A Biphasic Model for Micro-Indentation of a Hydrogel-Based Contact Lens

Introduction

Soft contact lenses are composed of polymeric hydrogels. The porous structure of these hydrogels allows for transport of oxygen, water, and other nutrients through the lens to the cornea of the eye. Numerous contact lens studies have focused on oxygen permeation through the lens [1,2]. However, the flow of water through the lens, governed by the hydraulic permeability property, may also contribute to important lens functions including on-eye comfort of contact lenses and the bulk stiffness of contact lenses. In addition, indentation of thin membranes (~100 μm) requires special consideration of boundary conditions at lens surfaces and at the indenter contact region. In this study, a biphasic finite element model was developed to simulate the micro-indentation of a hydrogel contact lens. The model accounts for a curved thin hydrogel membrane supported on an impermeable mold. A time-varying boundary condition was implemented to model the interface between the impermeable spherical indenter and the lens. Parametric studies varying the indentation velocities and hydraulic permeability show F-D curves have a sensitive region outside of which the force response reaches asymptotic limits governed by either the solid matrix (slow indentation velocity, large permeability) or the fluid transport (high indentation velocity, low permeability). Using these results, biphasic properties (Young’s modulus and hydraulic permeability) were estimated by fitting model results to F-D curves obtained at multiple indentation velocities (1.2 and 20 μm/s). Fitting to micro-indentation test data of Etafilcon A resulted in an estimated permeability range of $1.0 \times 10^{-15}$ to $5.0 \times 10^{-15}$ m$/^3$/N s and Young’s modulus range of 130 to 170 kPa. [DOI: 10.1115/1.2472373]

Keywords: hydraulic conductivity, pHMA-MAA, poroelastic, porous media, exudation, FEM, computational model, biphasic, microindentation

1 Introduction

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3 For example, stiffer contact lenses may not fit the cornea well and may exhibit edge fluting, causing a foreign-body sensation. In addition, highly stiff contact lenses increase the occurrence of complications, e.g., SEALs [3,4]. Hydraulic permeability and Young’s modulus of the hydrogel matrix can be determined by micro-indentation of the lens under certain loading conditions. In such cases, matrix deformation and fluid transport through the hydrogel can be related to bulk viscoelastic behavior through biphasic theory [6]. Therefore biphasic characterization may be useful in the development and testing of comfortable lenses.

4 Stiffness properties for various hydrogels have been reported by a number of researchers using traditional techniques, including tensile testing, compression testing, and dynamic mechanical analysis [7–12]. For the hydrogel used in this study (Etafilcon A), Enns [12] used tensile tests to measure the Young’s modulus, obtaining a bulk value of approximately 255 kPa. Hydraulic permeability has been measured directly by permeation experiments. Yasuda et al. [13] used low-pressure ultrafiltration cells to measure hydraulic permeability of hydrogels with different equilibrium water content, which is the weight percentage of water in the equilibrium hydrogel. Measured values were $2.89 \times 10^{-17}$ m$/^3$/N s for 21% EWC pHMA-EG and $1.25 \times 10^{-15}$ m$/^3$/N s for 64% EWC PCGA. Testing pHMA membranes, Refojo [14] measured the hydraulic permeability of 38.7% 10−15 m$/^3$/N s and 53.8% EWC to be $8.4 \times 10^{-18}$ and 1.05 $\times 10^{-17}$ m$/^3$/N s, respectively, using a pressure-driven permeameter. More recently, Monticelli et al. [15] used a similar system to test 38% EWC HEMA-based hydrogel membranes (polymacon) and measured hydraulic permeability was $4.0 \times 10^{-18}$ m$/^3$/N s. Besides such studies that measure stiffness and permeability properties separately, Chiarelli et al. [16] used a poroelastic analysis of the stress relaxation response of thin strips to estimate poroelastic properties of the hydrogel polyvinyl alcohol-polyacrylic acid. For 19-mm-thick samples, Young’s modulus was estimated to be 750 kPa and hydraulic permeability was estimated to be $1.2 \times 10^{-17}$ m$/^3$/N s. In addition, biphasic analysis by LeRoux and Setton [17] have extracted properties from tensile tests on canine meniscus. In their study, custom biphasic FEM codes were used to predict the stress-relaxation behavior, and permeabilities were obtained by fitting computational predictions with experimental data.

