Hydraulic Permeability of a Hydrogel-Based Contact Lens Membrane for Low Flow Rates

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ABSTRACT: Hydrogels, widely used for contact lenses, are a class of materials that consists of both fluid and solid components. The aqueous fluid phase is supported by a solid polymer matrix. In this study, we characterize the water transport characteristics of an Etafilcon-A (copolymer of 2-hydroxyethyl methacrylate and methacrylic acid) membrane. A flow rate-controlled permeameter consisting of a syringe pump, membrane holder, pressure transducer, and tubing was developed and used to measure the pressure drop across a flat membrane (average thickness $\sim$ 686 μm $\pm$ 40). The relation between velocity and pressure drop was measured. These data were fit to rigid media and biphasic models of 1-D flow to determine hydraulic permeability, $k = 1.80 \times 10^{-14}$ m^4/N s. The results provide insight into the fluid flow properties of this hydrogel under low flow and low pressure conditions (<3 kPa). Physiological implications of these measured parameters on flow and deformation across the lens due to blinking are discussed. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 104: 3730–3735, 2007

Key words: contact lens; poly-HEMA; hydraulic conductivity; poroelastic; permeameter

INTRODUCTION

The transparency and softness of certain poly-HEMA (polyhydroxyethyl methacrylate)-based hydrogels have made them especially applicable in ophthalmology. Specifically, they are most commonly used in daily disposable contact lenses. Such hydrogels consist of a solid polymer matrix and a fluid phase, both of which may support mechanical loads. Biphasic and poroelastic models that account for coupled fluid flow and solid deformation models have been used for soft tissues[1] and hydrogels.[2,3] In a contact lens, variable pressure across the surface may cause flow across the lens. Also, flow-induced compression of the polymer matrix can lead to overall redistribution of fluid and changes in water transport properties. Since the material response to loading is coupled between fluid and solid phases, contact lens design may benefit from biphasic characterization.

Porous media flow is governed by the hydraulic permeability, which measures the conductance to fluid flow through the membrane. Measurement of this property may provide data for the dynamic analysis of contact lenses,[4,5] i.e., lens flow and variable thickness of the postlens tear film. Hydraulic permeability in poly-HEMA-based hydrogels has been measured previously. Yasuda et al. used ultrafiltration cells to measure hydraulic permeability in membranes with different equilibrium water content.[6] Measured values were 2.89×10^{-17} m^4/N s for 21 wt % water pHEMA-EG (polyhydroxyethyl methacrylate-ethylene glycol) and 1.25×10^{-15} m^4/N s for 64 wt % water pGMA (polyglycerol methacrylate). Testing 2-hydroxyethyl metacrylate (HEMA) membranes, Refojo used a pressure-controlled permeameter to measure hydraulic permeability of 38.7 and 53.8 wt % water membranes to be 8.4×10^{-18} and 1.05×10^{-17} m^4/N s, respectively.[7] More recently, Monticelli et al. used a similar system to test silicone (36 wt % water) and HEMA hydrogels (38 wt % water). Measured hydraulic permeability was 1.0×10^{-17} and 4×10^{-18} m^4/N s, respectively. The applied pressure gradient across the membrane was in the range of 35–100 kPa.[5]

In this study, we test the hydrogel, Etafilcon A (copolymer of 2-hydroxyethyl methacrylate and methacrylic acid). A dynamic mechanical method has been previously implemented by Enns to measure the bulk Young's modulus in compression, and a value of $\sim$ 255 kPa was obtained.[8] Besides, such studies that measure apparent bulk properties independently, Chiarelli et al.[2] used a poroelastic analysis of the stress-relaxation response to estimate Young's modulus of the polymer matrix and hydraulic permeability properties. Using thin strips of polyvinyl alcohol-polyacrylic acid hydrogel (80 wt %), Young's modulus was estimated to be 750 kPa and hydraulic permeability was estimated to be 1.2×10^{-17} m^4/N s.[2] More recently, our group has used a finite element (FE)

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approach to determine the biphasic properties from microindentation tests performed on a contact lens.[9] By fitting to force-displacement data, Young's modulus of the polymer matrix was estimated to be 130–170 kPa, and hydraulic permeability was estimated to be 1–5 $\times 10^{-15}$ m^4/N s for an Etafilcon A lens.

