



## Equilibrium water and solute uptake in silicone hydrogels



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### ABSTRACT

Equilibrium water content of and solute partitioning in silicone hydrogels (SiHys) are investigated using gravimetric analysis, fluorescence confocal laser-scanning microscopy (FCLSM), and back extraction with UV/Vis-absorption spectrophotometry. Synthesized silicone hydrogels consist of silicone monomer, hydrophilic monomer, cross-linking agent, and triblock-copolymer macromer used as an amphiphilic compatibilizer to prevent macrophase separation. In all cases, immiscibility of the silicone and hydrophilic polymers results in microphase-separated morphologies. To investigate solute uptake in each of the SiHy microphases, equilibrium partition coefficients are obtained for two hydrophilic solutes (i.e., theophylline and caffeine dissolved in aqueous phosphate-buffered saline) and two oleophilic solutes (i.e., Nile Red and Bodipy Green dissolved in silicone oil), respectively. Measured water contents and aqueous-solute partition coefficients increase linearly with increasing solvent-free hydrophilic-polymer volume fraction. Conversely, oleophilic-solute partition coefficients decrease linearly with rising solvent-free hydrophilic-polymer volume fraction (i.e., decreasing hydrophobic silicone-polymer fraction). We quantitatively predict equilibrium SiHy water and solute uptake assuming that water and aqueous solutes reside only in hydrophilic microdomains, whereas oleophilic solutes partition predominately into silicone microdomains. Predicted water contents and solute partition coefficients are in excellent agreement with experiment. Our new procedure permits a priori estimation of SiHy water contents and solute partition coefficients based solely on properties of silicone and hydrophilic homopolymer hydrogels, eliminating the need for further mixed-polymer-hydrogel experiments.

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### 1. Introduction

Silicone-hydrogel (SiHy) soft contact lenses (SCLs) are an important alternative to conventional hydrogel SCLs (i.e., lenses composed of only hydrophilic polymers, typically 2-hydroxyethyl methacrylate (HEMA)). Compared to conventional hydrogel SCLs, SiHy lenses allow six to ten times larger corneal oxygen supply, providing improved ocular health, especially for extended wear [1–5]. To date, SiHy SCLs have significantly reduced several serious hypoxia-related problems such as red eye, cornea swelling, and eye discomfort [3–5]. Accordingly, about two thirds of all contact lenses prescribed between 2011 and 2013 in the United States were silicone based [6–8].

Despite the importance of SiHy SCLs, their phase structure and morphology are not well understood [4]. It is commonly accepted that distinct phases occur in various morphologies due to

immiscibility of the silicone and hydrophilic polymers. Two typical examples include dispersions [4] (with microdomains isolated within a continuous phase) and co-continuous networks [4,9]. Conventional wisdom is that for SCL on-eye wear, the SiHy structure must contain interconnected silicone domains for sufficient oxygen permeability, as well as a co-continuous ion-conducting water phase localized within the hydrophilic-polymer domains [1–4,10–13].

Hydrophilic-domain water uptake largely dictates mechanical and transport properties (e.g., lubricity, elasticity, aqueous solute uptake, and ion/water permeability) that contribute directly to lens performance [1–4,10–18]. For example, water content must be large enough to provide sufficient lubricity for comfortable wear and sufficient salt permeability for prevention of corneal lens-adherence [13,17,19,20]. However, if the lens water fraction is too large, mechanical stability may be compromised due to lack of polymer volume, rendering the material unsuitable as a SCL. Additionally, an increase in water content through an increase in hydrophilic-phase fraction must be accompanied by a decrease in silicone-phase fraction that may compromise oxygen permeability [1–4,11].

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Hydrophilic-domain water uptake also governs loading and release of water-soluble drugs, tear-film components, preservatives, and wetting agents [11,13–15,18,21–24]. When on eye, SCLs are continually exposed to and uptake tear-film components, such as proteins, lipids, mucins, and salts. During wear, SCLs release pre-impregnated drugs, preservatives, and wetting agents in the form of salts, polymers, and polymeric surfactants. In either case, absorbed solutes may result in beneficial effects, such as improved wettability and comfort, or harmful effects, such as contamination and loss of comfort. All else being equal, higher water content, reflective of larger water-filled hydrophilic domains, leads to greater partitioning of aqueous solutes into SCLs [13–15,18,21–24]. However, with higher water content, oleophilic solutes (with low water solubility) partition less, due to a decrease in the hydrophobic silicone-phase fraction.

