Transactions on Biomedicine and Health vol 2, © 1995 WIT Press, www.witpress.com, ISSN 1743-3525

Review and overview of net bone remodeling

R.T. Hart
Department of Biomedical Engineering, Tulane University, New Orleans, LA 70118, USA

Abstract

The observations and ideas behind current thinking and simulation of the functional adaptation of bone are presented. Several phenomenological models and mechanistic models are summarized. In addition, the use of computational implementations for some of the theoretical notions is briefly introduced.

Introduction

The adaptation of bone shape to its mechanical usage has been a topic of considerable recent interest. First, the relationship between bone form and function raises questions of basic physiological interest. Additionally, advances in understanding bone's adaptation to mechanical use are expected to result in specific strategies to improve the design and success of implanted endoprostheses, and to improve clinical treatment of specific bone disorders.

It has been known since at least Gallileo's time [14] that bone's form is based in part on its structural function. In the 1800's a number of investigators made observations about bone form and function (e.g., Ward, von Meyer, Culman, Roux) as described in Julius Wolff's classic book *Das Gesetz der Transformation der Knochen* (*The Law of Transformation of Bone*) [31, 32]. Although the book contains a large number of ideas and observations, perhaps the most concise statement of "Wolff's Law" is that "Every change in the...function of bone...is followed by certain definite changes in...internal architecture and external conformation in accordance with mathematical laws," Roesler [27]. Thus there are two distinct portions to "Wolff's Law." One has to do with the architecture of the trabecular bone that is composed of small struts of calcified tissues found internally near the ends of long bone, see Figures 1 and 2.

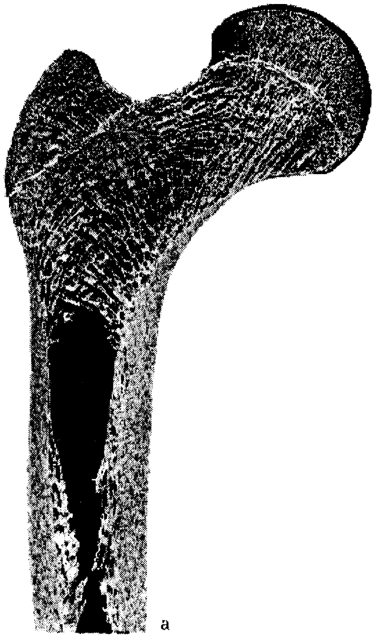

Figure 1. Copy of the plate from Wolff [31, 32] showing the thin longitudinal section of a human femur. His technique of using a steam powered saw for making the sections, and photographing the sections on a black velvet background enhances the visibility of the trabecular architecture.

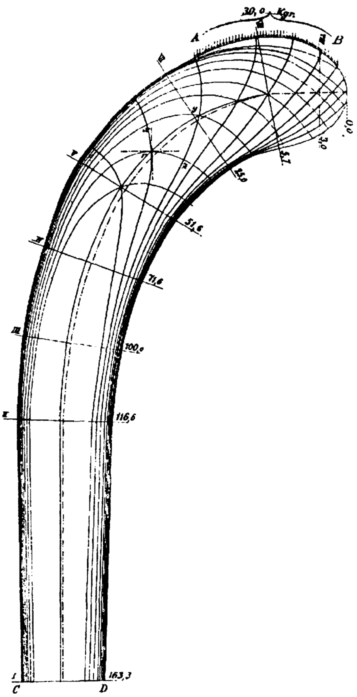

Figure 2. Copy of the plate from Wolff [31, 32] showing the patterns of principle stresses in the Fairbairn crane.

The stress patterns are a good first estimate of the stresses (for a detailed account, see Roesler [27]) as estimated by Culmann, an engineer. Wolff, a surgeon, found that the orientation of trabecular bone in the proximal portion of the femur was remarkably similar to the lines of principal stress that would be expected in this bent structure called a "Fairbaine crane." Wolff took this as proof that trabecular bone was oriented along the principal stress trajectories. This portion of "Wolff's Law" is called the Trajectoral Theory of Trabecular Bone.

