Chapter 2

Literature Review

2.1 Bone

Bone is a truly remarkable structural material, with properties that make it ideal for its functions of structural and physiological support. It's relatively light, but it has very high tensile and compressive strength, and a good deal of elasticity. Bone deposition and resorption typically occur continuously throughout our life. Bone protects our organs, and it is the site of attachment of our muscle and tendon. Bone is also the major reservoirs of calcium and phosphate necessary for a wide variety of metabolic functions. When studying the mechanical properties of bone, it is important to understand the mechanical properties of its components phases, and their structural relationships at the various levels [3, 4].

From a macroscopic point of view, bone tissue is non-homogeneous, porous and anisotropic. Although porosity can vary continuously from 5 to 95%, most bone tissues have either very low or very high porosity. Accordingly, we usually distinguish between two types of bone tissue (**Figure 2-1**). The first type is trabecular or cancellous bone with 50-95% porosity, usually found in cuboidal bones, flat bones and at the ends of long bones. The pores are interconnected and filled with marrow (a tissue composed of blood vessels, nerves and various types of cells, whose main function is to produce the basic

blood cells), while the bone matrix has the form of plates and struts called trabeculae, with a thickness of about 200 μm and a variable arrangement [7].

The second type is cortical or compact bone with 5-10% porosity and different types of pores [8]. Vascular porosity is the largest (50 μm diameter), formed by the Haversian canals (aligned with the long axis of the bone) and Volkmanns's canals (transverse canals connecting Haversian canals) with capillaries and nerves. Other porosities are associated with lacunae (cavities connected through small canals known as canaliculi) and with the space between collagen and hydroxyapatite. Cortical bone consists of cylindrical structures known as osteons or Haversian systems (**Figure 2-2**), with a diameter of about 200 μm formed by cylindrical lamellae surrounding the Haversian canal. The boundary between the osteon and the surrounding bone is known as the cement line.

Cortical bone is usually found in the shafts of long bones and surrounding the trabecular bone forming the external shell of flat bones. This combination of trabecular and cortical bone forms a "sandwich-type" structure, well known in engineering for its optimal structural properties.

2.1.1 Hierarchical Structure of Bone

Structurally, bone is a composite material with a complex hierarchical structure. Generally, following five structural levels can be distinguished [4]: (1) the macrostructural level, which represents the overall bone: trabecular (or cancellous) and cortical (or compact) bone; (2) the microstructural level at an observation scale of 10-500

μm: osteons, single trabeculae; (3) the sub-microstructural level at an observation scale of 1-10 μm: lamellae; (4) the nanostructural level (from several nanometers to one micron) including fibrillar collagen and crystallites; (5) the sub-nanostructural level involving molecular structure of constituent elements, such as collagen, mineral and non-collagenous proteins (**Figure 2-3**).

The basic building block of the bone is the mineralized collagen fibril (**Figure 2-4**). It is mainly composed of the collagen fibrils, apatite crystals, and water. The collagen fibrils are about 30-200 nm in diameter, of a circular or ellipsoidal cross section, and made of triple helix molecules with a diameter of about 1.2 nm and a length of about 300 nm [9]. They are reinforced with apatite crystals, which have irregular platelet-like shapes consisting of impure hydroxyapatite (HA; $Ca_{10}[PO_4]_{6\text{-}x}[OH]_{2\text{-}y}[CO_3]_{x+y}$, $6 \geq x \geq 0$ and $2 \geq y \geq 0$) with an average size of 50x25x2 nm [10-12]. The crystals are located both within and outside collagen fibrils, but the exact fibril-crystal interaction is not fully understood. However, the collagen fibrils and apatite crystals locally parallel each other.

At the next hierarchical level, mineralized collagen fibrils are present in bundles or arrays aligned along their lengths [13]. These bundles are, however, not discrete and may fuse with a neighboring bundle. They are arranged in a roughly parallel manner and form lamellae (3-7 μm thick) (**Figure 2-5** and **Figure 2-6**). At the next scale, these lamellae are stacked at different orientations to form laminated structures. In cortical bone, these lamellae wrap in concentric layers (3-10 lamellae) around a central canal to

form composite cylinders called osteons or Haversian systems, while in trabecular bone, they form crescent-like laminated structures called trabecular pockets.

At the macrostructural level, the collection of osteons and interstitial bone make up cortical bone; the trabecular pockets along with interstitial bone make up struts or plates called trabeculae, which, at the next structural scale, form a random porous network, with cavities being filled with bone marrow. Although these two types of bone (cortical and trabecular) are most easily distinguished by their degree of porosity or density, sometimes the structure of bone is fuzzy and it is difficult to tell them apart with any clarity.

