# A Computer-aided Multi-scale Modeling and Direct Fabrication of Bone Structure

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**ABSTRACT**

A multi-scale voxel modeling approach was presented to model the bone structure both in macroscopic and microscopic level. Based on the digital image, the overall macroscopic geometry of the vertebrate was acquired by traditional reverse engineering technology and the microscopic random trabecular network was described by two-point correlation function and the function was then used to reconstruct the bone microstructure. It was shown that the reconstructed model is statistically equivalent to the original structure in the microscopic level and the design intension can be integrated in the developed model. A direct-fabrication process planning was also developed based on the voxel model. The advantage is that there is no need for slicing process in this process which is a costly and essential process for traditional rapid prototype technology.

**Keywords:** biomedical imaging; bone microstructure, modeling, fabrication

## 1. INTRODUCTION

Osteoporosis, a common condition in aged person, is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a concomitant increase in bone fragility and fracture risk. It is recognized that osteoporosis is an important public health problem because of the large size of the affected population and because of the devastating impact of osteoporotic fractures on morbidity and mortality and on social costs. It is reported that osteoporosis affects 300 million people worldwide and the health care expenditures in the United States alone attributable to osteoporosis fractures were estimated at $13.8 billion in 1995 [1]. Patients with osteoporosis suffer a loss of bone mass with aging, making them prone to fractures of the proximal femur and vertebrate. In both locations, the load is carried by the cortical bone and the trabecular bone. The cortical bone is a dense bone structure with irregular geometry in macroscopic level which makes up of an outer shell of the bone and the trabecular bone is a random interconnected network in microscopic level. Developing and understanding the bone structure both in macroscopic and microscopic level may be essential in delineating the etiology of those devastating age-related vertebral fractures.

On the macroscopic level, trabecular bone is different with the age and health condition for different people while on the microscopic level, trabecular bone forms a porous random network [2]. There have been many open literatures available on bone modeling methods. Ulrich ed, al [3] used the architectural indices microstructural model to describe microscopic trabecular networks with structural topological indices such as Tr.Th (trabecular thickness) and Tr.N (trabecular number) and the microstructural topological indices are then used to evaluate the bone quality. However, this model can not capture the macrostructure and there is no evidence so far for its ability to predict the bone mechanical behavior accurately. Sun ed, al [4] used an computer-aided bone modeling approach to develop a femur model. In their approach, the conventional sliced imaged were acquired and a 3D CAD model were then built. To understand the microstructural behavior, they used quantitative computed tomography value (QCT) to characterize the bone mechanical properties. Hollister ed al [5] used an image-based approach to develop an Mandibular Condyle bone model and used the homogenization theory to evaluate the bone properties. To simulate the osteoporotic bone properties, Gibson ed al [6] developed a voronoi cell based microstructural model to simulate the bone strut thinning and bone micro-architectural deterioration.

Currently, there is a lack of an effective modeling approach to accommodate both bone macroscopic irregular anatomic shape and the inter-connected random trabecular network. In this study, we proposed an image based multi-scale modeling approach to simulate the bone structure both in macroscopic and microscopic level. This model will use patient-specific bone digital images to develop bone macroscopic shape as well as the statistically equivalent bone

microscopic network. To model the bone both in macroscopic and microscopic level, the conventional low resolution bone images were used to reconstruct the bone overall shape; the high resolution of the bone microstructure image was used to predict the correlation function, a micro-structural descriptor function, to describe the random natural of the bone microstructure network. Based on the reconstructed bone macroscopic bone structure and micro-structural descriptor, a multi-scale voxel model of bone was reconstructed through designed algorithm. We also proposed a direct fabrication process planning to fabricate the physical mode of multi-scale voxel bone model. This process can direct convert the voxel model into machine instruction to avoid the slicing procedure which is essential and costly process for traditional free-form fabrication techniques.
The paper is organized as following: the second details the image-based multi-scale modeling process regarding the steps involved. For demonstration purpose, a multi-scale vertebrate model was presented. The section 3 details the direct fabrication process planning. The traditional fabrcication used to fabricate the developed voxel model through conversion of STL file was also shown in this section.