Transactions on Biomedicine and Health vol 2, © 1995 WIT Press, www.witpress.com, ISSN 1743-3525

The second portion of Wolff's Law is that the external form of bone is dependent upon its function. This theory was based on observations made possible by having access to a large collection of unusual bone specimens from scientists throughout Europe. Of particular interest are the bones from a human lower limb from a specimen collection assembled by Professor Roux. The tibia has been broken some time before death, and the fracture never healed ("the fragments are smoothed at their extremities and freely mobile over one another," Wolff [32]). As a consequence, the fibula has taken the role of providing structural support due to the compromised tibia, and has increased its cross section so that "its cross section is six to eight times thicker than normal," Wolff [32].

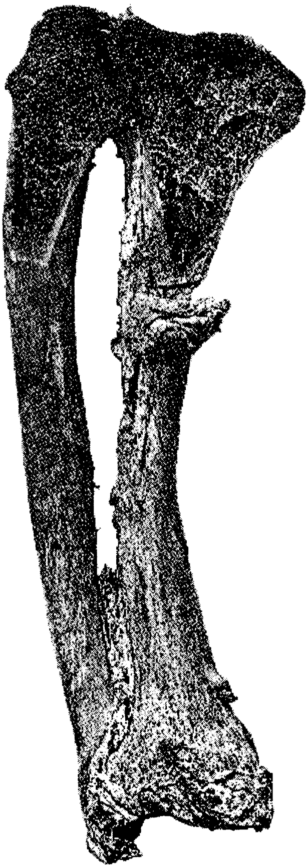

Figure 3. Copy of the plate from Wolff [31, 32] showing the specimen that Wolff obtained from Prof. Roux of Innsbruck.

Despite the continued fascination with bone's behavior as a living structural material, progress in developing a full understanding of the process has been slow.

A number of theories about bone adaptation have been proposed in the past century. A selection is presented in Table 1 that does not include the many investigations that have been primarily experimental. Many of the listed researchers continue their investigations.

Table 1. Representative list of Net Remodeling Theories

Principal Investigators	Description of Theory
Wolff, 1892 [31]	The Law of the Transformation of Bone
Frost, 1964 [10-12] –	Cortical Drift Models, Intermediary Organization
Pauwels, Kummer 1968-72 [26, 22]	Observational summaries, mathematical models
Gjelsvik, 1973 [15]	Piezoelectric models
Cowin, Hegedus and Van Buskirk, 1976 [3-5]–	Adaptive Elasticity: Surface, Internal, Trabecular Adaptation. Computational implementations
Davy, Hart and Heiple, 1983 [9, 18, 19]–	Computational implementation, cell-based theory
Guzelsu and Saha, 1984 [17]	Electromechanical model
Carter, Fyhrie, Beaupre, Orr, 1986 [1, 2, 13]–	Trabecular reorientation: Objective Functions, Computational Implementations
Huiskes, Weinans, Grootenboer, Kuiper, 1987[21]–	Strain energy density, Computational Implementations, Application to implants
Mattheck [23]–	Notch stress minimization, computational implementation
McNamara, Prendergast, and Taylor, 1992 [24]–	Fatigue damage repair, computational implementation

Theoretical Models

Phenomenological Models

There have been two broad classes of theoretical development for describing and predicting bone's functional response. The first, phenomenological models, try to simulate cause and effect, without much attention to the mechanism. The process may be modeled, or just the "end points" of the adaptation. A major advantage of this approach is that it can represent a convenient "what-if" framework to unify and test ideas and their consequences. The limitations have to do with the number of arbitrary constants needed to model additional behaviors which can increase unreasonably.

Examples of some of the phenomenological model developments are summarized in the following. Although not inclusive, the selected models are illustrative of the range of ideas that have been proposed.