This complicated hierarchical composite structure gives bone its unique mechanical properties: high stiffness and strength due to stiff crystals, high fracture toughness due to relatively compliant collagen, and light weight due to porosities at several scales.

2.1.2 Bone Quality

Although a consentaneous definition of bone quality remains pending [14], the concept of bone quality has been associated with the characteristics of healthy bone that maintain normal functions and, in particular, prevent the formation of non-traumatic fractures. Broadly, the factors most likely to influence the resistance to fracture include: (1) the overall composition (i.e., proportion of mineral, collagen, water, and proteins); (2) the physical and biochemical characteristics of these components (i.e., size and structure of hydroxyapatite crystals, degree of mineralization, nature of the collagen, degree and

type of collagen cross-linking); (3) the morphology and architecture (i.e., bone size, geometry, porosity, density and microarchitecture); (4) the amount and nature of preexisting microdamage (i.e., crack length, density and location). It is also critical to combine this information with knowledge of how the bone is loaded during situations that produce fractures. In order to understand better why bones fracture, additional research is needed to determine which failure mechanism (or combination thereof) governs fragility fractures.

2.1.3 Microdamage

Bone microdamage is generally defined as matrix failure detectable by light microscopy. By analogy with other materials, however, we know that damage must begin at the molecular level and have manifestations through all levels of the hierarchical structure of bone [15]. It is generally accepted that repetitive mechanical loading can lead to ultrastructural-level damage. The most prevalent form is discrete microcracks in the bone extracellular matrix that are easily visible under brightfield light microscopy [15-20]. Although younger people are more active and subject to repetitive loading of greater magnitude and duration, they typically have a greater physiological capacity to withstand the functional demands, and microdamage in bone is repaired by remodeling. Nevertheless, with age and/or pathological conditions, these compensatory mechanisms become impaired. In consequence, microdamage, which may no longer be repaired as efficiently, can play a role in the etiology of osteoporotic and stress fractures [19, 21].

Therefore, there is an inter-relationship between fatigue loading, microdamage accumulation, remodeling, bone matrix repair and fracture **(Figure 2-7**). Remodeling is triggered by microdamage accumulation through cell sensory mechanisms and it leads to bone matrix repair. However, remodeling can also enhances microdamage accumulation or directly leads to fracture upon exceeding a threshold stress. Because there is less bone to sustain loading upon resorption induced by remodeling, stresses and strains on the remaining bone would increase, generating even more microdamage, which stimulates another sequence of remodeling and so on and so forth [15, 22]. As a result, high remodeling as well as microdamage accumulation can lead to fracture. Dr. Schaffler suggested that in "healthy" bone, there is a balance between expected accumulation of damage due to daily loading and its repair [23]. In other words, too much, as well as too little, remodeling can accelerate microdamage accumulation and lead to fractures.

Micro- and ultrastructural features of bone can create stress concentrations that initiate crack formation. Reilly [24] observed tensile microdamage to initiate around the osteocyte lacunae through examination of specimens to which low levels of strain were applied. In such specimens, microcracks were shown to appear either in close proximity to the lacuna or at the lacuna boundary, leading to the hypothesis that lacunae serve as stress concentrators. Additionally, after applying increasing strains, the number of cracks that form outwards from lacunae was observed to increase, indicating damaging effect around the osteocyte lacuna. O'Brien et al. [25, 26] found similar results, supporting the hypothesis that incremental increase in strain levels increases the crack density, consequently suggesting that microcracks accumulated at all stress levels, but that lower

stress levels result in an accumulation of microcracks without failure occurring, while high stress levels result in a more rapid accumulation of microcracks with failure occurring. Besides lacunae, vascular canals can also initiate crack formation [27]. In addition to stress concentrations, higher mineralization can increase the probability of microcracking. Although heavily mineralized bone is stiffer than less mineralized bone, it is more brittle and associated with more microcracks [28].

Based on the mechanical behavior of composites, there is an expected association between microdamage accumulation and mechanical property degradation, in particular modulus degradation. However, the specific relationship between these two indicators of damage is unclear. It is likely that the testing method plays an important role in determining their relationship [18, 29]. For example, strain rate has an effect on the amount of damage produced and the degree of modulus degradation [30]. In addition, the amount and nature of microdamage may differ between different loading conditions. Even within a specified testing method, subtle differences in experimental conditions could change damage processes. In order to better identify relations between damage, mechanical properties and remodeling, better techniques are required to detect, monitor and visualize damage. Besides, a better model is needed to relate compositional changes to mechanical and morphological changes.

2.1.4 Toughness

Bone is a composite material with a complex hierarchical structure which is imbued with several mechanisms to resist fracture at multiple scales. These scales relate

to the characteristic structural dimensions in bone, which vary from tropocollagen at the nanoscale, mineralized collagen fibrils at the scale of tens of nanometers, collagen bundles to form the lamellar structure above micrometer dimensions, to the osteon structures, which are several micrometers in size [31]. It is the simultaneous operation of toughening mechanisms at these different size scales that provides bone with its prominent strength and toughness.

