# Bone structure and the dynamics of bone adaptation in response to accumulative damage

*Key Engineering Materials Vol. 86-87 (1993) pp.187-192*


# BONE STRUCTURE AND THE DYNAMICS OF BONE ADAPTATION IN RESPONSE TO ACCUMULATIVE DAMAGE

P.J. Prendergast (a), H. Weinans, R. Huiskes (b) and D. Taylor (a)

(a) Bioengineering Research Centre & Department of Mechanical Engineering, Trinity College, Dublin 2, Ireland

(b) Biomechanics Section, Institute of Orthopaedics, University of Nijmegen, NL-6500 HB Nijmegen, The Netherlands

*Keywords: porosity, bone, dynamical model, damage*

**ABSTRACT** - *A brief review of the structure of bone as a material is given. In particular, its capacity to adapt its structure (both internally and externally) to suit the load it supports is described. Computer-based models for the simulation of bone adaptation are investigated from the dynamical point of view; specifically, the hypothesis* (Weinans, Huiskes & Grootenboer, J. Biomechanics), *that bone arranges its internal structure in a process of self-organisation is studied for an accumulative damage stimulus.*

One of the functions of the animal skeleton is to transmit forces; both the everyday forces due to organ support, load bearing and locomotion and the "once off" large forces due to impact. The skeleton, therefore, is a structure in the engineering sense, and its members (the bones) are submitted to mechanical stress.

The structure of the skeleton and the shape of the individual bones in any species are the result of many millions of years of development during which time they have become adapted for their mechanical function (Thompson, [1]). Figure 1 shows the proximal part of the human femur. One of our interests is with the mechanical adaptation that results when a bone is subjected to a load which it was not meant to support. For example, an orthopaedic device such as hip joint replacement prosthesis, will generate non-physiological stresses in the femur causing it to adapt.

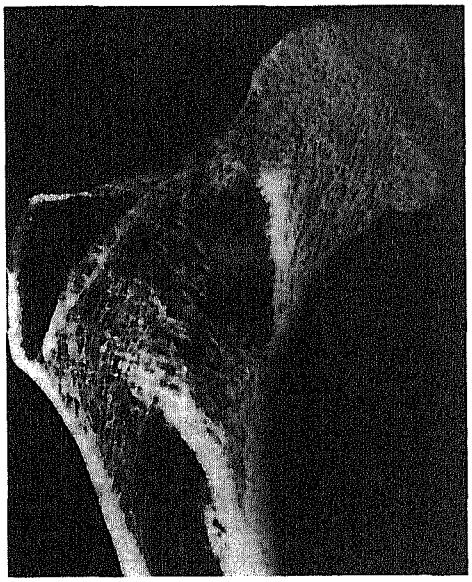

FIGURE 1: A CROSS-SECTION THROUGH A FEMUR SHOWING TRABECULÆ ORIENTED IN THE PRINCIPAL STRESS DIRECTIONS

Mathematical models have been used to simulate bone adaptation on computers by, among others, Huiskes et al. [2], Beaupre et al. [3] and, recently, by Weinans [4]. The principle they employ is that bone adapts as a function of the difference of stress and/or strain before and after a change in load. One mathematical form that has been used is

$$d/dt = C.\ (\ SED/\rho^n - k) \qquad (1)$$

where SED is the strain energy density and $\rho$ is the density, n is a constant transducing the continuum stress to the microstructural level and k is a remodelling equilibrium stimulus. An alternative approach proposed by Prendergast and Taylor [5] is based on the hypothesis that bone adapts to obtain an optimum level of accumulated damage, i.e. bone allows a site-specific amount of damage to accumulate despite the fact that this will increase the chances of bone fracture, the benefit being that of having to maintain less bone mass (Prendergast et al. [6]). The mathematical form required for computer simulation is given by

$$d/dt = \int (\dot{\omega} - \dot{\omega}_{RE}) . dt \qquad (2)$$

where $\dot{\omega}$ is the rate of production of damage at a new stress and $\dot{\omega}$RE is the repair rate (equivalent, in the model, to the damage production rate at the physiological stress).

Clearly there are fundamental differences between these predictive approaches. In particular the accumulative nature of the stimulus in equation 2 means that it is a second-order dynamical system whereas equation 1 simulates a first-order dynamical system. In this paper the authors use a dynamical model, previously employed to ascertain the characteristics of the first-order remodelling system by Weinans [4], to investigate the accumulative-damage model.

