



On the description of anisotropy and evolutionary phenomena in bone

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A MATHEMATICAL FORMULATION is outlined for describing the mechanical properties of bone, including the process of age-related degradation as well as functional adaptation. Bone is considered as an anisotropic material, with the microstructure described in terms of distribution of void space. Both the elastic and elastoplastic formulations are provided, relevant to cortical and highly porous cancellous bone, respectively. The description of aging process invokes the concept of a physiological time, whose evolution depends, among other factors, on the level of activity of a living bone. Short term remodelling due to hyperphysiological stress is described within a framework which is conceptually similar to that of age-related degradation, with bone being considered as a hypoelastic/plastic material.

1. Introduction

OVER THE LAST FEW DECADES, there has been a considerable research effort devoted to description of living bone as a material. The research was prompted by various clinical problems, such as age-related bone fractures, prostheses loosening, etc. In macroscopic terms, both cortical (compact) and cancellous (trabecular) bone represent a heterogeneous, anisotropic material. In a typical bone structure (femur, tibia, etc.), the material properties strongly depend on the anatomical location of the specimen. This is due to the fact that the distribution of porosity as well as the principal directions of anisotropy vary throughout the whole bone. The mechanical characteristics also change according to the biological variations (age, sex, etc.) and possible state of pathological degradation. The existing constitutive theories, commonly adopted for computational/analytical analyses, describe the bone tissue as an orthotropic linearly elastic continuum (e.g. [1, 2]). As an alternative, micromechanically based formulations are used incorporating the homogenization technique (e.g. [3]).

Living bone is a material which undergoes a continuous evolution with time. One form of such an evolution is known as functional adaptation. The idea is partly derived from Wolff's law, which states that there is a direct correlation between the stress field in the bone and its overall architecture. In other words,

bone is an optimal structure relative to its mechanical environment and it has the ability to maintain an optimal configuration by adopting its external form and internal microstructure to changes in the load environment. The phenomenon of short-term adaptation is commonly described within the framework of adaptive elasticity [4]. A variety of mechanical stimuli have been considered, which include strain [4], strain rate [5], stress [6], strain energy [7], etc.

In parallel with studies on functional adaptation, a considerable research has been undertaken on age-related changes in the structure and composition of bone tissue. These changes influence the mechanical properties of bone and are largely responsible for the increased incidence of fractures in elderly. The problem is becoming increasingly important as people continue to live longer. Although several experimental studies have examined the degradation of mechanical properties of bone associated with aging process (e.g. [8 – 11]), the existing information is still too fragmentary to draw any quantitative conclusions from this research. Moreover, there is no comprehensive mathematical framework available addressing the issue of bone aging process.

The main objective of this paper is to outline a general mathematical formulation for the description of mechanical properties of bone. The bone tissue is considered as an anisotropic material, with the microstructure described in terms of a fabric tensor. The definition of the fabric tensor is derived from a scalar-valued function characterizing the spatial distribution of voids within the bone. The cortical and cancellous bone are considered as the same tissue with different porosity characteristics. The age-related degradation is attributed to mechanical as well as hormonal influences. The former are assumed to be closely related to the level of activity of a living bone, whereas the bone itself is considered as a material which possesses a limited memory of mechanical events. Finally, the formulation for functional adaptation of a living bone is discussed as a special case of that corresponding to aging process. The differences in the mathematical treatment of these two evolutionary phenomena are pointed out.

One of the primary reasons for studying the bone degradation process is to assess the risk of bone fracture in individuals subjected to a prolonged period of reduced physical activity or immobilization. Typical example relevant to the latter case involves patients with spinal cord injuries, who can develop osteoporosis already in the first year after the injury. In these cases, fractures are caused by relatively minor trauma; most occur due to transfers or during turning in bed. Also, long bone fractures (typically within proximal tibia or distal femur) have a high incidence of non-union and delayed union. The other class of problems where the evolutionary phenomena are of importance, are those associated with the long-term performance of bone implants. In this case, the analysis requires the prediction of shape changes in whole bones as well as adaptation of spongy bone tissue architecture to the insertion of an implant. A rapid progress has be-

en made toward this goal, particularly in the context of computational analyses based on finite element algorithms (cf. [12]).

2. Description of mechanical properties of trabecular/cortical bone

The existing experimental evidence indicates that both cortical and trabecular bone represent an inhomogeneous anisotropic material. The anisotropy effects are primarily due to geometric arrangement of the porous microstructure, while the matrix material itself may be considered as isotropic. In order to describe the mechanical properties of such a "structured medium", it is convenient to implement the notion of a fabric tensor ([1, 13]). Over the last few decades, several different internal structure measures have been proposed, including mean intercept length, volume orientation, star length distribution, etc. A comprehensive review may be found, for example, in ref. [14]. The emphasis in this work is not specifically on quantification of bone architecture but rather on incorporation of one of its measures in the formulation of the problem. The particular measure employed here is analogous to that proposed in refs. [15, 16] and it attributes the anisotropy of bone fabric to the bias in the spatial distribution of lineal/areal porosity.

In order to define the distribution of lineal porosity, isolate in the neighbourhood of a material point a sphere (S) of a unit radius, which encloses a representative volume of the material. Consider now a test line of length \bar{L} , emanating from the centroid, with the orientation ν_i with respect to the fixed Cartesian coordinate system. Denoting by $l(\nu_i)$ the total length of interceptions of this line with the void space, one can write

$$(2.1) \quad L(\nu_i) = l(\nu_i)/\bar{L}; \quad L_{av} = \frac{1}{4\pi} \int_S L(\nu_i)g(\nu_i)dS,$$

where $L(\nu_i)$ represents the fraction of \bar{L} occupied by voids, and $g(\nu_i)$ is a scalar-valued function describing the spatial distribution of test lines. It can be shown that the mean value of $L(\nu_i)$ is the measure of the average porosity of the material, n , whereas the lineal fraction occupied by pores is an unbiased estimator of the volume fraction of voids in the direction ν_i , i.e.

$$(2.2) \quad n = L_{av}; \quad \bar{n}(\nu_i) \equiv L(\nu_i).$$

Note that the distribution of void fraction may also be described in terms of *areal* porosity. In this case the function $L(\nu_i)$ will be defined as the areal fraction of voids on a plane with unit normal ν_i , i.e.

$$(2.3) \quad L(\nu_i) = \frac{1}{4\pi} \int_{C(\nu_i)} l(\mu_i)g(\mu_i)dC,$$

where $C(\nu_i)$ is a unit circle rounding the centroid of the sphere and μ_i , which is orthogonal to ν_i , specifies the orientation of the test line.