Frost. Beginning in the early 1960's, Frost developed the descriptive "Flexure-neutralization Theory" to formalize some of the clinical observations of bone realignment [10]. He stated that repeated nontrivial dynamic bending loads cause strains that cause bone formation drifts to build up upon concave-tending surfaces, while resorption drifts tend to erode convex-tending surfaces [11, 12]. In addition to many observations of the biology and mechanics of bone adaptation, Frost has recently been quantified in his "3-way Rule" which symbolically represents the observations of the flexure neutralization theory.

Cowin and co-workers: Of key interest among many investigators has been

Transactions on Biomedicine and Health vol 2, © 1995 WIT Press, www.witpress.com, ISSN 1743-3525

Cowin's theory of adaptive elasticity [5]. The grounding of the adaptive theory in elasticity theory has also led to it's computational implementation [7, 18, 28]. One key feature is the use of an assumed error signal to drive the remodeling process. The error signal is the difference between the mechanical state in its equilibrium configuration (a quiescent state with no net remodeling) and the current mechanical state (following some perturbation to the bone such as a changed mechanical load). The error signal is then used to drive the net remodeling process. The theory has three major parts: one for the shape change of cortical bone (net surface remodeling); one for the density changes of cortical bone (net internal remodeling); and one for changes in the density and the orientation of continuum representations of trabecular bone tissue.

For net surface remodeling, Cowin and Van Buskirk [4] proposed the following equation:

$$U = C_{ij}(Q)[(\varepsilon_{ij}(Q) - \varepsilon^0_{ij}(Q)] \qquad (1)$$

where U is the "velocity" (change in position over time) of the bone's external bone surface at point Q, C_{ij} are remodeling rate parameters, $\varepsilon_{ij}(Q)$ is the strain at point Q, and $\varepsilon^0_{ij}(Q)$ is the remodeling equilibrium strain at point Q.

For net internal remodeling, Cowin and Hegedus [3] proposed

$$\dot{e} = a(e) + tr[A(e)\varepsilon] \qquad (2)$$

where $\dot{e}$ is the rate of change in solid fraction of bone, A is a remodeling rate parameter, and ε is the strain tensor.

For the trajectoral theory of trabecular orientation, Cowin [6] develops a continuum model that segregates changes in the density of the trabecular bone from changes in the predominant orientation of the struts of trabecular bone as measured by a "fabric tensor" (defined as the inverse square root of the mean intercept length, easily measured steriologically). By describing the elastic material properties, **D**, as a function of the solid volume fraction, ν, and the fabric tensor, **H**, the stress, **T**, is written as: $\mathbf{T} = \mathbf{T}(\nu, \mathbf{E}, \mathbf{H})$. He then presents a mathematical expression of Wolff's trajectoral theory [6] as the commutative multiplication property of the relevant tensors: $\mathbf{T}^*\mathbf{H}^* = \mathbf{H}^*\mathbf{T}^*$ and $\mathbf{T}^*\mathbf{E}^* = \mathbf{E}^*\mathbf{T}^*$ and $\mathbf{H}^*\mathbf{E}^* = \mathbf{E}^*\mathbf{H}^*$, where the * indicates a remodeling equilibrium value. Cowin [8] has also written trabecular rate equations for the evolution of the fabric tensor re-orientation back to the remodeling equilibrium configuration (assumed dependent on the deviatoric portion of the strain), simultaneously with the change of the density (assumed dependent upon the dilatational portion of the strain).

Huiskes and co-workers: An approach similar to Cowin's has been developed by Huiskes *et al*. [21]. One difference was implemented to model the observed bone behavior that shows some threshold of mechanical stimulus is required to start the process of net remodeling, sometimes referred to as a "lazy zone" or a "dead zone." In addition, the mechanical stimulus is not taken to be the strain tensor, but a scalar, the strain energy density, $U = 1/2\mathbf{E}_{ij}\mathbf{T}_{ij}$.

