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Percolation theory relates corticocancellous architecture to mechanical function in vertebrae of inbred mouse strains

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Abstract

Complex corticocancellous skeletal sites such as the vertebra or proximal femur are connected networks of bone capable of transferring mechanical loads. Characterizing these structures as networks may allow us to quantify the load transferring behavior of the emergent system as a function of the connected cortical and trabecular components. By defining the relationship between certain physical bone traits and mechanical load transfer pathways, a clearer picture of the genetic determinants of skeletal fragility can be developed. We tested the hypothesis that the measures provided by network percolation theory will reveal that different combinations of cortical, trabecular, and compositional traits lead to significantly different load transfer pathways within the vertebral bodies among inbred mouse strains. Gross morphologic, micro-architectural, and compositional traits of L5 vertebrae from 15 week old A/J (A), C57BL6/J (B6), and C3H/HeJ (C3H) inbred mice ($n=10$/strain) were determined using micro-computed tomography. Measures included total cross-sectional area, bone volume fraction, trabecular number, thickness, spacing, cortical area, and tissue mineral density. Two-dimensional coronal sections were converted to network graphs with the cortical shell considered as one highly connected node. Percolation parameters including correlation length (average number of connected nodes between superior and inferior surfaces), chemical length (minimum number of connected nodes between surfaces), and backbone mass (strut number) were measured. Analysis of the topology of the connected bone networks showed that A and B6 mice transfer load through trabecular pathways in the middle of the vertebral body in addition to the cortical shell. C3H mice transfer load primarily through the highly mineralized cortical shell. Thus, the measures provided by percolation theory provide a quantitative approach to study how different combinations of cortical and trabecular traits lead to mechanically functional structures. The data further emphasize the interdependent nature of these physical bone traits suggesting similar genetic variants may affect both trabecular and cortical bone. Therefore, developing a network approach to study corticocancellous architecture during growth should further our understanding of the biological basis of skeletal fragility and, thus, provide novel engineering approaches to studying the genetic basis of fracture risk.

Keywords: Percolation theory; Inbred mouse strains; Vertebrae; Corticocancellous architecture; Trabecular network; Biomechanics

Introduction

Growth and development greatly affect peak adult bone properties, which are important determinants of fracture risk early in life and skeletal fragility late in life. Bone mineral density (BMD), which is a measure of the amount of bone, is an important clinical tool used to diagnose fracture risk. However, to study how cancellous architecture arises during growth, multiple measures of bone architecture and tissue quality must be examined rather than simply the amount of bone. Advances in our understanding of genetic variation in growth and development offer insight into the degree of integration among skeletal features that highlights the flaws in analytical approaches that

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attempt to reduce the skeleton into discrete, supposedly independent traits, each with its own adaptive story [1]. Prior work examining details of trabecular bone architecture revealed that differences in mechanical properties could be explained by regional variation in trabecular architecture [2–4]. However, these studies failed to reveal fully how the entire bone structure is designed (or adapts) to handle the transfer of loads because they focused on a region of interest (ROI) of cancellous bone and did not consider the critical interactions of cortical bone with the flow of stress or were incomplete in that they did not include the variability in material quality. Therefore, a new integrated approach is needed to understand more completely how the underlying biological processes during growth and development determine the load transferring capability of complex corticocancellous structures.

Network science offers an approach that can help shed new light on an old problem [5]. In networks, structure almost always affects function. Researchers are most interested in the relationships between a network's components because they affect the behavior of the system as a whole. Networks are dynamic, yet robust; maintaining a given function despite adaptive changes in their components with time. The study of a network's connectivity (its ability to transfer information from point A to point B) is the focus of the percolation theory. The main objectives of the percolation theory are to characterize the distribution of cluster sizes in the network and to determine how the transfer of information depends on network architecture [5]. Although it was originally developed to answer questions in organic chemistry, percolation models have been used successfully to study network related phenomena including forest fires, electrical conductivity, epidemics of disease, and signal transfer in neurons [6].