The scalar-valued function $\bar{n}(\nu_i)$, as defined in Eq. (2.2), can be represented by the generalized double Fourier series. The desired best fit approximation can be established by the "least square" method leading to representation in terms of symmetric traceless tensors Ω_{ij} , Ω_{ijkl} , ... (cf. [17])

$$(2.4) \quad \bar{n}(\nu_i) = n(1 + \Omega_{ij}\nu_i\nu_j + \Omega_{ijkl}\nu_i\nu_j\nu_k\nu_l + \dots).$$

The higher rank tensors Ω_{ijkl} ... relate to the higher order fluctuations in void space distribution. Thus, in order to describe a smooth orthogonal anisotropy it is sufficient to employ an approximation based on the first two terms of the expansion (2.4). In such a case, the function $\bar{n}(\nu_i)$ may be defined as

$$(2.5) \quad \bar{n}(\nu_i) = 3nA_{ij}\nu_i\nu_j; \quad A_{ij} = \frac{1}{3}(\delta_{ij} + \Omega_{ij}) \Rightarrow A_{ii} = 1,$$

where A_{ij} , referred to as fabric tensor, is a non-singular measure of the spatial distribution of voids.

With the notion of fabric tensor, as defined above, the mechanical properties of bone should be considered as an explicit function of its architecture. Thus in the elastic range, the constitutive relation will assume the form

$$(2.6) \quad \sigma_{ij} = D_{ijkl}\varepsilon_{kl}; \quad D_{ijkl} = D_{ijkl}(A_{pq}, n)$$

in which the components of D_{ijkl} are a function of the fabric tensor and the average porosity.

In the above formulation, viz. Eq. (2.6), no explicit distinction has been made between the cortical and cancellous bone. Thus, both are considered here as the same material (in phenomenological sense); the only discriminating factor being $\bar{n}(\nu_i)$, Eq. (2.4). Cortical bone, which occurs for example on the cortex of central sections of femur, is compact (average porosity 3% – 5%), contains no marrow (other than in the central medula) and its blood vessels are microscopically small. For a broad range of external loads, it may be considered as an elastic material. Cancellous bone, which is predominant in the neighbourhood of the joints, is much softer; it consists of a network of trabeculae interspersed with marrow and a large number of small blood vessels. Given the fact that the porosity of the cancellous bone may be as high as 90%, it is reasonable to expect that this material, *under certain loading conditions*, will exhibit some irreversible (plastic) deformations. It is recognized that in an intact bone subjected to typical physiological loads, the response of the trabecular network will still be predominantly elastic. However, for problems involving a surgical intervention, e.g. bone/prosthesis interaction, the irreversible deformations are likely to occur

in the region adjacent to bone-implant interface. This may be an important factor contributing to loosening of the implant and it should be properly taken into account.

The properties in the elastoplastic range should also be considered as fabric-dependent. In general, the yield function can be expressed as an isotropic function of stress and fabric tensors as well as the average porosity n . This leads to a rather complex form which employs ten independent invariants of both tensors and a set of material functions which depend on n . A simpler formulation may be established by following the framework similar to that recently proposed by the author in ref. [16]. In this case, the expression for the yield function incorporates directly the void space distribution \bar{n} , i.e.

$$(2.7) \quad f = f(\sigma_{ij}, \kappa, \bar{n}(l_i)) = 0; \quad \kappa = \kappa(\varepsilon_{ij}^p),$$

where \bar{n} is evaluated in the so-called "loading direction" $l_i = l_i(\sigma_{kl})$. According to Eq. (2.7), the consistency condition reads

$$(2.8) \quad \dot{f} = \left(\frac{\partial f}{\partial \sigma_{ij}} + \frac{\partial f}{\partial l_k} \frac{\partial l_k}{\partial \sigma_{ij}} \right) \dot{\sigma}_{ij} + \frac{\partial f}{\partial \varepsilon_{ij}^p} \dot{\varepsilon}_{ij}^p = \dot{h} + \frac{\partial f}{\partial \varepsilon_{ij}^p} \dot{\varepsilon}_{ij}^p = 0.$$

In order to specify the irreversible (plastic) deformations, assume that the flow rule takes the form

$$(2.9) \quad \dot{\varepsilon}_{ij}^p = \dot{h} G_{ij}; \quad G_{ij} = \hat{G}_{ij}(\psi_{ij}, \omega_{ij})$$

where

$$(2.10) \quad \psi_{ij} = \frac{\partial \Psi}{\partial \sigma_{ij}} \Big/ \left\| \frac{\partial \Psi}{\partial \sigma_{kl}} \right\|; \quad \omega_{ij} = \Omega_{ij} / \|\Omega_{kl}\|; \quad \Psi(\sigma_{ij}, \bar{n}(l_i)) = \text{const}$$

and $\Psi = \text{const}$ is a parametric equation defining the plastic potential. Apparently $\dot{h} \rightarrow 0 \Rightarrow \dot{\varepsilon}_{ij}^p \rightarrow 0$, so that the plastic deformation vanishes for all neutral loading histories. In Eq. (2.9), G_{ij} is an isotropic tensor-valued function. Assuming that G_{ij} is linear ψ_{ij} , leads to the general representation, which incorporates six functions of ten independent invariants of both tensors defined in (2.10). A particular form of this representation, as discussed in ref. [16], is given by

$$(2.11) \quad \dot{\varepsilon}_{ij}^p = \dot{\lambda} \left(\psi_{ij} + (b_1 \psi_{kk} + b_2 \omega_{kl} \psi_{kl}) \omega_{ij} \right)$$

where b_1 and b_2 are constants. Equation (2.11) represents a simple generalization of the flow rule, which incorporates the effect of material fabric. It is noted that the functional form (2.11) has, to some extent, similar numerical repercussions to those of incorporating a rotation of the plastic potential surface. In general, the deviation from isotropy results in a progressive deviation of the direction of plastic

flow from that specified by the gradient of the potential function. Apparently, for an isotropic material, $\omega_{ij} = 0$, so that the classical formulation is recovered.

3. Modelling of the evolution of bone architecture

(i) Aging of bone

Consider now the question of degradation of mechanical properties of bone with age. Apparently, the existing experimental evidence is insufficient to provide a complete formulation of the problem. Therefore, the main objective here is to introduce a set of hypotheses which lead to a general mathematical framework. These hypotheses in themselves, may serve to define appropriate experimental procedures, which are required in order to quantify the problem.

In general, the aging process will result in an increase in average porosity, n , of the bone material. At the same time, the bias in the spatial distribution of voids may also be altered. The question of age-related changes in the trabecular bone architecture was addressed by a number of researchers (cf. [10, 11, 18]). In a typical plate-like structure, the process of bone loss involves a progressive perforation of plates combined with the thinning and subsequent disappearance of the supporting horizontal rods [19]. A similar mechanism occurs in rod-like structures, where the age-related changes invoke primarily the thinning and disappearance of the horizontal struts leading, in extreme cases, to an advanced breakdown of the continuous trabecular network [10]. In both these cases, the bone resorption leads to an increase in the bone porosity as well as to the change in the bone architecture.

