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NECESSARY AND SUFFICIENT CONDITIONS FOR GLOBAL STABILITY AND UNIQUENESS IN FINITE ELEMENT SIMULATIONS OF ADAPTIVE BONE REMODELING

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Abstract—Conditions which can guarantee the global stability and uniqueness of the solution to a bone remodeling simulation are derived using a specific rate equation based on strain energy density. We modeled bone tissue as isotropic with a constant Poisson ratio and the elastic modulus proportional to volumetric density of calcified tissue raised to the power n. Our remodeling rate equation took the rate of change of volumetric hard tissue density as proportional to the difference between a stimulus (strain energy density divided by volumetric density taken to the power m) and a set point. In previous studies we defined state variables which are conjugate to the remodeling stimulus, and the function which acts as a variational indicator for the remodeling stimulus. In this study, we use the properties of this variational indicator to establish the stability and the uniqueness of the solution to the remodeling rate equations for all possible density distributions. We show that the solution is the global minimum of a weighted sum of the total strain energy and the integral of density to the power m over the remodeling elements. These results are proven for $n < m$, and we show that taking $n > m$ will eliminate the possibility that a unique solution exists.

INTRODUCTION

Although people and animals exist in a wide variety of sizes, a degree of similarity in bone structure exists in many vertebrate bones (Bertram and Biewener, 1992; Biewener, 1989; Alexander *et al.*, 1979). A comparison of bone structure with the expected loading which bones are expected to support suggests that, subject to the requirements placed on animal size and shape by natural selection, mechanical factors are important in maintaining bone structure throughout adult life. This is the basis for an often-cited concept known as Wolff's Law (Wolff, 1986). As reviewed by Roessler (1981), Wolff was convinced that bone is able to produce the best possible structure for a given amount of material, as was Roux, a contemporary. These early investigators and others established the idea that heavily loaded regions of bone are dense, and that less loaded regions are more porous. Also, bone was noted to become more dense if overloaded, and less dense if unloaded.

Bone is generally of two types: Cortical and cancellous. Cortical bone is the dense outer layer in the mid-shaft of bones. Cancellous bone, the material which supports nearly all weight-bearing animal joints, resembles an open celled foam (Netter, 1987; Warwick and Williams, 1973) and has elastic properties which depend heavily on the volumetric density of calcified tissue present (Carter and Hayes, 1977). In many cases, the distinction between the two tissues is arbitrary, since cortical bone can become porous, and cancellous bone can become very dense. In many bone remodeling studies, and in ours, the distinction between cancellous and cortical bone is not explicitly made, and where the remodeling study predicts high density, we expect cortical bone.

Bone formation and remodeling is mediated by many biological factors in addition to mechanical stress. Although the general character of the responses to non-mechanical factors is known, the interaction between such factors and stress is not well known (Brown *et al.*, 1990). In this study, we will not consider biological factors. Thus we assume either that the influence of biological factors is small, or that the biological factors are applied evenly over the region of interest, and do not substantially interact with the stress-mediated response of the tisue. We do not have direct evidence to support these assumptions, however.

Bone shape and size is determined by many biological factors which we cannot hope to adequately mimic using a purely mechanical model (Bertram and Swartz, 1991). Although Bertram and Swartz acknowledge a substantial role for stress in bone remodeling, they detail many biological effects which can confound bone remodeling experiments. The mechanical effects discussed in this paper are therefore restricted in their application to adult adaptation, since we have concentrated on remodeling simulations in which bone shape is held fixed, and bone density is allowed to vary with time.