Some toughening mechanisms contribute to limit the microdamage. For example, plasticity ahead of the crack dissipates energy and reduces local stresses. Other mechanisms shield the crack tip from the applied external force responsible for crack propagation, e.g. crack bridging. The following toughening mechanisms have been reported for cortical bone, including sacrificial bonds between fibrils [32], plasticity ahead of the crack [33], constrained microcrack [34], crack deflection [35, 36] and crack bridging [35]. For individual microcracks, bridging by collagen fibrils might be significant since the substantially smaller collagen fibrils would be able to bridge a large percentage of the crack length [37] .

2.2 Micromechanics and Representative Volume Element

Traditional continuum mechanics deals with idealized materials assuming that: (1) the elastic properties of a solid at a given point are the same in every direction (isotropy); (2) the material properties are the same at all points within the solid (homogeneity). These two assumptions render the uniform stress and strain distribution within an infinitesimal material element. However, from the microscopic and realistic points of

view, an infinitesimal material element has its own complex microstructure. Therefore, the stress and strain field within such a material element is not uniform at the microscopic level. The major objective of micromechanics is to characterize such infinitesimal material element and its neighborhood with a rigorous theoretical framework. In order to capture the effects of inhomogeneities, the concept of RVE (Representative Volume Element) is introduced. The RVE for a material point of a continuum mass defines a material volume which statistically represents the infinitesimal material neighborhood of that material point [38]. In other words, RVE features the mesoscopic length scale which is much larger than the size of inhomogeneity, but much smaller than macroscopic length scale.

Based on the concept of RVE, the continuum constitutive relations are evaluated in terms of the properties and structure of the constituents within RVE. The methodology to estimate the effective material properties is named "homogenization", which is performed by the statistical and volume averaging within an RVE. Mathematically, this type of procedure is related to the ensemble-volume averaging process, and leads to the overall governing constitutive equations. We will employ this homogenization method rigorously in the following chapters and more detailed formulations will be addressed.

2.2.1 Eshelby's Equivalence Principle

Based on micromechanics, when a material contains inhomogeneities of different material properties such as inclusions, voids, or cracks, etc., it is subjected to an internal stress (eigenstress) field even if it is free from external load. Such stress field is caused by

the eigenstrain inside the inhomogeneities due to the misfit and phase transformation. Eshelby [39] pointed out that that the stress perturbation in an applied stress due to the presence of an inhomogeneity can be simulated by an eigenstress caused by an inclusion when the eigenstrain is chosen properly.

Let us now consider an infinitely extended matrix domain D (stiffness $\boldsymbol{C}_0$) with an inclusion (inhomogeneity) domain Ω (stiffness $\boldsymbol{C}_1$). Suppose that the applied stress at infinity is σ^0 and the corresponding strain is ε^0. Furthermore, the perturbed stress field and strain field are denoted by σ' and ε', respectively. Therefore, the Hooke's law takes the form

$$\sigma^0 + \sigma' = \boldsymbol{C}_0 : \left(\varepsilon^0 + \varepsilon'\right) \qquad \text{in} \quad \Omega \tag{2.1}$$

$$\sigma^0 + \sigma' = \boldsymbol{C}_1 : \left(\varepsilon^0 + \varepsilon'\right) \qquad \text{in} \quad \text{D-}\Omega \tag{2.2}$$

Eshelby's equivalent eigenstrain principle is to replace the inhomogeneity with a homogenized inclusion, with which an eigenstrain field is prescribed, such that the homogenized field is mechanically equivalent to the original inhomogeneous field. By introducing an eigenstrain ε^* within the inclusion domain Ω and applying the Eshelby's equivalence principle, the Hooke's law yields

$$\sigma^0 + \sigma' = \boldsymbol{C}_0 : \left(\varepsilon^0 + \varepsilon' - \varepsilon^*\right) \qquad \text{in} \quad \Omega \tag{2.3}$$

$$\sigma^0 + \sigma' = \boldsymbol{C}_0 : \left(\varepsilon^0 + \varepsilon'\right) \qquad \text{in} \quad \text{D-}\Omega \tag{2.4}$$

Apparently, the necessary and sufficient condition for the equivalency of the stresses and strains in equations (2.3) and (2.4) is

$$\boldsymbol{C}_1 : \left(\varepsilon^0 + \varepsilon'\right) = \boldsymbol{C}_0 : \left(\varepsilon^0 + \varepsilon' - \varepsilon^*\right) \tag{2.5}$$

In the case of uniform stress σ^0 at the far field, the eigenstrain ε^* is also uniform within inclusion domain Ω.

