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Review

Materials characterization and mechanobiology of the eye

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ABSTRACT

The eye responds to a great deal of internal and external stimuli throughout its normal function. Due to this, a mechanical or chemical analysis alone is insufficient. A systematic materials characterization is needed. A mechanobiological approach is required for a full understanding of the unique properties and function of the eye. This review compiles the mechanical properties of select eye components, summarizes mechanical and chemical testing platforms, and overviews modeling approaches. Analysis is done across studies, experimental methods, and between species in order to summarize what is known about the mechanobiology of the eye. Several opportunities for future research are identified.

Contents

1. Introduction

Mechanobiology has become an increasingly important topic across multiple research fields. Biochemical analysis alone does not allow full explanation for the complexity of tissues, and researchers have realized that mechanical properties must also be taken into account. Mechanobiology has grown to cover a few specific areas: dimensions (or topography) [1,2], mechanical properties [3],biochemistry [4], and the interactions of all the above. Mechanobiology is certainly important in rationalizing the function and pathology of the eye. This organ presents some unique materials characterization challenges. The eye is a complex organ, composed of different functional parts that depend on one another [5]. From a clinical point of view, the cornea, lens, vitreous, sclera, optic nerve and retina are particularly important. Each of these has specific mechanical properties that allow them to perform their required functions. Changes in these properties can lead to specific pathologies [6] or loss of function [7]. Additionally, damage done to the eye can lead to major alterations of the mechanical strength and elasticity [8]. While large scale changes are more easily recorded, changes on the cellular level are just as important [9]. These changes can lead to altered development, regeneration, or functionality of full tissues or individual cells [10,11]. Treatments for a multitude of damage and/or diseases can be developed from the quantification of these changes and how they affect individual cells and tissues alike [12]. Understanding of mechanical properties can occur through experimentation, in vivo monitoring, or computational modeling. While some mechanical properties of parts of the eye have been summarized before [13,14], this review will provide an overview of mechanical features of each of the above listed eye components, an insight into in vitro mechanobiology experiments, and a look into modeling approaches. The conclusions will focus on trends that have

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the potential to provide new knowledge into the mechanobiology of the eye.

2. Anatomical structures

2.1. Cornea

The cornea provides protection from infection and physical damage to the eye and acts as a clear window for light to pass into the eye [15,16]. The corneal mechanical properties have been well characterized through many different tests. Indentation, inflation, and tensile/compressive testing remain common methods for analyzing mechanical properties. Indentation has been used and improved upon for use in determining elastic and viscoelastic properties of the cornea [17]. Inflation testing has also consistently been utilized to understand corneal tissue, and a study by Elsheikh et al. has investigated how much more effective inflation testing is when compared to strip extensometry [18]. Samples from multiple species [19,20] have been examined and their stress–strain behavior recorded [3,21]. Tensile and compressive testing, using uni-axial, bi-axial, or pressure testing, has been applied extensively [22]. In addition to standard mechanical testing, the cornea has been characterized through high resolution microscopy techniques such as atomic force microscopy (AFM). One of the tests that has gained popularity is indentation testing using an AFM tip, Fig. 1 [23]. Some of the benefits include the ability to test both elastic and viscoelastic properties and continuous axisymmetrical testing. This indentation testing has been compared to normal tensile testing by McKee et al. [13]. McKee et al. used AFM indentation with multiple tip designs to determine the Young's Modulus of corneal samples, among others. The indentation results were greatly different from the tensile data