Because of their importance, significant effort has been expended towards predicting SCL hydrogel water content [25–29] and solute partitioning [11,13–15,18,21–24]. Water-content predictions typically modify Flory–Rehner theory, where hydrogel swelling arises from a balance between the tendency of the polymer to dissolve in the aqueous phase and elasticity of the cross-linked network that opposes dissolution. With water content specified, solute-partition-coefficient models then account for solute/hydrogel-network interactions including: size exclusion, electrostatic interaction, and specific adsorption onto the polymer strands [14]. Currently, however, all systems where equilibrium water or solute uptake is predicted are conventional hydrogels (i.e., those containing no silicone) [11,13–15,18,21–29]. To our knowledge, no studies attempt prediction of water content or solute partitioning in SiHys.

This work reports experimental and theoretical equilibrium water content and solute uptake in thirty SiHys over a wide range of hydrogel compositions and water contents (3–82%). Silicone hydrogels are synthesized using thermally initiated free-radical polymerization, and consist of silicone monomer, hydrophilic monomer, cross-linking agent, and triblock-copolymer macromer used as an amphiphilic compatibilizer to prevent macrophase separation. Equilibrium water contents and partition coefficients of four solutes are measured using gravimetric analysis, fluorescence confocal laser-scanning microscopy, and back extraction with UV/Vis-absorption spectrophotometry. SiHy equilibrium water contents are predicted assuming that water is localized within the hydrophilic-polymer domains. Therefore, aqueous solutes (with high water solubility) primarily partition into water-swollen hydrophilic microphases. Conversely, oleophilic solutes (with low water solubility) largely partition into hydrophobic silicone microdomains. To account for aqueous-solute size exclusion in the hydrophilic phase and oleophilic-solute specific adsorption in the silicone phase, enhancement-factor partitioning theory is adopted [14]. In all cases, predicted water contents and solute partition coefficients are in excellent agreement with experiment.

## 2. Materials and methods

### 2.1. Chemicals

Synthesized silicone hydrogels (SiHys) consist of silicone monomer, amphiphilic macromer, hydrophilic monomer, cross-linking agent, thermoinitiator, and solvent. Silicone monomers, 3-methacryloxypropyltris(trimethylsiloxy)silane (97%, TRIS, Cat. No. 1713, Lot 1713-020514), and methacryloxypropyl-terminated polydimethylsiloxane (97+%, M-PDMS, 8–14 cSt, Cat. No. DMS-R11, Lot 3J-21494) were acquired from Silar Laboratories (Wilmington, NC) and Gelest Inc. (Morrisville, PA), respectively. The amphiphilic macromer acryloxy-terminated ethyleneoxide

dimethylsiloxane–ethyleneoxide ABA triblock copolymer (95+%, DBE-U12, 80–120 cSt, Cat. No. DBE-U12) was purchased from Gelest Inc., and used to prevent macrophase separation. Sigma Aldrich (St. Louis, MO) provided all other chemicals used in SiHy preparation: hydrophilic monomers: 2-hydroxyethyl methacrylate (97%, HEMA, Cat. No. 128635-500G) and methacrylic acid (99%, MAA, Cat. No. 155721-500G); cross-linking agent: ethylene glycol dimethacrylate (98%, EGDMA, 335681-100ML); thermoinitiator: 4,4'-azobis(4-cyanovaleric acid) (98+%, Cat. No. 11590-100G); and solvent: ethanol (99.5+%, Cat. No. 459844-1L). Following free-radical polymerization, hydrogels were swollen for a minimum of 3 d in pH 7.4 phosphate-buffered saline solution (PBS) prepared as described previously [14–16].