Contributed by the Bioengineering Division of ASME for publication in the Journal of Biomechanical Engineering. Manuscript received December 9, 2005; final manuscript received September 13, 2006. Review conducted by Jacques M. Huynh. Paper presented at the 2005 ASME Summer Bioengineering Conference, Vail, CO.
In addition to traditional testing methods, which generally involve complex sample preparation, indentation exists as an alternative, nondestructive testing technique for measuring the mechanical properties of materials [18–25]. Micro-indentation refers to indentation on the micrometer scale, and nanoindentation refers to submicrometer scale testing. In practice, an indenter tip is pushed into the surface of the sample. The applied force and the penetration depth of the tip into the sample are used to create a force-displacement curve. Indentation is increasingly being used in the mechanical assessment of soft hydrated materials, e.g., biological tissues, because of its nondestructive nature, small sample capacity, and ability to hone in on localized regions of interest [19,22,25]. For its application to soft hydrated materials, various data analysis techniques have been used to determine mechanical properties. Using the analysis technique developed by Oliver and Pharr [18] for elastic/plastic materials, Ebenstein et al. [19] determined reduced modulus values of porcine aorta by nanoindentation (indentation depth 1–2 μm). In addition, biphasic analysis has been used to address the complex indentation response during indentation tests (indentation depth ~0.1–0.5 mm) on cartilage and hydrogels [23–27]. Mow and co-workers [24,26] solved for the displacement of a cylindrical porous indenter during creep and then used the analytical solution to extract Young’s modulus, Poisson ratio, and permeability from indentation tests (~0.2 mm indentation depth) of cartilage. FEM models are able to account for complex boundary conditions and allow for the consideration of spherical and impermeable indenters, for which analytic solutions are not mathematically tractable. A linear biphasic FEM model has been developed by Spilker et al. [27] to predict the indentation stress-relaxation response of articular cartilage taking into account friction at the indenter-tissue interface and tissue thickness. Using the same linear biphasic model, Hale et al. [23] have predicted the indentation F-D response for canine articular cartilage. They modeled an impermeable spherical tip moving with a constant indentation speed (~0.3 mm indentation depth and ~25% compression), and these predicted F-D profiles were used to determine Young’s modulus, Poisson ratio, and permeability.

In this study, we use a linear biphasic model to predict the rate-dependent behavior of a curved contact lens during microindentation (~20 μm indentation depth). A FEM model was developed that accounts for the thin geometry, the spherical indenter shape, and the time-varying contact interface between the impermeable indenter and hydrogel surface. Specifically, the FEM model was used to predict F-D behavior during constant velocity indentation. The effect of varying experimental parameters, including indenter velocity, hydrogel permeability, and matrix stiffness, on predicted F-D curves were parameterized. The results of this sensitivity analysis were used as a guide for experimental design, and model results were optimally fit with test data obtained at multiple indentation rates. The results of this study provide data for hydraulic permeability and Young’s modulus of the polymer matrix of the contact lens material, Etafilcon A.

Materials and Methods

Material and Experimental Testing. The contact lenses (ACUVUE®, Vistakon, Jacksonville, FL) used in this study were composed of Etafilcon-A (copolymer of 2-hydroxyethyl methacrylate and methacrylic acid), which has an equilibrium water content of 58% (by weight). Lenses were approximately 100 μm thick at the apex and had a 7.68 mm base radius of curvature along the apex. Samples were fixed onto a rigid, impermeable, and conformal polymer foundation (which is rigid and impermeable in comparison to the hydrogel). A NanoTribometer™ (CSM Instruments, Peseux, Switzerland) was used to perform indentation tests. The test apparatus consisted of a cantilever arm whose base was coarsely controlled by a stepper motor and finely controlled by a piezoelectric cell (maximum vertical movement ~100 μm, and vertical resolution, ~20 nm; Fig. 1). The stainless steel spherical indenter (radius=1 mm) was bonded to the end of the cantilever, which had a measured cantilever stiffness of 0.7194 mN/μm. The cantilever displacements were measured at a fixed location along the cantilever using built in optical sensors. The entire apparatus was located on a vibration isolated granite table. For analysis, force versus time (F-t), and force versus penetration depth (F-D) into the hydrogel were collected and plotted. The experiments were conducted by moving the base of the cantilever using a controlled velocity through the initial gap and into the lens until a penetration depth of approximately 20 μm was reached (strain ~20%). Two indenter velocities exhibiting distinct F-D behavior were used: a high velocity ~20 μm/s (19.7–21.8 μm/s, n=5) and a low velocity ~1.2 μm/s, (1.1–1.3 μm/s, n=4). A new lens from commercial packaging was used for each test. For experiments that were performed in air, the assembly and indentation process occurred in less than 2 min from the time the lens was removed from the packing; this was done to minimize lens dehydration. For these tests, three distinct stages were identified from the F-t curve: (1) indenter movement through air, (2) indenter movement through the fluid film on the surface of the contact lens (determined to be several micrometers thick), and (3) indenter contact with the hydrogel. The indenter contact point was determined by first fitting a line to the force response for stage 2, then determining the point from which there was a departure from this line (due to contact with a stiffer material, i.e. the hydrogel; Fig. 2). For low velocity tests, the contact point was distinct, marked by a discrete change in slope. However, at high indenter velocities, determination of the contact point was difficult because of limited sampling of data through stage 2 and difficulty in separating out meniscus effects (the adhesion of fluid to the indenter due to surface tension). For high velocity tests, the sample was indented using a submerged configuration. These submerged tests reduced meniscus effects and increased the number of data points.
sampled in the fluid before contact, facilitating the determination of the contact point. (Submerged tests at low velocity were found to have increased noise. Therefore, unsubmerged tests were used at low velocity.) For these tests, a polymer dam was created around the contact lens setup. The dam was filled with deionized water, and the contact lens was held in place by overlaying a steel plate with a circle hole cutout.

