An Investigation of the High Cycle Fatigue Behavior of Bovine Trabecular Bone

By

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Submitted to the Department of Materials Science and Engineering in Partial
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ABSTRACT

Fractures can be caused by fatigue loading due to prolonged exercise and age-related
fragility. Fatigue loading causes microdamage in bone that leads to both a loss of
stiffness and strength. Some engineering materials, such as steels, have a fatigue limit,
which is represented by a stress plateau in the stress-life (S-N) curve. When loaded to
levels below the stress plateau, these materials have an infinite fatigue life. Other
materials, such as aluminum, do not exhibit a fatigue limit. For these materials, the
endurance limit is defined as the stress amplitude corresponding to a somewhat arbitrary
large number of cycles of fatigue (e.g. various texts suggest $10^6$ to $10^8$ cycles ). In
previous work on compressive fatigue of bovine trabecular bone, it was hypothesized that
there was a fatigue limit at a normalized stress, $\Delta \sigma/\sigma_{p}$, of approximately 0.0035. This
study tested this hypothesis by fatigue testing bovine trabecular bone loaded to one of
four normalized stresses ranging from 0.0015 to 0.0035. Failure was defined as a 10%
loss in the secant modulus of the specimen. The data show that the rate of decrease of
modulus reduction per cycle increased with increasing normalized stress. A fatigue limit
in bovine trabecular bone was not found. While a threshold below which the fatigue life
is infinite was not found, an endurance limit corresponding to $10^6$ cycles to failure was
found at a normalized stress of about 0.00137. The study also showed that normalized
secant modulus decreased with normalized number of cycles in the same manner for all
normalized stresses.

Thesis Supervisor:  Lorna J. Gibson
Biographical Note

Abel Hastings attended Hampshire College in Amherst, Massachusetts from 1991 to 1995. While there he completed research in physiology, biomechanics, and exercise science. In 1994, he won a Lemeson scholarship to pursue his research into the interaction of high-level kayakers with their kayak paddle. This research included the design and fabrication of a data acquisition system to help re-design the paddle blade based on athlete performance. In 1995, Abel presented this research at the National Conference on Undergraduate Research.

From 1995 to 2000, he pursued a career as an athlete, twice qualifying for the US Team in marathon kayak. He represented the United States in international and World Cup competition in 13 countries.

From 2001 to 2002, he completed the Master of Engineering program at the Massachusetts Institute of Technology. His research into microfabrication culminated in a thesis entitled “An Assessment of Various Metallic Microfabrication Techniques.” In addition, Abel represented the Massachusetts Institute of Technology at the 2002 Foundry Education Foundation Conference.

From 2002 through 2003, Abel worked with Lorna Gibson to study the high cycle fatigue behavior of bovine trabecular bone. This research was conducted as a continuation of several years of research completed by Dr. Gibson and many other esteemed researchers and graduate students.
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Lorna Gibson has been an wonderful advisor, teacher and friend for the past three years. When I arrived at MIT I was inexperienced in engineering discipline due to my previous education in physiology. Lorna is a challenging yet encouraging professor and advisor who inspires inquisitive enthusiasm in students. She has allowed me to explore engineering through success and failure and for this I am very appreciative.

The cellular solids group at MIT is made of many talented individuals, with their own fortes and experiences. I would like to especially thank Dr. Fergal O’Brien for his technical guidance and advice. In addition, I would like to thank Dr. Debbie Chachra for helping with data analysis. I would also like to thank Dr. Tara Moore for her assistance in procedural continuity.

Sample preparation took place at the Beth Israel Orthopedics and Biomechanics Laboratory. I would like to thank Beth Israel and the staff of the OBL for their time, space, and effort. Robert Adamson deserves special thanks for helping with sample preparation.

There are a few people at MIT outside of the cellular solids group who deserve acknowledgement too. Tim Hanlon helped with troubleshooting Instron nuances on many occasions. Fred Cotes and David Robertson helped fabricate mechanical and electronic devices that were crucial to this study’s success.

Finally I’d like to thank my family who cheered me on, even when I wasn’t cheery. They’ve provided me with lots of support and guidance. My wife Jennifer has been my biggest supporter and my best friend. To her, I owe the world.
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Chapter 1: Motivation

It is believed that microdamage of bone may be the result of the repetitive loading of day-to-day activities such as walking. Microdamage can take the form of small cracks or diffusely damaged areas [1]. If not repaired, microdamage has been shown to cause the bone to decrease in stiffness and strength [2]. With continued loading microdamage may coalesce and subsequently cause fracture. While a small amount of microdamage seems to be present in vivo, in healthy bone most microdamage is typically resorbed and remodeled into fracture free bone tissue. Some studies suggest that microdamage may be the stimulus for bone remodeling [3]. The control mechanism that remolds bone is limited in its capacity to repair microdamage, which can result in both stress fractures and age-related fragility fractures. Knowledge of the method by which microdamage accumulation causes the degradation of bone may help point toward solutions for related illnesses such as osteoporosis and microgravity-related bone loss. For example, the study of fatigue in bone can make important contributions to the effort to reduce and treat osteoporotic fragility fractures through treatments such as therapeutic exercise and drug based treatments. Understanding rates and mechanisms of fracture propagation can make improvements in our analysis of the viability of therapeutic exercise as well as help determine an optimal regimen. The understanding of bone mechanics can also play a role in the selection of drug based treatment regimens aimed at slowing or stopping bone loss or point towards new drug designs made to counteract the effects of osteoporosis. A model of the implications of compromised bone may help guide the protocol for long duration space exploration which, in part, is limited due to microgravity-related bone loss complications. Fatigue studies will also allow us to test the validity of many of the
assumptions made in the modeling methods used in computational mechanics. In turn, these models can be used to analyze the risk of fracture for people with bone illnesses or astronauts attempting new missions in space.
Chapter 2: Literature Review

2.1. Bone Structure

The bones of the human skeleton provide structure, support, protection and mineral storage for the human body [4]. Each bone is comprised of two types of bone: compact and cancellous. Compact bone is almost fully dense, with a porosity of less than 15% [5]. Cancellous bone is made up a network of struts and plates, called trabeculae, with a porosity of greater than 50% [5]. Cancellous bone is found at the ends of the long bones and in the core of the vertebrae; it is always surrounded by a shell of compact bone [4]. The two types of bone, compact and cancellous, are sometimes sandwiched together - compact bone on the exterior surface, cancellous in the inside - as in the skull and the pelvis. Much like an engineering sandwich panel, the two work together to optimize mechanical properties.

The trabeculae of cancellous bone (sometimes called trabecular bone) are geometrically arranged in a manner that corresponds with the loading requirements of the particular region of the bone: the trabeculae are aligned with the directions of principal stress and the trabecular bone is denser in regions of higher stress [6]. The trabeculae are typically on the order of 100μm in diameter and 600μm in length [7]. The trabeculae are perforated with canals (called canaliculi) that lead to lacunae, which are pockets within which osteocytes live [4].

There are three main cell types within bone: osteocytes, osteoblasts, and osteoclasts. Osteocytes are the bone cells that account for most of the cellular population inside the
bone tissue. They have long processes that extend though the canaliculi. Osteocytes maintain and monitor the mineral and protein content of the surrounding bone. They are responsible for intercellular communication. Osteoblasts are responsible for promoting the solidification and deposition of the mineral that make up solid bone through the deposition of extracellular matrix. Osteoclasts are related to monocytes. They are very large cells, often containing 50 or more nuclei. During resorption, they release proteolytic enzymes and acids that dissolve the crystallized hydroxyapatite [8].