## THE STRUCTURE OF BONE AND MICROSTRUCTURE PROPERTY RELATIONSHIPS

The composite structure of bone can be described on several levels. These can be;

(i) Hydroxyapatite (HAP) crystals reinforce a soft organic collagen matrix.
(ii) HAP/Collagen composite layers are arranged to form either (a) tubular fibre-like structures called osteons each consisting of 20-30 laminates or (b) lamellar bone.
(iii) Osteonal bone or lamellar bone arranged with pores and water to form bone material that is either Compact (Porosity between 10% and 30%) or Trabecular (30% to 90%).

There are two sets of relationship we can consider with regard to bone as a material; firstly the relationship between the stress and the micro/ultra structure and secondly the relationship between the micro/ultra structure and the mechanical properties.

Stress/microstructure relationships have been investigated by, for example, Ascenzi and co-workers (see Ascenzi, [7]). They found that, in the tensile side of osteons, the HAP crystals tend to orientate in the direction of the stress (i.e. axially) and that in the compressive side they were orientated at 45 degrees to the axis. Based on this, the hypothesis that HAP is orientated to best prevent bone fracture was proposed. The relationship between stress and ultrastructure is seen in the development of long bones; compact bone material is found on the surface in high stress areas and trabecular bone material is found where multi-axial stresses of a lower magnitude exist (e.g. near bone ends).

The relationship between microstructure (e.g. HAP phase) and mechanical properties has been reviewed by Katz [8], who presents, for example, relationships between volume concentration of HAP and Young's modulus. The relationship between ultrastructure (for example density) and mechanical properties is more pronounced and has been thoroughly reviewed for bone by Linde et al. [9]. One expression that has been used in analytical studies is due to Carter and Hayes [10] in equation 3. More complex steriological modulus/porosity relationships are also proposed (Turner et al. [11])

$$E[MPa] = C.\ \rho[g/cm3]^\gamma \quad C= 3790,\ \gamma = 3 \qquad (3)$$

Low porosity Compact bone has a density of up to 1.8 g/cm3 and high porosity Trabecular bone has a density in the range 0.3 to 1.0 g/cm3 with little bone found at intermediate densities. It is hypothesised (Weinans et al. [12]) that the non-linear nature of the bone remodelling process generates an instability that can cause the bone to remodel from a homogenous structure into an organised porous structure.

HYPOTHESIS OF TRABECULAR BONE FORMATION DUE TO WEINANS (1991)

Computer simulations of bone density evolution have shown continuous smoothed density distributions. The simulations done by Weinans [4], without element averaging, allowed density to vary only in different elements; each individual element responded to its own remodelling sensor. These simulations resulted in a discontinuous distribution where element densities either attained the remodelling objective or the maximum density or they went to zero. The result was along the lines of a previous result of Carter et al. [13]. Based on this result, it was hypothesised that a discontinuous and non-homogenous structure (i.e. porous bone) is the end-configuration resulting from the non-linear dynamical equations governing bone remodelling. This hypothesis was investigated further using both simple analytical models and finite element models. The simple analytical models are based on 'two-units' of bone in parallel to which equal strain was applied (figure 2). It was shown that, if the density is perturbed about equilibrium, the conditions for returning to a homogeneous equilibrium depend on the parameters characterising the non-linearity (i.e. n and $\gamma$ in equations 1 and 3 above).

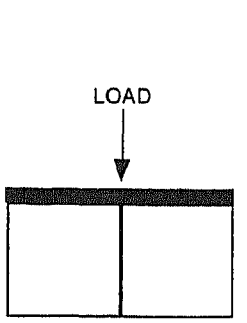


Figure 2A

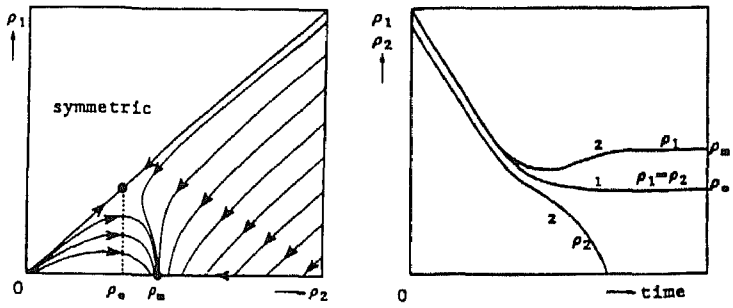


Figure 2B

FIGURE 2: (A) SCHEMATIC OF THE 2 D.O.F. MODEL: (B) PHASE PLOT WITH ρ1 AGAINST ρ2 FOR $\gamma$ = 2 AND n = 1: TIME COURSE OF ADAPTATION (PATH 1 $\gamma$ < 1, n = 1; PATH 2, $\gamma$ > 1, n = 1) [ From Weinans 4]