Mechanics Model. Hydrogels are composed of a polymer network saturated with water. The water in hydrogels exists in two forms, i.e. bound water and free water [28]. It is reported that Etafilcon A has approximately 54% free water out of a total 58% water content [29]. The free water is responsible for the fluid transport properties of hydrogels. Polymer chains and bound water create the polymer network that contributes to the solid properties of the hydrogel. The mechanical behavior of porous hydrogels can be described by the biphasic model by Mow et al. [6], which has been used extensively in the analysis of articular cartilage [6,24,26]. Biphatic theory is based on theory of mixtures in which each spatial point in the mixture is assumed to be occupied simultaneously by a material point of a fluid and solid phase. In the application of the biphasic theory to hydrogel contact lens, it is assumed that both the solid and fluid phases are incompressible and the fluid is inviscid. The constitutive equation for the bulk material is [6]

\[ \sigma = -pI + \lambda Tr(e)I + 2\mu e \]  

where \( \sigma \) is the stress tensor of the solid matrix (defined by \( \sigma = \frac{1}{2}(T + T^T) \)), \( \lambda, \mu \) are the Lamé elastic constants of the solid matrix; \( p \) is the pore fluid pressure. Lamé constants are related to Young’s modulus and Poisson ratio \((E, v)\) of the solid matrix, which are used in following sections, by \( \lambda = E/(1 + v)(1-2v) \) and \( \mu = E/2(1+v) \).

The balance of momentum results in the equation:

\[ \nabla \cdot [\lambda Tr(e)I + 2\mu e] - \nabla p = 0 \]  

Fluid flow is described by Darcy’s law as

\[ k \nabla p = \nabla v = -v \]  

where \( v = \delta \nabla \cdot \dot{v} + \delta \nabla \cdot \dot{v} \) is the volume-averaged bulk velocity; \( \dot{v}, \dot{v} \) are the velocity vectors of solid and fluid; \( \delta, \delta \) are the volume fraction of the solid and fluid phases in the bulk material respectively; and \( k \) is the hydraulic permeability (constant \( k \) is assumed). Using Eq. (3) with the conservation of mass (\( \nabla \cdot v = 0 \)) results in

\[ \nabla \cdot (k \nabla p) = \frac{\partial (Tr(e))}{\partial t} \]  

Equations (2) and (4) comprise the governing equations for the coupled fluid-solid problem. A \( u-p \) (displacement-pressure) formulation was used in finite element discretization [30].

Finite Element Modeling. Micro-indentation of the lens was modeled as a 2-D, axisymmetric, contact problem with the spherical indenter contacting the center of the lens and moving downward at a constant velocity (Fig. 3). The contact lens hydrogel was modeled as a biphasic isotropic material and the indenter was modeled as a rigid, impermeable body. The hydrogel was assumed to have constant thickness and an equal radius of curvature on the top and bottom surfaces of the test region. The boundary conditions for the hydrogel were: (1) fixed displacement and no fluid flux at the bottom of the hydrogel (rigid foundation boundary); (2) free displacement and zero fluid pore pressure at the surface of the hydrogel; (3) impermeable indenter, i.e., zero normal flow flux in the contact region; and (4) frictionless contact between the indenter and the hydrogel.

