



Gemunu Gunaratne

Using Vibrational Assessment To Estimate Bone Strength

Gemunu Gunaratne
Department of Physics

Abstract—Astronauts in flight tend to lose bone mass, some suffering damage to their bones. New non-invasive tools are available to estimate bone damage during space flight. UH researchers have developed a program designed to analyze and quantify possible types of damage. They are using “extreme value statistics” to estimate loss of strength in bone. *Photo—Downtown Houston, within sight of the University of Houston campus.*

LOSS OF BONE MASS AND THE RESULTING DAMAGE TO BONE are serious consequences of manned space flights.¹⁻³ Although rigorous exercise regimens and the use of new powerful therapies can stabilize bone loss, the level and type of damage is subject dependent; hence, some astronauts may be expected to suffer detrimental long-term residual effects. Moreover, therapies often have adverse side-effects and should be administered with great care because indiscriminate use can exacerbate bone damage.⁴ Hence, the availability of easily implemented, reliable diagnostics of mechanical properties of bone can be extremely helpful in timely and optimal therapeutic intervention. UH researchers are analyzing the feasibility of using vibrational assessment to identify new, non-invasive diagnostic tools that can be used to estimate bone damage during space flight.

Currently, bone density tests and ultrasonic scans are the principal clinical means for detecting age-related osteoporosis.

However, they only partially account for bone strength and likelihood of fracture.⁴ One underlying reason is that bone consists of two distinct segments with vastly different mechanical characteristics. They are the outer solid bone (the cortex) and the inner porous region (trabecular bone). Moreover, age-related damage modalities in the two segments are vastly different. Consequently, it is a non-trivial task to identify reliable surrogates for bone strength. Researchers expect that vibrational assessment of bone—using characteristics such as linear and nonlinear response functions, resonant modes—can provide a comprehensive profile of its mechanical properties. Although such vibrational methods are routinely used for damage assessment in engineering structures, the fact that both cortical and trabecular components are important for load transmission complicates the interpretation of results.

In order to identify an optimal class of diagnostics for the strength profile of bone, it is necessary to implement a pro-

gram where changes in strength caused by all possible types of damage are analyzed and quantified. It is extremely difficult, however, to conduct such an analysis using clinical or experimental studies because no protocols are known that can control individual facets of bone. Our approach to this problem is predicated on an analysis of mathematical models. The conclusions are then validated by two independent means. The first uses anatomically accurate computer models constructed from digitized images of human bones. The second involves experiments conducted by a colleague, M. Liebschner of the Department of Bioengineering, Rice University.

Anatomy of Bones

Bone is a composite of hydroxyapatite crystals and collagen fibers. The axial and cross sectional dimensions of hydroxyapatite crystals are ~ 20 and 5 nm, respectively. The crystals and collagen fibrils typically lie along the length of a bone; thus bone material is anisotropic.⁵ The porous domains consist of trabecular elements whose length and cross section are of the order of 1 mm and 0.1 mm, respectively, and typically exhibit a structure reminiscent of a disordered cubic network (see Fig. 1).

Material turnover is critical in maintaining the quality and strength of bone. During aging, micro-fractures, which occur during routine activity, are repaired by resorption (through osteoclasts) and regeneration (through osteoblasts).⁵ Because of inactivity during space flight and due to reductions in sex-steroid hormones (estrogen and testosterone), bone loses material from its surface at an excessive rate. If the connectivity of trabecular bone were to remain unchanged during this degradation, it would be possible to regenerate its strength with rigorous exercise regimens and therapy following return to earth. However, this is not the case if there is loss of connectivity.

Methodology

The proposed research is aimed at identifying surrogates for bone strength. Note however that *in vivo* measurements can only be made on the whole bone and not on the cortical and trabecular segments. In order to use vibrational assessment to estimate bone strength, it is thus necessary to be able to calculate vibrational responses of cortical and trabecular bone from measurements made on the whole bone. The next step is to determine how the strength of trabecular and cortical components can be estimated from their responses to external vibrations. The methods used to implement these are described next.