Numerical simulations of bone remodeling have shown qualitative agreement with the natural bone density distribution, but have shown a number of problems with stability (Carter *et al.*, 1989; Weinans *et al.*, 1989, 1990, 1992; Weinans, 1991). These problems indicate that the numerical methods need improvement, and they also show that the dynamics of the postulated remodeling feedback mechanisms need more careful study. In recent studies (Harrigan and Hamilton, 1992a; Weinans *et al.*, 1992) the remodeling rate equations used by many investigators have been shown to be unstable. Modifications have been used to make the simulations stable prior to these studies, and other possibilities for stable simulations were arrived at. Huiskes *et al.* (1991) and Beaupré *et al.* (1990) have used a "dead zone" around the equilibrium value of the remodeling stimulus, so that the rate of change of density due to stress changes is zero for a range of stimuli. The dead zone accounts for the observations that small changes in the stress state in a bone do not seem to generate a remodeling response. This procedure produces results which agree qualitatively with experimental results, but the use of a dead zone (with zero slope) thwarts a unique or an optimal solution. Harrigan and Hamilton (1992a) have proposed modifying the stimulus according to a derived stability limit, so that a zero-slope dead zone is not necessary.

The approach taken in this and previous studies is conceptually different from many in the literature, in that the global behavior of the remodeling simulation is used to provide a limit on the stimulus to be used in the local remodeling rule. This contrasts with many prior studies in which a local stimulus is proposed based on mechanical concepts, and the behavior of the global structure with time is studied. We have been able to take this approach because we have found a direct link between the local and global behavior of a remodeling simulation.

Although the numerical simulations in the literature can represent many facets of the natural response to stress, these simulations generally operate by time stepping a rate equation, without assessing whether the simulations are stable or optimal in a certain sense. Also, since an optimization function is not derived for many of these simulations, the questions of solution uniqueness and path dependence are left unanswered. Also, the connection between a common medical interpretation of Wolff's Law of bone remodeling—that bone is an optimal structure—and the remodeling rate simulations had not been made until recently (Harrigan and Hamilton, 1992b; Kuiper *et al.*, 1992; Huiskes and Kuiper, 1993).

In this paper, we build on the results of two recently published studies in which we derived the form of the state variables needed to make a specific bone remodeling stimulus part of an optimization routine (Harrigan and Hamilton, 1992c), and we derived the form of the indicator function being optimized by the remodeling rate equation (Harrigan and Hamilton, 1992b). Using this information, we show here that if a simple condition is satisfied, then (a) the remodeling rate equation developed using the state variables used previously is stable for all possible density distributions; and (b) the solution of the remodeling rate equations for an equilibrium density distribution is unique, since the remodeling rate equation arrives at a global minimum of the indicator function in this case. We then show that if this condition is not satisfied, the results will be unstable and non-unique.

These results follow directly from the remodeling rate equations, and are thus restricted in their applications to situations where the rate equations apply. Thus, the concept of bone as an optimal mechanical structure is primarily a mathematical convenience used here to assess solution stability and uniqueness. We do not assess the generation of bone shape during growth using this formulation, so we can not make any statements regarding the optimal nature of bone shape.

METHODS

In this paper, we use the mathematics associated with fine element analysis to prove that we can obtain a unique stable solution for a particular bone remodeling rate equation. In the development, we assume that the volumetric density of calcified bone, and thus the elastic properties of the tissue, are constant within a finite element. We assume that the finite element mesh chosen is the same throughout the simulation, and thus we do not assess shape changes explicitly. Changes in the shape of the resulting structure due to element densities becoming zero are allowed, however.

Using the direct stiffness finite element method, we add local element stiffness matrices together to form a global stiffness matrix (Bathe, 1982). In the development for this paper, we write the element matrices in global coordinates. The element matrix indices span the range of global coordinate indices, with non-zero entries only in the positions in which the global coordinates couple to the "local" element coordinates. Thus, we never refer to local coordinates for the element stiffness matrices we use here. Also, implied summation over repeated indices is only used when the repeated indices are subscripts that follow displacements or stiffness matrices. When we require summation over elements, we use a summation sign. We will also use the subscripts f, g, p and q to indicate particular (global) degrees of freedom. The subscripts and left superscripts e and s refer to element number. A right superscript (used here only on density) indicates exponentiation. Thus, we have restricted our notation to maintain clarity in the operations we intend.