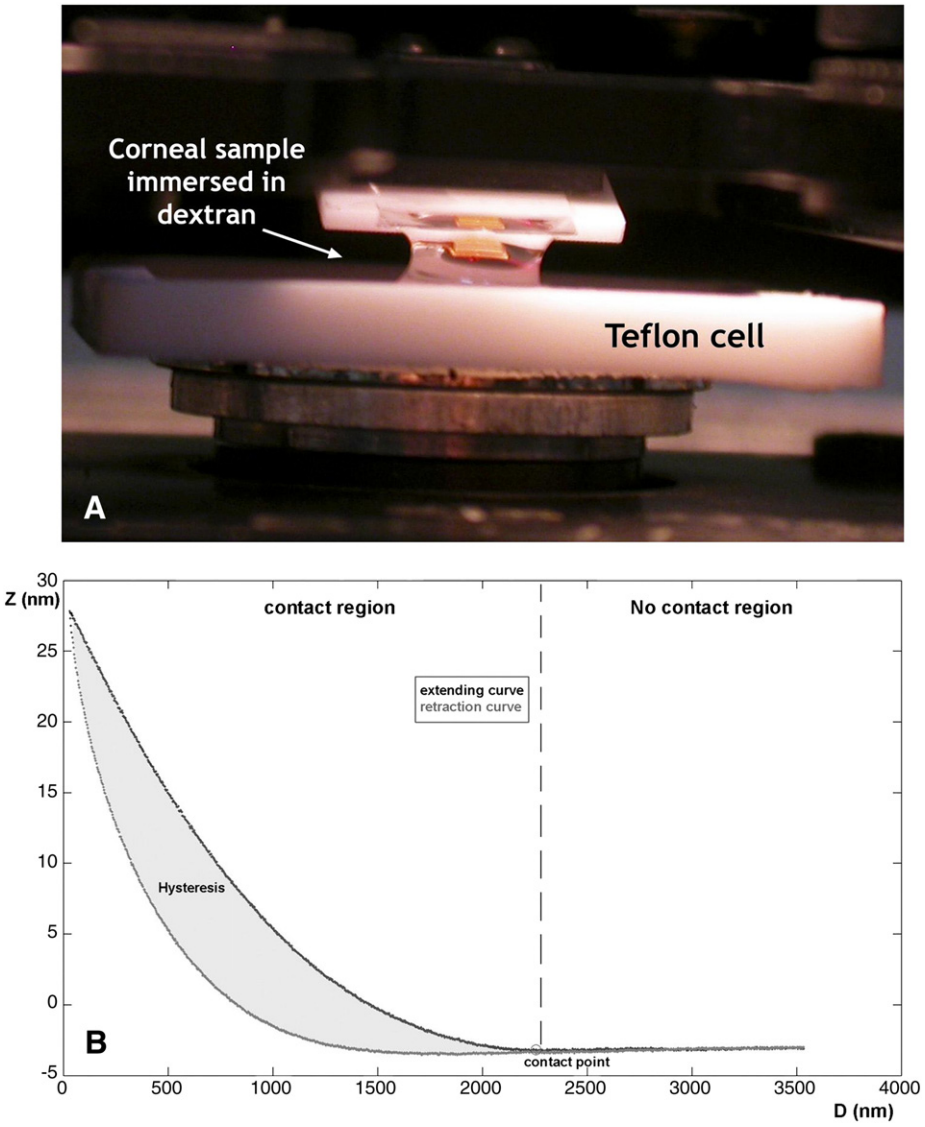

Fig. 1. (A) Mechanical measurements of the anterior stroma were performed with the AFM tip, and the tissue was completely immersed in 15% dextran solution on a custom-built Teflon cell. The storage medium was used to maintain the stromal thickness during the experiment. (B) A typical extension–retraction cycle obtained in this study. In a force–distance (*f*–*d*) plot, *Z*c and *Z*p are the cantilever deflection and the piezo displacement, respectively. Within each extension–retraction cycle, a signal proportional to the deflection of the cantilever is recorded as a function of the vertical position of the piezoelectric stage. At large separation, the interaction between the sample and probe is 0 (no contact region), and the curve consists of a straight line, until the probe comes into contact with the sample when the gradient of forces (attractive) exceeds the spring constant of the cantilever (contact point). The absence of jump-to-contact indicates negligible interactions of the tip with the surface in dextran solution. As the tip comes into contact with the stroma, there is a gradual increase in the deflection of the cantilever, as expected with soft samples. On retraction of the corneal surface from the probe, the approach and retraction curves do not overlap. This phenomenon is due to the material's hysteresis (*shaded area*). On retraction, the absence of a pull-off jump of the tip from the sample's surface is typical of viscoelastic materials.
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