Vibrational Assessment

Vibrational analysis was first used in orthopedics in 1932, by Lippman,⁶ who used his finger to percuss the femur, humerus, and clavicle of fractured patients to assess healing. He used a stethoscope to pick up the response of the bone and concluded that pitch and quality changes resulted from free vibration of separate fragments. Thus a bone state was identified anywhere between a healed fracture or an incomplete union.

In 1970, Jurist exploited the fundamental equation describing a vibrating bar to relate the resonant frequency times the bone length (F_0L) to the Young's modulus, a value which it was hoped would correlate with resistance to fracture.⁷ He used an apparatus, which applied a vibratory stimulus via the olecranon process and monitored the response at the distal end of the ulna using a small instrumentation accelerometer. He found the reproducibility of the F_0L determination was at 5 percent precision, if forearm position and muscle tension were standardized. He concluded, therefore, that acoustic analysis has potential value to screen for metabolic bone disease, early detection of osteoporosis, and evaluation of general bone health (including responses to therapeutic treatments) because the elastic response could be predicted *in vivo*.

In a subsequent study involving 480 volunteers, Jurist and Diamond found that a normal subject's F_0L increases beginning at age 6 for approximately 15-20 years, following which there is a steady decrease in its value.⁸ In males, the rate of reduction is uniform between 25 and 80 years. Females older than 45 years showed a bimodal distribution. In the first group, F_0L values decreased at approximately the same rate as men. In the second group, F_0L declined rapidly after 45 years of age. By age 60 most individuals in the second group were diagnosed as osteoporotic. The F_0L diagnostic was shown to provide a 82 percent effective discrimination between women with symptomatic osteoporosis and their age-matched controls.⁹ The results indicate that vibrational analysis can provide early diagnosis on loss of bone strength.

Differentiating Responses of Cortical and Trabecular Bone

Our approach to differentiate the acoustic responses of various structural levels from those of the whole bone will be adapted from techniques used in undersea petroleum exploration. It is based on an algorithm for analyzing non-linear inverse scattering problems. These series methods were first introduced and adapted to exploration seismology in the early 1980s and practical algorithms first demonstrated in 1997.¹⁰

Inverse scattering series methods were first developed by Moses,¹¹ Prosser,¹² and Razavy¹³ and were transformed for application to a multi-dimensional earth and exploration seismic reflection data by Weglein et al.¹⁴ and Stolt and Jacobs.¹⁵ The inverse scattering series is the only multi-dimensional direct inversion formalism that can accommodate arbitrary heterogeneity directly in terms of the reference medium, through its Green function G_0 , i.e., with estimated rather than actual propagation, G . Serious conceptual and practical hurdles in the theoretical evolution have been overcome through algorithm development, and robust industrial application of the inverse scattering methods. This new acoustic signal processing method can be expected to have high potential for the medical field and in particular for the non-destructive diagnostic of bone.

For vertebral bone, the separate domains are (1) trabecular bone, (2) cortical bone, and (3) the outer skin and muscle layers. An ultrasonic wave sent into the body experiences multiple reflections at the skin/cortical and cortical/trabecular interfaces due to impedance mismatch. The measurement at

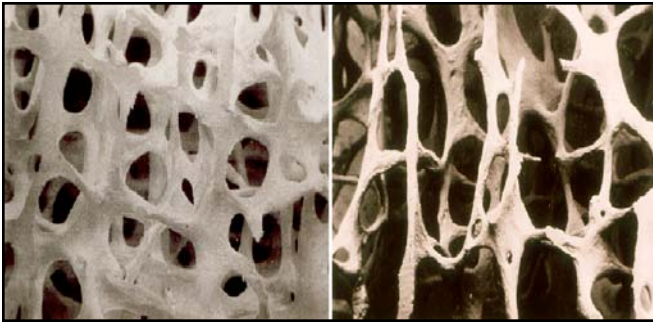


Figure 1. Scanning electron micrographs of a normal and osteoporotic bone, illustrating age-related changes including loss of connectivity

any receiver combines components that have reflected once and those from multiple reflections. The latter include “free surface multiples” which have reflected from the skin layer (from the inside) and “internal multiples” which have had multiple reflections within the bone. We can extract each of these components by analyzing signals from *multiple receivers* and *multiple sources* through the inverse scattering series.¹⁰ Researchers are currently developing methods to extract response functions of cortical and trabecular bone using signals collected at multiple receivers. These studies are performed on computer models constructed from digitized images of cadaveric samples that include both cortical and trabecular segments. The input data are the signals received at neighboring locations due to sinusoidal driving at a point.