In order to address the problem, it may be convenient to introduce the notion of *physiological* time (t'), as opposed to the linear *chronological* time (t). The physiological time may be defined through an incremental relation

$$(3.1)_1 \quad dt' = g_1(w, \dot{w})g_2(x_\alpha)dt; \quad x_\alpha = x_1, x_2, \dots, x_n,$$

where

$$(3.1)_2 \quad w = \frac{1}{\Delta \bar{t}} \int_{\Delta \bar{t}} W dt; \quad W = \int \sigma_{ij} d\varepsilon_{ij}.$$

In general, both functions g_1 and g_2 are scalar-valued functions defined within the range between 0 and 1. The function g_1 defines the mechanical influences, while g_2 is introduced to account for complex hormonal, nutritional and genetic ($x_\alpha, \alpha = 1, \dots, n$) influences. Recognizing the apparent difficulty in quantifying g_2 , the discussion here is focused primarily on the mechanical aspects. In the first approximation, g_1 may be defined as a scalar-valued function of w alone,

i.e. $g_1 = g_1(w)$. The function w , Eq. (3.1)₂, represents the average strain energy density input due to loading over a fixed time interval $\Delta\bar{t}$. Thus, the main assumption embedded here is that, in the absence of any degenerative bone disease and at a given hormonal/nutritional level ($g_2 = \text{const}$), the degradation process is an implicit function of the level of physical activity of a living bone which, in turn, is measured by w . The bone is said to possess the memory of mechanical events which extends over a time interval $\Delta\bar{t} = \text{const}$. As time elapses, the events occurring before $t - \Delta\bar{t}$ are continually erased from the memory. In general, the bone tends to degrade with time towards a pathological state; this process however can be slowed down, and even partially reversed, depending on the degree of physical activity. The dependence of g_1 on w alone, implies that a systematic activity involving moderate strain energy inputs is, in general, more efficient than a sporadic intensive exercise. If this assumption is at variance with experimental observation, then a more general form (3.1)₁, incorporating \dot{w} should be employed.

Apparently, the incremental relation (3.1)₁ is not, in general, integrable, implying that it cannot be reduced to a unique relation between t and t' . Also, Eqs. (3.1)₁ and (3.1)₂ are formulated in *local* sense, so that for a particular boundary value problem the physiological time will not be uniform in space. A somewhat simpler, though more restrictive formulation may be obtained by postulating that Eq. (3.1)₂ may be defined in the context of a specific structural bone as a whole (e.g. femur, tibia, etc.). In this case,

$$(3.1)_3 \quad w = \frac{1}{\Delta\bar{t}} \int_{\Delta\bar{t}} \bar{w} dt; \quad \bar{w} = \frac{1}{V} \int_V W dV,$$

where w represents the strain energy per unit volume (V) of the entire structural system. The hypotheses (3.1)₁ and (3.1)₃ imply that the physiological clock runs uniformly throughout the entire bone as a structural element, leading to a homogeneous degradation process.

The specification of the functions g_1 as well as $n = n(t')$, i.e. the evolution of average porosity, requires a comprehensive experimental programme. As an example, the following simple representations may be suggested

$$(3.2) \quad g_1(w) = \frac{\langle w_{\text{opt}} - w \rangle}{w_{\text{opt}}}; \quad n = n_p + (n_i - n_p)(1 - t'/t'_p)^\xi.$$

Here, w_{opt} represents a certain optimum strain energy input over $\Delta\bar{t}$ and the expression within the angular bracket is defined as $\langle x \rangle = x$ for $x > 0$, otherwise $x = 0$. Thus, for a very active person (in terms of physical exercise), $w \rightarrow w_{\text{opt}}$ implying $dt' \rightarrow 0$, so that the aging process can be substantially slowed down. (Note that an activity resulting in $w > w_{\text{opt}}$ has the same effect as that corresponding to $w \rightarrow w_{\text{opt}}$). On the other hand, for an immobilized individual $w \rightarrow 0$

so that $dt' \rightarrow dt$, which results in a progressively increasing rate of degradation. This case corresponds to, for example, persons with spinal cord injury which develop osteoporosis, a metabolic disorder of bone leading to increased risk of fracture, already in the first year after the injury. In the second equation of (3.2), $\zeta = \text{const}$, $0 \leq t' \leq t'_p$, n_i is the initial average porosity and n_p corresponds to the maximum pathologically admissible value of n . Thus, $n = n_i$ at $t' = 0$, whereas for $t' \rightarrow t'_p$ there is $n \rightarrow n_p$.

Given the definitions (3.1), the constitutive relation in the elastic range can be derived by differentiation of Eq. (2.5) with respect to time

$$(3.3) \quad \dot{\sigma}_{ij} = \dot{D}_{ijkl}\varepsilon_{kl} + D_{ijkl}\dot{\varepsilon}_{kl}.$$

The specification of the first term in Eq. (3.3) requires an evolution law for the components of the fabric tensor A_{ij} . According to the experimental evidence, mentioned earlier in this section, the age-related changes in the microstructure invoke primarily the thinning and disappearance of the supporting rods with no significant reorientation of the vertical trabeculae. Such a mechanism is not likely to promote any significant changes in the principal directions of anisotropy, thus rendering \dot{A}_{ij} to be coaxial with A_{ij} , and thus Ω_{ij} . In this case,

$$(3.4) \quad \dot{A}_{ij} = g_1 g_2 (c_1 \delta_{ij} + c_2 \Omega_{ij} + c_3 \Omega_{ip} \Omega_{pj})$$

where c_1, c_2, c_3 are functions of t' and the basic invariants of Ω_{ij} . Restricting the formulation to an approximation which retains terms of the order two in Ω_{ij} yields the evolution law in the form

$$(3.5) \quad \dot{A}_{ij} = g_1 g_2 \left(d_1 \Omega_{ij} + d_2 (\Omega_{ip} \Omega_{pj} - \frac{2}{3} \Pi_{\Omega} \delta_{ij}) \right),$$

where Π_{Ω} is the second invariant of Ω_{ij} and d_1, d_2 are function of t' alone.

In general, at this preliminary stage of considerations, a simplified approach may be advocated in which the degradation of properties is attributed to the changes in the average porosity alone, so that

$$(3.6) \quad \dot{D}_{ijkl} \approx g_1 g_2 \frac{\partial n}{\partial t'} \frac{\partial}{\partial n} D_{ijkl}.$$

Equations (3.3) and (3.6) represent a set of differential equations describing the aging process under the assumption that the bone is an anisotropic elastic material. Apparently, the elastic regime is defined in terms of

$$(3.7) \quad f < 0 \Rightarrow \dot{\sigma}_{ij} = \dot{D}_{ijkl}\varepsilon_{kl} + D_{ijkl}\dot{\varepsilon}_{kl}$$

whereas $f = 0$ implies the onset of irreversible deformations. The behaviour in the elastoplastic range can be defined by invoking the consistency condition, which according to Eqs. (2.8) and (2.12) takes the form

$$(3.8) \quad \dot{f} = \left(\frac{\partial f}{\partial \sigma_{ij}} + \frac{\partial f}{\partial l_k} \frac{\partial l_k}{\partial \sigma_{ij}} \right) \dot{\sigma}_{ij} + \frac{\partial f}{\partial \kappa} \frac{\partial \kappa}{\partial \varepsilon_{ij}^p} \dot{\lambda} (\psi_{ij} + b \omega_{ij}) + g_1 g_2 \frac{\partial f}{\partial \bar{n}} \frac{\partial \bar{n}}{\partial t'} = 0,$$

where $b = b_1 \psi_{kk} + b_2 \omega_{kl} \psi_{kl}$ and

$$(3.9) \quad \frac{\partial \bar{n}}{\partial t'} = 3 \left(\frac{\partial n}{\partial t'} A_{ij} + n d_1 \Omega_{ij} + n d_2 (\Omega_{ip} \Omega_{pj} - \frac{2}{3} \Pi_{\Omega} \delta_{ij}) \right) \nu_i \nu_j.$$