Then the rate equation is written as:

$$\frac{dX}{dt} = \begin{Bmatrix} C_x[U-(1+s)U_n]; & U > (1+s)U_n \\ 0; & U_n < U < (1+s)U_n \\ C_x[U-(1-s)U_n]; & U < (1+s)U_n \end{Bmatrix} \tag{3}$$

where X is the surface growth, C_x is the remodeling rate coefficient, $2s$ is the width of the "lazy zone," and U_n is a homeostatic strain energy density.

Beaupré, Orr, and Carter. Similar to the models of Cowin and Huiskes is the model proposed by Beaupré, Orr, and Carter [1]. However, it uses a "daily tissue level stress stimulus" defined as $\varphi_b = \left(\sum n_i \sigma_{bi}^m\right)^{1/m}$ where n_i is the number of cycles of load type i, σ_{bi} is a true bone tissue level effective stress, and m is an empirical constant, summed over one day. Then,

$$\frac{dr}{dt} = \begin{cases} c(\varphi b - \varphi_{bAS}) + c \cdot w; & \varphi_\beta - \varphi_{bAS} < -w \\ 0; & -w \le \varphi_\beta - \varphi_{bAS} \le w \\ c(\varphi b - \varphi_{bAS}) - c \cdot w; & \varphi_\beta - \varphi_{bAS} > w \end{cases} \tag{4}$$

Mattheck. A somewhat different approach has been taken by Mattheck [23] in developing the "CAO," a Computer Aided Optimization Hypothesis. Mattheck makes the observation that "A good mechanical design is characterized by a homogeneous stress distribution at its surface." As a result, a computerized implementation of CAO was developed and has been used to simulate shape change of bone (and plants) [23]. The governing equation is

$$\dot{\varepsilon}_n = k(\sigma_M - \sigma_{ref}) \tag{5}$$

and $\dot{\varepsilon}_n$ is defined as the volumetric swelling rate, and σ_M is the von Mises equivalent stress.

Mechanistic Models

The second broad class of models are mechanistic models that try to incorporate portions of the biological processes. The chief advantage from this approach will come from successful linkage between mechanical and biological causes and effects, but the chief disadvantage is the complexity of the models, and uncertainty about which of the many mechanical and biological parameters are most important to measure and track.

Of course, the bone cells must somehow sense the need to either add new bone material or to remove it. This implies the need for a mechanico-biological transducer. An excellent 1981 review article by Treharne [29] summarizes a number of suggested transducers. Although the nature of the transducer is ignored here, such a biological transducing mechanism must exist or else the observed functional adaption could not ocurr.

McNamara, Prendergast, and Taylor. The first of the models presented here may be considered as a mechanistic model because of the hypothesis that bone adaptation is activated by accumulated damage, although it stops short of directly addressing the biological processes. McNamara *et al.*, [24] assume that there is some damage at RE (Remodeling Equilibrium), and that the rate of repair is associated with the damage rate. Mathematically, at RE, $\dot{\omega}_{eff} = 0$ and $\dot{\omega} = \omega_{RE}$, where ω_{eff} is the effective damage, ω is the current rate of damage production, and ω_{RE} is the rate of damage production at RE. Then,

$$\frac{dX}{dt} = C \cdot \omega_{eff} \quad (6)$$

Davy, Hart and Heiple. In an effort to begin to tie the mechanics and the biology into the net remodeling rate equations, a model based upon observable cellular measures was developed [9, 19]. The net remodeling was regarded as a manifestation of competing cellular activities and numbers. Then the rate equation was written as

$$\dot{d} = \lambda_b a_b n_b - \lambda_c a_c n_c \quad (7)$$

where the subscript b refers to osteoblasts and c refers to osteoclasts, λ is the surface area fraction available, a is a measure of cellular activity, and n is a measure of cellular number. Further equations were then written to relate each of the parameters in equation (7) to measures of the strain history. The theory has recently been used to make *a priori* predictions of experimentally induced net surface remodeling with encouraging results [25].