## 2. IMAGE-BASED MULTI-SCALE MODELING OF BONE STRUCTURE

Bone structure is a sandwich structure which is made up of an outer shell of irregular dense compact bone, enclosing a core of porous cellular, trabecular bone. To model a bone structure with irregular macroscopic structure and complicate random microstructural network remains to be a challenge to researches due to its complicity and heterogeneity. The traditional CAD model is difficult to model the heterogeneous structures. This is especially a case when the heterogeneous microstructure is a random network. In this study, a bionic multi-scale will be developed to model the natural trabecular bone. The overall process to get the voxel model of bone heterogeneous structure with random microstructure is shown in Fig. 1.

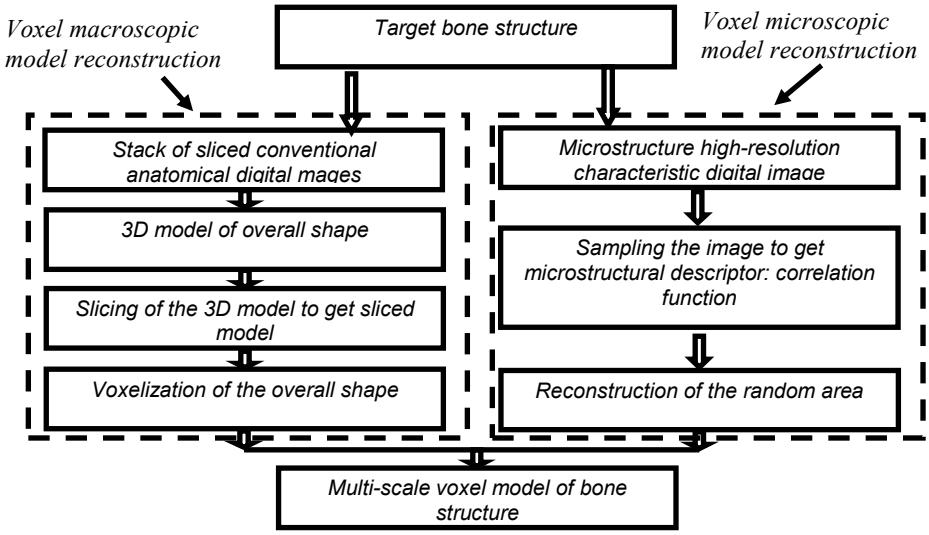



Fig. 1. The process to construct the voxel model of vertebrate bone structure with random microscopic network

As shown in Figure 1, the process is divided into two functional activities, the macroscopic voxel model reconstruction and the microscopic voxel model reconstruction. The two functional activities all start from the digital imaging acquisition of patient-specific data. The functional activates as shown in the right of Fig.1 is to generate the voxel model of the bone overall shape through conventional image reconstruction and in-house developed slicing and voxelization algorithm detailed in section 2.1. Images used in this function are low-resolution. The functional activates in the left side is to generate the voxel model in the microscopic level. The digital image used in this activity is usually high-resolution image characterized the microstructure bone random network.

### 2.1 Macroscopic voxel model construction

The image-based macroscopic voxel model construction begins with the acquisition of noninvasive conventional images and its subsequent processing of appropriate bone region of interest. As a first step, an appropriate threshold range was found that could best capture the relevant information contained in the bone macrostructure. Using this

threshold value, all pixels of the images within this range were grown to a color mask and hence the segmentation process achieved by making use of region growing techniques available in the software. This color mask acts as the input to the 3-D reconstruction process. The 3D model created after segmentation is used as the starting point. The 3D dataset of the bone structure is converted to point data form and then these points are loaded into any reverse engineering software. Commercially available software Geomagic Studios (Raindrop Inc) [7] are then used to process these data points for surface processing and refinement. This is perhaps the best approach that can be followed since the process starts from the base level, i.e., points. The imported points first needs to be cleaned of noise points and decimation of points maybe necessary depending on the number of points. The points are then triangulated to form a faceted model. Further surface refining and enhancement is required to reduce file sizes and unwanted features maybe removed at this stage. Finally a CAD model as shown in the Figure 2(b) of the macroscopic bone model can be generated. To show the feability of this study, a slice of the vertebrate bone core was acquired by slicing of the 3D mode as shown in Figure 2(c) and (d). After this step, an in-house direct slicing program developed in out lab is used to generate sliced model of heterogeneous structure [8]. Then an in-house program developed in out lab was used to generate voxel model of macroscopic vertebrate bone slice. As shown in the figure 2(f), the black area is the space area and the white area is the trabecular area which can not be shown in the macroscopic scale and the gray area is the compact bone. The thickness of the bone was acquired from reference [9]. The following indicator function was used to save the voxel model,