Assuming the additivity of elastic and plastic strain rates

$$(3.10) \quad \dot{\sigma}_{ij} = \dot{D}_{ijkl} \varepsilon_{kl}^e + D_{ijkl} (\dot{\varepsilon}_{kl} - \dot{\varepsilon}_{kl}^p)$$

and substituting Eq. (3.10) in Eq. (3.8), the following constitutive relation may be established after some algebraic operations

$$(3.11)_1 \quad \dot{\sigma} = D_{ijkl}^{ep} \dot{\varepsilon}_{kl} - \left[\frac{1}{H} D_{ijrs} \left(\frac{\partial f}{\partial \sigma_{pq}} + \frac{\partial f}{\partial l_t} \frac{\partial l_t}{\partial \sigma_{pq}} \right) (\psi_{rs} + b \omega_{rs}) \right. \\ \left. - \delta_{ip} \delta_{jq} \right] \dot{D}_{pqkl} C_{klmn} \sigma_{mn} - \frac{1}{H} D_{ijkl} (\psi_{kl} + b \omega_{kl}) \frac{\partial f}{\partial \bar{n}} \frac{\partial \bar{n}}{\partial t'} g_1 g_2;$$

$$D_{ijkl}^{ep} = D_{ijkl} - \frac{1}{H} D_{ijrs} \left(\frac{\partial f}{\partial \sigma_{pq}} + \frac{\partial f}{\partial l_t} \frac{\partial l_t}{\partial \sigma_{pq}} \right) (\psi_{rs} + b \omega_{rs}) D_{pqkl}$$

where

$$(3.11)_2 \quad H = \left(\frac{\partial f}{\partial \sigma_{ij}} + \frac{\partial f}{\partial l_m} \frac{\partial l_m}{\partial \sigma_{ij}} \right) D_{ijkl} (\psi_{kl} + b \omega_{kl}) - \frac{\partial f}{\partial \kappa} \frac{\partial \kappa}{\partial \varepsilon_{ij}^p} (\psi_{ij} + b \omega_{ij}); \\ C_{ijkl} = D_{ijkl}^{-1}.$$

Equation (3.11) describes bone as an anisotropic elastoplastic material with degrading properties. Once again, the formulation may be simplified by neglecting the terms involving the evolution of fabric in Eq. (3.9). It should be emphasized, that for problems restricted to an intact bone subjected to normal physiological loads, there will be, in general, $f < 0$, in which case Eq. (3.11) will simplify to representation (3.7).

(ii) Bone as a regenerating material; internal adaptation process

The time scale associated with age-related degradation of bone may extend to several decades in humans. However, over a shorter time interval (of the order of months) the living bone may undergo yet another type of internal remodelling

process. The latter is related to functional adaptation to changes in the load environment, which are prompted by an increase in physical activity, i.e. taking up jogging or other form of athletic exercise. In this case, the mechanical stimuli trigger biological processes which occur at a cellular and microstructural level and manifest themselves in a progressive increase in density, which is again coupled with the reorganization of the trabecular architecture.

The phenomenon of short-term remodelling due to hyperphysiological stress may be described within a framework which is conceptually similar to that outlined in the previous section. In order to specify the required modifications, consider first the rate of energy dissipation due to the evolution of elastic properties under $\sigma_{ij} = \text{const}$. Inverting Eq. (2.5) and differentiating it with respect to time (under $\sigma_{ij} = \text{const}$), leads to

$$(3.12) \quad \varepsilon_{ij} = C_{ijkl}\sigma_{kl} \Rightarrow \sigma_{ij}\dot{\varepsilon}_{ij} = \sigma_{ij}\dot{C}_{ijkl}\sigma_{kl} \geq 0 \Rightarrow \det[C_{ijkl}] \geq 0.$$

In general, the above inequality is satisfied for a degrading material only, implying that the representation (2.6) is not suitable for our purpose here. Thus, the elastic properties of a regenerating material should be described by invoking *hypoelastic* relation

$$(3.13) \quad \dot{\sigma}_{ij} = D_{ijkl}\dot{\varepsilon}_{kl}; \quad D_{ijkl} = D_{ijkl}(A_{pq}, n)$$

which ensures that, under a sustained load, $\sigma_{ij}\dot{\varepsilon}_{ij} = 0$.

Equation (3.13) must be supplemented by an appropriate evolution law for the components of D_{ijkl} . Since the functional adaptation involves relatively short time intervals, the notion of a physiological time may now be abandoned. The formulation of the problem requires, among other factors, the specification of the evolution of n . In general, for a normal level of activity $n = \text{const}$, whereas hyperactivity will result in reduction of n to a finite, physiologically possible value. The level of activity can again be measured in terms of average strain energy density, Eqs. (3.1)₂ or (3.1)₃, with an understanding that the time interval associated with memory of mechanical events is now much shorter than that corresponding to age-related degradation. A possible form of evolution law, which may be adopted here, is

$$(3.14) \quad \dot{n} = h_1(w, \dot{w})\dot{h}_2(t); \quad 0 \leq h_1 \leq 1,$$

where h_1 reflects the level of physical activity, whereas $h_2(t)$ describes the maximum, physiologically admissible variation of n under $h_1 \rightarrow 1$. Apparently, for standard levels of activity $h_1 = 0$, which corresponds to remodelling equilibrium.

The response in the elastoplastic range can be obtained by following the same procedure as that outlined in the previous section, Eqs. (3.8) – (3.11). Invoking the consistency condition

$$(3.15) \quad \dot{f} = \left(\frac{\partial f}{\partial \sigma_{ij}} + \frac{\partial f}{\partial l_k} \frac{\partial l_k}{\partial \sigma_{ij}} \right) \dot{\sigma}_{ij} + \frac{\partial f}{\partial \kappa} \frac{\partial \kappa}{\partial \varepsilon_{ij}^p} \dot{\varepsilon}_{ij}^p + \frac{\partial f}{\partial \bar{n}} \dot{\bar{n}} = 0$$

and the assumption of additivity of elastic and plastic strain rates, the following constitutive relation may be established

$$(3.16) \quad \dot{\sigma}_{ij} = D_{ijkl}^{ep} \dot{\varepsilon}_{kl} - \frac{1}{H} D_{ijkl} (\psi_{kl} + b \omega_{kl}) \frac{\partial f}{\partial \bar{n}} \dot{\bar{n}},$$

where D_{ijkl}^{ep} and H are defined in Eq. (3.11). It should be noted that in a regenerating material, under $\sigma_{ij} = \text{const}$, there is $(\partial f / \partial \bar{n}) \dot{\bar{n}} < 0$ leading to $\dot{\lambda} < 0 \Rightarrow \sigma_{ij} \dot{\varepsilon}_{ij} = 0$. On the other hand, in a degrading material, Eqs. (3.11), $\dot{\lambda} > 0$ and $\sigma_{ij} \dot{\varepsilon}_{ij} > 0$, so that the evolution of microstructure under a sustained load leads to dissipation of energy. The above constraints are consistent with the second law of thermodynamics.

