C(\dot{\sigma}, \dot{A}^d, \dot{A}^h) \quad (20)$$

$$\dot{\alpha}_d = \nabla_{\dot{A}^d} j_C(\dot{\sigma}, \dot{A}^d, \dot{A}^h) \quad (21)$$

$$\dot{\alpha}_h = \nabla_{\dot{A}^h} j_C(\dot{\sigma}, \dot{A}^d, \dot{A}^h) \quad (22)$$

or in an equivalent form

$$\dot{\boldsymbol{\sigma}} = \nabla_{\boldsymbol{\varepsilon}} \cdot j \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) \quad (23)$$

$$\dot{A}^d = \nabla_{\alpha_d} \cdot j \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) \quad (24)$$

$$\dot{A}^h = \nabla_{\alpha_h} \cdot j \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) \quad (25)$$

or in a condensed form

$$\left(\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h \right) = \nabla j \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) \quad \Leftrightarrow \quad \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) = \nabla j_C \left(\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h \right) \quad (26)$$

Defining the region of admissible rates of thermodynamic forces as the negative polar cone of $\partial \text{Ind}_p(A)$:

$$\left(\dot{A}^* \right) \in \dot{P} = [\partial \text{Ind}_p(A)]^{-1} \Leftrightarrow -\dot{\alpha} \cdot \dot{A}^* \leq 0 \quad (27)$$

where

and using the same arguments than Hecke (1991) for elasto-plasticity model, it can obtained the relation:

$$\left(\dot{\alpha} \right) \in \partial \text{Ind}_p \left(\dot{A} \right) \quad (28)$$

Equation (28) makes it possible to account for the return to dead zone or unloading. If A represents a set of thermodynamic forces in the yield surface and \dot{A} represents rates in the interior of the admissible region \dot{P} , then $\partial \text{Ind}_p \left(\dot{A} \right) = 0$, which means that there is not process of gain and loss strength, $(-\dot{\alpha}) = (0)$. Table 1 present a summary of the constitutive relations presented above.

Table 1. Constitutive relations

$$\begin{aligned} \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) &= \frac{1}{2\rho(\alpha_d, \alpha_h)} \mathbf{ID}(\alpha_d, \alpha_h) \boldsymbol{\varepsilon} \cdot \boldsymbol{\varepsilon} \\ \rho(\alpha_d, \alpha_h) \psi_C(\boldsymbol{\sigma}, A^d, A^h) &= \sup_{\boldsymbol{\varepsilon}, \alpha_d, \alpha_h} [\boldsymbol{\sigma} \cdot \boldsymbol{\varepsilon} + A^d \cdot \alpha_d - A^h \cdot \alpha_h - \rho(\alpha_d, \alpha_h) \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)] \\ \boldsymbol{\sigma}(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) &= \rho(\alpha_d, \alpha_h) \frac{\partial \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)}{\partial \boldsymbol{\varepsilon}} = \mathbf{ID}(\alpha_d, \alpha_h) \boldsymbol{\varepsilon} \\ A^d(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) &= \rho(\alpha_d, \alpha_h) \frac{\partial \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)}{\partial \alpha_d} & A^h(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h) &= -\rho(\alpha_d, \alpha_h) \frac{\partial \psi(\boldsymbol{\varepsilon}, \alpha_d, \alpha_h)}{\partial \alpha_h} \\ \boldsymbol{\varepsilon} &= \frac{\partial}{\partial \boldsymbol{\sigma}} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) & \alpha_d &= \frac{\partial}{\partial A^d} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) & \alpha_h &= \frac{\partial}{\partial A^h} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \\ & & \left(\dot{\alpha}_d, \dot{\alpha}_h \right) &\in \text{Ind}_{p_s} \left(A^d, A^h \right) \\ j_C(\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h) &= \nabla_{\boldsymbol{\sigma}} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{\boldsymbol{\sigma}} \cdot \dot{\boldsymbol{\sigma}} + \nabla_{\alpha^d} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{\boldsymbol{\sigma}} \cdot \dot{A}^d + \\ &+ \nabla_{\alpha^h} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{\boldsymbol{\sigma}} \cdot \dot{A}^h + \nabla_{A^d A^d} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{A}^d \cdot \dot{A}^d + \\ &+ \nabla_{A^d A^h} \left(\frac{\psi_C(\boldsymbol{\sigma}, A^d, A^h)}{\rho(\alpha_i)} \right) \dot{A}^d \cdot \dot{A}^h \\ j \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) &= \sup_{\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h} \left[\dot{\boldsymbol{\sigma}} \cdot \dot{\boldsymbol{\varepsilon}} + \dot{A}^d \cdot \dot{\alpha}_d + \dot{A}^h \cdot \dot{\alpha}_h - j_C \left(\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h \right) \right] \\ \left(\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h \right) &= \nabla j \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) & \left(\dot{\boldsymbol{\varepsilon}}, \dot{\alpha}_d, \dot{\alpha}_h \right) &= \nabla j_C \left(\dot{\boldsymbol{\sigma}}, \dot{A}^d, \dot{A}^h \right) \end{aligned}$$