Remodeling is the method by which bone is maintained. Remodeling is the cycle of resorption of bone tissue followed by the deposition of new mineralized tissue by the specialized cells that reside in bone. Remodeling allows the bone to slowly adjust to new loading patterns, such as a change in gait, or a repetitive activity. This cycle also allows the bone to repair itself in the event of a fracture. In fact, studies suggest that microcracks are present in all bone and may even be the catalyst for remodeling. Microcracks are cracks in bone that are not long enough to, by themselves, propagate global fracture. Similarly, bone may contain groupings of microfractures which is generally termed microdamage. Some studies estimate that 0.5 to 2.5 cracks/mm² are present in vivo [9]. An exact balance between osteoclast activity, called resorption, and osteoblast activity, called osteogenesis, is required to yield a zero net loss of bone material. The process of remodeling carries on throughout the lifecycle of the human. A hypothesis for the mechanism by which the microdamage is repaired has been offered by Taylor [3]. His model suggests that crack growth rate is determined by crack length and shows a minimum at a specific crack length. This rate of crack propagation can be combined with
repair rate to show a “lazy band” of crack lengths within which crack lengths can be maintained. The predicted stable crack length ranges from 42µm under stress of 15MPa to 82µm under a stress of 35MPa. This model agrees well with data from Lee, who found a majority of crack length in vivo were between 38 µm and 62 µm. [3].

2.2 Osteoporosis

While there is a wide array of diseases that affect the structural integrity of bone this study will focus much of its attention on osteoporosis because of its pervasiveness, crippling affect on the patient, and its root in the structure of the bone itself. Much of the material discussed in this manuscript has implications for overuse related stress fractures as well. While the overuse related stress fracture has a significantly different population at risk than osteoporosis, the structural causes of the two diseases are similar: both are cases of repeated mechanical stresses on the bone which, over time, eventually exceed the mechanical strength of the tissue.

Osteoporosis, Latin for porous bone, is a disease that is characterized by low bone mass and causes a structural weakening of bone tissue leading to bone fragility and a decreased resistance to fracture. Clinically, osteoporosis is defined as a bone mineral density T score of –2.5, which is a bone mineral density 2.5 standard deviations below that of a young, healthy individual of the same gender and ethnicity.

There is no single cause associated with osteoporosis. Risk factors increasing susceptibility include: family history of osteoporosis, advanced age, and sex – women are
more likely to develop osteoporosis in part because of connection between estrogen and bone mineralization. During menopause, a reduction in estrogen causes a decrease in the mineralization of new bone [10]. Osteoporosis is a disease of the remodeling cycle of bone. Normally bone is continually remodeled with a zero net loss in bone mass. Bone tissue is resorbed and re-deposited in accordance with the structural requirements of the anatomical location [3, 6]. In osteoporosis, the mechanism responsible for mineralizing new bone falls behind, leaving a net loss of bone over time. In trabecular bone, the effect of osteoporosis is two fold - the net loss of bone causes a thinning of trabecular struts which is exacerbated by the loss of individual trabeculae [11]. The result is weak bone that is more susceptible to traumatic fractures as well as cyclic stress related fragility fractures [12].

Osteoporosis is a highly prevalent disease among the world’s aging population. In the US, an estimated 10 million people have osteoporosis, and another 34 million have osteopenia, or low bone mass that has not yet reached the clinical definition of osteoporosis. Women are four times more likely to get osteoporosis than men [13]. Fifty percent of women and twenty five percent of men over the age of 50 will suffer an osteoporosis related fracture. Osteoporosis costs the US an estimated $17 Billion in 2001 and is on the rise [10]. As our aging and elderly population grows, so will the prevalence of osteoporosis and the cost of treatment.
The most common fractures associated with osteoporosis are those of the hip, spine, wrist and ribs. Fractures can be the result of a sudden trauma, such as a fall, or of repeated loadings from the activities of daily living, over time.

Hip fractures are commonly the result of trauma. In a small fraction of the cases, patients report that they believe that their hip fracture caused them to fall, suggesting that the hip failed in fatigue prior to the fall. There are an estimated 300,000 hip fractures annually in the US costing an estimated $5.5 to $15 billion [14, 15]. In 90% of all cases, hip fractures are the result of a fall from standing height or less [10]. Not surprisingly, wrist fractures are often the result of the same traumatic accident. Hip fractures can sometimes prove fatal; estimates suggest a mortality rate of 2.5% during initial hospitalization [14]. When not fatal, they are responsible for reducing the life expectancy of the patient by as much as 1.8 years [14]. In 10-20% of cases, the patient will die within a year [10].

Vertebral and rib fractures are typically non-traumatic, meaning they develop over time rather than in a single incident. There are an estimated 700,000 vertebral fractures diagnosed in the US annually [15]. Pain associated with vertebral fractures can often go unchecked for long periods. These fractures are often only diagnosed as a result of routine radiology, and even then, only one third of abnormal radiographs lead to medical attention. This is because vertebral fractures rarely require significant acute medical attention; in fact, only 10% require hospital admission [10]. Because these fractures progress slowly, and with comparatively benign symptoms, the medical community often pays less attention to them than hip fractures. However some experts estimate that the
lifetime adverse affects of a vertebral fracture may be just as severe as that of the hip fracture. In fact, because of decreased activity levels, patients who suffer vertebral fracture have an elevated mortality rate due to cardiovascular and pulmonary diseases that extend for years after the fracture. In addition, a first fracture elevates the patient’s risk of a second by as much as 50-100% [10].

Because of the importance of the vertebral fracture as a public health concern and because of the structural nature of fragility fracture, this study will focus on the mechanism of fragility fracture and fatigue fracture. Fragility fractures, such as osteoporotic vertebral fractures, are due to repetitive minor traumas inflicted onto the microstructure of the bone. In a healthy individual, these traumas heal before the number of them becomes great enough to compromise the structural integrity of the bone. In fact, these fractures are thought to catalyze the normal resorption and deposition of new bone material [16]. This continual remodeling of the bone keeps the bone healthy and may adjust to changes in loading patterns. In older adults the accumulation of microdamage outpaces the remodeling and leads to reduced bone quality. Reduced quality coupled with a loss of bone mineral density (BMD) can put patient at risk of fracture in the case of a relatively minor fall or blow.

As a side note, it is important to notice that the fragility fracture, while most present in elderly patients, does have a close connection with stress fractures in younger people. Army recruits and runners are especially prone to fractures of the feet. Under normal conditions and activity levels, our bodies are able to repair microdamage at
approximately the same rate as the damage accumulates. When we increase the loading on our bones, the microdamage can accumulate faster than our normal remodeling can repair it. The result is the coalescence of microdamage, which can allow fractures to propagate. It is clear that while the underlying mechanism between osteoporosis and stress fractures may be very different, the resulting compromised mechanics leading to fracture are very similar. While this manuscript may be aimed at osteoporosis it stands to reason that much of the subject could be directly related to stress fracture.

It has been hypothesized that remodeling is instigated by loading of the bone itself. There are two possible signals that could produce accelerated remodeling: mechanotransduction or microdamage. It has been shown that increased microdamage due to cyclic stress is well correlated with increased resorption. These resorption spaces were, in fact, in direct association with the microcracks themselves [17]. This would seemingly point toward low-stress exercise as the treatment for osteoporosis. This hypothesis is supported by the finding that rates of hip fracture are also higher in urban areas. Urbanization is implicated in a lifestyle of decreased activity compared with rural areas. Similarly, an article by Karlsson probed the long term effect of exercise on fragility bone fractures in men. While avid exercisers were shown to have a lower risk of fracture the beneficial effects were reversed after the abandonment of exercise [18]. These investigations underscore the importance of investigating the fracture mechanics and low-stress, high cycle fatigue behavior of trabecular bone.
It has been estimated that vertebral trabecular bone carries 90% of the load on the vertebra [19]. Osteoporotic bone has a compromised microstructure. As remodeling takes place, diseased bone thins trabeculae as well as reduces the number of trabeculae. Studies have shown that this loss of trabeculae is a permanent loss. Even if the remodeling can be corrected and bone loss is stopped the number of trabeculae will not increase [11]. This points towards protection of the number of trabeculae as a critical step in treating osteoporosis. This protection would require the continued balance of resorption and mineralization.