Equation (3.16), supplemented by the evolution law (3.14), defines a simple framework for modelling of the bone tissue undergoing an internal adaptation process. Apparently, if the irreversible deformations are negligible, i.e. $H \rightarrow \infty$, then Eq. (3.16) reduces to the hypoelastic relation (3.13). The formulation may again be enriched by incorporating the effect of the changes in the trabecular architecture, which requires an appropriate evolution law for the fabric tensor A_{ij} . The latter issue was addressed, for example, in ref. [20], or more recently in ref. [21], where the evolution law employed the notion of optimally effective bone remodelling.

(iii) An example

In order to illustrate the mathematical framework outlined in this section, a simple numerical example is provided here. The objective is to demonstrate the effect of the age-related degradation of elastic properties on the mechanical characteristics of trabecular bone.

Consider the behaviour of the material under uniaxial compression ($\sigma_1 = \sigma_2 = 0, \sigma_3 < 0$) in the direction of principal material axes. Choose the properties which may be considered as representative of a trabecular bone from the human proximal tibia [22]. Assume that $\bar{n}(\nu_i)$ is defined in terms of, say, lineal porosity, i.e. Eq. (2.1), and let $\Omega_1 = 0.15$, $\Omega_2 = 0.1$, $\Omega_3 = -0.25$, $n_i = 0.53$, which corresponds to $\bar{n}(e_1) = 0.61$, $\bar{n}(e_2) = 0.58$, $\bar{n}(e_3) = 0.40$. Following ref. [23], assume that the orthotropic Young's and shear moduli are defined as

$$E_i = E_0 [\rho_s (1 - n)]^2 A_i^{-2}; \quad G_{ij} = G_0 [\rho_s (1 - n)]^2 A_i^{-1} A_j^{-1}.$$

In the above equations $i, j = 1, 2, 3 (i \neq j)$, A_i are the eigenvalues of the fabric tensor, ρ_s and n represent the density of the tissue and the average porosity, respectively, and E_0, G_0 are material constants. Take $\eta_{12} = \eta_{23} = 0.25$ (Poisson's

ratios) and $E_0 = 230$ (MPa cm³/g²), $\rho_s = 1.93$ g/cm³, so that $E_1 = 1.29$ GPa, $E_2 = 1.40$ GPa, $E_3 = 3.00$ GPa. The degradation of properties is described in terms of evolution laws (3.2) and (3.5). Assume that $\xi = 0.5$ and $t' \rightarrow 10$ ph.y (*physiological years*) results in an increase in the average porosity to its pathological value of $n_p = 0.85$. Moreover, take $a_1 = 0.01$ /ph.y and $a_2 = 0$ in the evolution law for the fabric tensor, Eq. (3.5).

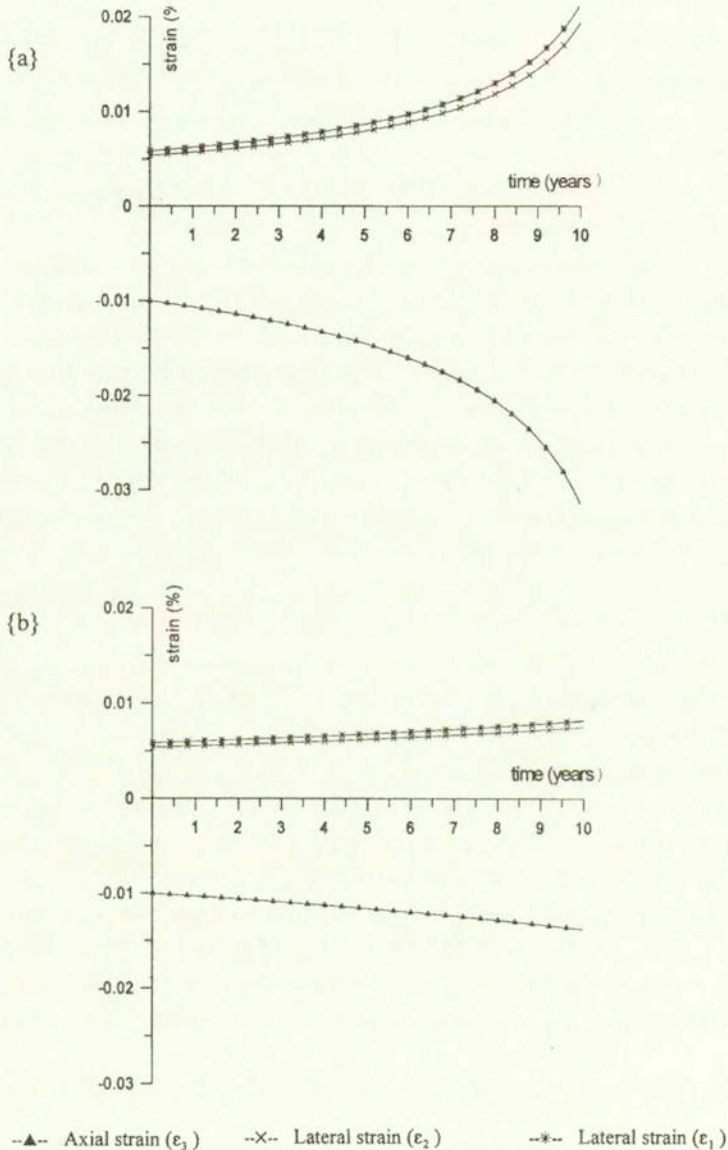


FIG. 1. Evolution of normal strain under a constant load of $\sigma_3 = 0.3$ MPa; solution for: (a) $w/w_{opt} = 0.1$, (b) $w/w_{opt} = 0.6$.

The results of numerical simulations are presented in Figures 1 and 2. The figures show the mechanical characteristics and the evolution of microstructure for the bone material subjected to a sustained axial load of $\sigma_3 = -0.3$ MPa.