PBS was used as the solvent for the hydrophilic solutes: theophylline (99+%, Sigma Aldrich, Cat. No. T1633-50G) and caffeine (99+%, Sigma Aldrich, Cat. No. C0750-100G), whereas silicone oil (500 cSt, Fisher Scientific, Pittsburgh, PA, Cat. No. S159-500) was used as the solvent for the oleophilic fluorescent solutes: Nile Red (99%, Life Technologies, Grand Island, NY, Cat. No. N-1142) and 4,4-difluoro-1,3,5,7,8-pentamethyl-4-bora-3a,4a-diaza-s-indacene (99%, Bodipy Green, Life Technologies, Cat. No. D-3922). Initial loading concentrations for the hydrophilic and oleophilic solutes were  $6 \times 10^{-3}$  and  $1 \times 10^{-5}$  M, respectively. Molecular weights and hydrodynamic radii of the four solutes are similar (i.e., 190–315 Da and 0.3–0.58 nm) [14,18]. All solutes are nonionic at pH 7.4. All chemicals were used as received. Water- and solute-uptake measurements were performed at ambient temperature.

### 2.2. Hydrogel synthesis

SiHys were synthesized using thermally initiated free-radical polymerization and cross-linking of monomers and macromer in ethanol. Hydrogel composition was varied by altering the relative amounts of silicone monomer (i.e., TRIS or M-PDMS), macromer, and hydrophilic monomer (i.e., HEMA, MAA, or a mixture of 10 vol.% MAA and 90 vol.% HEMA denoted as 10% MAA/90% HEMA) in the volume ratios reported in Table 1. Typical reaction solutions consisted of monomer, macromer, 0.25 vol.% EGDMA, 0.5 wt.% 4,4'-azobis(4-cyanovaleric acid), and 50 vol.% ethanol, where percentages are of total monomer plus macromer. Hydrogels are referred to by their corresponding solvent-free volume fraction of hydrophilic monomer,  $v_{hyphil}$ , where the volume fraction of hydrophilic monomer, macromer ( $v_{macromer}$ ), and hydrophobic monomer ( $v_{hyphob}$ ) sum to unity (i.e.,  $v_{hyphil} + v_{macromer} + v_{hyphob} = 1$ ). The reaction mixture was stirred magnetically until full dissolution of the thermoinitiator. Subsequently, nitrogen gas was bubbled through the solution for 15 min to remove dissolved oxygen. The stripped reaction mixture was injected between two upright glass plates separated by a 250- $\mu$ m spacer, and previously hydrophobized with RainX<sup>®</sup> Original (Sopos Products, Houston, TX). Free-radical, thermally initiated polymerization took place in an oven whose temperature was raised from 65 to 75 °C over a 60-min period and then maintained

**Table 1**  
SiHy composition and hydrophilic-monomer volume fraction,  $v_{hyphil}$ .

Constituent volume parts			$v_{hyphil}$
Silicone monomer <sup>a</sup>	Macromer	Hydrophilic monomer <sup>b</sup>	
10	1	1	0.08
5	1	1	0.14
1	1	1	0.33
1	1	5	0.71
1	1	10	0.83

<sup>a</sup> TRIS or M-PDMS.

<sup>b</sup> HEMA, MAA, or 10% MAA/90% HEMA.

at 75 °C for 60 min. When cooled, all hydrogels were boiled in DI water for at least 30 min to remove unreacted constituents. Use of ethanol as the extraction solvent yielded identical equilibrium water contents and solute partition coefficients as when boiling water was used indicating negligible unreacted silicone monomer. Following synthesis, all hydrogels were swollen for a minimum of 3 d in PBS (changing the solution daily). In PBS (pH 7.4), MAA moieties are fully ionized [14–16].

### 2.3. Equilibrium water content

Following others [13–16,18,25], hydrogel equilibrium water content, approximately the water volume fraction,  $\phi_1$ , was obtained gravimetrically. To determine water content, swollen 9-mm diameter SiHy discs were weighed in the PBS-equilibrated ( $m_{wet}$ ) and ambient-temperature dry ( $m_{dry}$ ) states. Let  $\Delta m_1 \equiv m_{wet} - m_{dry}$ . Equilibrium water volume fraction is given by

$$\phi_1 = \frac{\Delta m_1 / \rho_1}{\Delta m_1 / \rho_1 + m_{dry} / \rho_{dry}}, \quad (1)$$

where  $\rho$  is mass density, and subscripts 1, *wet*, and *dry* denote water, swollen hydrogel, and dry hydrogel, respectively. In Eq. (1),  $\phi_1$  is approximately water content, since  $\rho_1 \approx \rho_{dry}$ . Equilibrium water-uptake measurements were performed in triplicate.