We assume isotropy, a material Poisson ratio which is constant, and a power law relationship between density, ϕ, and elastic modulus (Carter and Hayes, 1977), i.e.

$$E = E_0 \phi^n, \tag{1}$$

with ϕ the volumetric density, n the material exponent, usually taken as 2 (Rice *et al.*, 1988) or 3 (Carter and Hayes, 1977). This results in a material property matrix $[C]$ which we express as

$$[C] = [C_0]\phi^n, \tag{2}$$

with $[C_0]$ the material property matrix for unit volumeric density (Bathe, 1982). Using this matrix in a standard finite element formulation for element stiffness matrices yields

$${}^eL_{fg} = \phi^{ne} K_{fg}, \tag{3}$$

with the left superscript e indicating the element, ${}^eL_{fg}$ the element stiffness marix and ${}^eK_{fg}$ the element stiffness matrix for unit density. We can thus write the global stiffness matrix K in terms of density as

$$K_{fg} = \sum_{e=1}^{N} \phi_e^{n\,e} K_{fg} + {}^cK_{fg}, \tag{4}$$

with ${}^cK_{fg}$ the part of the stiffness matrix which remains constant during the remodeling simulation (e.g. an orthopedic implant).

The average strain energy density within the element, ${}^e\Psi$, for a given displacement solution u is

$${}^e\Psi = \frac{\phi^n u_f {}^eK_{fg} u_g}{2V_e}, \tag{5}$$

with V_e the element volume. We assume the tissue stimulus for bone remodeling is

$$^{e}\Psi_t = \frac{^{e}\Psi}{\phi^m}, \tag{6}$$

with the exponent m being a material constant. This equation reflects the way that the microstructure magnifies continuum-level stresses, strains and strain energy density. That is, the stresses, strains and strain energy density at peaks within the microstructure are higher than the continuum-level variables (Beaupré *et al.*, 1990). Since we are not making specific assumptions about the physical stimulus for remodeling, we chose this relationship with the exponent m left as a parameter.

In a previous paper (Harrigan and Hamilton, 1992c), we showed that changing the state variable used in the remodeling equation allows that equation to be part of an optimizing process. By using density to the power m [the exponent in the denominator of eqn (5)] we can define a variable γ as

$$\gamma = \phi^m \tag{7}$$

and by taking the rate equation to be

$$\frac{\partial \gamma_e}{\partial t} = {}^{t}\Psi_e - \Psi_0 \tag{8}$$

or, more explicitly,

$$V_e \frac{\partial \gamma_e}{\partial t} = \frac{\gamma_e^{(n-m)/m}(u_f{}^{e}K_{fg}u_g)}{2} - \Psi_0 V_e \tag{9}$$

we can satisfy the requirements for an optimizing function. Note that when $\gamma = 0$, $\phi = 0$, and when $\gamma = 1$, $\phi = 1$. Since ϕ is the volumetric density of hard tissue, we add to our simulation the restriction that both ϕ and γ are between 0 and 1. Fully dense bone elements can thus simulate the development of cortical bone, and empty elements can simulate complete resorption. For reference, we can write the global stiffness matrix in terms of γ as

$$K_{fg} = \sum_{e=1}^{N} \gamma_e^{n/m}{}^{e}K_{fg} + {}^{c}K_{fg}. \tag{10}$$

The connection between the remodeling rate equations used and an optimizing function is very similar to the connection between Newton's laws and the energy in a structure. Finding the displacements in an elastic structure that satisfy the equations of equilibrium is equivalent to finding the displacements that minimize the stored elastic energy. By analogy, there is a connection between finding the bone density distribution that is a stationary point for a "remodeling potential" function and finding the density distribution in which the rate equations predict no change in density with time.

In a sense, we have shown that there is a function H such that $\mathrm{d}H = \Sigma(F_e\,\mathrm{d}\gamma_e)$, with F_e the remodeling stimulus in eqn (8) but there is no function G such that $\mathrm{d}G = \Sigma(F_e\,\mathrm{d}\phi_e)$ except for the special case where $m = 1$. That is, if H is similar to an energy function, γ_e is the state variable which is energetically conjugate to F_e.