A time-varying boundary condition was used to ensure impermeability at points of contact with the indenter. That is, since the contact region increased as the indenter moved downward at a constant velocity, the boundary condition assigned to nodes at the hydrogel surface that were in contact with the indenter had to be reassigned accordingly. Nodal contact points were determined at each time step using a pilot simulation (which initially assumed a zero pressure boundary condition along the contact surface). A version 6.5, The MathWorks Inc., Natick, MA) subroutine was developed to generate a FEM model at each solution time step as guided by the nodal contact information determined from the pilot simulation. Generated FEM models updated the surface boundary condition, setting normal fluid flux to zero at contact nodes, and imported the solution from the previous step as the initial condition. Biphatic equations were solved using the FEM package ADINA (version 8.2.2, ADINA R&D Inc., Water- town, MA), and the solution was transferred to the next time step, continuing the simulation.

Contact modeling was implemented by defining two potential contact surfaces: the indenter surface and the top surface of the hydrogel (Fig. 3). Displacement of the nodes on these two surfaces was checked and adjusted at each time step such that penetration of a node on one surface into another surface was avoided by imposing a penalty function [30]. The micro-indentation process was modeled as a quasi-static problem. Reaction force on the indenter was calculated for each time step during simulation. A sparse solver (a direct solution method) was used to solve the discretized form of Eqs. (2) and (4) [30]. The FEM mesh was generated using nine-node rectangular elements. The final mesh consisted of 1600 elements. To increase the accuracy of the computational results, a finer mesh was adopted in the contact region. Doubling the number of elements resulted in a negligible change in predicted force response.

Determination of Biphasic Properties. The calculated indenter displacement versus time from experiments was used as the input for indenter displacement in the FEM models. The predicted reaction force acting on the indenter in the vertical direction was calculated at each time step by summing vertical components of forces acting on all surface elements of the indenter. The predicted F-D curve was obtained for a combination of biphasic properties \( E, v, k \). Given the uncertainty in the material value of the Poisson ratio, a range of values were simulated (0.1, 0.2, 0.3, and 0.4). For each Poisson ratio, 16 × 20 simulations were carried out; 16 simulations with \( E \) varying between 100 to 400 kPa (\( \Delta E \) = 20 kPa) and 20 simulations varying \( k \) between 1.0 × 10\(^{-17}\) to 7.5 × 10\(^{-13}\) m\(^2\)/N s. The choice of these ranges was based on previous studies [12,13], where Enns measured a Young’s modulus of 255 kPa for this material and Yasuda et al. obtained permeability values between 2.78 × 10\(^{-17}\) to 1.25 × 10\(^{-13}\) m\(^2\)/N s for different hydrogels with different EWCs from 21% to 64%.

Computationally predicted F-D curves were compared with ex-
peripheral F-D data. Since material properties should be independent of indentation velocity, the set of material properties that result in the best-fitting F-D curve at the high indenter velocity should also provide the best-fitting results at the slower velocity. F-D curves were simultaneously compared at varying indentation velocities for a prescribed set of material properties ($E$, $v$, and $k$). The mean square error was calculated using the equation

$$\text{MSE} = \frac{1}{m} \sum_{i=1}^{m} \left( X_i^E - X_i^C \right)^2 / n_i$$

where $m$ is the total number of F-D curves ($m=7$), $n_i$ is the total number of points to be compared for the $i$th experimental F-D curve ($n_1=17$ for high velocity and $n_2=32$ for low velocity indentation), $X_i^E$ and $X_i^C$ are the experimental and computational reaction force values of the $i$th experimental F-D curve, respectively. A MSE map for varying $E$ and $k$ was plotted for each $v$. Potential optimal values that minimize MSE were then identified for each Poisson ratio.

**Results**

*Experimental Micro-indentation Results.* Figure 4 shows F-D data obtained during micro-indentation of the contact lens for two different indenter velocities: 1.2 μm/s ($n=4$) and 20.0 μm/s ($n=5$). There was an initial displacement region between 0 to ~12 μm, i.e., the toe region, where there was no obvious difference between F-D behaviors between the different indenter velocities. Forces in this region are quite low, up to approximately 1.5 mN. Upon further indentation up to 20 μm, two distinct curves were obtained, with the higher indenter velocity tests resulting in a larger force response. Response forces acting on the indenter were as high as 4.8 mN for the 20.0 μm/s velocity at maximum displacement (~20% strain). Corresponding reaction forces at 1.2 μm/s were ~20% lower.