The aim of this study was to characterize the biphasic and water transport properties of a contact lens material, Etafilcon A, for simple loading and for physically relevant loads. Blinking pressures are estimated to be low, in the range of 0.1–1 kPa.[10–12] To test within this range, we developed a flow-controlled permeameter and tested flat membranes over low flow rates. The pressure response was measured under varying flow rates, and experimental data was fit to biphasic and rigid media solutions for transmembrane flow. The influence of the fluid transport properties applied to models of postlens tear film depletion and blinking is discussed.[4,5]

MATERIALS AND METHODS

Permeameter and flow experiments

A permeameter system was developed to apply a constant flow rate across a flat membrane sample and measure the corresponding pressure drop. The experimental system consisted of a syringe pump, syringe, noncompliant tubing, fittings, a pressure transducer, and membrane holder (Fig. 1). A syringe filled with deionized water was connected to a membrane holder with PEEK (polyetheretherketone) tubing with a 0.062 in. inner diameter and brass tube fittings (Swagelok, Solon, OH). A syringe pump (Model 100, KD Scientific, Holliston, MA) drove water from a 250-μL gas-tight syringe (Hamilton, Reno, NV) through an acrylic membrane holder (9.53-mm diameter flow area) at constant flow rates. The membrane holder contained the hydrogel membrane placed between an O-ring, which provided a water-tight seal, and filter paper and wire mesh, which provided mechanical support (prevented buckling and fixed deformation along the outflow side). To eliminate air bubbles within the system, the experimental setup was assembled and stored underwater.

A variable reluctance differential pressure transducer (Validyne DP15-32, Northridge, CA) was connected upstream and downstream of the membrane holder to measure the pressure drop across the membrane. Output signals were sent to a demodulator (Validyne CD280-4, Northridge, CA) for amplification, and a DAQ (data acquisition) box for input to a computer. LabVIEW (v.7 Express, National Instruments, Austin, TX) was used to convert the voltage signal to a pressure reading. The transducer was calibrated by connecting it to a set of differential height water columns, which were varied from 0 to 14.7 kPa (150 cm H_2O). A linear relationship was determined between voltage and pressure. Pressure drop because of the tubing, fittings, filter paper, and mesh support was assumed negligible (pressure gradients measured without the membrane were less than the calculated error in pressure-transducer readings, $\pm$0.035 kPa). Also, only pressure readings obtained after infusion of 10 μL were used for steady-state calculations since the transducer membrane deflection volume was 10 μL or less. Outflow water was collected in a contained beaker and fluid output was compared to fluid input to ensure no system leakage.

Etafilcon A test membranes (58 wt % water, provided by John Enns, Vistakon, Jacksonville, FL) were in the form of a flat sheet with a thickness of ~686 μm $\pm$ 40 [Fig. 2(a)]. Thickness was determined by an optical method, viewing thin slices of membrane under a

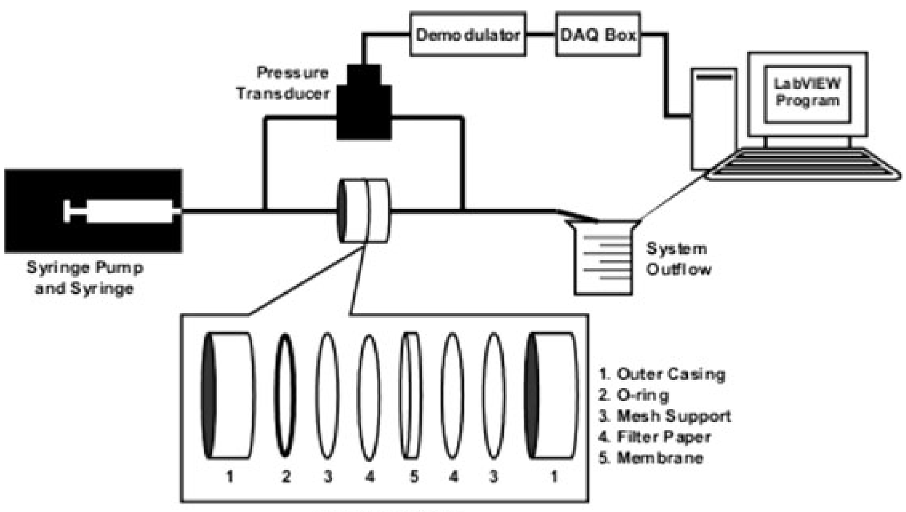

Figure 1 Permeameter system used to measure the pressure drop across a hydrogel membrane under various flow rates.