Put another way, we can assert that if there is an indicator function that measures some property of the density distribution, and results in a specific numerical value, then we can write that function as

$$H(\gamma_1, \gamma_2, \gamma_3, \ldots, \gamma_n). \tag{11}$$

If the remodeling rule used finds stationary points of this indicator function, then we can relate the remodeling rule to the indicator function by

$$F(\gamma_i) = -\frac{\partial H(\gamma_1, \ldots, \gamma_n)}{\partial \gamma_i}. \tag{12}$$

Thus we can show that

$$\frac{\partial F(\gamma_i)}{\partial \gamma_j} = -\frac{\partial^2 H(\gamma_1, \ldots, \gamma_n)}{\partial \gamma_i \partial \gamma_j} = -\frac{\partial^2 H(\gamma_1, \ldots, \gamma_n)}{\partial \gamma_j \partial \gamma_i} = \frac{\partial F(\gamma_j)}{\partial \gamma_i} \tag{13}$$

and we can derive a remodeling rule from an overall indicator function on density if and only if the derivatives of that rule follow this equation.

In a previous study, we have shown that eqn (13) is satisfied for the remodeling rule above, and in another previous study (Harrigan and Hamilton, 1992b) we found that the indicator function H was

$$H = \left(\frac{m}{n}\right) H_1 + H_2 \tag{14}$$

with

$$H_1 = \sum_{e=1}^{N} \frac{u_f(\gamma^{n/m\,e} K_{fg} + {}^{c}K_{fg}) u_g}{2} \tag{15}$$

the total strain energy in the structure (bone and possible implant), and

$$H_2 = \Psi_0 \sum_{e=1}^{N} V_e \gamma_e \tag{16}$$

equal to Ψ_0 multiplied by the integral of γ over the remodeling elements. Notice that H_2 is not proportional to the total mass of calcified tissue unless $m = 1$. Minimizing total tissue mass will result in a different remodeling equation unless $m = 1$.

Notice that the developments up to this point are valid for any values of n and m. This derivation does not depend on any stability conditions, and thus the indicator function H is as general as the remodeling equation.

Stability, global optimality and uniqueness

By using the remodeling rate equation, the defined optimizing functions, and the derivatives calculated in Harrigan and Hamilton (1992c), we can prove that the simulations are stable for all possible density distributions, and we can show that the solutions are a global optimum. If we consider the rate equations as

$$V_e \frac{\partial \gamma_e}{\partial t} = -\frac{\partial H}{\partial \gamma_e} = F(\gamma_e) \tag{17}$$

with H defined as above, then eqn (8) results. We can write a perturbation equation in γ as

$$V_e \frac{\partial(\delta\gamma_e)}{\partial t} = \left[\delta_{es}\left(\frac{n-m}{m}\right)\gamma_s^{((n-2m)/m)} \frac{(u_f{}^{s} K_{fg} u_g)}{2} - \gamma_e^{((n-m)/m)} (u_f{}^{e} K_{fp} K_{pq}^{-1\,s} K_{qg} u_g)\left(\frac{n}{m}\right)\gamma_s^{((n-m)/m)}\right]\delta\gamma_s \tag{18}$$

which can be written as

$$V_e \frac{\partial(\delta\gamma_e)}{\partial t} = -(T_{es}+P_{es})\delta\gamma_s \tag{19}$$

with

$$T_{es} = \delta_{es}\left(\frac{m-n}{m}\right)\gamma_s^{((n-2m)/m)}\frac{(u_f{}^s K_{fg} u_g)}{2},$$

$$P_{es} = \left(\frac{n}{m}\right)\gamma_e^{((n-m)/m)}(u_f{}^e K_{fp} K_{pq}^{-1\,s} K_{qg} u_g)\gamma_s^{((n-m)/m)} \tag{20}$$

and to prove stability for arbitrary distributions of γ, we need to show that $T_{es}+P_{es}$ is positive definite for all possible distributions. This will be done below in the context of global minimization.