Computational Implementation

Complementary to the theoretical development is the concurrent development and refinement of computational implementations. The study of bone mechanics involved complex geometries, anisotropic and inhomogeneous material properties with complex boundary conditions and loading conditions. Thus, in order to study the consequences of the various ideas and theories of bone's functional adaptation, numerical simulations are needed. These computational implementations then allow for a convenient "what-if" environment for testing ideas and their consequences while using complex models of bone and loading.

There have been a number of different approaches to the computational implementation of net bone remodeling ideas. Although one has been based on the use of beam theory [7], and some upon the Boundary Element Method [28], most have been based on the use of the finite element method for the spatial problem coupled with the finite difference method for the time dependence [1, 16, 18, 20, 23, 24, 25, 30]. Space does not permit a full discussion here, but a compation paper [20] shows the implementation of two of the theories discussed here to examine an idealized example of net surface bone remodeling.

Conclusion

The fascination with bone as a living structural material has continued for centuries. However, only recently have the theoretical notions and the computational resources required to explore the consequences of the various theories become available. Progress in the field is expected to accelerate, and the promise of linking biological form and mechanical function may finally be realized.

References

1. Beaupré, G.S., Orr, T.E., and Carter, D.R., An approach for time-dependent bone modeling and remodeling—theoretical development, *J. Ortho. Res.*, 1990, **8**:651-661.

2. Carter, D.R., Mechanical loading histories and cortical bone remodeling, *Calc. Tis. Int.*, 1984, **36**: S19-S24.

3. Cowin, S.C., and Hegedus, D.H., Bone Remodeling I: Theory of Adaptive Elasticity, *J. Elasticity*, 1976, **6**, 313-326.

4. Cowin, S.C., and Van Buskirk, W.C., Surface bone remodeling induced by a medullary pin, *J. Biomech.*, 1979, **12**, 269-276.

5. Cowin, S.C., Continuum models of the adaptation of bone to stress, *Mechanical Properties of Bone*, ed., Cowin, S.C., American Society of Mechanical Engineers, New York, N.Y., 193-210, 1981.

6. Cowin, S.C., Wolff's law of trabecular architecture at remodeling equilibrium, *J. Biomech. Eng.*, 1986, **108**, 83-88.

7. Cowin, S.C., Hart, R.T., Balser, J.R., and Kohn, D.H., Functional adaptation in long bones: establishing *in vivo* values for surface remodeling rate coefficients, *J. Biomech.*, 1985, **18**, 665-684.

8. Cowin, S.C., Sadegh, A.M., and Luo, G.M., An evolutionary wolff's law for trabecular architecture, *J. Biomech. Eng.*, 1992, **114**, 129-136.

9. Davy, D.T., and Hart, R.T., Computation of mechanically induced remodeling in bone, *36th Annual Conference on Engineering in Medicine and Biology*, Columbus, Ohio, 1983.

10. Frost, H.M., *The Laws of Bone Structure*, Charles C. Thomas, Springfield, 1964.

11. Frost, H.M., *Intermediary Organization of the Skeleton*, CRC Press, Boca Raton, 1986.

12. Frost, H.M., Skeletal structural adaptations to mechanical usage (SATMU): 1. redefining Wolff's Law: the bone modeling problem. *The Anatomical Record*, 1990, **226,** 403-413.

13. Fyhrie, D.P., and Carter, D.R., A unifying principle relating stress to trabecular bone morphology, *J. Ortho. Res.*, 1986, **4**, 304-317.

14. Galileo, G., Discorsi e dimonstrzioni mathematiche intorna a dure nuove scieze, in Treharne, R.W., Review of Wolff's law and its proposed means of operation, *Orthopaedic Review*, 1981, **10**, 35-47.