**Sensitivity of the Predicted F-D Response.** Different indenter velocities were simulated while keeping all the other parameters fixed ($E$, $v$, and the maximum displacement). As the indenter velocity increased, the response force acting on the indenter also increased, i.e., the F-D curve shifted upward, as shown in Fig. 5(a). Area under the curve was calculated to measure changes in the F-D response. AUC has physical relevance as the work done during micro-indentation. Sensitivity of AUC to changes in indenter velocity is shown in Fig. 5(b). This graph implies that, for a given hydrogel, there is a range of indenter velocities within which the response force increases with indenter velocity. Outside of this range, the F-D response changes little with indenter velocity. For materials with higher permeability, this sensitive range shifts to a range with higher indenter velocity values. These sensitivity results imply that it is necessary to test within the sensitive range of indenter velocities when using micro-indentation to back out hydraulic permeability of a given hydrated material. This can be insured by testing at multiple velocities that result in distinct F-D curves.

Micro-indentation of materials with different permeability values was also simulated while keeping all the other parameters fixed ($E$, $v$, and indenter velocity). F-D response was compared by plotting AUC as a function of permeability (Fig. 5(c)). This provided a method to compare results with experimental data.

**Fig. 4** Changes in the AUC correspond to changes in F-D behavior (A). Sensitivity of F-D curves to (B) indenter velocity and (C) permeability. Normalized AUC was calculated by dividing AUC with the asymptotic limit of AUC determined at high loading rate in (B) and at low permeability in (C) ($E$=270 kPa, $v$=0.3).

**Fig. 5** Fitting between computational and experimental curves at different indenter velocities (1.2 and 20 μm/s). The values used are $E$=150 kPa, $k$=2.5×10^{-15} m^4/N s, and $v$=0.3.
graph also suggests a sensitive range within which the response force increases as the permeability decreases. This sensitive range of permeability shifts to a range with higher values as indenter velocity increases.

**Biphasic Parameter Estimates.** Experimental \( F-D \) results were compared with the simulated \( F-D \) response over the prescribed range of \( E, v, \) and \( k \). A MSE map generated using the experimental \( F-D \) response at a single indenter velocity \( (1.2 \, \mu m/s) \) and a fixed Poisson ratio \( (v=0.3) \) is presented in Fig. 6. From this map it is evident that the MSE does not reach a unique minimum, and \( E \) and \( k \) cannot be estimated uniquely. The range of best fitting \( E \) and \( k \) values was reduced by using the MSE calculated from multiple indenter velocities \( (1.2 \) and \( 20 \, \mu m/s) \).

Figure 7 shows the corresponding MSE maps for different Poisson ratios. MSE maps did not show a unique value for \( v \), with the minimum MSE values being close in value; e.g., 0.0102 for \( v=0.4 \), 0.0098 for \( v=0.3 \), 0.0075 for \( v=0.2 \), and 0.0142 for \( v=0.1 \). Thus, estimates of \( k \) and \( E \) were made for each \( v \). By using results from a previous study by Yasuda et al. [13], permeability for a high EWC \((64\%)\) hydrogel was estimated as approximately \((10^{-15} \, m^4 /N \, s)\). By imposing this permeability range, the permeability values estimated using the MSE matrix were narrowed to the closed region with the smaller permeability values.

Estimates of \( E \) and \( k \) are summarized in Table 1. Presented ranges correspond to MSE <0.03. Experimental \( F-D \) response at a single indenter velocity \( (1.2 \, \mu m/s) \) and a fixed Poisson ratio \( (v=0.3) \) is presented in Fig. 6. From this map it is evident that the MSE does not reach a unique minimum, and \( E \) and \( k \) cannot be estimated uniquely. The range of best fitting \( E \) and \( k \) values was reduced by using the MSE calculated from multiple indenter velocities \( (1.2 \) and \( 20 \, \mu m/s) \).