2.2.2 The Ensemble-Averaging Procedure

Upon the solution of the local stress/strain field, the ensemble averaging procedure (homogenization) is typically performed within the aforementioned representative volume element (RVE) to obtain the overall effective constitutive equations and properties of the heterogeneous composites. For example , the volume-averaged stress and strain tensor are defined as [40]

$$\bar{\sigma} = \frac{1}{V}\int_V \sigma(x)dx = \frac{1}{V}\left[\int_{V_m} \sigma(x)dx + \sum_{r=1}^{n}\int_{V_r} \sigma(x)dx\right] \tag{2.6}$$

$$\bar{\varepsilon} = \frac{1}{V}\int_V \varepsilon(x)dx = \frac{1}{V}\left[\int_{V_m} \varepsilon(x)dx + \sum_{r=1}^{n}\int_{V_r} \varepsilon(x)dx\right] \tag{2.7}$$

where V is the volume of an RVE, V_m is the volume of the matrix, V_r is the volume of the r th-phase inhomogeneities, and n denotes the number of inclusion phases of different material properties (excluding the matrix). Combining the Eshelby's equivalence principle and the ensemble-averaging procedure, the effective constitutive relations as well as the overall elastic behavior of the composite can be derived.

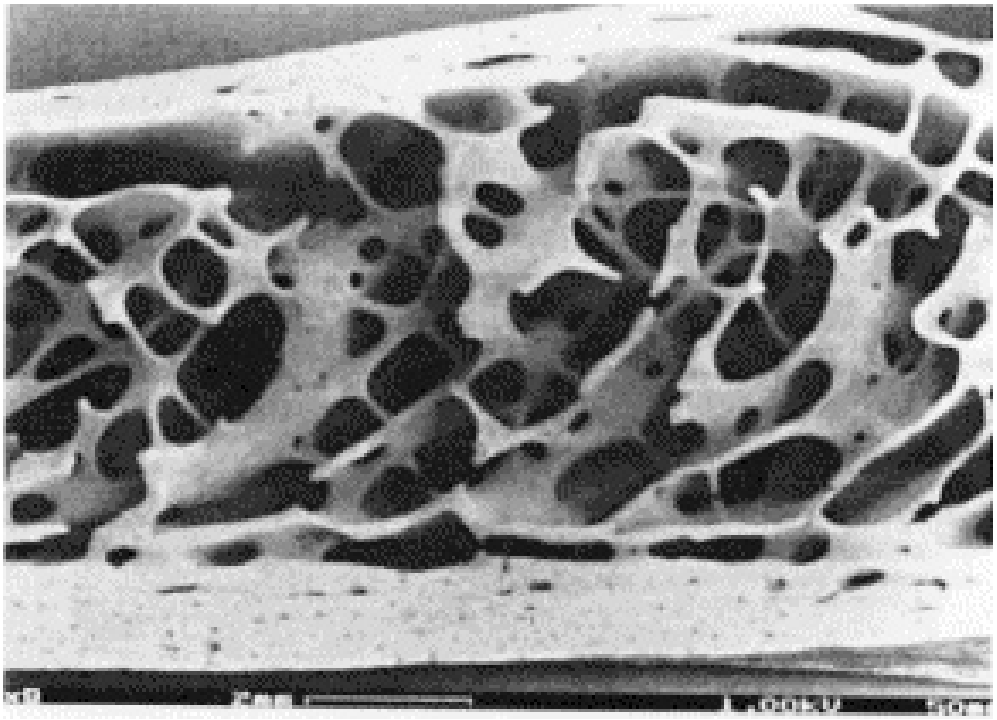

Figure 2-1. Bone section showing cortical and trabecular bone [2]**.**

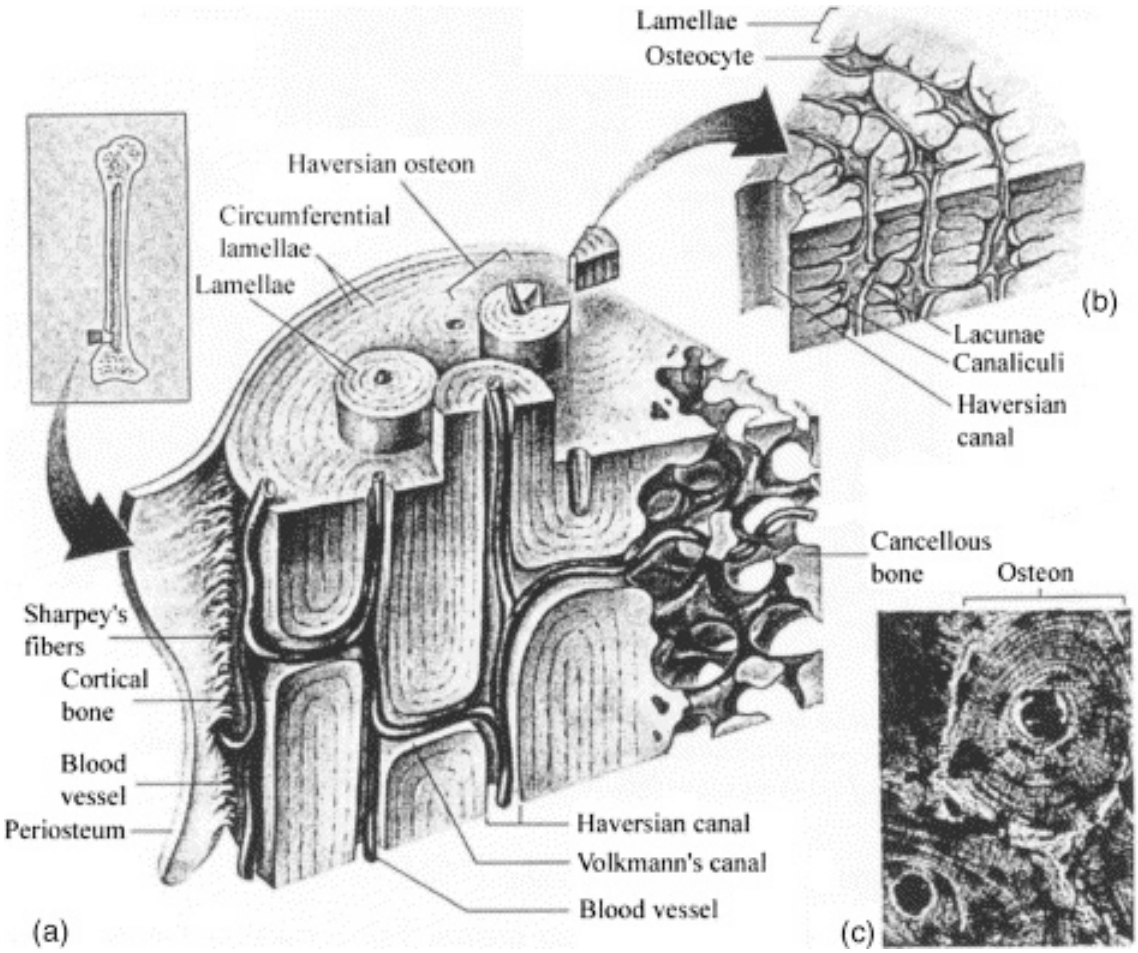

Figure 2-2. Microscopic structure of cortical bone. (a) 3D sketch of cortical bone, (b) cut of a Haversian system, (c) photomicrograph of a Haversian system [1].

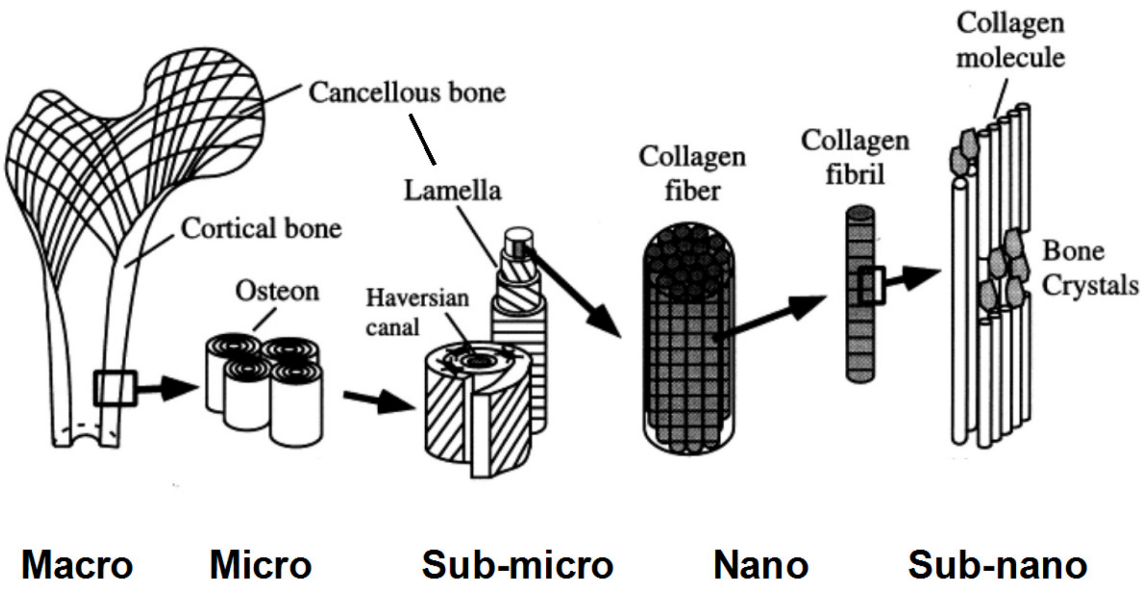

Figure 2-3. Hierarchical structural level of bone: (a) trabecular and cortical bone; (b) osteons and single trabeculae; (c) lamellae; (d) mineralized collagen fibrils; (e) collagen, mineral and non-collagenous proteins. [4]