### 2.4. Equilibrium solute partition coefficients

Aqueous-solute (i.e., theophylline and caffeine) partition coefficients in the SiHys were measured using back extraction with UV/Vis-absorption spectrophotometry, as described previously [14]. Equilibrium-swollen SiHys were soaked in aqueous-solute-containing PBS under magnetic stirring for at least 2 d. Following solute loading, solute-equilibrated hydrogels were removed from solution, blotted lightly with Fisherbrand® weighing paper, and immediately placed into PBS for solute release. Solute equilibrium supernatant concentration was obtained by pipetting 1 mL of solution into a 4-mm wide UV quartz cuvette (path length 10 mm), and measuring previously calibrated solution absorbance at 220–250 nm with an Ocean Optics spectrophotometer (Model ADC-1000, Dunedin, FL). The equilibrium partition coefficient,  $k_i$ , of solute  $i$  (i.e., the concentration of solute in the hydrogel phase divided by the concentration in bulk surrounding phase) is then calculated using the equilibrium-release PBS-solution concentration,  $C_i$ , by the expression [13]

$$k_i = C_i V / C_{io} V_G \quad (2)$$

where  $V$  is back-extraction-solution volume,  $V_G$  is water-swollen hydrogel volume, and  $C_{io}$  is equilibrium loading-solution concentration.

Oleophilic-solute (i.e., Nile Red and Bodipy Green) partition coefficients in the SiHys were obtained using two-photon fluorescence confocal laser-scanning microscopy (FCLSM), as described previously [15,16,18]. A Carl Zeiss 510 LSM META NLO AxioImager confocal microscope (Jena, Germany) equipped with a Spectra-Physics MaiTai HP DeepSee Laser (Santa Clara, CA) was used at 780-nm excitation. Nile-Red and Bodipy-Green fluorescence emissions were detected through a 685-nm short-pass emission filter and a 500–550-nm band-pass emission filter, respectively. Equilibrium aqueous-swollen SiHys were soaked in the solute-containing silicone oil under magnetic stirring for at least 2 weeks at 400 rpm. Subsequently, an equilibrium-solute-loaded SiHy was placed on the microscope for scanning in the vertical  $z$ -direction at the same laser power and detector setting as those during scanning of the bulk-solute solution. Detected solute intensities inside the hydrogel and in the surrounding bulk

solution were proportional to dye concentration in the concentration range studied [15,16,18]. Accordingly, the partition coefficient,  $k_i$ , is given by the ratio of solute intensity in the SiHy to that in the loading solution. Loading concentrations were varied over a factor of 10 with no change in measured partition coefficients. Additionally, gravimetric oil-uptake measurements of dry SiHys reveal little to no swelling when immersed in silicone oil [18].

## 3. Experimental results

Fig. 1 plots SiHy equilibrium water volume fraction,  $\phi_1$ , as a function of the solvent-free hydrophilic-monomer fraction,  $v_{hyphil}$ . The hydrophilic-monomer fraction consists of HEMA (triangles), MAA (squares), or a mixture of 10 vol.% MAA and 90 vol.% HEMA (circles), denoted as 10% MAA/90% HEMA. Filled and open symbols represent  $\phi_1$  for TRIS and M-PDMS-based SiHys, respectively. Water contents for conventional hydrogels that contain no silicone monomer or macromer (i.e., where  $v_{hyphil} = 1$ ) are also shown [14]. Solid lines are drawn according to theory discussed below. In all cases,  $\phi_1$  rises linearly with increasing  $v_{hyphil}$ . For a given value of  $v_{hyphil}$ , both TRIS- and M-PDMS-based SiHys have nearly identical  $\phi_1$  (compare open and filled symbols). As expected, the MAA-based hydrogels show consistently higher  $\phi_1$  than the HEMA-based and 10% MAA/90% HEMA-based hydrogels because fully ionized MAA moieties (at pH 7.4) have higher affinity for water compared to uncharged HEMA moieties yielding greater equilibrium swelling [14–16,26].