Given the functions which are minimized by the remodeling rule, we can explore the possibility that the minimum value of these functions is a global minimum, as opposed to a local minimum. If there exists only one global minimum, then the solution to the remodeling equations above is unique, and this can be important for remodeling simulations.

From calculus of variations, as applied to discrete problems (Ewing, 1985), a function has a single minimum over a set of variables if it is convex everywhere in that set. The mathematical definition of convexity for a function is H, which takes a multidimensional set K as an input and results in a real number, is convex over the set K if, given two states X and Y within the set K,

$$H(X)+\tau(H(Y)-H(X)) \geqslant H(X+\tau(Y-X)) \tag{21}$$

for $0 < \tau < 1$. We will take the optimization function here as $(m/n)H_1+H_2$. Notice that H_2 is linear in γ_e, and thus satisfies the equality in this relationship by default. If, as in this case, the second derivatives of H are continuous, then this inequality is satisfied if

$$\sum_{i=1}^{N}\sum_{j=1}^{N}\frac{\partial^2 H}{\partial x_i \partial x_j}\alpha_i\alpha_j \geqslant 0 \tag{22}$$

with x_i the components of X and α_i components of any vector in Euclidian N-space. This condition is in fact equivalent to requiring that the symmetric matrix, with components i,j given by the second partial derivative term above, is positive definite (Strang, 1986). Given the function H as defined above for bone remodeling, this mixed partial derivative matrix is simply the matrix $T_{es}+P_{es}$.

Thus we can prove that finite element simulations which use eqn (8) as a basis for stress-related bone remodeling are stable and have a unique solution which minimizes $(m/n)H_1+H_2$ if we can prove that eqn (22) is satisfied for all possible density distributions. This will establish the results for approximate finite element solutions, and we expect that corresponding results can be derived for continuous analytical situations, but we have not proven that.

RESULTS

Sufficient conditions

We can prove that this inequality is satisfied for all possible bone density distributions as follows. The matrices T_{es} and P_{es} are

$$T_{es} = \delta_{es}\frac{(m-n)}{m}\gamma_e^{-2}\frac{(u_f\gamma_e^{n/m\,e}K_{fg}u_g)}{2} \tag{23}$$

and

$$P_{es} = \left(\frac{n}{m}\right)\gamma_e^{((n-m)/m)}(u_f{}^e K_{fp} K_{pq}^{-1\,s} K_{qg} u_g)\gamma_s^{((n-m)/m)}. \tag{24}$$

If n is less than m, the terms in T_{es} are diagonal and all positive, since the matrix product corresponds to the strain energy stored in a particular element, and γ is defined between 0 and 1. Thus, T_{es} is positive definite if $m > n$. Since the sum of two positive definite matrices is positive definite, we can prove that eqn (22) is satisfied for all possible densities, and that a global minimum is found, if P_{es} is positive definite for all possible values of γ. In order to do this, we will write the matrix sum by explicitly showing some of the implied summations above. To prove that P_{es} is positive definite, we form the test as

$$\sum_{e=1}^{N}\sum_{s=1}^{N}\alpha_e\left[\left(\frac{n}{m}\right)\gamma_e^{((n-m)/m)}\left(\left(\sum_{f=1}^{N_d} u_f{}^e K_{fp}\right)K_{pq}^{-1}\left(\sum_{g=1}^{N_d}{}^s K_{qg} u_g\right)\right)\gamma_s^{((n-m)/m)}\right]\alpha_s \geqslant 0 \tag{25}$$

with the summation over p and q left implied. Notice that all the terms which refer to element e are to the left of K_{pq}^{-1}, and all the terms which refer to element s are to the right. Thus we can take the summation term in s over to the right of this summation as follows:

$$\left(\frac{n}{m}\right)\left[\sum_{e=1}^{N}\alpha_e\gamma_e^{((n-m)/m)}\left(\sum_{f=1}^{N_d} u_f{}^e K_{fp}\right)\right]K_{pq}^{-1}\left[\sum_{s=1}^{N}\left(\sum_{g=1}^{N_d}{}^s K_{qg} u_g\right)\gamma_s^{((n-m)/m)}\alpha_s\right] \geqslant 0. \tag{26}$$

