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Mathematical model of mechanical behavior of micro/nanofibrous materials designed for extracellular matrix substitutes

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A B S T R A C T

Electrospun micro/nanofibrous biomaterials are widely used as extracellular matrix substitutes in tissue engineering applications because of their structural and mechanical properties. To explore the influence of microstructure on the mechanical behavior of fibrous material, a mathematical model of the fiber system was developed. The model describes the microstructural properties of a fibrous matrix using a probability density function, and enables study of their mechanical properties. The results from the mathematical model were validated by qualitative comparison with the experimental results of mechanical testing of polystyrene electrospun nanofibrous materials. The analyses show a trend of three-phase load–displacement behavior. Initially, as an increasing number of fibers are recruited for load bearing, the load–displacement curve has a 'J'-shaped toe region, which is followed by a nearly linear load–displacement curve, in which the number of load-bearing fibers remains nearly steady. Finally, there is a phase when the load–displacement curve descends, indicating failure of the material. The increase in flexibility of the fibrous material makes it stronger, but the randomness of fiber orientation makes the fibrous structure more flexible at the cost of lower strength. The measured mechanical properties of a fibrous matrix were also observed to be dependent on sample size. Therefore, the analyses establish a clear link between the structure and strength of fibrous materials for optimized design and fabrication of fibrous biomaterials with targeted use in tissue engineering, regenerative medicine and drug delivery. The model also establishes a need for standardization of experimental protocols for mechanical characterization of fibrous materials for consistency.

1. Introduction

Fibrous materials are ubiquitous in biological systems because of their unique structural and mechanical properties, arising from the high length-to-diameter ratios of the individual fibers as well as their arrangement in the fiber systems. For example, load-bearing tissues such as the tendon, ligament and the articular cartilage are mechanically reinforced with collagen fibers in the extracellular matrix (ECM), which provide them with adequate tensile strength as well as an appropriate microenvironment for specific cell behavior [1–3]. These tissues achieve a wide spectrum of mechanical properties by the complex hierarchical arrangement of the fibrous system made up of collagen and base matrix composed of proteoglycans, minerals and crosslinking agents [1]. The tissue-specific structural arrangement of the fibers gives rise to the required mechanical strength by frictional sliding of the fibers over one another, followed by their stretching [2].

Inspired by the biological systems, synthetic fibrous materials are being engineered for biomedical applications including, but not limited to, tissue engineering scaffolds and drug delivery systems [3]. Scaffolds designed using the electrospinning technique are the most extensively used fibrous materials in tissue engineering because of their tunable structural properties, e.g. diameter, orientation/alignment, porosity and surface chemical properties, which allow for closer replication of the microenvironment present in the native ECM [4]. Scaffolds designed for load-bearing tissues require not only structural and chemical properties similar to that of the ECM of the tissue of interest, but also appropriate mechanical properties, as mechanical stimuli play a significant role in cell attachment, motility and proliferation in the scaffolds [5–7].

Although there have been multiple studies characterizing fibrous materials based on various geometric and mechanical properties of the fibers [8–14], the relationship between the structural and mechanical properties of fibrous materials remains poorly understood [15–17]. In most studies, the mechanical properties of the fibrous matrices have been characterized using the stress–strain diagram, from which characteristic moduli (elastic or tangential modulus) or characteristic stress and strain values

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(e.g. yield stress, ultimate tensile stress, breaking strain) have been estimated. These measurements and subsequent calculations have most often followed methodologies used to describe the mechanical strength of bulk solids, which may not be appropriate for fibrous materials because, unlike bulk solids, the properties of fibrous materials depend not only on the material of the bulk solid, but also on the structure of the matrix, e.g. fiber diameter, fiber curvature, fiber alignment, fiber density [18–21]. Therefore, analysis of the mechanical properties of the fibrous materials is important not only for the understanding of load–deformation behavior of such biomaterials, but also for optimizing the process parameters for engineering fibrous materials with targeted structural and mechanical properties for their end use in tissue engineering and other biomedical applications.

This paper reports on the development of a theoretical framework for establishing the relationship between the macroscopic mechanical properties and the structural properties of fibrous materials. By means of a statistical model of the fibrous system, the influence of fiber assembly on the macroscopic mechanical properties of the fibrous materials was explored.