Current treatments for osteoporosis include bisphosphonates, calcitonin, estrogen/hormone therapy, parathyroid hormone, and selective estrogen receptor modulators. The majority of these drugs are intended to inhibit the resorption of bone tissue by osteoclasts. While this may help balance the remodeling process it has been shown that remodeling is also a repair mechanism for propagating microfractures due to cyclic stress. Inhibiting resorption could stall fracture repair thereby allowing micro fractures to grow and coalesce. In fact, animals treated with bisphosphonates, which block resorption, have been shown to have an increase in microdamage accumulation [20]. This damage accumulation would have an adverse effect on the structural integrity and fracture resistance of bone.

2.3 Mechanical Properties of Trabecular Bone

A great number of investigations have probed the mechanical properties of both cortical and trabecular bone [21-31]. While this study focuses on trabecular bone, important
connections can be made between the mechanics of both types of bone. Studies have investigated the Young’s modulus, yield strain, creep behavior, and fatigue behavior of both trabecular and cortical bone. The damage accumulation, mechanical property degradation and subsequent mechanical overload of bone has also been experimentally characterized and modeled [9, 12, 19, 32-36]. While these studies may be difficult to combine and distill into a cohesive model of bone, the understanding of the mechanical properties of bone has become substantial.

A number of studies have been performed to determine the linearity of the stress-strain curve in the elastic regime as well as the yield strain. Keaveny et al. (1994) showed that when using an appropriate protocol, trabecular bone is both linearly elastic and fails at low strains [37]. This was expected because Gibson and Ashby (1997) demonstrated that cellular solids, made of linearly elastic constituent materials, should behave as linear elastic solids, despite their cellular microstructure [38]. Studies of trabecular bone have shown a strong relationship between apparent density and the Young’s modulus, thereby allowing a continuum of property comparison between trabecular and cortical bone [28].

Non-linearities in the stress strain relationship of trabecular bone have been found experimentally; however, these have been limited to high strain rates and studies involving low strain low cycle fatigue testing. Morgan et al. (2001) found non-linearities in the first three cycles of low strain testing of trabecular bone [30]. Linde and Hvid showed that there is an increased stiffness in the first 10 cycles of low strain testing of cortical bone, as well as an increased non-linearity. They hypothesized that this non-
linearity was due to the poro-viscoelastic response of the marrow interacting with porous bone and the lack of confinement at the boundary conditions (i.e. a porous boundary condition); thereby allowing fluid movement [29]. A study by Carter and Hayes showed that the role of the marrow was negligible except at very high strain rates [39]. These experimental findings can be supported through the use of modeling techniques, which show that nonlinear behavior is dependant on both strain rate and fluid movement. This porous boundary condition does not resemble in vivo conditions; therefore, these results are not considered to be of great importance [40].

In monotonic compression, bone loaded beyond the yield strength fails through the formation of shear bands as evidenced through experimental investigations as well as modeling techniques [19, 34, 35, 41]. In this situation, failure is due to the failure of individual trabeculae, which are loaded beyond their yield strain due to strain concentration. This strain concentration is dependent on the orientation of trabeculae, which has been shown to influence their microdamage accumulation [2].

The type and orientation of damage can also be affected by the type of loading [1]. Experimental investigations have shown that microfractures due to compressive loading are both of different orientation and are significantly longer than microfractures formed in tension [1]. There are two types of damage: microfracture and microdamage. Microfracture is defined as a single crack, whereas microdamage is defined as a conglomerate of small fractures. These two types of damage accumulate as monotonic experiments progress. This accumulation of damage reduces the stiffness of the sample
[1, 41, 42]. This loss of stiffness progresses until global failure ensues. Microdamage accumulation, measured by way of crack density, has been shown to reduce the stiffness of trabecular bone in a quadratic manner [42]. On the other hand, damage area reduced stiffness in a linear fashion. The same study showed that microcrack orientation has an important bearing on the loss of stiffness; however, the majority of cracks were homogeneously oriented in compression [42]. While the above study focused on microcrack accumulation, Yeh et al. (2001) showed that microdamage, as opposed to microfracture, is more likely responsible for modulus reduction [43]. This was shown by matching experimental evidence of microfracture with a model of the expected effect. The result showed that at a 2% strain failure criteria, 10% of trabeculae would need to include microfracture if only microfracture could occur, whereas only 2% to 10% was observed [43].

Microdamage observations done by Moore allowed modeling of the reduction of modulus in trabecular bone due to compressive loading due to damage accumulation. This model incorporated partially cracked trabeculae into the model to predict the modulus reduction of the sample [44]. Moore built on a model by Budiansky and O’Connell, which calculated the reduction in elastic modulus due to randomly located microcracks [44, 45]. The trabecular struts were modeled as beams in bending, which failed due to increasing amounts of damage. This model of trabecular damage allowed a three-tiered model of microdamage accumulation proceeding from the trabecular level through the cellular solids level and finally to the specimen level. This model predicted modulus degradation based on observed damage accumulation that correlated well with
experimental data. Another strength of this model was that it could take into account the
density of the bone by modifying the degree to which the system is modeled as plates
versus rods. As a part of this study, a parametric investigation was done to determine the
resulting type of microdamage, including damage bands. This model was not purported
by the researchers to accurately predict microdamage at low strains, because a
quantitative analysis of the performance of this model at low strains was not presented
[44]. To our knowledge, a more comprehensive model of low strain damage behavior has
not yet been done.

Both trabecular and cortical bone have been show to creep (i.e. they exhibit increasing
strain with time at a given constant load) [22, 46]. An example of a plot describing the
creep behavior of trabecular bone appears in Figure 2.1. The data showed that creep in
trabecular bone can be described with a power law:

$$\varepsilon_{ss} = A\sigma^B$$

Where $\varepsilon_{ss}$ is strain rate and A and B are experimentally determined constants. The time
to failure can also be described by a power law:

$$T_B = C\sigma^{-D}$$

Where $T_B$ is the time to failure, $\sigma$ is the stress and C and D are empirically determined
constants. This data showed no threshold below which the sample does not display
creep.
Experimentally determined values for the time to failure in cortical bone and trabecular bone are as follows (time is in seconds):

**Cortical Bone:**

\[ T_B = 1.45 \cdot 10^{-36} (\sigma)^{-15.81} \quad (r^2 = .95, \text{ n}=11, \text{ from Caler and Carter 1989 [23]}) \]

**Trabecular Bone:**

\[ T_B = 9.66 \cdot 10^{-33} \left( \frac{\Delta \sigma}{E_0} \right)^{-16.18} \quad (r^2 = .83, \text{ p}<.001, \text{ n}=24, \text{ from Bowman et al., 1994 [22]}) \]

![Graph showing creep behavior of trabecular bone](image)

**Figure 2.1 Creep behavior of trabecular bone, from Bowman et al. 1998**
Cyclic fatigue behavior relates the stress range over which the sample is loaded with the number of cycles to failure. This data is often plotted as an S-N curve. In many situations, this S-N curve can be described by a power law equation.

\[ N_f = X \left( \frac{\Delta \sigma}{E_o} \right)^y \]

Where \( N_f \) is the number of cycled to failure, and \( X \) and \( y \) are experimentally determined constants. An example of fatigue behavior for trabecular bone (i.e. an S-N curve) appears in Figure 2.2.