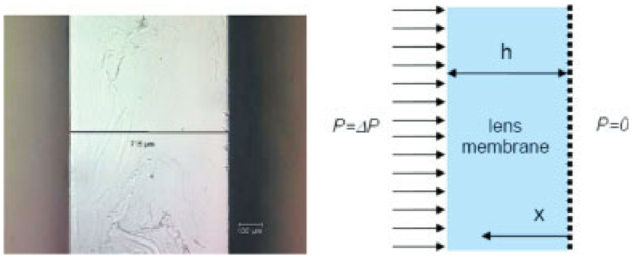

Figure 2 (a) View of cut membrane cross section (bar = 100 μm); and (b) schematic of the biphasic membrane model.

microscope (×100, Zeiss Axioplan II, Oberkochen, Germany). Membranes were cut into 9.53-mm diameter circles to fit the membrane holder. Once mounted in the membrane holder, samples were allowed to equilibrate for ∼1 h. Samples were tested at varying flow rates, 2, 5, 10, and 15 μL/h, for ∼1 h at each rate until an approximately steady pressure reading was achieved. Pressure was allowed to equilibrate ∼1 h between each flow rate test.

Leakage of the system was tested by replacing the test membrane with a thin, impermeable solid disk. Then, the inlet side of the system was pressurized by infusing at the syringe pump's lowest rate (1 μL/h). The pressure increase was monitored over a range of high pressures (∼ 7–18 kPa). A steady-state pressure was not obtained, and a steady pressure increase of about 1 kPa/h was observed in this range ($n = 4$). Assuming the leak to be a parallel fluid pathway to the membrane (circuit analogy), we calculated an equivalent permeability of the leak. For a flow rate of 1 μL/h and assuming a pressure-gradient equivalent to 15 kPa or greater, the calculated leak permeability was less than 8.90 10^{-18} m^4/N s. This value was orders of magnitude smaller than the measured membrane values (∼ 10^{-14} m^4/N s). Thus, we assumed that the effect of the leak on our measured permeability was negligible.

Rigid membrane analysis

Hydraulic permeability was calculated using Darcy's law for flow of water through porous media,

$$k_r = -\frac{vL}{\Delta P} \tag{1}$$

where k_r is hydraulic permeability of the rigid media, v is the average trans-membrane fluid velocity, ΔP is the pressure difference across the membrane, and L is the thickness of the membrane.

Biphasic analysis

Deformation of the porous media hydrogel during flow of fluid was analyzed. The hydrogel was modeled as an elastic, isotropic solid matrix saturated with viscous fluid. Both fluid and solid phases were assumed incompressible. Flow-induced compression of the bulk material and decreased fluid fraction are due to applied pressure. Osmotic pressure effects were not considered. The one-dimensional, steady-state biphasic compression solutions as solved and reviewed by Barry and Aldis[13] were used (refer to Ref. 13 for a detailed description of the governing equations and solutions, IDCON, and IDEXP models). These solutions assume axially confined, frictionless walls. The upstream end of the hydrogel ($x = h$) is a free boundary and the downstream end ($x = 0$) is fixed by the rigid mesh boundary [Fig. 2(b)].

The relationships between applied pressure difference, P, and macroscopic fluid velocity, v, are presented. The momentum and continuity relations yield,

$$\frac{dP}{dx} = \frac{d\sigma}{dx} = \frac{-v}{k} \tag{2}$$

where P is the fluid pressure, σ is the solid stress between constituents, and k is the hydraulic conductivity. In the case of infinitesimal deformation, the solid stress is

$$\sigma = \frac{H_a}{L}\frac{dU(x)}{dx} \tag{3}$$

where $U(x)$ is the displacement of the medium, L is the initial thickness of the membrane, H_a is the aggregate elastic modulus, $H_a = E(\upsilon - 1)/[(1 + \upsilon)(2\upsilon - 1)]$, and E is the Young's modulus. Boundary conditions assume zero displacement and pressure at the downstream end ($U(0) = 0$, $P(0) = 0$) and an applied pressure difference and zero contact stress at the upstream end $\left(P(H) = \Delta P, \frac{dU(h)}{dx} = 0\right)$. For a constant hydraulic permeability, $k = k_o$, the displacement and velocity solutions are then

$$U(x) = \frac{-vx}{H_a k_o}\left(\frac{x}{4} - \frac{H_a L}{2H_a + \Delta P}\right) \tag{4}$$

$$v = \frac{-\Delta P k_o}{L}\left(1 + \frac{\Delta P}{2H_a}\right) \tag{5}$$

where υ is the Poisson ratio. Solving eq. (5) for the hydraulic permeability,

$$k_o = \frac{-v}{\Delta P}\frac{2H_a L}{(2H_a + \Delta P)} = \frac{-vh}{\Delta P} \tag{6}$$

where h is the final thickness of the membrane. When the deformation of material is small, eq. (6) is equivalent to eq. (1).