$$\tau^{MA}(\tilde{x}) = \begin{cases} 0, \text{ if } \tilde{x} \in \text{cortical bone} \\ 1, \text{ if } \tilde{x} \in \text{space area} \\ 2, \text{ if } \tilde{x} \in \text{trabecular bone area} \end{cases} \quad (1)$$

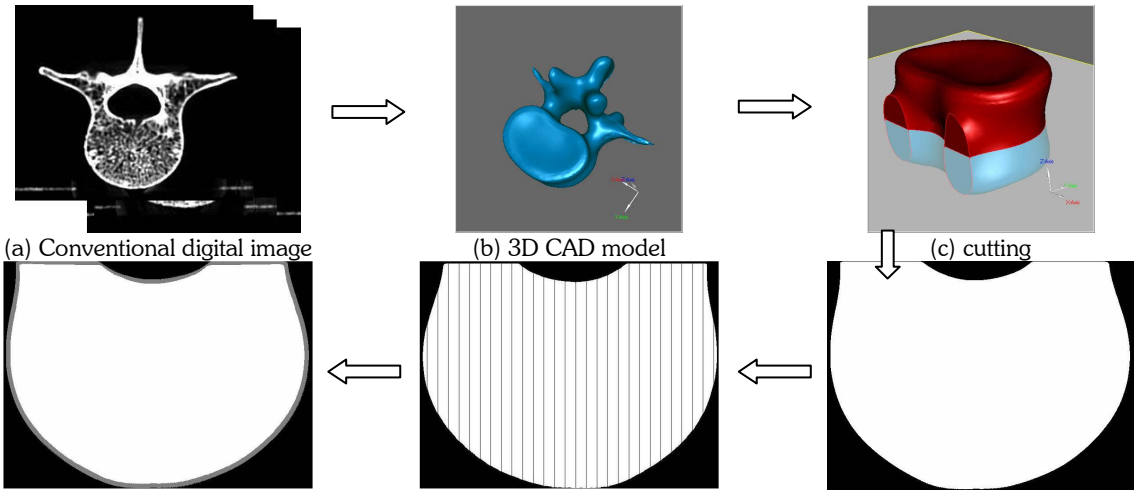



Fig. 2. The macroscopic voxel model construction

### 2.2 Microscopic voxel model construction

The microscopic construction shown in the right of Fig. 1 is used to describe and reconstruct the random microstructural network of bone. The aim of this microscopic model construction is to construct a large scale microscopic inter-connected random trabecular bone network which is statistically equivalent with the original bone sample. In order to characterize the original bone trabecular network, a high-resolution image of the sample was acquired. There are currently many methods to acquire the high-resolution image such as Micro-Computed Tomography (micro-CT) and Scanning electron photomicrograph. Based on the image, a systematic mathematic method (correlation function) is used to describe the randomness of the trabecular network. The mathematic description was then used to construct the microscopic voxel model using the developed algorithm described as following sections.