All else being equal, higher water contents, reflective of larger water-filled hydrophilic domains, allow for greater aqueous-solute partitioning in SiHys. Figs. 2 and 3 display aqueous theophylline and caffeine partition coefficients,  $k_i$ , as a function of the solvent-free hydrophilic-monomer fraction,  $v_{hyphil}$ . Also shown are theophylline and caffeine partition coefficients for conventional hydrogels that contain no hydrophobic polymer (i.e.,  $v_{hyphil} = 1$ ) [14]. Filled and open symbols correspond to TRIS- and M-PDMS-based SiHys, respectively. Solid lines are drawn according to theory discussed below. Identical to water content, aqueous-solute partition coefficients increase linearly with rising solvent-free hydrophilic-phase fraction in all cases. Again, the TRIS- and M-PDMS-based SiHys have similar values of  $k_i$  for a given value of  $v_{hyphil}$  (compare open and filled symbols). In PBS (at pH 7.4), both

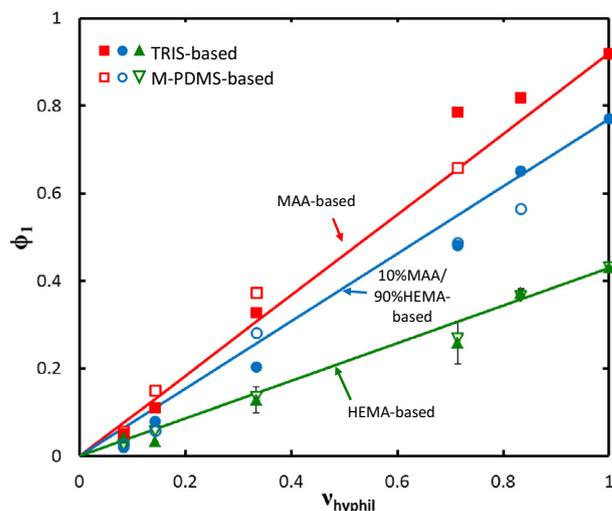
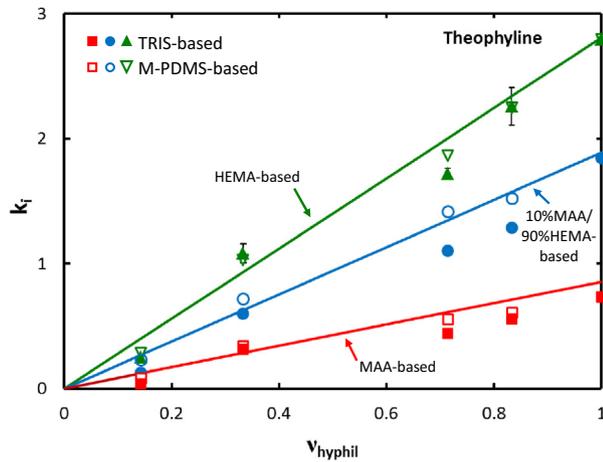
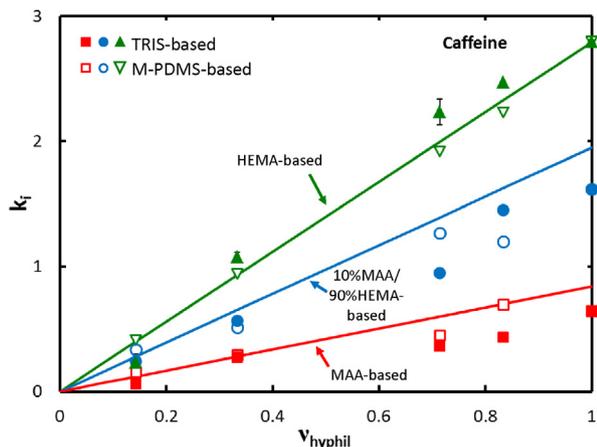


Fig. 1. Equilibrium water volume fraction,  $\phi_1$ , as a function of the solvent-free volume fraction of hydrophilic monomer,  $v_{hyphil}$ , for HEMA-(triangles), MAA-(squares), and 10% MAA/90% HEMA-based (circles) SiHys. Filled and open symbols denote TRIS- or M-PDMS-based SiHys, respectively. Typical error bars are shown. Lines are drawn according to theory.



**Fig. 2.** Theophylline partition coefficients,  $k_i$ , as a function of the solvent-free volume fraction of hydrophilic monomer,  $v_{hyphil}$ , for HEMA-(triangles), MAA-(squares), and 10% MAA/90% HEMA-based (circles) SiHys. Filled and open symbols denote TRIS- or M-PDMS-based SiHys, respectively. Typical error bars are shown. Lines are drawn a priori according to theory.