Vibrational Assessment and Strength of Trabecular Bone

The Mathematical Model is introduced to represent rod-like trabecular bone (Fig. 1) as a cubic network of struts and nodes.¹⁶ A disordered network is constructed by randomly displacing nodes on a cubic grid. In porous bone, trabecular elements do not pivot freely; changing angles between adjacent trabeculae requires energy. Bond-bending terms in the potential energy model this effect. An externally imposed strain on

such a configuration increases its potential energy via a combination of stretching ($1/2 k\delta r^2$) and bond bending ($1/2 \kappa\delta\theta^2$) contributions. Here k and κ are the relevant linear elastic moduli; δr and $\delta\theta$ are changes in the length of a strut and in the bond angle between adjacent struts respectively. Assigning random values for k and κ models the variability in thickness of trabecular elements.

Experiments on porous bone have demonstrated that, while breaking stress decreases significantly with aging, the corresponding strain remains nearly unchanged; we thus have a *strain-based* failure criterion for struts and bonds. During compression, we remove any failed strut and all bonds associated with it. When a bond fails, we remove its weaker neighbor (i.e., the strut with smallest elastic constant) from the network. We implement individual architectural changes as follows.

Random elimination of struts represents isotropic removal of trabecular elements. We assume that remaining struts retain their elastic moduli. In this scenario, the fraction of struts removed quantifies the level of osteoporosis.

A uniform reduction in the elastic moduli of all struts models trabecular thinning. Fractional reduction in elastic modulus gives the level of osteoporosis.

We can introduce anisotropy by directional reduction in the removal of struts and/or reduction in elastic moduli. Levels of trabecular removal and thinning estimate osteoporosis. It is thus possible to analyze consequences of changes in individual architectural characteristics of (the model) trabecular bone. Consequences of changes in combinations of architectural changes can also be easily studied. We describe the most significant conclusions made on the basis of this model.

The Most Damaging Architectural Change

We have shown that reduction in fracture load is attributed to trabecular perforation; hence, loss is significantly larger than that caused by equivalent changes in other architectural characteristics (e.g., thinning).^{17,18} This assertion has an interesting consequence. A network segments and its peak load vanishes

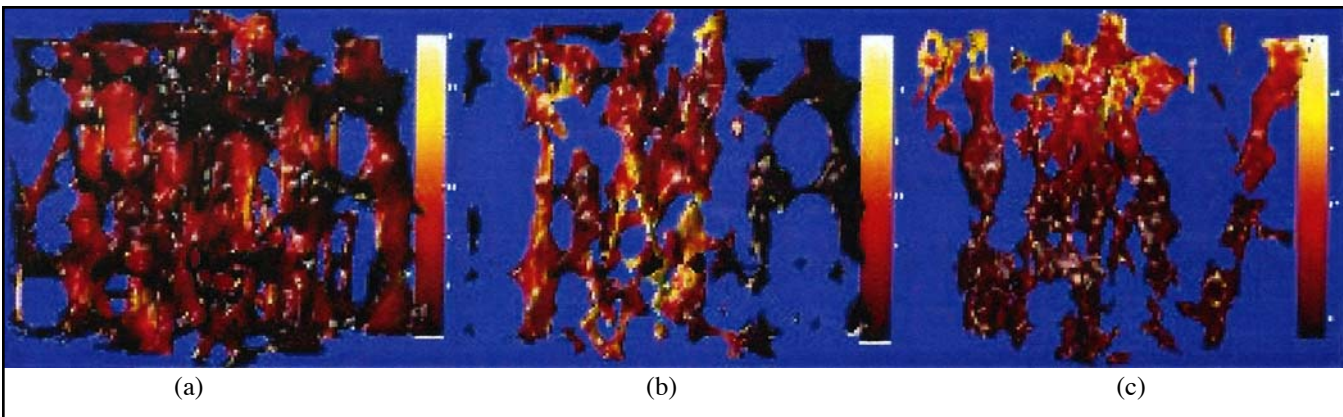


Figure 2. Stress distributions on (a) healthy and (b) osteoporotic samples of trabecular bone. Note that only a small “stress backbone” is used for load transmission in (b). In contrast, when the osteoporotic bone is subjected to vibrations (at resonance), all elements on the top layer are excited. This observation is the basis for the claim that Γ is a reliable surrogate for bone strength.