#### 2.2.1 Random microstructure descriptor and digital Image

The microstructure of the trabecular bone is an interconnected random network. To describe the randomness of the bone trabecular network, the random stochastic function of pore (characteristic or indicator function) $\tau(x)$, is defined as

$$\tau^{MI}(\tilde{x}) = \begin{cases} 1, \text{ if } \tilde{x} \in \text{pore} \\ 0, \text{ otherwise} \end{cases} \tag{2}$$

For fixed point $\tilde{x}$, the indicator function $\tau^{MI}(\tilde{x})$ has only two possible values; i.e., for point belongs to pore, it is 1, otherwise 0. The probabilistic description of $\tau^{MI}(\tilde{x})$ is given simply by the probability that $\tau^{MI}(\tilde{x})$ is 1, which we write as

$$p\{\tau^{MI}(\tilde{x}) = 1\} \tag{3}$$

Therefore, the 2-point correlation function can be defined as

$$\begin{aligned} S_2(\tilde{x}_1, \tilde{x}_2) &= p\{\tau^{MI}(\tilde{x}_1) = 1, \tau^{MI}(\tilde{x}_2) = 1\} \\ &= \Pr obability\ that\ 2\ point s\ at\ positoins\ \tilde{x}_1, \tilde{x}_2 \\ &\quad are\ found\ in\ bone \end{aligned} \tag{4}$$

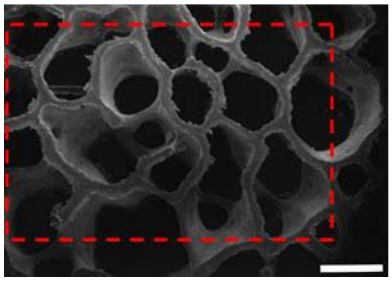
A simple physical way of understanding $S_2$ is to think of it as the probability of finding two randomly selected points that are both in the pore phase.

A digital image is a collection of individual, nonoverlapping elements or pixels that have distinct intensities (gray scale or color) indicating the size of the pixel, with high resolution meaning a small pixel is used. As the pixel size decreases, the number of pixels per unit length increases and a high-resolution digital image is generated. A digital image, as we used in this study, can be a gray –scale image, where the intensity of each pixel images from black (0) to white (N). For many imaging system, N=255, corresponding to 8 bit of intensity resolution. The original gray scale image needs to be analyzed to distinguish the bone and the pore. The thresholding process was applied to process the original sample image. Figure 2(b) shows the white and black image where white represent bone and black pore by using threshold value 210.

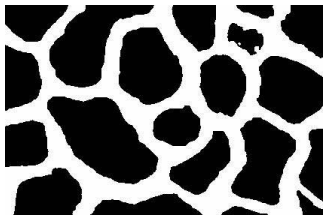
The two-point correlation function of bone can be measured from a finite size (*m* x *n*) digital image as following [10]

$$S_2(r) = S_2(x, y) = \sum_{i=1}^{M-x} \sum_{j=1}^{N-y} \frac{\tau^{MI}(i, j)\tau^{MI}(i+x, j+y)}{(m-x)(n-y)} \tag{5}$$

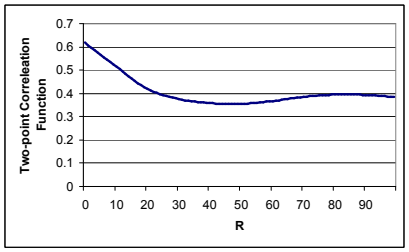
Where, $S_2(r)$ is the polar representing of 2-point correlation function, $r$ represent the distance of two random selected points. Figure 2(c) shows the measured 2-point correlation function of pore. It can be seen that when r=0 which represents the porosity of the bone is 62% while when r increases, the 2-point function converged to 0.4.



(a) Scanning electron photomicrograph of transverse slab of vertebral trabecular bone. The image is 8 bit gray scale image. The Scale line showed in image is 1 mm. The area inside the red dashed line represents the area of interest.



(b) The sample image after thresholding.