**Table 1** Estimates of biphasic properties at different Poisson ratios. Presented ranges correspond to MSE <0.03.

<table>
<thead>
<tr>
<th>Poisson ratio</th>
<th>Young’s modulus (kPa)</th>
<th>Permeability ( (m^4/N , s) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4</td>
<td>150–170</td>
<td>((1–5) \times 10^{-15})</td>
</tr>
<tr>
<td>0.3</td>
<td>150–170</td>
<td>((1–5) \times 10^{-15})</td>
</tr>
<tr>
<td>0.2</td>
<td>130–150</td>
<td>((1–5) \times 10^{-15})</td>
</tr>
<tr>
<td>0.1</td>
<td>138–142</td>
<td>((2.0–3.0) \times 10^{-15})</td>
</tr>
</tbody>
</table>

Fig. 6 MSE map generated to compare experimental and simulated \( F-D \) response for varying \( E \) and \( k \). A node on the mesh represents a combination of \((E, k)\) used in the FEM biphasic model. This map (at a fixed \( v=0.3 \)) compares experimental data at single indenter velocity of \( 1.2 \, \mu m/s \). Minimum values represent best fit with the experimental \( F-D \) data. Nonunique optimal values are found.

Fig. 7 MSE maps generated to compare simulated and experimental \( F-D \) responses at indenter velocities of \( 1.2 \) and \( 20 \, \mu m/s \). A node on the mesh represents a combination of \((E, k)\) used in the FEM biphasic model. Best-fit parameter values of \( E \) and \( k \) minimize the MSE at different Poisson ratio, \( v=0.1, 0.2, 0.3, \) and \( 0.4 \).
of estimated $E$ was from 130 to 170 kPa. Simulation curves (with minimal MSE) for the $F-D$ response with the corresponding experimental data are shown in Fig. 4. Good fits were achieved with MSE=0.012 for the indenter velocity of $\sim$20 $\mu$m/s and MSE=0.014 for the indenter velocity of $\sim$1.2 $\mu$m/s.

Simulated indentation at different indenter velocities (20, 1.2, and 0.05 $\mu$m/s) using estimated parameters ($E=140$ kPa, $k=2.5 \times 10^{-15}$ m$^3$/N s, $v=0.3$, $u_0=20$ $\mu$m, where $u_0$ is the maximum indenter depth, $t_0$ is the ramping time to reach $u_0$. The pink arc is the indenter. For $t_0=1$, 16, and 400 s (corresponding to indenter velocities of 20, 1.2, and 0.05 $\mu$m/s, respectively), the magnitude of maximum pore pressure are 50.9, 26.4, and 0.05 $\mu$m/s, respectively). The magnitude of fluid pressure was found at the bottom center of the contact region. To provide insight into flow-dependent behavior, we compared the magnitude of fluid pressure at different indenter velocities. For a slow indenter velocity of 0.05 $\mu$m/s, the contribution of fluid pressure to the total stress was quite small ($\sim$6%) and load was borne mainly by the solid. For higher indenter velocities of 1.2 and 20 $\mu$m/s, fluid pressure contributed $\sim$41% and $\sim$51%, respectively, to the total stress. In these two cases, both fluid and solid phases support the indentation load.

### Discussion

In this study, we investigated the mechanical behavior of a thin contact lens hydrogel under micro-indentation. Observed rate-dependent $F-D$ behavior suggests that previously developed micro-indentation analysis techniques for elastic/plastic materials [18] may be inadequate for analysis of soft hydrated material, since the resultant bulk modulus values may vary with indenter velocity. Rate-dependent behavior caused by fluid flow can be explained using biphasic analysis. In this study, a computational biphasic model was developed that accounts for the varying contact area and the thin, curved geometry of the lens. Indentation rate-independent material properties $E$ and $k$ were determined by fitting model results to experimental measures of $F-D$ response.

Sensitivity analyses of $F-D$ behavior showed a range of indenter velocities, outside of which the $F-D$ response changed little with increases or decreases in indenter velocity. A similar result was found when varying the permeability property and holding all other parameters constant. Limits in the mechanical response under conditions of changing loading conditions and material properties are well known [26] and exist because of limitations on the pore fluid response. For slow indentation rate tests or high permeability materials, the fluid within the hydrogel has enough time to redistribute through pores and the load is mainly borne by the solid matrix. For high indentation rate tests or low permeability materials, there is not enough time for pore fluids to redistribute, resulting in significant pressure gradients. Results from sensitivity studies highlight the need to test in the sensitive range of velocities when determining the hydraulic permeability; otherwise, a unique value cannot be obtained (Fig. 5c). To address this issue, we tested at multiple indenter velocities that result in distinct, nonoverlapping $F-D$ curves. In addition, MSE maps fitting to an $F-D$ curve obtained at a single velocity within the sensitive region showed nonunique optimal biphasic properties. This can be explained as a trade-off between properties; e.g., increases in the force response were predicted by increasing $E$ or by decreasing $k$ separately. However, by simultaneously fitting $F-D$ curves obtained at multiple indenter velocities, the common minimum region in MSE mappings was narrowed and these regions provided estimated ranges of $E$ and $k$.