If the 2 units are perturbed to a density different from the remodelling equilibrium density, the sensors will record a stimulus to adapt. Depending on n and $\gamma$, they will either both return to the equilibrium density (path 1) or the unit with higher density will take load from the one with lower density such that the lower will adapt to zero density (path 2). Since this is a equal strain case, it is not clear that the effect will be reproduced in complex loading states. However, Weinans et al. [4] found it to operate in a finite element model of a plate under a distributed ramp load when the condition $\gamma$ > n is satisfied. Harrigan and Hamilton [14] reported both analytical and numerical solutions showing, as do Weinans et al. [4], that $\gamma$ < n is a necessary but not sufficient condition to prevent growth of perturbations about equilibrium. However, they do not describe an effect related to sensor-cell density. Jacobs et al. [15] show the phenomena to be dependent on the choice of finite element and suggest a nodal averaging procedure to eliminate it. Notwithstanding this, if "sensors-of-adaptation" exist, then the real system is discrete in nature, and if so, some mechanism whereby local stress-shielding stimulates ordered Trabecular bone formation seams likely. In the following section, we examine this phenomenon in simulations based on damage-adaptive remodelling.

DYNAMICS OF BONE ADAPTATION WITH ACCUMULATIVE-DAMAGE CRITERIA

None of the above studies have analysed the effect of an accumulative or "strain-history" stimulus. The accumulative damage model integrates the difference between damage

produced and damage repaired and uses this accumulated change-of-damage, called effective damage ($\omega$eff), as the stimulus for remodelling (equation 2). Following Prendergast and Taylor [5], damage is measured using a remaining life variable and a linear damage growth law is used, i.e.

$$\omega = 1/Nf \tag{4}$$

where Nf is the number of cycles to failure in a fatigue test. Carter et al. [16] present comprehensive fatigue data for bone for different microstructural groups. The regression analysis relation is

$$\text{Log } (2Nf) = -7.79 \log \sigma + 2.364\rho - 0.0266T + MI \tag{5}$$

where $\sigma$ denotes stress and T denotes temperature. MI = 15.720 for remodelled bone with osteons. An increase in density will increase the fatigue life and decrease the damage rate and, in this way, the rate of remodelling depends on the density similarally to strain-adaptive remodelling. Using forward Euler integration to simulate adaptation after a perturbation, the constants of equation 5 give $\gamma \approx 1.2$ as the critical value for the formation of a non-homogenous structure. The effect of a perturbation with an accumulative-damage stimulus is given in figure 3. Figure 3(a) shows that, for $\gamma < \gamma$crit, a oscillation occurs in both units for a simulation with the time-step $\Delta t = 0.05$. The path did not settle into a repetative loop during the time of the simulation and it may be that this is a non-periodic or chaotic response though this remains to be confirmed by stability analysis. Figure 3(b) shows the time-course of this mass transfer between units showing an out of phase response between units. Figure 4(a) shows the response with $\gamma > \gamma$crit for perturbations above and below eqilibrium. This is similar to the non-accumulative stimulus in that the density in the lower unit goes to zero; however the higher unit continues to oscillate as shown in figure 4(b). If a maximum density is imposed, as it is physiologically, then the oscillations stop.

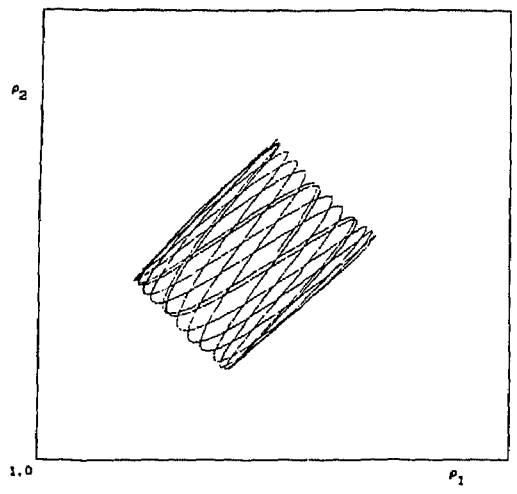


FIGURE 3(A)

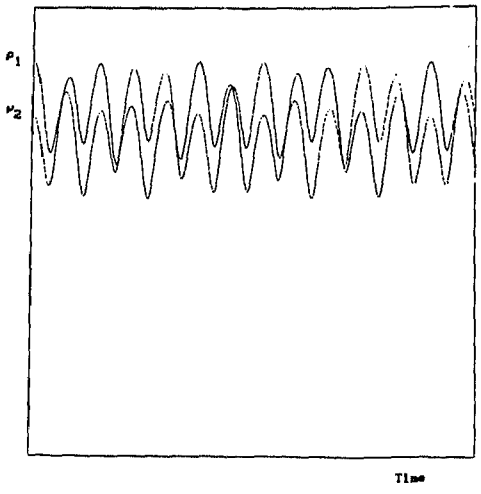


FIGURE 3(B)