15. Gjelsvik, A., Bone remodeling and piezoelectricity-I. *J. Biomech.*, 1973, **6**, 69-77.

16. Gupta, K.K., Knoell, A.C., and Grenoble, D.E., A bone biomechanical remodeling algorithm. 8th Annual Meeting, Association for Advancement of Medical Instrumentation, Washington D.C., 1973.

17. Guzelsu, N., and Saha, S., Electro-mechanical behavior of wet bone—part I: Theory. *J. Biomech. Eng.*, 1984, **106**, 249.

18. Hart, R.T., Davy, D.T., and Heiple, K.G., A computational method for stress analysis of adaptive elastic materials with a view toward applications in strain-induced bone remodeling, *J. Biomech. Eng.*, 1984, **106**, 342-350.

19. Hart, R.T., Davy, D.T., and Heiple, K.G., Mathematical modeling and numerical solutions for functionally dependent remodeling, *Calc. Tiss. Internat.,* 1984, **36**, S104-S109.

20. Hart, R.T., and Rust-Dawicki, Computational simulation of idealized long bone realignment, BIOMED '95, Milan, Italy, 1995.

21. Huiskes, R., Weinans, H., Grootenboer, H.J., Dalstra, M., Fudala, B., and Slooff, T.J., Adaptive bone-remodeling theory applied to prosthetic-design analysis, *J. Biomech.*, 1987, **20**, 1135-1150.

22. Kummer, B.K.F., Biomechanics of bone: mechanical properties, functional structure, functional adaptation, *Biomechanics: Its Foundations and Objectives*, eds., Y.C. Fung, N. Perrone, and M. Anliker, Prentice-Hall, Englewood Cliffs, 1972.

23. Mattheck, C., and Huber-Betzer, H., CAO: Computer simulation of adaptive growth in bones and trees, *Computers in Biomedicine*, Computational Mechanics Publications, ed. K.D. Held, C.A. Brebbia, and R.D. Ciskowski, 243-252, 1991.

24. McNamara, B.P., Prendergast, P.J., and Taylor, D., Prediction of bone adaptation in the ulnar-osteotomized sheep's forelimb using an anatomical finite element model, *J. Biomedical Eng.*, 1992, **14**, 209-216.

25. Oden, Z.M., Hart, R.T., Forwood, M.R., and Burr, D.B., implementation of a cell based mechanistic model for functional adaptation of bone,*Proc. Second World Congress of Biomechanics*, July 10-15, 1994, Amsterdam, p. II-55.

26. Pauwels, F, *Biomechanics of the Locomotor Apparatus: Contributions on the Functional Anatomy of the Locomotor Apparatus*, Springer-Verlag, Berlin, 1980.

27. Roesler, H., Some historical remarks on the theory of cancellous bone structure (Wolff's Law), *Mechanical Properties of Bone*, ed., Cowin, S.C., American Society of Mechanical Engineers, New York, N.Y., 27-42, 1981.

28. Sadegh, A.M., Luo, G.M., and Cowin, S.C., A Boundary Element Method for bone ingrowth at the bone-implant interface, *Computers in Biomedicine*, Computational Mechanics Publications, ed. K.D. Held, C.A. Brebbia, and R.D. Ciskowski, 207-218, 1991.

29. Treharne, R.W., Review of Wolff's law and its proposed means of operation, *Orthopaedic Review*, 1981, **10**, 35-47.

30. Umetani, Y., and Hirai, S., An adaptive shape optimization method for structural material using the growing—reforming procedure. Joint JSME-ASME Applied Mechanics Western Conf., 1975, 359.

31. Wolff, J. *Das Gesetz Transformation der Knochen*, Hirschwald Verlag, Berlin, 1892.

32. Wolff, J., *The Law of Bone Remodeling*, translated to English by P. Maquet and R. Furlong, Springer-Verlag, Berlin, 1986.

Acknowledgments

This research has been supported, in part, by a grant from the NIH (AR40655).