No obvious minimum for MSE was found for the wide range of Poisson ratio values input into the biphasic model (0.1 to 0.4). Few published data of Poisson ratios for hydrogel matrices are available with which to narrow the predicted range, though a small Poisson ratio is expected due to the large equilibrium water content. Goldsmith et al. [25] measured a Poisson ratio of 0.0 to 0.307 for the hydrogel polyNVP-MMA with cellulose acetate, which has 50% EWC. However, over the range of Poisson ratios simulated, the estimated ranges of $E$ and $k$ were found to be relatively insensitive to the changes of Poisson ratio (Table 1).

The estimated Young’s modulus for the solid matrix component of the hydrogel was 130 to 170 kPa. Comparing with bulk modulus values (which measures the combined matrix and pore fluid resistance) provided by the manufacturer [12], the estimated modulus was lower, as expected. The bulk modulus value of 255 kPa was obtained from tensile tests at 850 $\mu$m/s. Bulk modulus values calculated from biphasic FEM simulations of the tensile test using the estimated biphasic properties were 193 kPa. This predicted value is comparable to the experimentally measured value since some difference is expected given the different testing modes. The large difference in testing velocities between the tensile testing and the indentation tests. Estimated hydraulic permeability range was, $1 \times 10^{-13}$ to $5 \times 10^{-13}$ m$^2$/N s. Yasuda et al. [13] measured the permeability of 21% EWC pHEMA and 64% EWC pGMA. By interpolating their results, a 58% EWC Etafilcon A may be expected to have permeability range of $(0.8-1.0) \times 10^{-13}$ m$^2$/N s, similar to the range estimated. Our measured hydraulic permeability values were significantly larger than those by Refoj [14] and Monticelli et al. [15]. Differences may, in part, be attributed to different testing procedures. Monticelli et al. [19] used a high pressure gradient to drive flow across the hydrogel membrane, i.e., $\sim$35–100 kPa. Permeability has been found to decrease nonlinearly with compression [31–33], and large pressure gradient may significantly compress the membrane. Differences in measured values may also be due to differences in gel formulation; e.g., crosslinking density, pore size, and percentage of unbound water.

Previous studies by Hale et al. [23] and LeRoux et al. [17] also used a curve fitting to back out biphasic material properties. Hale et al. [23] fit to an $F-D$ curve obtained at a single velocity and searched for the optimal $E$, $v$, and $k$ of canine articular cartilage within potential ranges. When using this approach, unique values of $k$ or $E$ may not be obtained if property ranges and indentation loading rate are not carefully chosen. Most previous studies, including this study, limit analyses to isotropic material properties. When the number of unknown properties increases such as for anisotropic materials, additional direct experimental measurement is needed. LeRoux et al. [17] have also used a multi-step testing approach for transversely isotropic meniscus. In their study, ten-
sile tests were used to measure the $E$ and $v$, and then curve fitting of tensile stress relaxation data was used to find the transversely isotropic permeabilities. Instead of analyzing $F-D$ behavior during indentation, a number of researchers have used indentation creep tests to extract biphasic properties [24–26]. In this study, we limit our analysis to $F-D$ behavior. However, analysis of creep response provides a sensitive method for determining biphasic properties since the effects of $E$, $v$, and $k$ on the force response are more easily separable. Mow and co-workers [24,26] have presented an analytical solution for indentation creep tests using a cylindrical flat-ended porous indenter to which experimental data can be fit.

We assume an infinitesimal deformation in our biphasic formulation, and consider a maximum 20% strain. Previous studies by Spiker et al. [27] suggest that strain below 25% is reasonably modeled using linear biphasic theory. In addition, our current biphasic model uses a constant hydraulic permeability assumption. However, local changes of permeability due to compression may be significant and can be modeled using a strain-dependent relation as presented by Lai and Mow [33]. Implication of the constant hydraulic permeability assumption on the current estimates is that permeability may be underestimated, since we fit to data collected from a compressed material. A higher permeability is expected at a zero-strain state. FEM boundary conditions assume zero displacement and zero flow flux boundary conditions at the bottom surface of the contact lens. In reality, a thin fluid film may form at the hydrogel-foundation interface, and some relative sliding may occur during indentation. However, no obvious sliding or detachment of the lens was observed during micro-indentation test, and the no delamination assumption was assumed to be valid.