(c) The 2-poitn correlation of pore calculated by Eq.(5)

Fig. 3. The 2-point correlation computation. (Original image Figure 3(a)is provided by Dr. Paul Weinhold at University of North Carolina)

### 2.2.2 Reconstruction criteria

The reconstruction of microstructural trabecular network is an intriguing inverse problem. Clearly, it is extremely difficult to reconstructe, or to replicate the original structure because of the randomness of bone internal architecture, the inadequacy of bone internal architectural information, and the limited modeling capability and computing power. Therefore, the objective here is not to reconstruct the original structure but to reconstruct a target structure which is statistically equivalent to the original structure. In order to do this, we define a trial function

$$E = \sum_{r} [\hat{S}_2(r) - S_2(r)]^2 \tag{6}$$

where, $\hat{S}_2(r)$ represents the target 2-poitn correlation function while $\hat{S}_2(r)$ represents the original 2-poitn correlation function and the sum is over all value of *r*. The aim is to minimize the trial function to equal the target and original correlation functions. Therefore, the reconstructed structure and the original structure are statistically equivalent. In the practice, 3 sample points (*r=0, 40, 70*) were chosen to compute the trial function as following

$$E = \{[\hat{S}_2(r|_0) - S_2(r|_0)]^2 + [\hat{S}_2(r|_{40}) - S_2(r|_{40})]^2 + [\hat{S}_2(r|_{70}) - S_2(r|_{70})]^2\} \tag{7}$$

where, $\hat{S}_2(r|_0)$ represent the constructed 2-poitn correlation function at r=0 while $\hat{S}_2(r|_0)$ represent the original 2-poitn correlation function at r=0.

### 2.2.3 Reconstruction algorithm

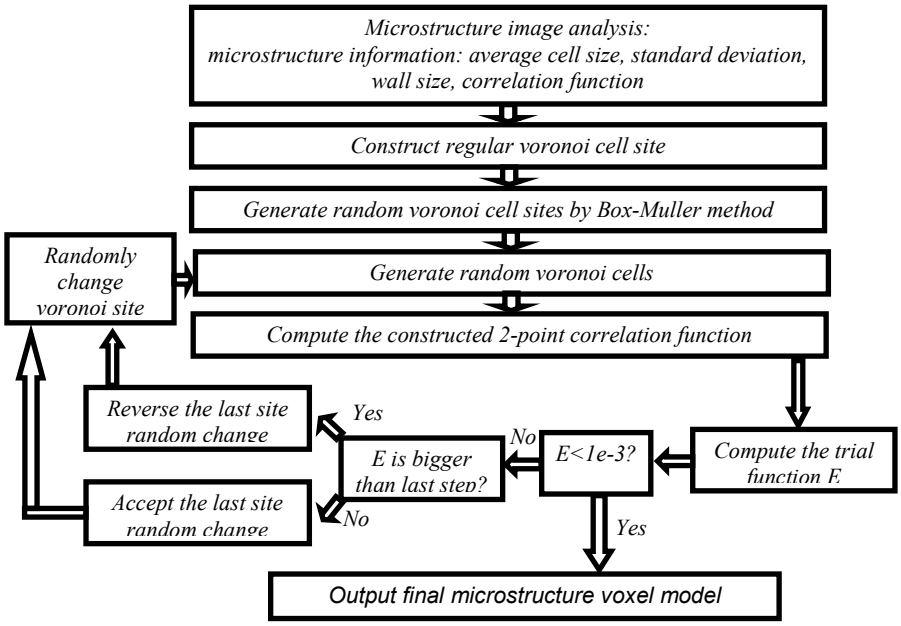
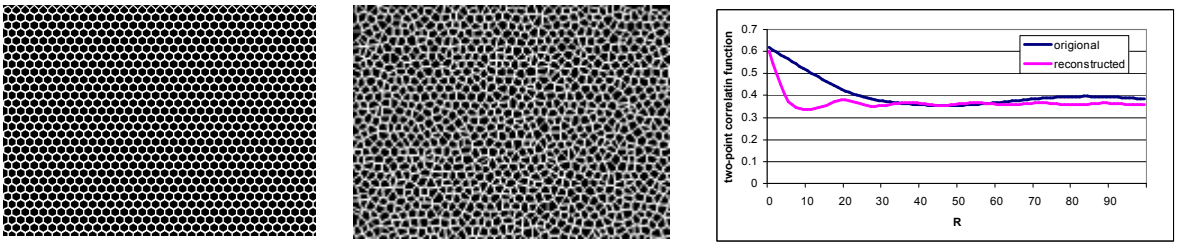