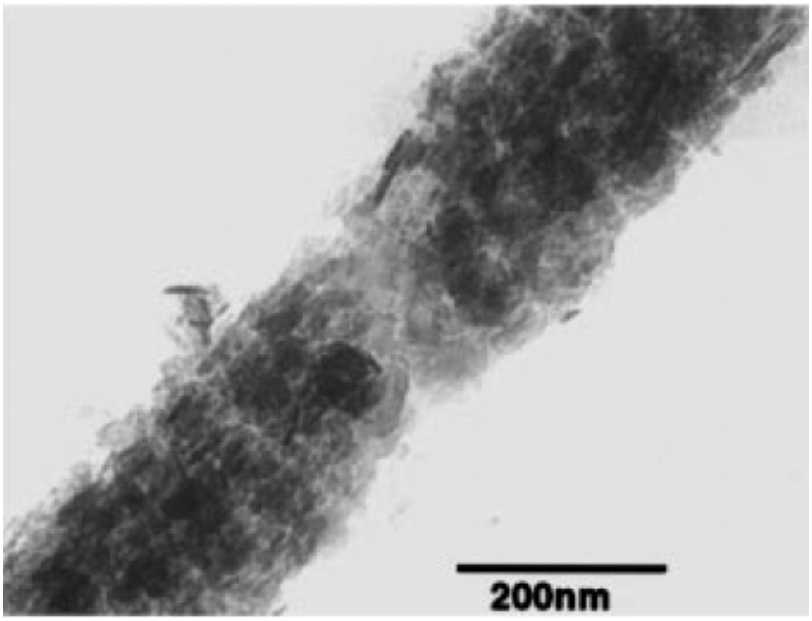

Figure 2-4. TEM micrograph of a mineralized collagen fibril from turkey tendon [6].

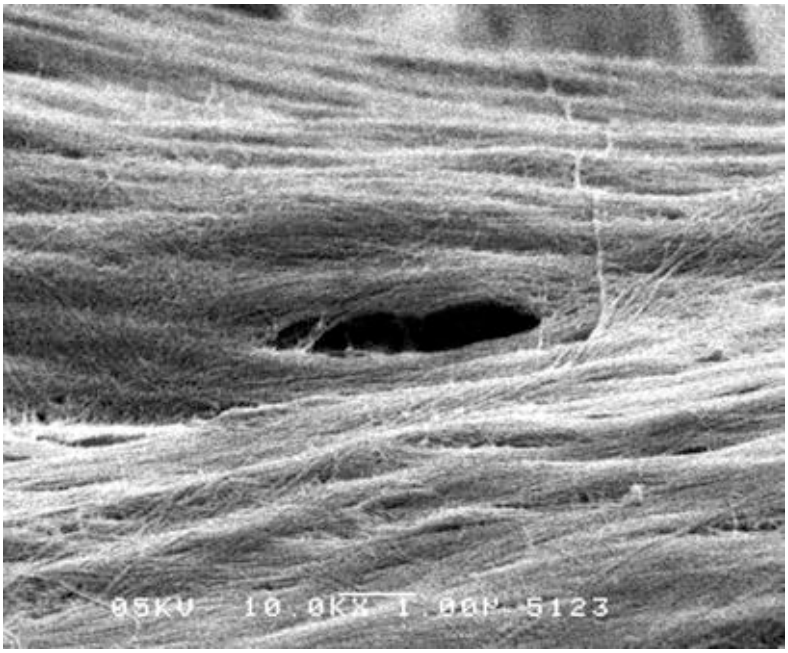

Figure 2-5. Scanning electron microscopy image of trabecular bone at a single lamella level. Fibrils are aligned in the preferential direction, forming bundles. A void in the center is called lacunae [5].

Figure 2-6. An isolated and flattened lamellar specimen from an alternate osteon (Dr. M.-G. Ascenzi).