![Figure 2.2 S-N curve for bovine trabecular bone. From Moore (2002)]
Assuming a superposition of creep and fatigue, Carter and Caler investigated the fatigue behavior of cortical bone [46]. Early cyclic fatigue studies showed that throughout each test the modulus of the specimen degraded and the stress strain loops were shown to translate along the strain axis with increasing cycles. Carter and Caler interpreted these tests as describing the combined effect of both creep and fatigue. Carter and Caler created a combined model of fatigue and creep as two separate yet additive power law functions to model the total time dependent response. While it is difficult to approximate the creep response of bone during cyclic fatigue the assumption was made that creep contributed to damage accumulation and subsequent modulus degradation of cortical bone [31]. A similar hypothesis was made for trabecular bone [21]. Recently, however, the maximum possible of this contribution of creep to cyclic fatigue was reanalyzed. This study used stress levels of \( \frac{1}{2} \) the maximal cyclic stress over a duration of \( \frac{1}{4} \) of the cycle to approximate the creep contribution. This estimate is reasonable, and in fact conservative, when considering the sinusoidal stress waveform of most cyclic fatigue tests. This analysis showed that the creep contribution of cyclic fatigue is an order of magnitude smaller than a contribution corresponding to the observed translation of the stress-strain loops along the strain axis during cyclic fatigue. This test shows that residual strain accumulation is due to fatigue not creep [47].
Figure 2.3 Modulus reduction throughout a single fatigue test (Ds/Eo=0.008, Sample TLA38C, Moore (2002)).

The global modulus of a specimen undergoing cyclic fatigue degrades as the test progresses until ultimately the sample fails. An example of the modulus reduction appears in Figure 2.3 above. The microstructural manifestation of this fatigue is microdamage and microfracture [23]. This damage accumulates until the fractures coalesce and the global structure is compromised. The accumulation of damage is associated an increase in the hysteresis in the stress strain loops, thereby showing that the damage accumulation is energetically based [1, 48]. In several studies the rate of modulus reduction under sufficiently low compressive strains has been found to be roughly linear [31]. Michel et al. showed that fatigue loading of trabecular bone results in modulus degradation [48]. Their experiment found that the modulus of low cycle fatigue samples (i.e. high cyclic stress) decreased steadily throughout the test while high cycle fatigue
samples showed a temporary increase in modulus before eventual degradation of stiffness. Michel et al. hypothesized that the increase in modulus was due to the boundary conditions of their test. They used unconfined rectangular samples and measured strain through displacement at the platens; this allowed strain concentration at the ends of the specimen thereby allowing the effective increase in secant modulus. This hypothesis was strengthened by the strain contour developed in association with the experiment [48].

Guo, Cheng, and Moore utilized a new protocol developed by Keaveny et al. to show that the fatigue life of trabecular bone was best described by a power law equation [49]. Prior to these studies, a hypothesis was made that damage in high cycle fatigue was predominantly due to fatigue while damage in low cycle high stress fatigue was due to creep. The expectation was that these two damage regimens would be evident from a change in slope of the S-N curve between high and low cycle fatigue. In the study by Guo, Cheng and Moore, no statistically different slope was found, thereby lending validity to the theory that while creep damage may be present in all loading conditions, it plays a significantly smaller effect than that of fatigue. Their experiment pointed towards the existence of an endurance limit for trabecular bone at a normalized stress level of $(\Delta \sigma/E_s=0.0035)$ [49]. This hypothesis parallels the finding of an endurance limit in cortical bone at strains of approximately 2500$\mu$e in tension and 4000$\mu$e in compression. Pattin et al. used an energy integral to show an energetic balance for the fatigue life of cortical bone, thereby lending validity to the hypothesis of an energetic threshold for crack propagation [31]. This thesis explores the hypothesized existence of an endurance limit in trabecular bone in further detail.
Crack growth in cortical bone has been shown to follow a Paris Law:

\[
\frac{da}{dN} = A (\Delta K)^b
\]

Finite element models of fatigue in trabecular bone have been developed, by assuming that crack growth within trabeculae also obeys the Paris law. Early studies used two dimensional honeycomb models to simulate the failure of trabecular bone. Guo randomly distributed cracks into the two-dimensional model and subjected the model to cyclic fatigue [33]. Cracks were assumed to grow at a rate given by the Paris Law. Struts were assumed to fail when the crack length reached 75% of the strut thickness. When the first strut failed, it was removed from the model, the new modulus of the remaining structure was determined, and the test re-run until the next failure. Guo found that the first strut to fail was the one with longest initial crack length. He also found that after the failure of three struts, subsequent failures tended to form a failure band, thereby increasing the probability of failure around that band. Finally, they found that a loss of 1.6% of the struts translated into an 11% loss in modulus. This modulus loss was characterized by an increasingly negative slope in the plot of secant modulus versus number of cycles throughout the test [33]. The inclusion of defects and the subsequent nucleation of shear bands was investigated by Guo et al. in a follow up study [34]. The group modeled two dimensional honeycombs with single and multiple initial defects of various sizes and relative proximities. They found that defects within 10 cells of each other tended to interact thereby allowing the formation of a shear band. This shows that initial geometry of damage can have a significant effect on observed fatigue life.
The two-dimensional honeycomb is an idealized version of bone. The simplified model differs from reality. When comparing a model of honeycomb to manufactured honeycomb Papka and Kyriakides have showed that geometric simplifications of the honeycomb structure used in two-dimensional model can cause a 12% overestimation of the modulus of manufactured honeycomb [50]. With regard to bone, Silva et al. compared the two dimensional periodic honeycomb to that of a Voronoi structure [36]. This study shows that non-periodic Voronoi structures had a 6% higher Young’s modulus and an 11% higher shear modulus than regular honeycomb models. When considering the effect this has on the fatigue failure in bone, which is typically chosen as a modulus loss of 5-10%, this underestimation of the Young’s modulus can have a significant effect. A later study by the same group, in which cell walls were randomly removed, showed that the non-periodic Voronoi structure results in higher strain concentration in individual struts as compared to the regular honeycomb. This strain concentration in individual struts resulted in a 30% reduction in the strength of the Voronoi structure over the honeycomb. This study showed that the struts failed primarily through yielding or buckling, which appropriately simulates osteoporotic bone. After the removal of four adjacent struts the structure began to show the appearance of a localized band of collapse [19]. The Voronoi structure was also modeled in fatigue. Using a method similar to that used by Guo, Shaffner et al. (2000) applied the Paris law of crack propagation to a two dimensional Voronoi structure. Again, damage bands were seen after only three to four were removed. The results showed that the Voronoi structure is more sensitive to fatigue than the regular honeycomb [35]. Trabecular bone differs from the two-dimensional honeycomb model and the two dimensional Voronoi structure in that trabecular bone is
three-dimensional. This lack of depth limits the relevance of either of these two modeling systems. Makiyama et al. (2002) used a three dimensional Voronoi structure to model fatigue in low-density osteoporotic bone. The study included a parametric investigation of the effect of crack shape and normalized stress on the fatigue life of the structures. Fatigue life was shown to be affected little by pre-existing crack shape. Fatigue life did, however, depend on loading level, defined by normalized stress. The study showed that a failure of 1-2% of the struts resulted in a 10% decrease in the elastic modulus of the sample. The model also showed that the fatigue life of low density structures was significantly greater than that of high density structures at the same normalized strain, however, when tested at the same applied stress, low density structures had a significantly lower fatigue life. For example, reducing the relative density from 10% to 5% reduced the fatigue life by a factor of 100 at the same applied stress [9].

The progression from two-dimensional regular honeycomb to three-dimensional Voronoi structure has increased the understanding of the effect of crack propagation on the mechanical properties of trabecular bone. With each iteration of experimental investigation or model development, the failure mechanism of bone becomes better understood.