By rearranging the order of the terms in this expression, the left double summation can be shown to be equal to the right. Thus, by rearranging the summations for elements and degrees of freedom, we can show that given any vector α, there corresponds a load vector given by the expressions in the square brackets. Since K_{pq} is the global finite element stiffness matrix, and is always positive definite (or positive semi-definite if enough elements have zero stiffness), the inverse K_{pq}^{-1} is also positive definite, if the remodeling simulation is restricted to elements with non-zero density. Thus, the inequality is satisfied for all density distributions, with the restriction that only elements with non-zero density are considered as part of the remodeling simulation. This means that the matrix P_{es} is positive definite for all possible density distributions, and that the sum of P_{es} and T_{es} is positive definite if $n < m$. Thus, H is convex for all possible density distributions, and has a unique minimum which can be found by finding the equilibrium points in the time-dependent remodeling rate equations, if $n < m$. As shown above, since T_{es} and P_{es} are positive definite, the bone remodeling simulations run using eqn (8) in a finite element discretization are always stable with $n < m$.

Necessary conditions

To see that the $n < m$ condition is necessary, consider the sum $T_{es} + P_{es}$. If we factor the sum as follows:

$$T_{es} + P_{es} = \gamma_e^{-1}(u_f\gamma_e^{n/m\,e} K_{pf})\left(\left(\frac{m-n}{2m}\right)\delta_{es}\gamma_e^{-1}u_p + \left(\frac{n}{m}\right)\gamma_s^{-1}K_{pq}^{-1}(\gamma_s^{n/m\,s} K_{qg})u_g\right) \tag{27}$$

we can then identify $\delta_{es}\gamma_e = \gamma_s$ and factor the total stiffness matrix K_{pq}^{-1} out of the sum in parentheses. We then have

$$T_{es} + P_{es} = \gamma_e^{-1}(u_f(\gamma_e^{n/m\,e} K_{pf}))K_{pr}^{-1}\left(\left(\frac{m-n}{2m}\right)\gamma_s^{-1}K_{rt}u_t + \left(\frac{n}{m}\right)\gamma_s^{-1}(\gamma_s^{n/m\,s} K_{rg})u_g\right) \tag{28}$$

and we can physically identify some terms. Note that we imply summation over repeated subscripts only in the stiffness matrices and the displacements, so that there are no implied sums over e and s. The terms $\gamma_e^{n/m\,e} K_{pf}$ and $\gamma_s^{n/m\,s} K_{rq}$ represent the actual stiffness matrices of

elements e and s, respectively. Since the terms referring to element e are all to the left of K_{pr}^{-1} and the terms referring to element s are to the right, we can now form the sum in eqn (22) as

$$\sum_{e=1}^{N}\sum_{s=1}^{N}(P_{es}+T_{es})\alpha_e\alpha_s = u_f\left(\sum_{e=1}^{N}\alpha_e\gamma_e^{-1}(\gamma_e^{n/m\,e}K_{pf})\right) \times K_{pr}^{-1}\left[\left(\frac{m-n}{2m}\right)K_{rt}u_t\left(\sum_{s=1}^{N}\alpha_s\gamma_s^{-1}\right)+\left(\frac{n}{m}\right)\left(\sum_{s=1}^{N}\alpha_s\gamma_s^{-1}(\gamma_s^{n/m\,s}K_{rg})\right)u_g\right]. \quad (29)$$