5. Discretized form:

The time interval $[0, T]$, in which the history is defined, is partitioned into N sub-intervals of size ΔT , not necessarily equal, according to

$$0 = t_0 < t_1 < t_2 < \dots < t_{n-1} < t_n < t_{n+1} < \dots < t_{N-2} < t_{N-1} < t_N = T$$

The problem of discrete evolution consists in evaluating variables at the end of a time step starting from their values at the beginning and the strain increment. If it is assumed that the value of variable β at time t_n is $\beta(t_n) = \beta_n$ and $\Delta\beta = \beta_n - \beta_{n-1}$, where β is any variable, the solution of the actual problem within the interval $[0, T]$ is then obtained by solving N successive finite-step problems. In order to ensure convergence and stability requirements, the implicit scheme is considered. As a result of a backward-Euler type approximation and using

$$\boldsymbol{\varepsilon}_{t+\Delta t} = \frac{1}{\rho_{t+\Delta t}(\alpha_d, \alpha_h)} \frac{\partial \psi_c(\boldsymbol{\sigma}_{t+\Delta t}, A_{t+\Delta t}^d, A_{t+\Delta t}^h)}{\partial \boldsymbol{\sigma}} \quad (29)$$

$$\boldsymbol{\sigma}_{t+\Delta t} = \boldsymbol{\sigma}_t + \Delta\boldsymbol{\sigma} \quad (30)$$

$$(\alpha_d)_{t+\Delta t} = (\alpha_d)_t + \Delta\alpha_d \quad (\alpha_h)_{t+\Delta t} = (\alpha_h)_t + \Delta\alpha_h \quad (31)$$

$$(A^d)_{t+\Delta t} = (A^d)_t + \Delta A^d \quad (A^h)_{t+\Delta t} = (A^h)_t + \Delta A^h \quad (32)$$

the constitutive relations

$$(\Delta\boldsymbol{\sigma}, \Delta A^d, \Delta A^h) = \nabla j(\Delta\boldsymbol{\varepsilon}, \Delta\alpha_d, \Delta\alpha_h) \quad (33)$$

are satisfied at the end of each time step. The advantage of this formulation is that the solution procedure takes the form of a minimization of a convex function on a convex set, i.e., a convex optimization problem.

The increments of stress and thermodynamic forces $(\Delta\boldsymbol{\sigma}, \Delta A^d, \Delta A^h)$ can be determined from the increments of deformation and internal variables $\Delta\boldsymbol{\varepsilon}, \Delta\alpha_d, \Delta\alpha_h$ by the constitutive relation (33). Equation (34) expresses the condition necessary and sufficient that the generalized stress $(\Delta\boldsymbol{\sigma}, \Delta A^d, \Delta A^h)$ must verify in order to be the solution of (33).

$$(\Delta\alpha_d, \Delta\alpha_h) \in \partial \text{Ind}_{P_n}(A_{t+\Delta t}^d, A_{t+\Delta t}^h) \quad (34)$$

In the case that the yield function f is a vector field with m components f_j called plastic modes, the differential inclusion (34) can be determined by the system:

$$(\Delta\alpha_d, \Delta\alpha_h) = \Delta\lambda \bullet \nabla f_A(A_{t+\Delta t}^d, A_{t+\Delta t}^h) \quad (35)$$

$$f(A_{t+\Delta t}^d, A_{t+\Delta t}^h) \leq 0 \quad (36)$$

$$\Delta\lambda \geq 0 \quad (37)$$

$$\Delta\lambda \bullet f(A_{t+\Delta t}^d, A_{t+\Delta t}^h) = 0 \quad (38)$$

When the stress and the thermodynamic forces can be related to the plastic multipliers by:

$$\boldsymbol{\sigma}_{t+\Delta t} = \boldsymbol{\sigma}_t + \Delta\boldsymbol{\sigma} \quad (A^d)_{t+\Delta t} = (A^d)_t + \Delta A^d \quad (A^h)_{t+\Delta t} = (A^h)_t + \Delta A^h \quad (39)$$