An increased understanding of the mechanism of failure may allow the application of this knowledge to treatment of osteoporosis. The experiments listed above show that trabecular bone, with its highly porous microstructure, has behavior that is very similar to that of cortical bone except that creep does not contribute to fatigue life in trabecular
bone. This research shows that bone is a linear elastic cellular solid that fails as a result of damage accumulation. This damage accumulation occurs at strains much lower than the yield strength. This research also points toward this damage as a catalyst for repair and remodeling. Therefore the subject of this thesis will be to answer the following questions:

1. Is there a stress level below which fatigue does not occur (i.e. an endurance limit)?
2. Can fatigue be accurately modeled with a power law?
3. Is residual strain accumulation similar in low cycle and high cycle fatigue?
Chapter 3: Materials and Methods

Whole fresh bovine proximal tibia were obtained from Bertolino Beef Company (South Boston, MA). Cylindrical cores of trabecular bone were harvested in accordance with the protocol developed by Keavney et al. [27]. First, all soft tissue was removed to expedite specimen preparation. The tibia were then sliced along the sagittal plane into 13 to 15mm thick sections using a bandsaw equipped with a metal cutting blade (Kaufman Co., Cambridge MA). Slices were kept moist by wrapping the sample with 4” by 4” gauze pads soaked in distilled water until the specimens were ready to be stored in the freezer. Typically one day of dissection was required to go from initial removal of soft tissue to freezing. The slices were radiographed using a Faxitron Model 43855 X-ray camera at 80kV for 20 Seconds (Hewlett Packard, McMinnville, OR). The radiographs were inspected for regions in which the trabeculae were homogeneous and axially aligned. Regions that included the epiphysis or gradients of trabecular density were excluded. Acceptable regions of aligned trabeculae with minimum dimensions of 45mm by 13mm were hand-traced onto acetate. The sections of aligned trabeculae were cut out of the tracing in order to provide a stencil of the region to be marked onto the sample using a wax crayon (Crayola Inc.). The marked sections were excised into parallelepipeds approximately 13mm by 13mm by 45mm using the same bandsaw. The sample was then securely mounted into a vise, submerged in water, and cored using an 8.3mm diameter Starlite diamond tipped coring tool (Starlite Tool Co., Rosemont, PA). Cores were numbered to correspond to each sagittal slice and radiographed again, using the same voltage and time settings, to check that the trabeculae were qualitatively aligned with the specimen axis. The marrow was removed using an ultrasound bath for 22 minutes

32
(Fischer Scientific, Inc, Hampton, NH), followed by a water jet of distilled water.

Samples were then dried using fresh gauze. Dry samples were mounted into specially
made brass endcaps using a custom fabricated alignment tool and were then affixed using
cyanoacrylate adhesive (Ross Adhesives Inc.). Once cured, the samples were removed
from the alignment jig, wrapped in plastic food film (Saran Wrap, SE Johnson and Sons)
and placed into a -80°C freezer for a minimum of 3 hours and a maximum of 12 hours
[Figure 3.1].

Within 3-12 hours, each sample was removed from the freezer and immediately mounted
into an EMCO compact 5 lathe (Maier & Co., Austria). The sample was waisted to a
diameter of 6mm by removing successive cuts of a maximum depth of 0.2mm using a
cutting speed of 300-350 rpm and a 6.35mm radius carbide cutting tool. Turning on the
lathe producing a specimen with a 6mm diameter and a gauge length of approximately
8mm. The geometry of the waisted section was designed to be consistent with that
developed by Keavney et al. (1994). Samples were then re-wrapped in plastic and stored
in a −20°C freezer until they were to be tested.

The above preparation method tended to yield three to five samples per bovine tibia. A
total of 24 samples were successfully prepared for use in this investigation.
Prior to testing, each sample was removed from the freezer, inspected, and allowed to thaw for 15-20 minutes. Once thawed, a water jet of distilled water was used to remove any excess marrow. The sample was then stained in a solution of 0.3% alizarin complexone in a vacuum desiccator for a minimum of 18 hours and a maximum of 24 hours to maximize stain penetration [49].

After staining, the sample was washed with distilled water to remove excess stain. The sample was then fitted with a fluid dispensing attachment and a fluid basin/drain attachment; these attachments were designed to keep the specimen moist during the mechanical testing. The diameter of the sample within the gauge length was measured five times and averaged.
The average diameter was used to calculate the average cross sectional area of the sample.

The sample was then mounted into an Instron 1321 loadframe fitted with a 5000 plus controller and a 500N static reversible load cell (Instron Inc., Canton MA). Fixturing was done with a set of three jaw chucks (Kaufman Tools, Cambridge MA). A nominal compressive load of 10N was applied. A miniature extensometer (MTS 632.290-30) with a 5mm gauge length was attached to the sample using the extensometer metallic clips similar to Figure 3.2. Care was taken to ensure that the extensometer was well-seated on the bone directly opposite the fluid dispensation port. A pump was connected to both the fluid dispensing attachment and the basin/drain attachment to facilitate the continuous hydration of the sample with a 0.9% NaCl solution at a rate of 0.5mL/min.

After the sample was loaded into the loadframe, the sample was preconditioned with ten cycles of strain controlled sine wave compression cycles to a strain of -0.2% at a rate of 2Hz. This level of preconditioning strain was selected to allow comparisons with existing data from prior studies. While this level of preconditioning could hypothetically induce a small amount of microdamage, in prior studies it was found that the preconditioning cycles did not significantly affect the mechanics of the sample or induce detectable microdamage [49]. Load, strain, and position data were recorded at a rate of 100 Hz on an HP Brio computer (Hewlet Packard, Palo Alto, CA) running a custom virtual instrument developed using LabView 6.0 (National Instruments, Austin, TX). The stress strain relationship from the tenth loading cycle was used to determine the initial modulus.
of the sample \( (E_0) \). The loading segment of the tenth cycle was inspected for linearity and the slope was calculated using Microsoft Excel (Microsoft Inc.). Using this initial modulus, a maximal compressive load corresponding to one of four values of normalized stresses was determined. The values of normalized stress \( (\Delta \sigma / E_0) \) used were 0.0015, 0.0025, 0.002, and 0.0035. The sample was then loaded from the nominal compressive load of 10N to the maximal compressive load of the nominal load plus a load corresponding to the normalized stress. Depending on the modulus of the sample in question, the nominal compressive load of 10N would correspond to a normalized stress range of 0.00006 to 0.0007. The sample was fatigued at a frequency of 2Hz. For the normalized stress levels of 0.0015, 0.0020, and 0.0025 seven-minute data sets at 30-minute intervals were recorded using the same HP Brio computer at a sampling rate of 50Hz. This method of taking data at intervals was used in order to allow a temporal measure of the secant modulus of the specimen without the overlapping effects of residual strain accumulation or extensometer signal drift. A more detailed account of selection of this procedure, as well as an quantitative assessment of the confidence of strain measurements appears in Appendix 1. For the normalized stress level of 0.0035, data were recorded continuously using a similar virtual instrument sampling at 50Hz throughout the test. Data sets were examined to determine the secant modulus of the sample. Tests were completed when the sample fractured or the secant modulus of the sample dropped below 90% of the original modulus.
Figure 3.3 Schematic of the stress-strain behavior of the first and following cycles of a fatigue test

A schematic of the relevant features of the stress strain behavior are seen in Figure 3.3. The initial modulus is labeled $E_\infty$. The secant modulus is given by the line drawn between the minimum strain of each cycle and the maximum strain on loading. During fatigue tests, it is observed that the stress-strain behavior translates along the strain axis. The strain at the end of each cycle is called the residual strain. The residual strain is labeled here as $\varepsilon_r$. The residual strain is inelastic strain.