Fig. 4. The microscopic voxel model reconstruction algorithm

The image-based microscopic voxel model reconstruction begins with the acquisition of high resolution digital characteristic image acquisition and its subsequent image processing. The characteristic image is the image which can represent the feature of the bone microstructure. In this paper, a high resolution microscopy tomography image obtained from a transverse cut of a vertebrate was used. By measuring some morphologic parameters such as average cell size, standard deviation, wall size and computing the correlation function, the reconstructed algorithm starts with the regular voronoi cell site generation as shown in Figure 5(a). In this case, a honey-comb shape was used. According to the standard deviation of the cell size, the random voronoi cell site can be generated by Box-muller method [11]. Then the initial deformed voronoi cells were generated according to Fortune's algorithm [12]. Based on the generated voronoi cell configuration, the initial correlation function and initial trial function can be computed. An iteration process was adopted to minize the value of trial function by random moving the voronoi sites. For each iteration step, the trial function is checked for convergence, If the trial function is smaller than a certain allowance, the final configuration is outputted. If the trial function is larger than the allowance, the current trial function was checked with

the previous trial function, if the current value is bigger than the previous one, the previous random sire movement was recovered. If the current value is smaller the previous one, the next random voronoi site changed will be proceed for next step until the trial function is converged.
Figure 5(a) shows the initial regular voronoi cells. It can be seen that the voronoi cells are regular honey-comb structure. Figure 5(b) show the final random voronoi cells. It can be see that the voronoi cells are random in term of cell size as well as the cell shape. To show the equivalent of the original and final structure, the original correlation function and the reconstructed correlation function is plotted in the Figure 5(c), it can be seen the two functions converged well.




(a) The initial regular voronoi cell structure

(b) The final random voronoi cell structure

(c) The comparison of target 2-point correlation function with the original 2-poitn correlation function

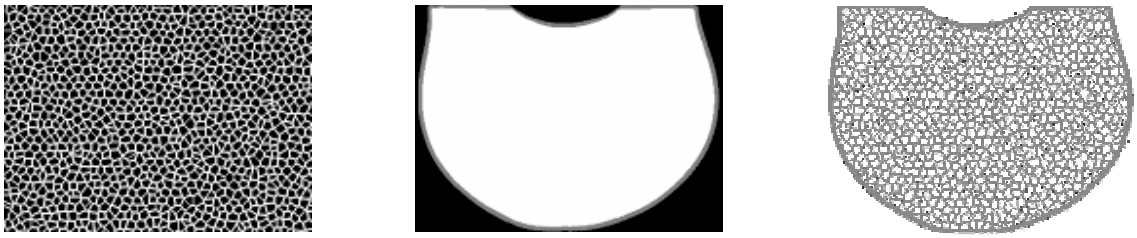
Fig. 5. microscopic trabecular voxel model

### 2.2.4 Multi-scale voxel bone model

To combine macroscopic and microscopic model together, a simple Boolean operation on one voxel was conducted as following,

$$\tau(\tilde{x}) = \begin{cases} \tau^{MI}(\tilde{x}),\ if\ \tau^{MA}(\tilde{x}) = 2 \\ 0,\ if\ \tau^{MA}(\tilde{x}) = 0 \\ 1,\ if\ \tau^{MA}(\tilde{x}) = 1 \end{cases} \tag{8}$$

Where, $\tau(\tilde{x})$ is the voxel indication function of multi-scale bone model. $\tau(\tilde{x}) = 0$ represents the solid bone voxel while $\tau(\tilde{x}) = 1$ represents the pore. As shown in the Figure 6, the final reconstructed multi-scale bone model has a overall geometry as the macroscopic model shown in Figure 6(b) and the same microscopic random voronoi cell structure as shown in the Figure 6(a).



(a)Microscopic voxel model

(b) Macroscopic voxel model

(c) multi-scale voxel model

Fig. 6. (a) The macroscopic CAD model of trabecular bone. (b) A typical layer of trabecular bone include compact bone (gray) and trabecular bone (white). (c) The reconstructed vertebrate bone voxel multi-scale model.