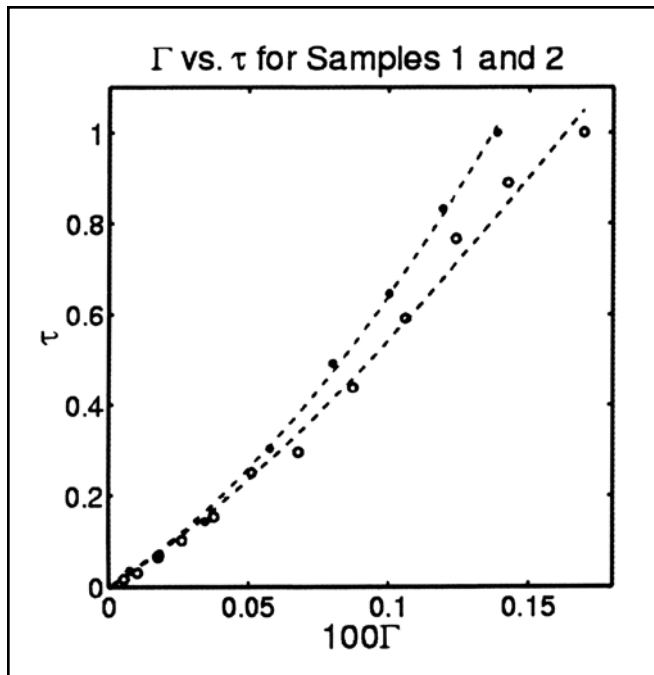


Figure 3. The relationship between Γ and τ (Equation 1) for two computer models constructed from digitized images of cadaveric trabecular bone. As predicted theoretically, they converge for small values of Γ (i.e., for weak bones). This observation suggests that Γ can be used as a non-invasive diagnostic for bone strength.

when we remove a fraction ν_0 of elements randomly. The value ν_0 , known as the bond-percolation threshold, depends on the class of network. Thus, *the strength of trabecular bone will vanish at a finite density*. Consequently, an almost universally accepted power-law relationship between the density and strength of trabecular bone can only be approximate.^{19,21} The deviation will be most dramatic for weak bone, where diagnostics are most needed.²²

Only a Small Stress Backbone Used in Load Transmission

Consider a network with a fraction ν of elements removed. As ν increases, we expect occasional long fractures, which will significantly reduce the strength of the network. In particular, they prevent large swaths of the network (such as elements immediately above and below the fracture) from transmitting stress. For sufficiently large values of ν , only elements in a small “stress backbone” transmit an externally applied load, the remaining regions are highly under-utilized. It is thus conceivable that a network becomes increasingly inefficient as ν increases; this inefficiency is possibly the primary cause of bone degradation (see Figs. 2(a) and 2(b)).²³ Model computations have confirmed these expectations and have shown that other architectural changes, like trabecular thinning and anisotropy, only incrementally change the inefficiency.¹⁷ We have also observed this progressive inefficiency in anatomically accurate computer models.²⁴

Linear Response as a Surrogate for Bone Strength

Since the strength of a network depends primarily on its efficacy (i.e., what fraction of trabeculae are used in transmitting externally applied loads), we hypothesize that fracture load increases with the fraction of elements that belong to the stress backbone. Thus, we need to estimate the number of elements in the stress backbone and the total number in the network. We have shown that we can estimate these quantities from the elastic modulus $\chi(0)$ and the linear response of the network $\chi(\Omega)$ at the resonance frequency Ω . Consequently, we expect $\Gamma = \chi(0)/\chi(\Omega)$ to be a surrogate for the *fractional loss of strength* of a network. Analysis shows that:

$$\tau = a\Gamma + h(\Gamma), \quad (1)$$

where τ denotes the *fractional reduction of bone strength from its peak value* (i.e., from young adulthood).²³ The nonlinear term $h(\Gamma)$ depends on model parameters (e.g., the ratio of the elastic and bond-bending coefficients) while a depends on more general characteristics like the class of network. When we consider removal of elastic elements in isolation, ignoring factors like trabecular thinning, $a = M(1 - \nu_0)$ where M denotes the number of layers in the network in the direction of driving. Results from model networks (Fig. 3) validate these assertions. The fit near the origin is independent of $h(\Gamma)$. The calculation of Γ does not require comparisons with a sample population and can form the basis for a new diagnostic for the strength of trabecular bone.