The data from all tests was combined with the data from previous investigations (Guo [51], Cheng [52], and Moore [41]). The results of the normalized stress versus number of cycles to failure were plotted. Logarithmic regressions for the data from experiments done during this investigation were obtained. This regression was compared with those of the previous investigations of Cheng [52], Guo [51], and Moore [49]. In addition, a logarithmic regression of the combined data from this and previous investigations was
performed. The regression from this investigation was compared with that of the previous investigation to see if there was a statistically significant difference between the two regression curves [41]. The normalized modulus reduction \( (E/E_0) \) from the beginning of the test to failure was also plotted against the number of cycles normalized by the number of cycles to failure \( (N/N_f) \) for each category of normalized stress. A linear regression of the modulus reduction versus normalized number of cycles was performed. This data was combined with data from the previous study by Moore. The modulus reduction for all samples from this study and Moore were plotted versus the normalized number of cycles to failure. A linear regression was performed to test for statistically similar rates of modulus reduction.

Once the failure criterion had been met, the sample was removed from the load frame, the hydration fixturing was removed, and the sample was stained with a .09% Calcein solution for a minimum of 18 hours and a maximum of 24 hours. The sample was then washed with distilled water and placed in 80% ETOH for 24 hours in order to remove excess stain. The gauge length of the sample was removed using a low speed diamond blade saw (Buehler Isomet, Lake Bluff, IL). Care was taken to support the specimen while cutting in order to minimize microdamage incurred during the cutting process. Samples were then dehydrated using a protocol developed by Moore and then infiltrated with Methyl Methacrylate (MMA) in a vacuum desiccator for three days [49]. The MMA mixture was refreshed with new embedding fluid each of the three days. Finally, the MMA was allowed to solidify by placing specimens in a water bath at 45°C in accordance with a protocol developed by Moore [49].
This study had intended to include an assessment of microcrack accumulation and the
distribution of microcracks and microdamage. An error in the solidification of the
PMMA embedding solution lead to the loss of most of the embedded samples.
Chapter 4: Results

Fifteen samples tested in high cycle fatigue resulted in satisfactory data: that is, they were tested to the failure criteria of at least a 10% reduction in modulus, or $10^6$ cycles. Data from nine samples was not included for the following reasons: samples used for protocol development (4), stress-strain data became nonlinear (2), equipment failure (3). Figure 4.1 shows a representative section of the stress-strain data from a typical sample (sample 15, $\Delta \sigma/E_0=0.0015$, cycles 86400-86500)

![Graph showing stress-strain data](image)

**Figure 4.1 Stress strain data from sample 15 cycles 86400-86500**
Table 4.1 shows a summary of the samples tested successfully. Samples that exceeded 1,000,000 cycles have a failure value listed as “run out”. For regression purposes, the number of cycles to failure for these specimens was estimated by extrapolating the rate of modulus reduction to the failure criteria of a 10% loss in secant modulus. Failure of all other samples was estimated using the slope of the modulus reduction curve and the data points before and after failure in order to calculate an accurate number of cycles to failure.

<table>
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<th>Specimen</th>
<th>Δσ/E₀</th>
<th>Modulus (Mpa)</th>
<th>Nf</th>
<th>Extrapolated Nf</th>
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</thead>
<tbody>
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<td>1873</td>
<td>103920</td>
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<td>2267</td>
<td>579,000.00</td>
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</table>

Table 4.1 Summary of results for high cycle fatigue tests successfully completed
Several samples were excluded from the data set for various reasons. Samples one through three were used to verify the testing protocol and the data acquisition system and were tested under a less regimented or modified protocol; all these samples were excluded from the analysis. Sample number 5 was stopped before completion due to a computer failure. Sample number 7 failed due to a fracture propagation that was outside of the gauge length of the extensometer. This fracture lead to an erroneous modulus value due to the opening and closing of this fracture. It is likely that the fracture was due to damage as a result of improper loading into the loadframe. Samples 13, 14 and 17 failed due to an error in use of the extensometer. These samples exceeded the predetermined maximum compressive strain yet the modulus of these samples had not yet decreased to that corresponding to the failure criteria. Sample 20 increased in modulus throughout the test. This test was stopped when the apparent modulus reached 160% of its original value. This sample exhibited a nonlinear stress strain relationship at low strains and a linear stress strain relationship at high strains [Figure 4.2]. Due to this irregularity this sample was excluded from data analysis.
Figure 4.2 Stress strain relationship from sample 20 showing non-linear behavior
During each test, the secant modulus of the sample was calculated using either incremental data sets, for samples tested at a normalized stress of 0.0015, 0.002, and 0.0025 or continuous data sets, for samples tested at a normalized stress of 0.0035. This secant modulus was used to determine when the sample met the failure criteria of the secant modulus being equal to or less than 90% of the initial modulus. The data representing modulus reduction appear in four figures corresponding to the four experimental regimes of normalized stress; Figures 4.3, 4.4, 4.5, and 4.6. For comparison between the various normalized stresses it is possible to plot the modulus reduction versus the number of cycles normalized by the number of cycles to failure. This data has been plotted in Figure 4.7. The data from all samples tested using the same normalized stress are plotted with the same symbol thereby representing the data in a clearer manner. This data can also be compiled with similar results from Moore’s experiments, which were done at significantly higher normalized stresses. This data appears in Figure 4.8.
Figure 4.3 Modulus reduction for samples tested at a normalized stress of .0035

Figure 4.4 Modulus reduction for samples tested at a normalized stress of .0025
Figure 4.5 Modulus reduction for samples tested at a normalized stress of .002

Figure 4.6 Modulus reduction for samples tested at a normalized stress of .0015
Figure 4.7 Normalized modulus reduction ($E/E_0$) for fatigue samples from this study plotted against normalized number of cycles to failure ($N/N_f$).

\[ y = -0.0883x + 0.9944 \]
\[ R^2 = 0.624 \]

Figure 4.8 Normalized modulus reduction ($E/E_0$) for fatigue samples from this and previous studies plotted against normalized number of cycles to failure ($N/N_f$).

\[ y = -0.0893x + 0.994 \]
\[ R^2 = 0.6722 \]
Linear regressions from the modulus reduction data were performed with StatView (SAS Institute Inc.). The results of the linear regression for the fatigue data from this investigation is as follows:

\[
\frac{E}{E_o} = -0.088 \left( \frac{N}{N_t} \right) + .994 \quad (R^2=.62, \ p<.001, \ n=16 \ samples)
\]

Linear regression of the data from this investigation as well as the data from the Moore investigation resulted in similar findings [49].

\[
\frac{E}{E_o} = -0.089 \left( \frac{N}{N_t} \right) + .994 \quad (R^2=.67, \ p<.001, \ n=22 \ samples)
\]

The data shows a strong tendency towards a linear decrease in modulus throughout these tests.
Using the statistical program StatView (SAS Institute Inc.) a linear regression of the normalized stress and number of cycles to failure from the successful experiments was performed [Figure 4.3]. The number of cycles to failure is given by:

\[ N_f = 1.57 \cdot 10^{-18} \left( \frac{\Delta \sigma}{E_o} \right)^{-8.59} \]  
\( (R^2=.37, \ p<.001, \ n=15) \)

---

**Figure 4.9 S-N curve for fatigue specimens from this study.** For specimens with \( N_f > 10^6 \) cycles, \( N_f \) was extrapolated from the data for \( E/E_o \) versus \( N/N_f \) (see above)
The $R^2$ value from the high cycle fatigue is fairly low due to the high degree of scatter that exists in the number of cycles to failure for a given normalized stress. This scatter, in many cases, is as large as two orders of magnitude. When the data from this investigation is combined with the data from the tests performed by Cheng [52], Guo [51], and Moore [49], the data can give a much clearer picture of the total S-N curve in a wider spectrum of normalized stress conditions. Table 4.2 summarizes the data from all four investigators, the sample number indicated the investigator responsible for each data point.
<table>
<thead>
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<th>$\Delta\sigma/E_o$</th>
<th>$N_f$</th>
<th>Sample#</th>
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Table 4.2 Fatigue life data from all four investigators.