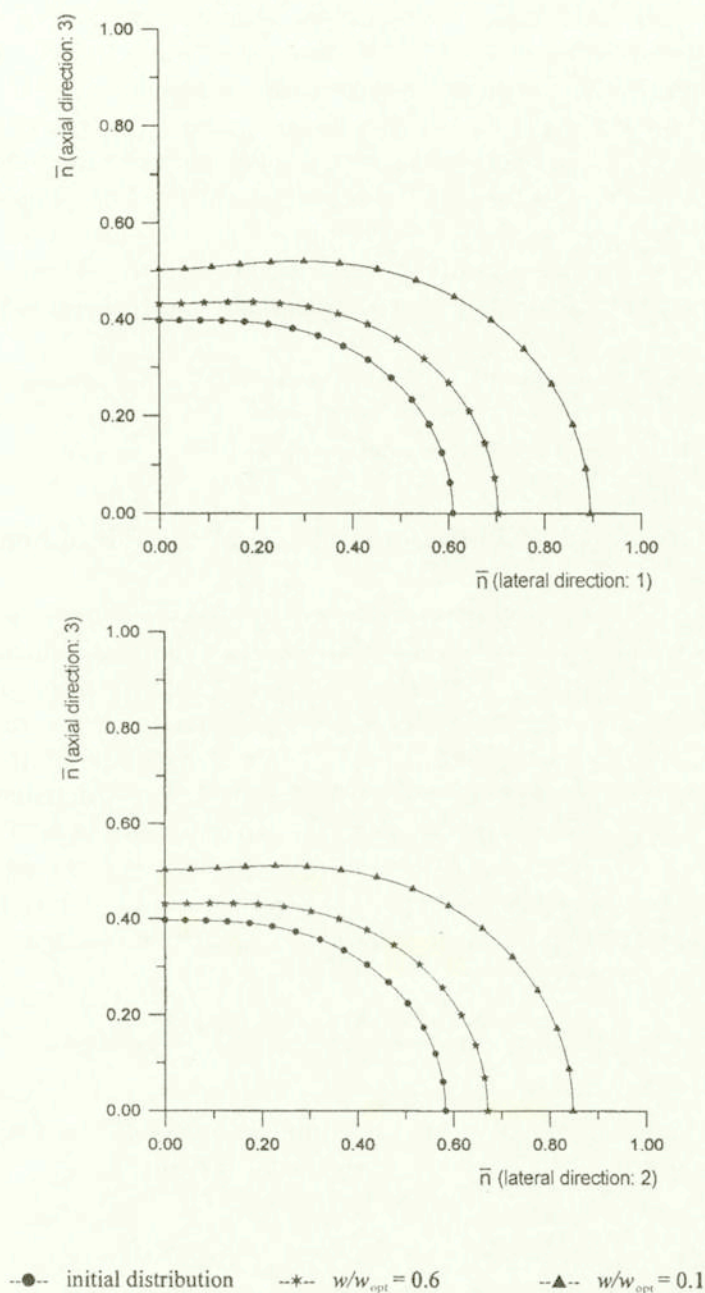


FIG. 2. Spatial distribution of $\bar{n}(\nu_i)$ at $t = 10$ years.

Figure 1 provides the time history of normal strain for $w/w_{\text{opt}} = 0.1$ and 0.6 , respectively. In the former case, a continuous development of deformation takes place and the strain rates progressively increase with time. When the *chronological* time approaches 10 years, the deformation gradients become very high, which is triggered by a significant degradation in material microstructure. On the other hand, the response for $w/w_{\text{opt}} = 0.6$ is characterized by a relatively slow progress in degradation, resulting in constant deformation gradients.

Figure 2 presents the evolution of bone architecture for both of these scenarios. The initial distribution of void fraction displays an orthotropic characteristic. For the case of $w/w_{\text{opt}} = 0.1$, the lineal porosity in the lateral direction increases to nearly 0.9 , prompting a severe degradation of mechanical properties. At $w/w_{\text{opt}} = 0.6$, the average porosity as well as the bias in the directional distribution of voids are only marginally altered, implying a much slower progress of the degradation.

Finally, it should be pointed out that a similar loading history imposed on a regenerating material, Sec. 3(ii), would trigger a progressive decrease in the average porosity accompanied by no deformation.

4. Specification of material functions; numerical analysis of bones

The identification of bone architecture requires the use of modern 3D imaging techniques such as high resolution magnetic resonance imaging, micro-computed tomography, etc. Apparently, the microstructure and thus the mechanical properties of bone depend on several factors including the anatomic location, age, sex, etc. In general, given an image of a fixed volume of bone material, in the form of 3D binary data, one can determine a set of \bar{n}_α ($\alpha = 1, 2, \dots, N$) defining, according to Eq. (2.1) or (2.3), the values of $\bar{n}(\nu_i)$ for discrete orientations ν_i . The obtained distribution can be approximated by the first two terms of the representation (2.4) using the least squares approach. The error involved is the sum of squares of the differences between the given values of \bar{n}_α and those due to approximation (2.4), i.e.

$$(4.1) \quad E = \sum_{\alpha} \left[\bar{n}_{\alpha} - n(1 - \mathbf{\Omega}^T \mathbf{N}_{\alpha}) \right]^2$$

where $\mathbf{\Omega}^T = \{\Omega_{11}, \Omega_{22}, \Omega_{12}, \Omega_{13}, \Omega_{23}\}$; $\mathbf{N}^T = \{(\nu_1^2 - \nu_3^2), (\nu_2^2 - \nu_3^2), -2\nu_1\nu_2, -2\nu_1\nu_3, -2\nu_2\nu_3\}$. The constants $\mathbf{\Omega}$ should minimize the total least squares error, i.e. $\partial E / \partial \mathbf{\Omega} = \mathbf{0}$, which leads to a set of simultaneous equations

$$(4.2) \quad \left(\sum_{\alpha} \mathbf{N}_{\alpha} \mathbf{N}_{\alpha}^T \right) \mathbf{\Omega} = \sum_{\alpha} \mathbf{N}_{\alpha} - n^{-1} \sum_{\alpha} \bar{n}_{\alpha} \mathbf{N}_{\alpha}$$

which can be solved for individual components of $\mathbf{\Omega}$.

The properties in the elastic range are defined by Eq. (2.6). The general representation of the elasticity tensor D_{ijkl} in terms of the fabric tensor, has been derived by COWIN [1]. The representation employs nine scalar functions of the three basic invariants of the fabric tensor. In the same reference Cowin has also developed an approximation based on retaining the terms of order two in A_{ij} and expanding the scalar functions in powers of A_{ij} . The result of this approximation is

$$(4.3) \quad d_\alpha = B_{\alpha\beta} k_\beta(n)$$

where d_α denotes the individual non-zero components of D_{ijkl} , k_β are functions of n only and $B_{\alpha\beta}$ depends on the basic invariants of the fabric tensor.