### 2.3 The Design Intension and Representation

The presented model is not only replicate the vertebrate bone structure, it allows to add other design consideration such as add non-random features in the model. This is very important in the bone tissue engineering scaffold design field. Bone tissue engineering scaffolds is designed to shape regenerating issue, provide temporary mechanical support and enhance tissue regeneration. The bone scaffolds should have a precise overall shape to fit into the defect bone site as well as a suitable microstructural environment to enhance the cell growth and proliferation. In order to introduce the design intension in our multi-scale bone voxel model, on the macroscopic voxel model level, model is divided into two

areas. One area is controlled by the correlation function predicted from the sampling image and one area is designed area which is controlled by the design shape. The other step will follow the steps stated in the previous section. As an example, one rectangle shape and one circular shape hole (shown middle of the model) were added in the trabecular bone area as shown in Figure 7(a). The final reconstructed model includes these 2 features as shown in Figure 7(b). It can be seen that the design shape was integrated in the final model successfully.

(a) (b)

Fig. 7. (a) The design intension adding on the trabecular bone area shown in the middle. (b) The reconstructed vertebrate model with the designed feature, a circular and rectangle holes.

## 3. DIRECT FABRICATION BASED ON VOXEL MODEL

All Solid Free-form Fabrication (SFF) techniques currently start from computer-aided model [13]. By slicing the 3-dimensional CAD model into 2-dimension slice, SFF techniques allow to build 3-dimesional objects by adding material according to 2-dimensional slices. It can be seen that CAD model and slicing are the core for traditional approach. To build a 3D CAD model of the random heterogeneous structure even in a small scale is difficult due to the complexity of the microstructure. Currently, there is no method to fabricate the tissue construct with random heterogeneous microstructure and designed shape. In this study, a Direct Fabrication (DF) process planning is presented regarding this issue.

The DF process follows the SFF technique to build 3D objects layer by layer. Since the voxel model is a volumetric discrete model, unlike traditional SFF method, it is unnecessary to slice the model. The process to build one slice of tissue construct is shown in Figure. 5. The nozzle used in the DF process system is a drop-on-demand mode nozzle. This nozzle can fabricate the object drop by drop. Each drop can be treated as a voxel in 3D voxel model. The voxel model of heterogeneous structure is feed into the direct fabrication analysis software. The software will then decide for each layer and for each voxel what material should be dropped. After one voxel layer is finished, the process goes to next layer, by this manner, a 3D structure will be built.

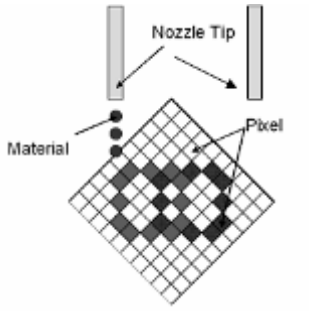
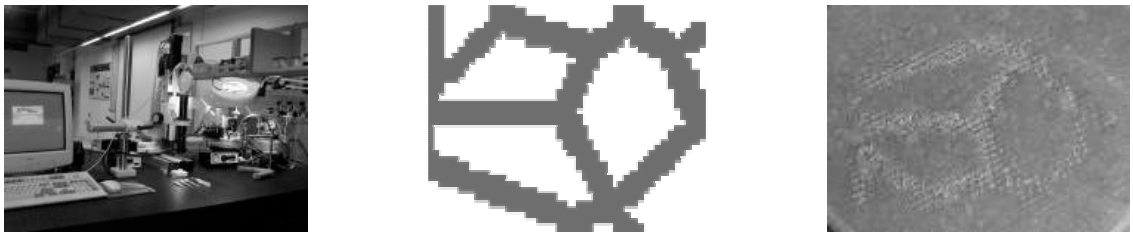



Fig. 8: Schematic of direct fabrication of one layer

A direct fabrication system was built in our lab. The Direct Fabrication system shown in figure 9(a) is a liquid-to-solid inkjet plotter with a separate Z-axis input. The inkjet subsystem rides on a precision X/Y drive carriage and deposits both materials on the build substrate under program control. The deposited material is Na-Alginate solution.