XEG=Guo, TLA = Arthur-Moore, AZH = Hastings, other = Cheng
The results of the high cycle endurance tests from this investigation are shown in Figure 4.4. These results have been combined with the data from the previous investigators for all samples. A linear regression of this data yields the following equation:

\[
N_f = 1.87 \cdot 10^{-19} \left( \frac{\Delta \sigma}{E_o} \right)^{-9.30} \quad (R^2=0.85, \ p<.001, \ n=76)
\]

Figure 4.10 S-N curve for combined data from all four investigators
An ANOVA comparison between this investigation and the pooled data from the prior three investigators showed no statistical difference (p<.001). The graphs of these two regressions are shown in Figure 4.5.

![Figure 4.11 Linear regressions of fatigue data.](image)

Figure 4.11 Linear regressions of fatigue data.
Some of Moore’s samples were tested at normalized stresses much greater than those necessary to produce failure in one cycle. Tests at these normalized stresses are indistinguishable from those at lower normalized stresses that also produced failure in a single cycle. Because of this, the data from samples which failed during a single cycle are not useful in determining the S-N curve for trabecular bone. After removing these data points from the data under assessment the new data pool appears in Table 4.3. The graph of this data appears in Figure 4.12. A linear regression of these values was performed using SPSS, the equation appears below:

\[ N_f = 4.70 \cdot 10^{-19} \left( \frac{\Delta \sigma}{E_o} \right)^{-0.31} \quad (R^2 = 0.78, p<.001, n=61) \]
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<th>Nf</th>
<th>sample#</th>
<th>Δσ/Eo</th>
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**Table 4.3 Data for samples surviving more than one cycle**
Figure 4.12 S-N curve for samples surviving greater than one cycle
Chapter 5: Discussion and Conclusions

Moore proposed an endurance limit for the fatigue behavior of trabecular bone at $\Delta\sigma/E_0 = 0.0035$. This hypothesis of an endurance limit was based on a change in slope of the best-fit lines of the S-N data with a slope of almost zero for $\Delta\sigma/E_0 = 0.0035$, as well as an absence of microdamage at $\varepsilon_{res} < 0.5\%$. This investigation attempted to prove or disprove this hypothesis by characterizing the fatigue behavior of trabecular bone at a range of normalized stresses less than 0.0035 and corresponding to $N_f$ between 3000 cycles up to and exceeding $10^6$ cycles.

As a continuation of studies by Guo [51], Cheng [52], and Moore [49], this study characterized the fatigue behavior of trabecular bone exposed to normalized stresses ranging from 0.0015 to 0.0035. The existence of an endurance limit would have been indicated by a slope of the S-N curve of zero for high cycle fatigue, indicating a threshold for fatigue. When compared with the findings from Moore et al., no significant difference in slope between the data from this investigation and the data from the previous investigation was found. The slope of all the S-N data, when combined with data from previous studies, described a common fatigue behavior from normalized stresses from 0.0015 to 0.01. This study found no statistically significant endurance limit corresponding to an infinite fatigue life. While no level of stress corresponding to zero stiffness degradation, and therefore an infinite fatigue life was found, this study did find an endurance limit corresponding to $10^6$ cycles. This effective endurance limit can be conservatively estimated based on the lower bounds of the S-N data from the four investigators. A selection of samples from the lower bounds of the SN data appears in
Table 5.1. Using these data points, an effective endurance limit was found to be a normalized stress of approximately 0.0013. This normalized stress would have a high probability of producing at least $10^6$ cycles.

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Table 5.1 Data used to estimate a conservative endurance limit (i.e. stress level which can be confidently used to produce a number of cycle to failure greater than $10^6$)

This finding contradicts the hypothesis by Moore et al. and shows a difference in behavior between trabecular and cortical bone [49]. It also suggests an energetic difference between the fracture mechanics of cortical and trabecular bone. Pattin, Carter and Caler found of an endurance limit in cortical bone at a strains ranging from 2500$\mu$ε to approximately 4000$\mu$ε [31]. This finding was supported by their energy integral method of investigating crack propagation. This endurance limit and the associated energetic balance suggests a stress threshold that must be met for fracture to propagate in cortical bone.

The finding that no true endurance limit exists for trabecular bone is supported by the data showing the modulus reduced throughout the tests. The data from this investigation shows a linear correlation between test progression ($N/N_i$) and modulus reduction ($E/E_0$).
This linearly reducing modulus throughout each test parallels the energetic contribution to modulus reduction modeled by Carter and Caler. The linear reduction in modulus suggests that the lowest normalized stress used in this investigation was either high enough to overcome this threshold, or, that no threshold exists. This data supports the theory that crack growth and microdamage contributes to modulus reduction, even at very low normalized stresses.

The implications for these findings are many fold. From modeling investigations to osteoporosis research, the data from this set of experiments will contribute to the understanding of bone mechanics. For example, the findings of this study help to shed light on the strengths and weaknesses of many the modeling investigations. The linear decrease in modulus seen in this study reinforces this assumption made by Makihama et al. when modeling fatigue in low modulus trabecular bone [9]. The rapid loss of modulus modulus after the loss of the first 10% of the original modulus as seen in this investigation lends credence to the assumptions made in many of the models including those presented by Guo, Silva and Makihama, that structural failure could be defined by a 10% loss in secant modulus. This study could not completely evaluate the phenomena of residual strain accumulation due to the drift in the data acquisition system. To this researcher’s knowledge, the phenomena of residual strain accumulation has not yet been sufficiently investigated. Residual strain accumulation may prove to be an important contributor to the mechanics of fatigue in trabecular bone.
Osteoporosis research takes many forms, all of which interact in the most basic sense. The failure mechanics of bone has a bearing on the treatment of those afflicted with osteoporosis. The finding that no endurance limit exists for trabecular bone suggests that the use of exercise as a treatment protocol for osteoporosis should be prescribed carefully. If trabecular bone had exhibited an endurance limit, the use of exercise below this strain threshold could be helpful in stimulating osteogenesis without propagating fracture. After completing this study it is clear that any prescription for exercise must also take into account the fracture mechanics of osteoporotic bone. To do this, a superposition of the fatigue behavior with that of the regenerative time course properties could allow the progression of osteoporosis to be slowed. In a healthy adult, the human body replaces one fifth of its bone material each year. This regeneration can be combined with the fatigue behavior induced by an estimated activity level of cycles per year at $1.8 \times 10^6$ cycles for a healthy adult. Assuming a steady state of fatigue behavior coupled with regeneration, an average loading profile similar to a normalized strain could be computed. Modifying this steady state behavior using the reduced regenerative properties of osteoporotic bone would allow an optimum of the interaction between fatigue and exercise induced regeneration and failure propagation to be estimated. This optimum might help researchers prescribe exercise regimens to minimize osteoporotic bone loss.

This study benefited from a pool of knowledgeable researchers, both past and present, as well as a well defined protocol. Previous studies investigated the effect of specimen geometry, fixturing technique and protocol variations. This study was able to utilize a methodology that would minimize random errors and maximize data relevance [53].
While bovine trabecular bone differs from human and other mammalian trabecular bone these differences can be treated appropriately.

The findings of this study, as with many biologically based studies, suffer from a high degree of scatter. For example, number of cycles to failure for a given normalized stress vary by as much as two orders of magnitude. This scatter may be due to differences in the specimen geometry, specimen microstructure or pre-existing fractures. While an increased number of samples would have more clearly defined the upper and lower limits for a given normalized stress it is unlikely that significantly different conclusions would have been found.