FIGURE 3: (A) PHASE PLOT WITH $\gamma < \gamma$ CRIT SHOWING OSCILLATORY BEHAVIOUR: (B) TIME-COURSE OF MASS TRANSFER BETWEEN UNITS

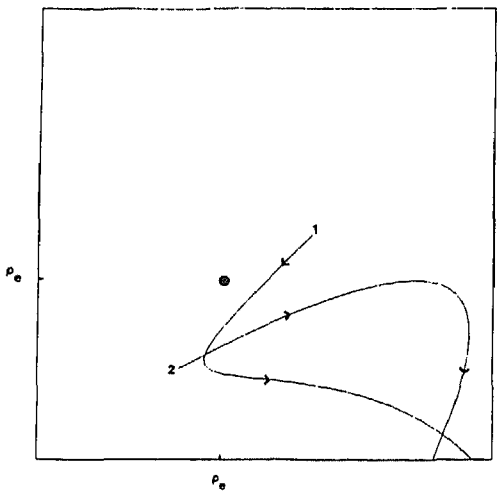


FIGURE 4(A)

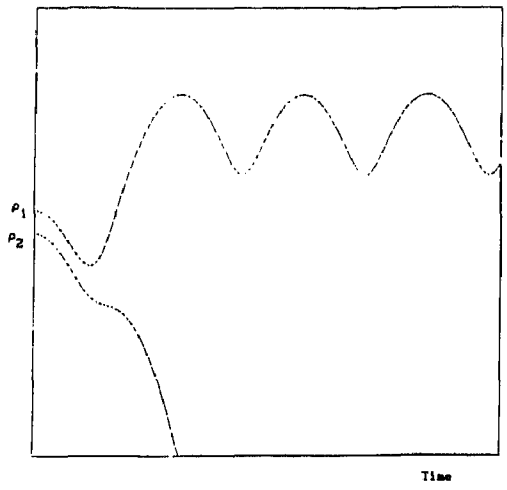


FIGURE 4(B)

FIGURE 4: (A) PHASE PLOT WITH $\gamma > \gamma_{CRIT}$ SHOWING INSTABILITY AFTER PERTURBATION TO A HIGHER DENSITY {Path 1} AND A PERTURBATION TO A LOWER DENSITY {Path 2}: (B) TIME-COURSE OF MASS TRANSFER BETWEEN UNITS SHOWING THAT THE LARGER UNIT CONTINUES TO OSCILLATE

## DISCUSSION

There are several assumptions in the remodelling rule in the above analysis the most important of which is that the sensors in each unit are uncoupled and operate independantly of each other. The limit of coupled sensors is a "whole bone stimulus" analysed by Kuiper et al. [17] who compare it with local adaptation and find that local adaptation gives density distribution more like that observed in reality. Several hypotheses as to the physiological nature of the sensor are proposed. For example, Martin and Burr [18] present a mechanism whereby osteonal debonding damage activates remodelling at a site. Cowin et al. [19] review strain-adaptive hypotheses one of which is that osteocyte-containing lacunae are the sensor sites.

However, it is clear that when an accumulative or integral stimulus is used to simulate bone adaptation a new class of remodelling solutions exist. These are oscillatory where either one or both of the units oscillate. With Strain-Adaptive remodelling, the condition $\gamma <$ $\gamma$crit [12,14] if it is imposed in Damage-Adaptive remodelling then the oscillations continue around both sensors and otherwise one sensor reduces to zero mass and thE other will oscillate unless a maximum density is imposed.

## CONCLUSIONS

We can enumerate the following points to summarize on the above
(i) Bone has a structure that is adapted in both microstructure and ultrastructure by its mechanical stress environment/
(ii) At the ultrastructural level, trabecular organisation is influenced by a process of stress-transfer and stress-shielding around sensor-sites. This depends critically on the non-linearity of the relationships governing bone remodelling for both strain-adaptive

remodelling and damage -adaptive remodelling.
(iii) An accumulative-damage remodelling criterion predicts that oscillatory adaptation will occur untill the repair rate eventually adjusts to the new stress.

We can sumarize that the present results indicate that, in principal, it would be possible to have a remodelling algorithm which not only produces a continuous trabecular-like end configuration but that it would also be possible to end up in a process of an ever continuing remodelling process. This hypothesis that normal homeostatic bone turnover is regulated by such a process is an extremely provocative speculation.

ACKNOWLEDGEMENTS

PJP thanks the Institute of Orthopaedics, University of Nijmegen for having him as a Guest Researcher from October to December 1991

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