RESULTS

Flow rate versus pressure gradient

After infusion of ∼ 10 μL, measured pressure across the membrane reached steady values. Steady-state

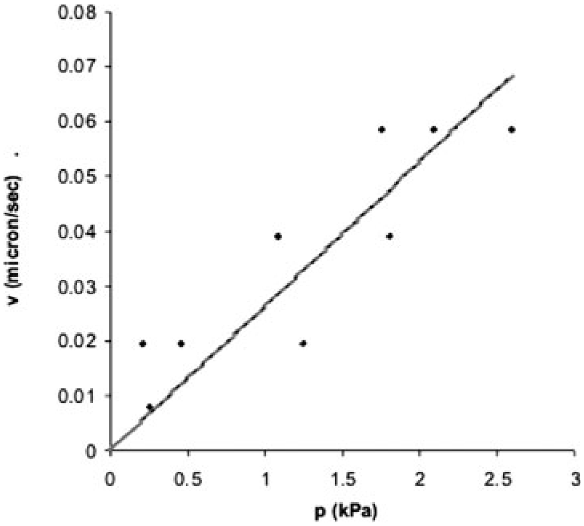

Figure 3 Steady-state velocity versus measured pressure difference across a 0.686-mm thick Etafilcon-A hydrogel membrane (58 wt % water). Curve fits for flow through a rigid membrane (dotted line) and biphasic material (gray line) overlap.

pressure gradients (0.25–2.60 kPa) increased with trans-membrane velocity (0.008, 0.020, 0.039, and 0.059 μm/s) (Fig. 3). Plotted data was fit to a linear solution for rigid membranes [eq. (1)] and the nonlinear solution [eq. (5)] for flow-induced deformation in biphasic media. The biphasic solution closely matched the linear solution. Predicted biphasic plots were only sensitive to changes in k. The parameter k was adjusted by minimizing the squared deviation (Genfit, Mathcad, Mathsoft, Cambridge, MA). Best fits estimate $k_r = 1.796 \times 10^{-14}$ and $k_o = 1.804 \times 10^{-14}$ m^4/N s for the rigid media and biphasic models, respectively.

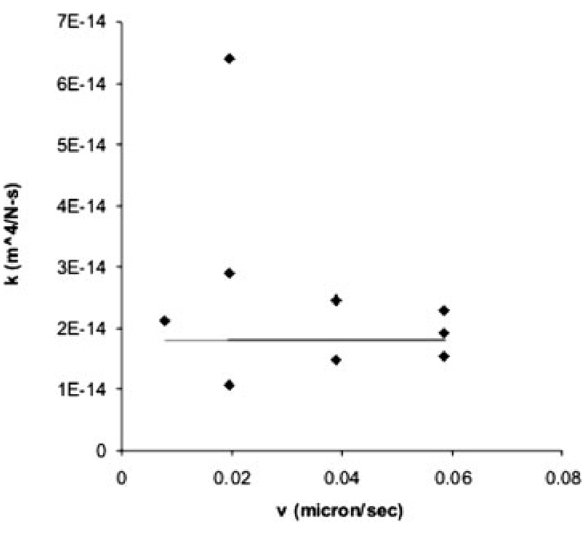

Figure 4 Variation in measured hydraulic permeability of the Etafilcon-A hydrogel membrane (58 wt % water). Best fits estimate $k_r = 1.796 \times 10^{-14}$ and $k_o = 1.804 \times 10^{-14}$ $m^4/$ N s for the rigid media and baseline models (solid line), respectively.

For the biphasic model, baseline parameters were $E = 180$ kPa and $\upsilon = 0.2$. The biphasic fits to k_o were not very sensitive to changes in E or υ. Fixing υ and varying E from 100 to 250 kPa, predicted k_o increased from 1.789×10^{-14} to 1.798×10^{-14} m^4/N s (0.5% change). The Young's modulus range was determined from a previous microindentation study[9] and a dynamic mechanical method by Enns[8] using the same material. Fixing E and varying υ from 0.1 to 0.35, predicted k_o increased from 1.795×10^{-14} to 1.799×10^{-14} m^4/N s (0.2% change). Measured and best fitting values for k ($k_r \sim k_o$) are presented in Figure 4. Variation in the hydraulic permeability was greater at lower velocities because of the increased variation in measured pressure difference over the longer time scales of the low velocity experiments. Increased error in pressure at longer times may be because of small systemic fluid leakage and/or electronic drift.