The experimental equipment used in this study were some of the highest precision instruments currently in production. However, with future devices under development, the precision of delivered fatigue stresses, as well as the recorded data, will most certainly increase. For example, this study utilized an extensometer with high precision over short temporal durations. The data from this device, when tested over long periods of time, can drift and thereby reduce the accuracy. This may have contributed to inaccuracies in the measurement of residual strain although subsequent research has found that, over long times, the drift contribution of residual strain is at least an order of magnitude smaller than the residual strain seen in the specimens.

A final shortcoming of this study is that it relies on consistency between researchers. While the protocol used in these studies was established in order to minimize random
errors, some sources of errors remain. These errors would reduce the combined statistical power of these findings. It is this investigator’s opinion that just such an inconsistency might have lead to the statistically insignificant, yet visually compelling difference in the two logarithmic regressions presented in Figure 4.11. Example inconsistencies may include handling details such as cutting speed and cutting force during sample preparation, water jetting to remove marrow, and method used to load specimens into the Instron. Each of these steps included possible inconsistencies and protocols that would be difficult, if not impossible to quantify.

In conclusion, this study has shown that trabecular bone does not exhibit an fatigue limit corresponding to an infinite fatigue life. In addition, this study has shown that a power law equation can be used to describe the S-N fatigue behavior of trabecular bone. Finally, this study has shown that modulus degradation occurs in the same manner independent of normalized stress applied.

The results of this study point towards several interesting recommendations for future research. For example, the description of the failure mechanism described by the data from this and previous studies is based on the global failure of the specimen. The new findings regarding the absence of an fatigue limit coupled with the finding that cortical bone does exhibit a fatigue limit shows that the microstructural implications of trabecular bone are more complex than originally thought. In addition, it seems that understanding the inconsistencies between residual strain accumulation and modulus degradation may hold the answers to how and why trabecular bone has no fatigue limit. When combined,
these two research areas may point towards a unified failure criterion based on strain or strain energy density. This research is imperative if human activity levels are to be connected to the progression or slowing of osteoporosis.

The research conducted in this study assumes that trabecular bone includes an initial density of microfractures. It did not account for the possibility that a wide range of in vivo crack densities may have been present prior to testing, or for loading to occur differently based on crack propagation, orientation or influence in any way. It seems relevant to attempt to visualize crack growth and subsequently understand their influence on each other.
References


Appendix 1

![Stress-strain behavior graph](image)

**Figure A.1:** Relevant features of the stress-strain behavior during fatigue testing. $E_0$ is initial modulus, $E_{sec}$ is secant modulus, $\varepsilon_r$ is residual strain, and $\varepsilon_{max}$ is maximum single cycle strain.

This study attempted to decouple the overlapping effects of residual strain accumulation, secant modulus degradation, and possible extensometer signal. In previous studies, tests were completed when the specimen reached a failure criteria of a predetermined maximum strain. In this study, a failure criteria of a 10% reduction in secant modulus was chosen. Assessing this required separating residual strain accumulation from changes in secant modulus. See Figure A.1 for a graphical representation of the relevant features of the stress-strain behavior observed during fatigue testing. This was accomplished through evaluating the secant modulus of the intermittent data sets while fatigue tests were underway. In addition, the data from the residual strain accumulation was required for an ongoing study. This long term extensometer signal drift study was performed in order to evaluate the confidence in and the quality of data from both secant modulus changes and residual strain accumulation.
Methods and Materials

An Instron 1321 loadframe with a 5000 plus controller and a 500N static reversible load cell (Instron Inc., Canton MA) was fitted with a miniature extensometer (MTS 632.290-30) with a 5mm gauge length. The zero set gauge of the extensometer was installed and held in place with a size 10 elastic band (Alliance Rubber Company, Hot Springs, AR). The extensometer was placed on a flat lab bench next to the Instron. The hydraulic pump of the Instron was turned on and strain channel of the Instron was zeroed and balanced. Two types of data sets were recorded according to the following procedure. In the first data set, data from the strain channel was recorded continuously for 35 minutes at a rate of 25 Hz on an HP Brio computer (Hewlet Packard, Palo Alto, CA) running a custom virtual instrument developed using LabView 6.0 (National Instruments, Austin, TX). In the second set of data, 7 minute data sets were recorded at 50 minute intervals using the same computer and sampling protocol. Recording proceeded for a total of 4 days.

The strain data was analyzed using two separate protocols: the first tested the short term drift, the second tested the long term drift. Using the first 35 minute long data sets, Matlab release 12 (Mathwork Inc., Natick, MA) was used to calculate fast Fourier transform and power spectral density of the strain data in order to quantify the error in secant modulus assessment due to high frequency drift. A minimum of 10 averages was used to improve the precision of the power spectral densities. The power spectral densities from these trials were compared with 3 data sets of equal data points from three randomly selected bovine fatigue samples.
The long term drift data from each intermittent data set was used to calculate an intermittent average strain. This strain was plotted versus effective cycles. Effective cycles were defined as time in seconds multiplied by two. Effective cycles allowed a more relevant comparison to fatigue data. Linear regressions of the long term data was used to calculate a drift based strain accumulation rate. This strain accumulation rate was compared with the strain accumulation rate of bovine fatigue samples.

Results

The signal drift as well as the power spectral density from a representative data set is shown in Figures A.2 and A.3. This power spectral density can be compared with the power spectral densities from the a selected bovine fatigue sample shown in Figure A.4. The power spectral densities from the drift data are true random noise. No consistent peaks are evident, and of the peaks, the maximum value was approximately $5.5 \times 10^{-7}$. This can be compared to the power spectral density from the bovine fatigue samples. As expected, these samples show a sharp peak at 2Hz. The minimum power shown in these samples is approximately .05, over 90,000 times that of the signal drift. This indicated that under the worst case scenario, in which the drift frequency is exactly 2Hz, the signal drift would contribute only a .0011% error in the secant modulus assessment.
Drift Test #1

Figure A.2: A representative set of strain data from the short duration drift study

Figure A.3 A representative power spectral density from above short duration drift data set
Figure A.4: A representative power spectral density from fatigue testing

(sample #8)
The mean strain of long term drift data over time (in cycles) is shown in Figures A.5 and A.6. These plots include linear trend lines. These strain accumulation rates can be compared to strain accumulation data from a fatigue sample is shown in Table A.7. The lowest strain accumulation rate seen in actual fatigue data is from sample 15. The data from sample 15 is compared to the drift data in Figure A7.
Figure A.5 Long term extensometer signal drift from test #1

Figure A.6: Long term extensometer signal drift from test #2
Figure A.7: Data from long duration drift study compared with representative strain accumulation data from actual fatigue testing

Discussion and Conclusion

The purpose of this study was to investigate what contribution extensometer signal drift made to the evaluation of secant modulus and residual strain accumulation. High frequency drift would impact secant modulus evaluation if there was a dominant frequency similar to the driving sinusoidal signal for fatigue. The finding of this study is that there are no dominant frequencies in the signal drift and the frequencies that are present have low amplitude. From this, it may be concluded that while drift may impact single cycle modulus assessment, it has a very small impact on secant modulus evaluated by averaging many cycles, such as was done in this study. Low frequency drift was also
assessed and determined to be on the order of 10 to 100 times smaller than the slowest strain accumulation rate observed in this study. The strain accumulation rates observed in this study range from $5 \times 10^{-7}$/cycle to $2 \times 10^{-9}$/cycle. The range of observed strain rates indicate that in the future, it is possible that some sample’s strain signal drift may rival that of the actual residual strain accumulation, but in this study, no significant error was observed.