In order to prove that $n < m$ is necessary for a convex function, we need only to prove that there is at least one set of perturbations which make the sum negative for any density distribution. We also require, for a stable distribution, that the inequality in eqn (22) holds for progressively finer finite element meshes, i.e. as the number of elements becomes very large. Consider the perturbation in which $\alpha_e = \gamma_e$. This will make the $\alpha_e\gamma_e^{-1}$ factors above unity, and we can recognize the sums over e and s as the overall stiffness matrix for the modeling elements. Substituting $K_{pf} - {}^cK_{pf}$ for those summations [using eqn (10) above] and rearranging terms yields

$$\sum_{e=1}^{N}\sum_{s=1}^{N}(T_{es}+P_{es})\alpha_e\alpha_s = N\left(\frac{m-n}{2m}\right)[u_f(K_{pf}-{}^cK_{pf})u_p]+\left(\frac{n}{m}\right)[u_f{}^cK_{pf}K_{pr}^{-1}{}^cK_{rt}u_t - u_r{}^cK_{rt}u_t] \quad (30)$$

with N the number of remodeling elements. Clearly, as N becomes large, the first term on the right will dominate. The matrix product in the first term on the right $(u_f(K_{pf}-{}^cK_{pf})u_p)$ is the energy stored in the remodeling elements, and is always positive. The last matrix product $(u_r{}^cK_{rt}u_t)$ is the energy stored in the non-remodeling portion of the structure, and the middle term on the right is harder to interpret, but seems to be a co-energy of some sort. We expect the two rightmost terms to be similar in magnitude, and we expect the terms to converge to constant values as the finite element mesh is refined.

This expression shows that if $n > m$, and a finite element mesh containing non-remodeling elements is progressively refined, then the simulation may appear stable at first, but will become unstable. Also, if the remodeling simulation contains no elements which do not remodel, the simulation will always be unstable with $n > m$.

The implications for optimization with $n > m$ and no remodeling elements are that there are no purely minimal points, and that every stationary point for the optimization function is in fact a higher-order saddle point, if the finite element mesh is sufficiently refined.

Multiple loading cases

The influence of multiple loading situations on the results shown here can be given for a simple characterization of these effects. If multiple load cases result in a stimulus which is a weighted sum of their influence, as used by Huiskes *et al.* (1991), then the remodeling rate equation becomes

$$V_e\frac{\partial\gamma_e}{\partial T} = \sum_{k=1}^{N_l}\beta_k\left(\frac{\Psi_{e,k}}{\gamma_e}\right)-\Psi_0 \quad (31)$$

with β_k a set of weighting factors to account for number of loading cycles and loading rates. Using this equation, the overall optimization function becomes a weighted sum of the strain energy in a number of load cases, and the integral of γ over the remodeling elements. The result of an analysis of global stability will be the same, since each load case will result in a corresponding strain energy term, which will in turn result in a matrix of the form $T_{es}+P_{es}$.

Thus, since the sum of any number of positive definite matrices is positive definite, we can prove that the solutions to eqn (31) are globally stable and unique as well.

DISCUSSION

Although the results here are encouraging for a finite element simulation of bone remodeling using eqn (8) or (31), the assumptions implicit in this formulation should be reiterated. We have made these assumptions so that our model will capture the important phenomena in bone remodeling, and for simplicity in the mathematical relationships used. We have chosen these assumptions based on the available experimental data for bone material properties. We do not intend the remodeling rule we use here to be a complete description of bone remodeling in any sense. Rather, we propose this development as a reference and a guide to further development of bone remodeling theories.

The material property assumptions are simplifications for the known mechanical properties of cancellous bone, but capture the most important trend. We have assumed elastic isotropy for bone tissue, and we have assumed that the Poisson ratio is independent of density. Cancellous bone is known to be substantially anisotropic (Cowin, 1985, 1986). The difference in elastic moduli in different directions in a specimen of cancellous bone can be over 300% in some cases. This is a limitation on the applicability of the remodeling theory developed here, but we have accepted this limitation in order to arrive at a tractable result for this study.