Vibrational Assessment and Strength of Cortical Bone

Accumulation of long micro-fractures is one of the principal causes for weakening of cortical bone. Such long fractures grow under stress and make the material brittle. A part of the study is to model implications and signatures of this form of damage. Healthy cortical bone is represented by a complete network representing a block of uniform material and damaged samples by blocks with 100 μm scale “fractures” whose sizes and locations are chosen randomly. Higher densities and/or larger mean sizes of fractures models increasing levels of damage.

We are conducting vibrational analysis on these model networks to quantify the damage caused by increasing occurrences of micro-fractures. Consider a single large fracture in the middle of a network. The high frequency response will not change because attenuation prevents the signal from reaching the fracture. On the other hand, low frequency responses will change because of reductions in the stress backbone. Thus, fractures will change the spectral energy distribution.

Reductions in bone strength depend on the statistics of extreme events. We are using “extreme value statistics” to identify additional characteristics to estimate loss of strength in bone.²⁵

References

- ¹W. S. S. Jee, T. J. Wronsky, E. R. Morey, and D. B. Kimmel, “Effects of Space flight on Trabecular Bone in Rat,” *Am. J. Physiol.* 244 (1983): R310-14.

²V. S. Oganov, A. I. Grigor'ev, L. I. Voronin, A. S. Rakhmanov, A. V. Bakulin, V. S. Schneider, and A. D. LeBlanc, "Bone Mineral Density in Cosmonauts after Flights Lasting 4.5-6 Months on the Mir Orbital Station," *Aviaskosmicheskaja I Ekologicheskaja Meditsina* 26 (1997): 20-24.

³E. Zerath, C. Nogues, M. Borne, and P. Sourdain, "Bone Effects of 13 Days of Weightlessness on Rat and Monkey: Some results on Biocosmos 1887 and Ground Simulations," *Physiologist* 33 (1990): S94-95.

⁴R. S. Weinstein, "True Strength," *J. Bone. Miner. Res.* 15 (2000): 621-25.

⁵Y. C. Fung, *Biomechanics: Mechanical Properties of Living Tissue*, New York: Springer-Verlag, 1993.

⁶R. K. Lippman, "The Use of Auscultatory Percussion for the Examination of Fractures," *J. Bone and Joint Surgery* 14 (1932): 118.

⁷J. M. Jurist, "In-vivo Determination of the Elastic Response of Bone: I. Method of Ulner Resonance Frequency Determination," *Phys. Med. Biol.* 15 (1970): 417-26.

⁸J. M. Jurist and A. M. Dymond, "Reproducibility of Ulner Resonant Frequency measurement," *Aerosp. Med.* 41 (1970): 875-78.

⁹K. Hasegawa, C. H. Turner, R. R. Recker, E. Wu, D. B. Burr, "Elastic Properties of Osteoporotic Bone Measured by Scanning Acoustic Microscopy," *Bone* 16.1 (Jan. 1995): 85-90.

¹⁰A. B. Weglein et.al., "Inverse Scattering Series and Seismic Exploration," *Inverse Problems* 19 (2003): R27-R83.

¹¹H. E. Moses, "Calculation of Scattering Potential from Reflection Coefficients," *Phys. Rev.* 102 (1956): 559-67.

¹²R. T. Prosser, "Formal Solutions of Inverse Scattering Problems," *J. Math. Phys.* 10 (1969): 1819-22.

¹³M. Razavy, "Determination of Wave Velocity in an Inhomogeneous Medium from Reflection Data," *J. Acoust. Soc. Am.* 58 (1975): 956-63.

¹⁴A. B. Weglein, F. A. Gasparotto, P. M. Carvalho, and R. H. Stolt, "An Inverse Scattering Series Method for Attenuating Multiples in Seismic Reflection Data," *Geophysics* 62 (1997): 1975-89.