Taking d_α as $\mathbf{d}^T = \{D_{11}, D_{22}, D_{33}, D_{44}, D_{55}, D_{66}, D_{12}, D_{13}, D_{23}\}$ one has

$$(4.4) \quad [\mathbf{B}] = \begin{bmatrix} 1 & \text{II} & 2A_{11} & 2A_{11}^2 & A_{11}^2 & 2 & 2\text{II} & 4A_{11} & 4A_{11}^2 \\ 1 & \text{II} & 2A_{22} & 2A_{22}^2 & A_{22}^2 & 2 & 2\text{II} & 4A_{22} & 4A_{22}^2 \\ 1 & \text{II} & 2A_{33} & 2A_{33}^2 & A_{33}^2 & 2 & 2\text{II} & 4A_{33} & 4A_{33}^2 \\ 0 & 0 & 0 & 0 & 0 & 1 & \text{II} & (A_{22} + A_{33}) & (A_{22}^2 + A_{33}^2) \\ 0 & 0 & 0 & 0 & 0 & 1 & \text{II} & (A_{11} + A_{33}) & (A_{11}^2 + A_{33}^2) \\ 0 & 0 & 0 & 0 & 0 & 1 & \text{II} & (A_{11} + A_{22}) & (A_{11}^2 + A_{22}^2) \\ 1 & \text{II} & (A_{11} + A_{22}) & (A_{11}^2 + A_{22}^2) & A_{11}A_{22} & 0 & 0 & 0 & 0 \\ 1 & \text{II} & (A_{11} + A_{33}) & (A_{11}^2 + A_{33}^2) & A_{11}A_{33} & 0 & 0 & 0 & 0 \\ 1 & \text{II} & (A_{22} + A_{33}) & (A_{22}^2 + A_{33}^2) & A_{22}A_{33} & 0 & 0 & 0 & 0 \end{bmatrix}$$

where

$$\text{II} = A_{11}A_{22} + A_{11}A_{33} + A_{22}A_{33}; \quad A_{11} + A_{22} + A_{33} = 1.$$

The question of the specification of $k_\beta(n)$ has been addressed in ref. [22]. In that study, k_β were approximated as power functions of normalized density and fitted (using the least squares analysis) to an extensive set of experimental data. The representation (4.3), although attractive, has a serious limitation. Namely, the matrix $[B]$, Eq. (4.4), is singular implying that there is no unique set of k 's describing the given material properties. Over the recent years, other approximations have been developed (e.g., [20, 24]). However, most of them are restrictive, as they neglect certain terms in the general representation, which may be of significance. The formulation adopted here is based on the approximation developed in ref. [23], quoted earlier in this paper. The estimates of elastic properties are derived from general representation theorems which incorporate an assumption of homogeneity of the constitutive relation with respect to the measures of the material fabric. Following this work, the orthotropic elastic moduli are defined as

$$(4.5) \quad E_i = E_0 A_i^{-2}; \quad G_{ij} = G_0 A_j^{-1}; \quad \eta_{ij} = \eta_0 \frac{A_i}{A_j}$$

subject to the constraint $\eta_0 = E_0/(2G_0) - 1$. In the above expressions, E and G are the Young's and shear moduli, respectively, and η is the Poisson's ratio. Moreover, $i, j = 1, 2, 3 (i < j)$, A 's are the eigenvalues of the fabric tensor, whereas E_0, G_0, η_0 are considered to be material functions which depend on structural density. A specific form of (4.5) has been employed in the example given in Sec. 3(ii).

A simple fracture criterion for bone, consistent with general representation (2.7), has been recently proposed by the author and his coworkers [25]. This criterion is expressed in the functional form

$$(4.6) \quad F = \bar{\sigma} - g(\theta)\bar{\sigma}_c = 0; \quad \bar{\sigma}_c = \frac{-a_1 + \sqrt{(a_1^2 + 4a_2(a_3 + I/f_c))}}{2a_2} f_c,$$

where $I = -\sigma_{ii}, \bar{\sigma} = (1/2s_{ij}s_{ij})^{1/2}, \theta = -1/3 \sin^{-1} \{(\sqrt{3}s_{ij}s_{jk}s_{ki})/2\bar{\sigma}^3\}$ and s_{ij} denotes the stress deviator. In Eq. (4.6), a_1, a_2, a_3 represent dimensionless material constants and the function $g(\theta)$ satisfies $g(\pi/6) = 1, g(-\pi/6) = K$, where $K \leq 1$ is a constant. Moreover, f_c which represents the uniaxial compressive strength of bone tissue, is assumed to be an explicit function of the void space distribution, i.e.

$$(4.7) \quad f_c(l_i) = f_{c0} \left(\frac{\rho}{\rho_0} \right)^\gamma = f_{c0} \left(\frac{1 - \bar{n}(l_i)}{1 - n_0} \right)^\gamma$$

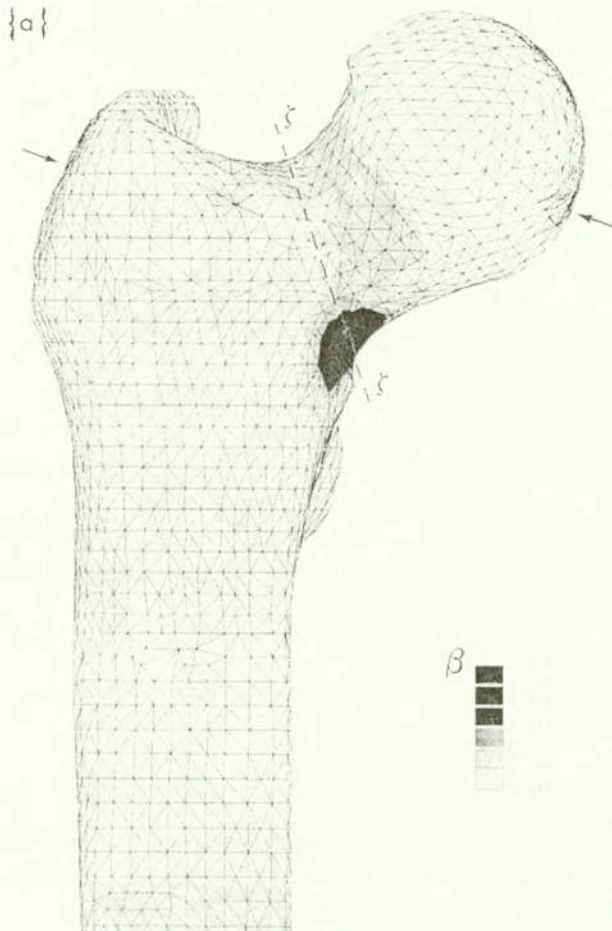
where n_0 and γ are constants and γ is typically within the range $1 \leq \gamma \leq 2$ (cf. [26]). The function \bar{n} is evaluated in the "loading direction" l_i which has been defined as the direction of the average stress vector t_i at a point,

$$(4.8) \quad l_i = \frac{t_i}{\|t_i\|}; \quad t_i = \sigma_{ij}(e_j^{(1)} + e_j^{(2)} + e_j^{(3)}) = \sqrt{3}\sigma_{ij}m_j,$$

where e_i are the base vectors associated with the principal material axes and $m_i = \{1, 1, 1\}/\sqrt{3}$ is a unit vector along the space diagonal.