The currently existing relationships which are meant to predict anisotropic elastic coefficients for cancellous bone do not represent the experimental data in a substantially more accurate fashion than the isotropic approximation we use here. Also, the anisotropic characterization for cancellous bone given by relationships between mechanical test results and structural anisotropy measurements is usually incomplete. Nine material property coefficients are needed for an orthotropic material model and 27 for a fully anisotropic material model, and experimental measurement of these coefficients is very difficult, since human bone tissue is relatively homogeneous only over a distance of approximately 1 cm. Thus, if we used the anisotropic relationships available in the literature, we would need another set of assumptions to complete the material model, and we would substantially complicate the analysis.

At this point, the choice for the left-hand side of eqn (8) can be rationalized as follows: We have shown that the remodeling stimulus is the rate of change of an indicator function with respect to state variables γ_e and we have defined the indicator function. It seems appropriate that in a minimizing procedure, we should take

$$\frac{\partial \gamma_e}{\partial t} = -\frac{\partial H}{\partial \gamma_e}$$

as in eqn (7).

The right-hand side of the remodeling rate equation used here is similar to many in the literature. Our model differs from those of Huiskes *et al.* (1991) and Beaupré *et al.* (1990) in the choice of the exponent m in the denominator. The a priori choice of $m = 1$ by Huiskes *et al.* is based on the idea that the strain energy per unit volume of calcified tissue is the primary stimulus for bone remodeling. Beaupré *et al.* (1990) used a modified stimulus which was an "energy stress", defined as the square root of the product of strain energy density and elastic modulus. The exponent on density in the denominator of their remodeling stimulus was taken a priori as 2, based on the idea that cancellous bone strength was proportional to the square of density. By contrast, we have initially left the exponent m undefined and then restricted it based on the physical behavior of the bone remodeling simulation itself. Thus we have arrived at an a posteriori bound on m, as opposed to making an a priori assumption.

Physically, taking $m > n$ is an assumption that the bone structure in the adult is stable, i.e. it remodels so that small perturbations in density (due to maintenance processes, for

example) tend to decay away with time. Put another way, changes in bone structure which increase exponentially with time do not occur.

The form of the equations used in bone remodeling reflects the qualitative observation that increased bone loading leads to denser bone tissue, while decreased loading leads to more porous tisssue. We have shown that our model produces equilibrium density distributions which are similar to those in the literature, and which are in qualitative agreement with what would be expected (Harrigan and Hamilton, 1993). Thus, while we have shown a substantial mathematical framework for the bone modeling rate equation we have studied here, we have not proven that this model is a better predictor of bone remodeling. However, given the substantial improvements in the mathematical characteristics of this model as compared to others in the literature, we believe we can test this model in much more detail than others have been tested. We also believe we can make improvements in this model in a much more knowledgeable fashion, given the mathematical framework we have developed.

The proof that $n < m$ is necessary for a stable remodeling simulation is similar to the work of Weinans *et al.* (1992) and Harrigan and Hamilton (1992a), but is more general. Weinans *et al.* showed a two component model which predicted limits for stability for a number of bone remodeling rate equations. Harrigan and Hamilton showed instabilities for a continuous one-dimensional problem (that of a composite beam). Here, we show that the predicted instability in both of those prior studies is a general phenomenon, since, given a proper discretization, any elastic structure can be effectively modeled with finite element techniques.

CONCLUSIONS

In this paper, we have shown that the bone remodeling theory we have developed in previous studies has solutions which are globally stable and unique. This model is built on two assumed relationships which have been shown to be reasonable, given the information available at this time. They are (a) an isotropic elastic material model with a constant Poisson ratio, and (b) a remodeling rule with a stimulus which is strain energy density divided by volumetric density taken to a power. These relationships are used within a finite element formulation to show that the resulting solutions are stable with $n < m$ for any density distribution, and that the solutions obtained using the remodeling algorithm are unique. We have also shown that simulations with $n > m$ are generally unstable, and that the solutions for equilibrium points are saddle points for a global indicator function.

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