¹⁵R. H. Stolt and B. Jacobs, "Inversion of Seismic Data in a Laterally Heterogeneous Medium," *SEP Rep.* 24 (1980): 135-52.

¹⁶G. H. Gunaratne, C. S. Rajapakse, K. E. Bassler, K. K. Mohanty, and S. J. Wimalawansa, "Model for Bone Strength and Osteoporotic Fractures," *Phys. Rev. Lett.* 88 (2002): 068101.

¹⁷Y. Song, M. A. K. Liebschner, and G. H. Gunaratne, "A Study of Age-Related Architectural Changes that are Most Damaging to Bones," *Biophysical J* 87 (2004): 3642-47.

¹⁸J. S. Espinoza Ortiz, C. S. Rajapakse, and G. H. Gunaratne, "Strength Reduction in Electrical and Elastic Networks," *Phys. Rev. B.* 66 (2002): 144203.

¹⁹G. H. Bell, O. Dunbar, J. S. Beck, and A. Gibb, "Variations in Strength of Vertebrae with Age and their Relation to Osteoporosis," *Calcified Tissue Research* 1 (1967): 75-86.

²⁰D. R. Carter and W. C. Hayes, "The Compressive Behavior of Bone as a Two-Phase Porous Structure," *J. Bone*

and Joint Surgery 59 (1977): 954-62.

²¹J. C. Rice, S. C. Cowin, and J. A. Bowman, "On the Dependence of the Elasticity and Strength of Cancellous Bone on Apparent Density," *J. Biomechanics* 21 (1988): 155-68.

²²C. S. Rajapaksa, J. S. Thomsen, J. S. Espinoza-Ortiz, S. J. Wimalawansa, E. N. Ebbesen, L. Mosekilde, and G. H. Gunaratne, "An Expression Relating Breaking Stress and Density of Trabecular Bone," *J. Biomechanics* 37 (2004): 1241-49.

²³G. H. Gunaratne, "Estimating the Strength of Bone Using Linear Response," *Phys. Rev. E.* 67 (2002): 061904.

²⁴M. A. K. Liebschner, R. Muller, C. S. Rajapakse, S. J. Wimalawansa, and G. H. Gunaratne, "Testing Two Predictions for Fracture Load Using Computer Models of Trabecular Bone," *Biophysical J (accepted)*.

²⁵E. J. Gumbel, *Statistics of Extremes*. New York: Columbia University Press, 1958.

Publications

Alejandro-Quinones, A. L., K. E. Bassler, M. Field, J. McCauley, M. Nicol, I. Timofeyev, A. Torok, and G. H. Gunaratne. "Theory of Fluctuations in Stock Prices," *Physica A (accepted)*.

Gunaratne, G. H., J. L. McCauley, M. Nicole, and A. Torok. "Variable Step Random Walks and Self-Similar Distributions," *J. Stat. Phys. (accepted)*.

Liebschner, M. A. K., R. Muller, C. S. Rajapakse, S. J. Wimalawansa, and G. H. Gunaratne. "Testing Two Predictions for Fracture Load Using Computer Models of Trabecular Bone," *Biophysical J. (accepted)*.

Presentations

Gunaratne, G. H. "How to Find out When Bones May Break," Boston University, Feb. 2004; Northwestern University, Feb. 2004; University of Connecticut, April 2004

—. "Summer School for Advanced Electronic and Bio-Materials," International Center for Materials Physics, Chinese Academy of Sciences, Shenyang, China, June 2004; Dalian University, China, June 2004.

—. "Characterization of Complex Patterns," Summer School for Advanced Electronic and Bio-Materials, International Center for Materials Physics, Chinese Academy of Sciences, Shenyang, China, June 2004; 8th US National Congress on Computational Mechanics, Austin, TX, July 2005.

—. "Random Walks and Anomalous Diffusion," Summer School for Advanced Electronic and Bio-Materials, International Center for Materials Physics, Chinese Academy of Sciences, Shenyang, China, June 2004.

—. "Variable Step Random Walks and Self-Similar Distributions," Fluctuation and Noise, Annual Meeting of the International Society for Optical Engineering, Austin, TX, May 2005.