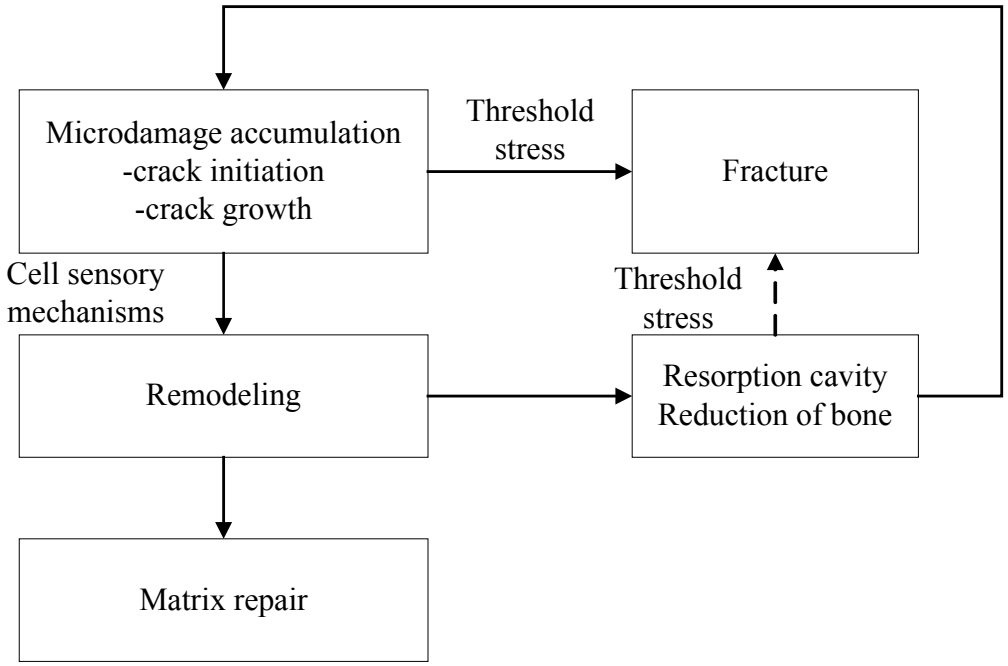

Figure 2-7. Schematic inter-relationship between microdamage accumulation, remodeling, bone matrix repair and fracture

2.3 References

1. Doblare, M., J.M. Garcia, and M.J. Gomez, *Modelling bone tissue fracture and healing: a review.* Engineering Fracture Mechanics, 2004. **71**(13-14): p. 1809-1840.
2. Williams, P.L., *Gray's anatomy. (38th ed.)*1995, Churchill Livingstone.
3. Weiner, S. and W. Traub, *Bone structure: from angstroms to microns.* FASEB J., 1992. **6**(3): p. 879-885.
4. Rho, J.-Y., L. Kuhn-Spearing, and P. Zioupos, *Mechanical properties and the hierarchical structure of bone.* Medical Engineering & Physics, 1998. **20**(2): p. 92-102.
5. Jasiuk, I. and M. Ostoja-Starzewski, *Modeling of bone at a single lamella level.* Biomechanics and Modeling in Mechanobiology, 2004. **3**(2): p. 67-74.
6. Weiner, S. and H.D. Wagner, *The material bone: Structure mechanical function relations.* Annual Review of Materials Science, 1998. **28**: p. 271-298.
7. Martin, R.B., D.B. Burr, and N.A. Sharkey, *Skeletal tissue mechanics.*1998, New York: Springer-Verlarg.
8. Cowin, S.C., *Bone poroelasticity.* Journal of Biomechanics, 1999. **32**(3): p. 217-238.
9. Lees, S., *Considerations regarding the structure of the mammalian mineralized osteoid from viewpoint of the generalized packing model.* Connect Tissue Res, 1987. **16**(4): p. 281-303.

10. Robinson, R.A., *An electron-microscopic study of the crystalline inorganic component of bone and its relationship to the organic matrix.* J Bone Joint Surg Am, 1952. **34-A**(2): p. 389-435; passim.

11. Ziv, V. and S. Weiner, *Bone Crystal Sizes - A Comparison of Transmission Electron-Microscopic and X-Ray-Diffraction Line-Width Broadening Techniques.* Connective Tissue Research, 1994. **30**(3): p. 165-175.

12. Landis, W.J., *The strength of a calcified tissue depends in part on the molecular structure and organization of its constituent mineral crystals in their organic matrix.* Bone, 1995. **16**(5): p. 533-544.

13. Reid, S.A., *Micromorphological Characterization of Normal Human-Bone Surfaces as a Function of Age.* Scanning Microscopy, 1987. **1**(2): p. 579-597.

14. Bouxsein, M.L., *Bone quality: where do we go from here?* Osteoporos Int, 2003. **14 Suppl 5**: p. 118-27.

15. Burr, D.B., et al., *Bone Microdamage and Skeletal Fragility in Osteoporotic and Stress Fractures.* Journal of Bone and Mineral Research, 1997. **12**(1): p. 6-15.