In order to provide an illustration to the notions brought up above, the results of numerical simulations pertaining to evaluation of the risk of fracture in a proximal femur are reviewed here (after ref. [25]). A 3D model of the proximal two thirds of an adult human right femur has been created based on external surface contours extracted from CT scans. A set of elastic constants was assigned to each element to model a heterogeneous distribution of orthotropic material properties. In particular, representation (4.5) has been employed with average porosity values obtained from CT data. At this preliminary stage, the bias in the distribution of void fraction was assumed to be constant, with the principal magnitudes of the tensor Ω_{ij} taken as $\Omega_1 = -0.15, \Omega_2 = 0.04, \Omega_3 = 0.11$. The latter

choice gives $E_1/E_3 = 1.7$, $E_1/E_2 = 1.5$ and $G_{12}/G_{23} = 1.3$, $G_{12}/G_{13} = 1.07$, which is consistent with typical experimental data for human femoral bone [27] over a broad range of average porosities. The numerical analysis has been carried out in two stages. First, a supplementary finite element simulations were conducted in order to estimate the distribution of the principal material directions. The problem was solved by performing a linear elastic analysis of the femur subjected to loading conditions corresponding the one-legged stance phase of gait under the constraint that the matrix multiplication of the stress and fabric tensors is commutative. The latter follows directly from Wolff's hypothesis, which postulates that the principal stress axes coincide with the principal trabecular directions at remodelling equilibrium. The second phase of the analysis involved the numerical simulations of a fall from standing height to the lateral aspect of the greater trochanter.



[FIG. 3.]

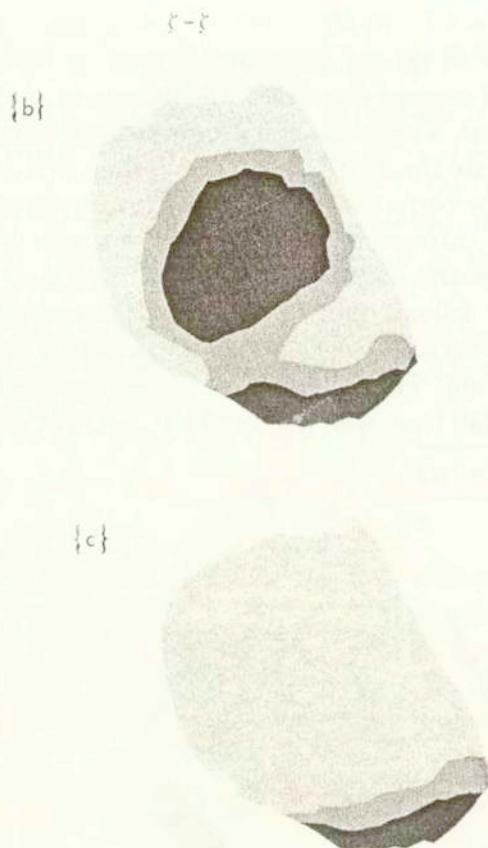


FIG. 2. Predicted contours of damage factor β in an osteoporotic bone; (a) anterior view of the proximal femur; (b) transcervical cross-section (orthotropic formulation); (c) transcervical cross-section (isotropic formulation).

The main results of the simulations are presented in Fig. 3. Figure 3a shows the anterior view of the proximal femur together with superimposed surface distribution of the *damage factor* β . The latter has been defined, based on the proposed fracture criterion (4.6), as

$$(4.9) \quad \beta = \frac{\bar{\sigma}}{g(\theta)\bar{\sigma}_c}.$$

It should be noted that, according to Eq. (4.6), $F \leq 0$ requires $0 \leq \beta \leq 1$. The case of $\beta \rightarrow 1$ results in $F \rightarrow 0$ and signifies the local failure of the bone material associated with formation of macro/micro cracks (e.g. fracture of individual trabeculae). Clearly, $\beta > 1$ is physically inadmissible as the stress state corresponds to $F > 0$. The distribution shown in Fig. 3 corresponds to an osteoporotic bone. It is evident that in the inferior region of the femoral neck, the stress field vio-

lates the fracture criterion, implying that a lateral fall to the hip will trigger a transcervical fracture. The fracture zone will initiate at the outer cortical shell and propagate through the trabecular network in the femoral neck. In general, given the fact that the porosity in the region of trabecular bone is relatively high, the propagation of the fracture zone will require little mechanical effort. In this context the elastic analysis alone, incorporating the criterion (4.6), may be sufficiently accurate for estimating the potential for fracture risk. Finally, Figs. 3b and 3c present the distribution of damage in the transcervical cross-section. The distribution shown in Fig. 3c corresponds to the case of isotropic formulation ($\Omega_{ij} = 0$). Comparing both results it is evident that the isotropic representation will, in general, overestimate the fracture potential.

5. Final remarks

An appropriate representation of the effects of aging on the mechanical properties of bone is essential for numerical evaluation of the risks of fractures and the design of prosthetic implants in elderly. With this objective in mind, a set of hypotheses has been put forward in order to form a general mathematical framework for the description of age-related degradation of bone structure. In general, the degradation phenomenon manifests itself in a progressive increase in the average porosity of the material coupled with the reorganization of the microstructure. The latter usually involves a thinning of vertical and horizontal trabeculae. This would indicate a possible simplification in the evolution law of the fabric, whereby the primary effect is that of the change in the eigenvalues of the fabric tensor. The formulation presented here distinguishes between the mechanical and hormonal/nutritional influences. The discussion is essentially restricted to mechanical effects, which is particularly relevant to studies on the degradation of bone due to prolonged periods of reduced physical activity.

Apparently, the most important clinical problems in orthopaedics today involve the regions which are dominated by the cancellous bone. Therefore, an adequate description of its mechanical properties is important. In general, the mechanical competence of the entire bone, as a structure, is enforced by the presence of cortical bone, which constrains the deformation. In this context, under typical physiological loads, the system may be considered as elastic. This is not the case however, when considering for example the bone-implant interaction. In order to predict the relative micromotions at the bone-prosthesis interface, it is important to recognize that the trabecular tissue has a high average porosity and it will experience some irreversible deformations (c.f. [24]). The formulation given in this paper is still in its preliminary stage and falls short of quantifying some of the material functions involved. It is believed that this and similar approaches are useful in directing the experimentation towards more specifically defined objecti-

ves. Clearly, the identification of properties in the elastoplastic range will require a series of uniaxial compression tests on trabecular bone specimens, performed at different values of confining pressures (within a range typically experienced in the region adjacent to bone-stem interface). Such tests should be performed in the principal material direction, which could be identified through measurements of material fabric involving high resolution imaging.

Various evolutionary phenomena in bones may be described within a similar conceptual framework. It has been demonstrated that the formulation for functional adaptation of the bone may be derived from that corresponding to aging process, by imposing different evolution laws for the material fabric. It is important to emphasize that the approach adopted for description of a regenerating material requires the framework of *hypoelasticity*, Eq. (3.13), rather than the conventional elasticity. This fact has been generally ignored in the existing formulations of the problem. Finally, it is apparent that much work needs still to be done on the development of quantitative theories, their verification and finally, the numerical simulations of specific clinical problems.

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