Maximum calculated displacements [eq. (4), $x = h$] are graphed in Figure 5 for a range of mechanical properties ($100 \leq E \leq 250$ kPa, $0.1 \leq \upsilon \leq 0.35$). Displacements increased approximately linearly with increasing applied pressure gradient. Maximum predicted compression of the membrane (at $x = h$) ranged from 1.0 to 4.0 μm for an applied pressure gradient of 2.6 kPa. These displacements correspond to small strains of 0.15–0.58%, which is consistent with the infinitesimal deformation assumption. Continuing the deformation analysis at higher flow rates and elevated pressures, displacement, and velocity diverge from infinitesimal solutions at a pressure gradient value of ~ 110 kPa ($\sim 10\%$ strain for $E = 180$ kPa and $\upsilon = 0.2$). This corresponds to a velocity of 3.69 μm/s, which is well above the experimental range of this study.

DISCUSSION AND CONCLUSIONS

Experimental flow rates were selected over a low pressure range considered relevant for physiological processes, i.e., blinking. Over these low flow and

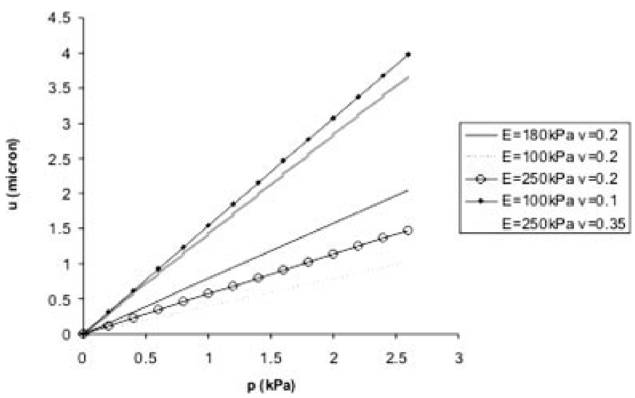

Figure 5 Predicted flow induced deformation at $x = L$ versus applied pressure gradient for the 0.686 mm hydrogel membrane for varying mechanical properties (E and υ).

low pressure ranges, an approximately linear relation was found between the trans-membrane velocity and steady-state pressure measurements, and small changes in membrane thickness were predicted. Thus, measured permeability was found to be approximately constant. Measured hydraulic permeability was larger than previously measured values of poly-HEMA. Values determined from FE analysis of microindentation range from 7.5×10^{-16} to 5×10^{-15} m^4/N s for the same Etafilcon A lens material.[9] Monticelli et al. and Refojo measured values which were on the order of 10^{-17} m^4/N s.[5,7] This difference in measured values may be due to different testing procedures which induced differing amounts of compression. Indentation tests measured tissue properties under local compression, up to ~20% strain. Monticelli et al.[5] applied a high pressure gradient in the range of 35–100 kPa. Such a large pressure gradient may significantly compress the membrane. Hydraulic permeability has been found to decrease nonlinearly with compression,[3,14–16] If the material permeability response is nonlinear, it may be reasonable to assume that hydraulic permeability may decrease by orders of magnitude with increased strain and pressure gradient. Also, some variation is expected because of differences in material composition between the poly-HEMA membranes, e.g., crosslinking density, pore size, and/or water content.

A possible mechanism for water transport across the lens is during blinking. As the eye lid closes, a normal force is applied and the thin fluid film between the lens and lid is pressurized. Local tear pressure on the anterior and posterior sides of the lens are different, and can either drive water into or out of the postlens tear film (PoLTF). Lens settling analysis for a permeable membrane has been previously conducted by Monticelli et al.[5] They model the lens as a rigid porous disk where water transport is due to a pressure gradient. The influence of water transport across the lens on the rate of lens settling velocity was determined to be minimal (less than 1%) for hydraulic permeability values less than 10^{-8} m^4/N s (assuming PoLTF thickness = 10 μm, lens radius = 6 mm, h = 70 μm). Our measured hydraulic permeability values were well below this threshold value, indicating that little tear fluid may be ''squeezed through'' as the lens settles towards the cornea upon lens insertion.