In addition, friction at the indenter-fluid interface may contribute to shear force acting on the indenter. However, measured friction coefficients values for contact with stainless steel are very small [34]. Even with a perfect adhesion, i.e., no sliding between indenter and sample, Spiker et al. [27] showed only about a 10% increase in force response using a flat-ended solid indenter compared with a lubricated indenter.

Accuracy of the experimental data was also affected by several factors. For samples tested in air, the meniscus force due to surface tension between the indenter and fluid layer was estimated to be 0.05 mN (∼1.0% of maximum contact force). These small forces were considered to be constant during indentation. However, changing meniscus forces at the initial contact point may have had some effect on contact point calculation. Submerged configuration tests helped to reduce these effects. The rate of data collection and potential noise may also affect the estimated biphasic properties via shifting of the $F-D$ curve. At low sampling rates, an earlier data point, which does not correspond to the physical contact, may be determined as the contact point, resulting in a smaller $E$ or higher $k$ estimate. Given the sensitivity of the results to contact point determination, care was taken to minimize error introduced by these effects.

Experimental micro-indentation tests were run at two different indenter velocities. To check whether these indenter velocities were adequate to capture fluid-flow-dependent behavior, an a posteriori analysis was made by using the characteristic time,$t^* = a^2/(H_k k)$, where $a$ represents the characteristic distance and $H_k$ the aggregate modulus ($H_k = k + 2\mu E(1-\nu)/[(1-\nu)(1-2\nu)]$) [24,35,36]. A small characteristic time corresponds to a fast escape of the fluid from the bottom center of the indenter to the outer free drain surface. By using the estimated values for the hydrogel ($E = 130–170$ kPa, $k = (1–5) \times 10^{-5}$ m$^2$/N s, $\nu = 0.1–0.3$, and $a = 200$ µm, the maximum contact length), $t^*$ was conservatively calculated to be ∼35 s. Reaching an indentation depth of ∼20 µm at 1.2 and 20 µm/s requires a period of time 2 and 35 times smaller than $t^*$, respectively, indicating that fluid does not have time to redistribute at 20 µm/s, and the fluid redistribution time is the same order as the solid deformation time for 1.2 µm/s. For a much slower indenter velocity of 0.05 µm/s, maximum indentation takes a period of time nearly 11 times larger than $t^*$. Thus, fluid has time to redistribute, and the load is supported mainly by the polymer matrix (Fig. 8). This simple analysis using $t^*$ supports our argument that the distinct $F-D$ behavior exhibited at the indenter velocity of 1.2 µm/s is due to being in the sensitive range for which fluid flow affects the $F-D$ response.

In practice, such $t^*$ analysis provides an a priori means for estimating indenter velocity ranges provided that a range of material is known. Micro-indentation in combination with biphasic analysis may provide a useful way to measure the rate independent biphasic properties of thin contact lenses. This study demonstrates a method to extract the biphasic properties by fitting to the $F-D$ response during micro-indentation. Sensitivity analyses using the biphasic FEM model acts as a guide for understanding of the flow-dependent behavior of hydrated soft materials and improving experimental design. Estimated Young’s modulus and hydraulic permeability for the Etafilcon A contact lens, together with its clinical performance data, may provide important parameters for the design of more comfortable contact lenses. These material properties may also be used in other computational models; e.g., modeling on-eye movement of contact lenses, drug delivery, fluid transport through the lens, and lens buckling.

Acknowledgment

The authors would like to thank Dr. Jim Jen and Dr. John Enns of Vistakon for providing testing materials (Etalicon A) and data of bulk modulus properties.

Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
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<tbody>
<tr>
<td>AUC</td>
<td>area under curve</td>
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<tr>
<td>EWC</td>
<td>equilibrium water content</td>
</tr>
<tr>
<td>F-D</td>
<td>force-displacement</td>
</tr>
<tr>
<td>FEM</td>
<td>finite element method</td>
</tr>
<tr>
<td>MSE</td>
<td>mean square error</td>
</tr>
<tr>
<td>pGMA</td>
<td>poly-glycerol methacrylate</td>
</tr>
<tr>
<td>pHEMA-EG</td>
<td>poly-hydroxyethyl methacrylate-ethylene glycol</td>
</tr>
<tr>
<td>polyNVP-MMA</td>
<td>N-vinyl pyrrolidone methyl methacrylate</td>
</tr>
<tr>
<td>SEALS</td>
<td>Superior epithelial arcuate lesions</td>
</tr>
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