Equations (36) to (38) represent a nonlinear complementarity problem. Newton's method solves it by generating a sequence $\{\Delta\lambda^k\}$ in the following way. Given $\Delta\lambda^k$, $\Delta\lambda^{k+1}$ is defined to be the exact solution of the linear complementarity subproblem:

$$w = F(\Delta\lambda^k) + B(\Delta\lambda^k) (\Delta\lambda - \Delta\lambda^k) \geq 0 \quad (36)$$

$$\Delta\lambda \geq 0 \quad (37)$$

$$\Delta\lambda^T \cdot w = 0 \quad (38)$$

where the matrix $B(\Delta\lambda^k)$ is the Jacobian matrix. In the present work, Lemke's Method was applied to solve the linear complementarity subproblem of the constitutive formulation.

5. Discussion:

A great consensus in biomechanics literature (from odontology and orthopedics) exists around the idea that the mechanical stimulus, its variation and its history, have a great influence in the bone remodeling process. Several constitutive models have been proposed to describe it; however none of them can exactly describe the theory of mecanodifferentiation and mecanoregulation. The great difficulty in the attainment of "in vivo" experimental results, an accurate interpretation of its results, the definition of the most important parameters to consider, the formulation of a coherent model from the mathematical and thermodynamic points of view, as also the choice of the adjusted numerical method for its simulation are obstacles to be transposed for its proper use and application in medicine, with a good performance and reliability.

In this work, a variational approach, also used successfully to describe the developed constitutive equations in mesoscale, of the elasto-plasticity (determination of the plastic strains in materials with constitutive laws associated and not associated that presents or not strain hardening) and damage (appearance of microcracks that reduces the rigidity of the inert materials, in special the granular materials) was generalized an implemented to describe the bone remodeling (loss and gain of bone rigidity). The process of bone repairing, that incorporates the density gain, and as a consequence the rigidity gain, can be seen as the contrary process of increase porosity and with a consequent loss of rigidity, common in granular materials. The proposed model, within this work, is based on the method of internal variables, when, after a proper choice of the most important internal variables to be considered, it is possible to describe the process, as also its mechanisms of variation with time. Making use of concepts derived from the convex analysis, potential laws are developed and proposed, in such a way that it's possible to incorporate a consistent formalism, that automatically satisfies the thermodynamic restrictions. In special, the model generalizes the ideas discussed and proposed by Feijóo et al [23,24,25], Hecke [26], Zouain et al. [27], and also Han & Reddy [28]. They have used concepts from the Convex Analysis [22], from the Thermodynamics ([33], [34]) and from the Mechanics of the Continuous considering the Damage and the Repairing

(CDHM- Barbero et al, [40]). Moreover, the constitutive equation was written in a short way, thus it can be solved with the use of efficient algorithms of the Mathematical Programming [31]. In the presented model, only internal scalar variables were considered proper to describe isotropic models, however this procedure can be generalized to include tensorial variables, proper for application to anisotropic models. The main contribution of this work is presented in the formalism considered in table 1, and its major goal is its adaptation to a great amount of specific constitutive models, existing in literature, by a proper choice of the internal variables, the constitutive potentials and the permitted regions for tensions and thermodynamic forces. With such formalism, it is possible to easily recognize the conjugated thermodynamic forces, associated to the mechanisms of gain and loss of rigidity. In consequence, we are able to propose coherent criteria for the development of such processes and through associated or not associated laws (common in the elasto-plasticity) propose evolution laws for such variables. The considered variables must be of some form measured and evaluated in an "in vivo" experiment.

6. Conclusion:

Based on the formalism considered above, for the constitutive model and its application, is possible to conclude that:

1. The same formalism, used to solve problems that involve the elasto-plasticity and the damage, can be used successfully in problems of bone remodelling. In this in case, the loss and bone gain were been identified as internal variables;
2. To describe the constitutive model of bone remodelling, using the proposed method, its only necessary the knowledge of two potentials: an energy potential (free energy of Helmholtz) and the other related to the energy inwards and outwards the system, generating consistent and coherent formulations (one distinguishes two classes of materials the associated and not associated, that uses respectively a potential or a bi-potential);
3. No additional assumption, such as, the definition of the stress-strain relation are necessary to define the evolution laws for the variables of loss and gain of rigidity, because they arise as an explicit result from potential functions.

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7. References

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