In addition to ''squeeze through,'' tear fluid may also be ''squeezed out'' of the lens as it deforms. Transient biphasic models can account for fluid leaving the lens due to both deformation, i.e., ''squeeze out'' and pressure gradients, i.e., ''squeeze through.'' Steady-state analysis can be applied to predict ''squeeze out'' fluid volumes. To estimate the maximum displaced fluid, we calculated deformation across a biphasic layer (L = 100 μm) resting on a thin PoLTF layer (10 μm). Over a 0.1–1 kPa pressure range,[10–12] the maximum predicted deformation is 0.125 μm. Change in the PoLTF layer because of ''squeeze out'' is on the order of ϕU or less, where ϕ is the fluid volume fraction of the membrane. If $\phi \sim 0.60$,[7,17] this contributes ~ 0.75% of the PoLTF layer thickness. Higher physiological pressures in the range of 5 kPa or higher are required to influence the PoLTF layer. It should be noted that this analysis assumes equilibrium conditions, which may overestimate the total displaced fluid, since the applied pressure gradient may not be applied for a long enough time to reach equilibrium. Thus, even considering the higher measured permeability, we predict little water transport across the lens during blinking because of either ''squeeze through'' or ''squeeze out.''

Features that are not included in the current model are material heterogeneity or anisotropy. Material parameters such as modulus and hydraulic permeability may change through the membrane thickness over the surface due to variation in crosslinking. In this study, we assume such variation in properties to be small. Also, for the permeameter tests, steady-state pressure conditions were determined. For blinking analysis, the loading time is short, <1 s. Additional studies characterizing transient response for over short time scales would be useful in determining contact lens behavior.

In addition to pressure-driven flows, water can also be transported by the diffusion-gradient of water as water is evaporated from the surface of the lens into adjacent air.[18,19] In the opposite direction, transport into the postlens tear film can be driven by salt osmotic gradients and mechanical lid stress. Quantitative knowledge of water transport through the hydrogel is necessary to establish the importance of these phenomena.[20] In this study, we measured one water transport property, the hydraulic permeability, at low rates of flow and pressure. Measured values, although larger than previous studies, are not large enough for significant blink-induced water transport. However, measured hydraulic permeability values may be useful in other porous media-swelling analysis. Hydrogel-swelling response may contribute to lens geometry (e.g., curvature and thickness) with changes in water content.

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References

1. Mow, V.C.; Kuei, S.C.; Lai, W.M.; Armstrong, CG. J Biomech Eng 1980, 102, 73.
2. Chiarelli, P.; Basser, P.J.; Derossi, D.; Goldstein, S. Biorheology 1992, 29, 383.
3. Holmes, MH.; Mow, V.C. J Biomech 1990, 23, 1145.
4. Raad, P.E.; Sabau, A.S. J Appl Mech Trans ASME 1996, 63, 411.

5. Monticelli, M.V.; Chauhan, A.; Radke, C. J. Curr Eye Res 2005, 30, 329.
6. Yasuda, H.; Lamaze, C.E.; Peterlin, A. J Polym Sci Part A-2: Polym Phys 1971, 9, 1117.
7. Refojo, M.F. J Appl Polym Sci 1965, 9, 3417.
8. Enns, J.B. Proc 54th Annu Tech Conf 1996, 3, 2852.
9. Chen, X.; Dunn, A.C.; Sawyer, WG.; Sarntinoranont, M. J Biomech Eng, to appear.
10. Miller, D. Arch Opthalmol 1967, 78, 328.
11. Chauhan, A.; Radke, C.J. J Colloid Interface Sci 2002, 245, 187.
12. Martin, D.K.; Holden, B.A. Phys Med Biol 1986, 30, 635.
13. Barry, S.I.; Aldis, GK. J Biomech 1990, 23, 647.
14. Gu, W.Y.; Yao, H.; Huang, C.Y.; Cheung, H.S. J Biomech 2003, 36, 593.
15. Johnson, E.M.; Deen, W.M. AIChE J 1996, 42, 1220.
16. Lai, W.M.; Mow, V.C.; Biorheology 1980, 17, 111.
17. Manetti, C.; Casciani, L.; Pescosolido, N. Polymer 2002, 43, 87.
18. Fornasiero, F.; Prausnitz, J.M.; Radke, CJ. J Membr Sci 2006, 275, 229.
19. Refojo, M.F.. Leong, F.L. Contact Intraocular Lens Med J 1981, 7, 226.
20. Hoch, G.; Chauhan, A.; Radke, C.J. J Membr Sci 2003, 214, 199.