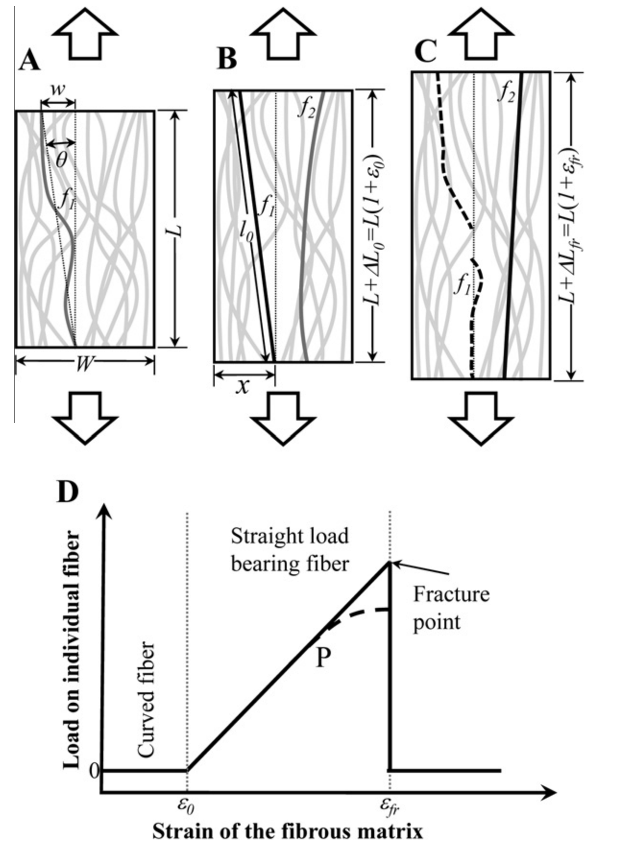

Fig. 1. Schematic showing tensile load applied on a fibrous material model. (A) The fibrous matrix is shown at the beginning of longitudinal stretching when all fibers are curved. At this stage, the scaffold material has very little mechanical resistance. (B) The scaffold is stretched to length $L+\Delta L_0$ when fiber f_1 becomes straight and begins to resists stretching, thereby providing mechanical strength to the matrix. (C) As the fibrous matrix is stretched to length $L+\Delta L_{fr}$, fiber f_1 breaks, but fiber f_2 straightens and resists stretching. (D) Load–displacement characteristic of a single fiber. The material of the model of the fibers can be linear (solid line) or non-linear (dashed line), depending on the fiber material.

2. Modeling details

The development of the theoretical model for load bearing by the fibrous materials is based on the approximation that most fibers in a fibrous matrix are initially curved until mechanically loaded. With very limited flexural strength of the fibers, the curved fibers have little load-bearing capacity until the fibers straighten and begin to resist longitudinal elongation. Therefore, when a tensile load is applied to it, a curved fiber first straightens before bearing the load. As a result, at any stretch value, only a fraction of the fibers that are straight bears the load. Thus, the tangent modulus of the fiber system depends not only on the modulus of elasticity of individual fibers, but also on the 'recruitment' of load-bearing fibers, which, in turn, depends on the organization of the fibers, all of which contribute to the observed mechanical behavior of the fibrous materials.

2.1. Model construction

The theoretical model analyzes the tensile strength of a rectangular piece of fibrous matrix of length L and width W, as shown in Fig. 1. The material is subjected to tensile load along the length, which results in lengthening of the sample (Fig. 1B and C). The thickness of the electrospun fibrous matrix being very small (0.2–0.4 mm) compared with the width (1 cm), all the fibers are assumed to be lying in the same plane. Each fiber present in the fibrous matrix can be described by its contour length l, diameter a (approximated to be uniform over the length of a fiber) and end-to-end lateral separation w. Within the rectangular piece of the fibrous matrix, the probability of finding a fiber that has length between l and $l+dl$, diameter between a and $a+da$, and end-to-end separation between w and $w+dw$ is $p(l,w,a)dldwda$. The probability density function (PDF) $p(l,w,a)$ satisfies the normalization condition

$$\int_{a_{\min}}^{a_{\max}}\int_{w_{\min}}^{w_{\max}}\int_{l_{\min}}^{l_{\max}} p(l,w,a)dldwda = 1 \tag{1}$$

where $a_{\min}$, $a_{\max}$, $w_{\min}$, $w_{\max}$ and $l_{\min}$, $l_{\max}$ are the minimum and maximum values of fiber diameter, end-to-end lateral separation and length of fibers in the fibrous matrix, respectively. The minimum and maximum fiber diameters $a_{\min}$ and $a_{\max}$ of the fibrous matrix are limited by practical limitations of the electrospinning process without any theoretical limits [22]. In the case of a fibrous matrix with fiber diameters ranging from $a_{\min}$ to $a_{\max}$, an effective fiber diameter can be calculated as

$$a_{effective} = \sqrt{\int_{a_{\min}}^{a_{\max}} a^2 p_{dia}(a)da} \tag{2}$$

where $p_{dia}(a)$ is the PDF of fiber diameters. In the base model, it is assumed that the fibers are not fused to each other, and the friction between the fibers is negligibly small. Therefore, the fibers that do not span the entire fibrous matrix longitudinally cannot bear the tensile load, and those fibers are ignored in the model. In the Appendix, a simplified model of fused fibers is also presented. Thus, in a fibrous matrix, the shortest load-bearing fiber would be straight and parallel to the longitudinal dimension of the fibrous matrix. Therefore, $l_{\min} \geqslant L$ and $w_{\min} \geqslant 0$. While there can be no theoretical limit for $l_{\max}$, $w_{\max} \leqslant W$. Length and end-to-end separation parameters of all end-to-end fibers must satisfy the condition that length of the fiber along the longitudinal direction of sample must be greater than or equal to the length of the sample, i.e.

$$l^2 - w^2 \geqslant L^2. \tag{3}$$

The length of the longest fiber in the matrix is dependent on the curvature of the fiber, with highly curved fibers being longer and vice versa. Thus, l/L represents the curvature of the fibers, and