The corticocancellous architecture of a complex skeletal site such as the vertebra or proximal femur is a connected network of bone capable of transferring mechanical loads, which are the "information" transferred through the network. The adaptive nature of these networks results in bone structures similar in mechanical function, but different in design. Previously, the percolation theory has been used in the description of age-related changes of mechanical competence in an ROI of normal and osteoporotic trabecular bone [4]. A network percolation model can also be used to study how genetic differences in bone growth affect mechanical function. Genetic variation gives rise to variation in the biological activity of each cell population leading to mechanically functional bone networks built with different combinations of trabecular bone, cortical bone, and mineral content. Bone has an inherent adaptive response to modify the apposition, resorption, and mineralization processes that determine bone structure and tissue quality to meet mechanical demands [7]. For example, inbred mice have the capability of modulating compositional and morphological bone traits to meet mechanical demands associated with weight bearing [8,9]. The coupling between bone morphology and tissue quality appears advantageous for ensuring that adequate whole bone stiffness is achieved for day-to-day activity (i.e., create a functional skeleton). However, the disadvantage is that the tissue quality factors that tend to make bone stiff also tend to make bone less ductile, less tough, and more damageable [10]. Thus,

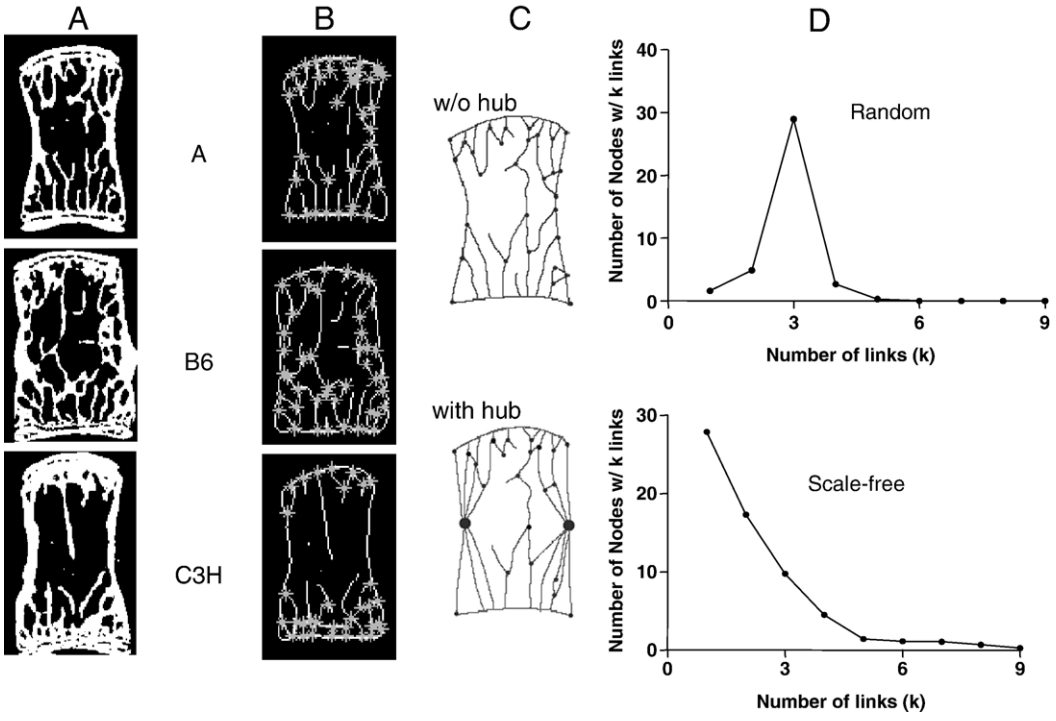

Fig. 1. Conversion of 2D vertebral images into network maps. (A) Two-dimensional coronal sections were (B) skeletonized and nodes were identified. (C) The skeleton graphs were converted into network maps by considering the cortical surface as one highly connected node or hub (large circles). (D) Graphical representation of random (no hub) and scale-free (cortical hub) networks.