16. Burr, D.B. and C. Milgrom, *Musculoskeletal fatigue and stress fractures*2001, Boca Raton: CRC Press.

17. Courtney, A.C., W.C. Hayes, and L.J. Gibson, *Age-related differences in post-yield damage in human cortical bone. Experiment and model.* Journal of Biomechanics, 1996. **29**(11): p. 1463-1471.

18. Zioupos, P. and J.D. Currey, *Changes in the stiffness, strength and toughness of human cortical bone with age.* Bone, 1998. **22**(1): p. 57-66.

19. Schaffler, M.B., K. Choi, and C. Milgrom, *Aging and matrix microdamage accumulation in human compact bone.* Bone, 1995. **17**(6): p. 521-525.

20. Currey, J.D., K. Brear, and P. Zioupos, *The effects of ageing and changes in mineral content in degrading the toughness of human femora.* Journal of Biomechanics, 1996. **29**(2): p. 257-260.

21. Sahar, N.D., S.-I. Hong, and D.H. Kohn, *Micro- and nano-structural analyses of damage in bone.* Micron, 2005. **36**(7-8): p. 617-629.

22. Weinans, H. and A. Odgaard, *Bone structure and remodeling : Amsterdam, 10-15 July 1994*. Recent advances in human biology ; v. 21995, Singapore ; River Edge, NJ: World Scientific. ix, 257.

23. Schaffler, M.B., *Role of bone turnover in microdamage.* Osteoporosis International, 2003. **14**: p. S73-S77.

24. Reilly, G.C., *Observations of microdamage around osteocyte lacunae in bone.* Journal of Biomechanics, 2000. **33**(9): p. 1131-1134.

25. O'Brien, F.J., et al., *The behaviour of microcracks in compact bone.* Eur J Morphol, 2005. **42**(1-2): p. 71-9.

26. O'Brien, F.J., D. Taylor, and T. Clive Lee, *The effect of bone microstructure on the initiation and growth of microcracks.* J Orthop Res, 2005. **23**(2): p. 475-80.

27. Carter, D.R. and W.C. Hayes, *Compact bone fatigue damage: A microscopic examination.* Clinical Orthopaedics and.Related Research, 1977. **127**: p. 265-274.

28. Sobelman, O.S., et al., *Do microcracks decrease or increase fatigue resistance in cortical bone?* Journal of Biomechanics, 2004. **37**(9): p. 1295-1303.

29. Burr, D.B., et al., *Quantification of bone damage and crack morphology and its effect on skeletal fragility: response to Zioupos.* Journal of Biomechanics, 1999. **32**(2): p. 213-215.

30. Schaffler, M.B., E.L. Radin, and D.B. Burr, *Mechanical and morphological effects of strain rate on fatigue of compact bone.* Bone, 1989. **10**(3): p. 207-214.

31. Launey, M.E., M.J. Buehler, and R.O. Ritchie, *On the Mechanistic Origins of Toughness in Bone.* Annual Review of Materials Research, 2010. **40**(1): p. 25-53.

32. Fantner, G.E., et al., *Sacrificial bonds and hidden length dissipate energy as mineralized fibrils separate during bone fracture.* Nat Mater, 2005. **4**(8): p. 612-616.

33. Baohua, J. and G. Huajian, *Mechanical properties of nanostructure of biological materials.* Journal of the Mechanics and Physics of Solids, 2004. **52**(9): p. 1963-1990.

34. Vashishth, D., K.E. Tanner, and W. Bonfield, *Experimental validation of a microcracking-based toughening mechanism for cortical bone.* Journal of Biomechanics, 2003. **36**(1): p. 121-124.

35. Nalla, R.K., et al., *Fracture in human cortical bone: Local fracture criteria and toughening mechanisms.* J. Biomech., 2005. **38**: p. 1517-1525.

36. Peterlik, H., et al., *From brittle to ductile fracture of bone.* Nature Materials, 2006. **5**(1): p. 52-55.

37. Ritchie, R.O., et al., *A fracture mechanics and mechanistic approach to the failure of cortical bone.* Fatigue & Fracture of Engineering Materials & Structures, 2005. **28**(4): p. 345-371.

38. Nemat-Nasser, S. and M. Hori, *Micromechanics: overall properties of heterogeneous materilas*. Second ed1993, Amsterdam, The Netherlands: Elsevier Science B.V.

39. Eshelby, J.D., *The Determination of the Elastic Field of an Ellipsoidal Inclusion, and Related Problems.* Proceedings of the Royal Society of London. Series A, Mathematical and Physical Sciences, 1957. **241**(1226): p. 376-396.

40. Ju, J.W. and T.M. Chen, *Micromechanics and Effective Moduli of Elastic Composites Containing Randomly Dispersed Ellipsoidal Inhomogeneities.* Acta Mechanica, 1994. **103**(1-4): p. 103-121.