The voxel can be direct converted to machine instruction based on the material status for each voxel. The voxel model shown in Figure 9(b) can be directly plotted by the direct fabrication system as shown in figure 9(c). As an example to show the feasibility of the current direct fabrication process planning, the voxel model shown in Figure 9(b) is very simple and the size is fairly large (overall size is 1.5 inches). By improving the fabrication precision and adjust the manufacture parameter, it is possible to plot small scale model.



(a) (b) (c)

Fig. 9. (a) a Direct-Fabrication plotter system. (b) a designed simple voxel model. (c) the fabricated Na-Alginate sample based on voxel model.

## 4. CONCLUSIONS AND DISCUSSIONS

To explore new design and modeling method and develop a novel manufacturing process for bone structure, an image-based multiscale model of vertebrate bone both in macroscopic and microscopic level and a direct fabrication process planning were presented. Based on the digital image and the rigorous mathematical description, the reconstructed microstructure model is equivalent in the sense of correlation function to the original bone structure. The macroscopic geometry of the reconstructed is identical of the original model. We also showed that the design feature can also be incorporated in the reconstructed model which makes it possible to design the optimized bone implant and replacement. A direct fabrication system was developed based on the voxel mode. Unlike the traditional Rapid Prototype Technology, the voxel can be direct convert to machine instruction without expensive slicing algorithm.

This model and fabrication method can be extended to bone tissue engineering area. Tissue engineering aims to replace the defect bone structure by designing and fabricate a tissue scaffold and seeding the cell in the scaffold. The requirements for tissue scaffold are (1) to fit the defect site in macroscopic level and (2) to have similar porous microstructure network with the natural bone in microscopic level to stimulate the cell growth and proliferation. It can be seen that the current modeling and fabrication method have great potential in this application.

## 5. ACKNOWLEDGEMENT

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## 6. REFERENCES

[1] WHO Technical Report, The Burden of Musculoskeletal Conditions at the Start of the New Millennium, Series Number 919, 2003.

[2] Torquato, S. Random Heterigeneous Materials: Microscopic and Macroscopic properties, Springer-verlag New York, 2002

[3] Ulrich, D., Van Rietbergen, B., Laib, A., Ruegsegger, P., 1999. "The ability of three-dimensional structural indices to reflect mechanical aspects of trabecular bone" Bone 25, 55 – 60.

[4] Sun, W., Starly B, Darling, A., Gomez, C., "Computer-Aided Tissue Engineering: Application to biomimetic modeling and design of tissue scaffolds", Biotechnology and Applied Biochemistry, Vol. 39, Issue 1, 2004, pp. 49-58

[5] Hollister SJ, Kikuchi N. 1994. Homogenization Theory and Digital Imaging: A Basis for Studying the Mechanics and Design Principles of Bone Tissue. Biotechnology and Bioengineering. 43:586-96

[6] Vajjhala, S., Kraynik, A.M., and Gibson, L.J. (2000) "A Cellular Solid Model for Modulus Reduction due to Resorption of Trabeculae in Bone." J. Biomech. Eng., 122, 511-515.

[7] http://www.geomagic.com/, Raindrop Geomagic, Inc.

[8] Satrly, B. Lau, A., Sun, W. Lau, W. and Bradbury T., "Direct Slicing of STEP Based NURBS Models for Layered Manufacturing," Computer-Aided Design Journal, in press

[9] Overaker, D, Langrana, NA, and Cuitino, AM, "Finite Element analysis of Vertebral Body Mechanics with a Nonlinear Microstructural Model for the Trabecular Core", Journal of Biomechanical Engineering, Transaction of ASME, Vol. 121, pp.542-550, 1999.

[10] Garboczi, E. J, ed, Digital images and computer modeling, in Experimental methods in the physical sciences, Vol, 35 , Academic Press, San diego, 1999

[11] B.S. Everitt, The Cambridge dictionary of statistics, Cambridge, UK ; New York : Cambridge University Press, 2002

[12] S. Skiena, The Algorithm Design Manual , Santa Clara, Calif. : TELOS--the Electronic Library of Science, c1998
[13] Marcel Dekker, Rapid prototyping technology : selection and application, Kenneth G. Cooper, New York, 2001