**Fig. 3.** Caffeine partition coefficients,  $k_i$ , as a function of the solvent-free volume fraction of hydrophilic monomer,  $v_{hyphil}$ , for HEMA-(triangles), MAA-(squares), and 10% MAA/90% HEMA-based (circles) SiHys. Filled and open symbols denote TRIS- or M-PDMS-based SiHys, respectively. Typical error bars are shown. Lines are drawn a priori according to theory.

nonionic caffeine and theophylline exhibit specific adsorption to HEMA strands, but not to anionic MAA chains. This result accentuates that, unlike HEMA strands, charged MAA strands have a higher affinity for water than for neutral caffeine and theophylline [14]. Consequently,  $k_i$  is largest for the HEMA-based SiHys, followed by the 10% MAA/90% HEMA-based SiHys, and finally by the MAA-based SiHys.

In contrast to the aqueous solutes that partition into the SiHy water-filled microphases (Figs. 2 and 3), oleophilic solutes (with low water solubility) have higher affinity for the hydrophobic-silicone microdomains [18]. Fig. 4 shows oleophilic partition coefficients (i.e., Nile Red and Bodipy Green),  $k_i$ , as a function of the solvent-free hydrophilic fraction,  $v_{hyphil}$ , for the HEMA-based SiHys. Filled and open symbols denote TRIS- and M-PDMS-based SiHys, respectively. Oleophilic-solute partition coefficients were not obtained for 10% MAA/90% HEMA- and MAA-based SiHys because these hydrogels were translucent, preventing accurate FCLSM measurement. Solid lines are drawn according to theory discussed below. In this calculation, we classify the small amount of amphiphilic macromer as hydrophobic because the water

content of a homopolymer macromer hydrogel is negligible (<0.1). In all cases,  $k_i$  diminishes linearly with increasing  $v_{hyphil}$  (i.e., decreasing silicone-phase fraction). Further, strong specific adsorption of the solutes to the silicone phase is observed (with  $k_i$  ranging from 3 to 43). Additionally, Nile Red exhibits a higher affinity for the silicone microphase than does Bodipy Green for both the TRIS- and M-PDMS-based SiHys.

#### 4. Theory

Water contents in Fig. 1 clearly increase linearly with increasing solvent-free hydrophilic-phase volume fraction. When  $v_{hyphil} = 0$ , water content is zero. When  $v_{hyphil} = 1$ , water content is simply the water content of the conventional hydrophilic hydrogel of the corresponding type (i.e., HEMA, MAA, or 10% MAA/90% HEMA). These findings suggest that overall SiHy water volume fraction is given by

$$\phi_1 = v_{hyphil} \phi_{1,hyphil} \quad (3)$$

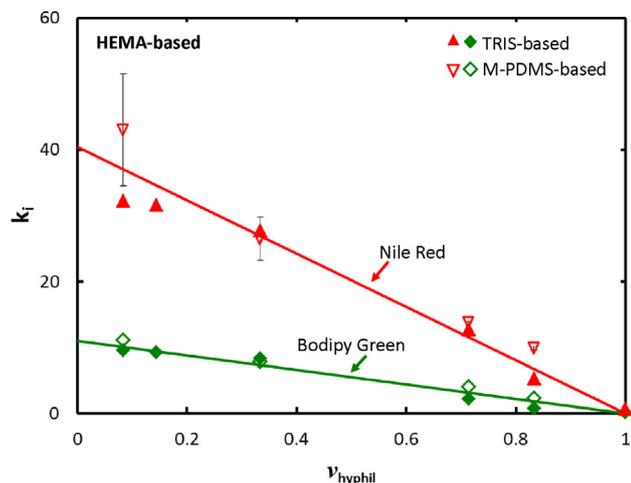
where  $\phi_{1,hyphil}$  is the water content of the conventional hydrophilic hydrogel. Solid lines in Fig. 1 are drawn according to Eq. (3) using no adjustable parameters. In all cases, agreement between theory and experiment is excellent. Eq. (3) reiterates that water primarily resides within the hydrophilic-polymer microdomains. In comparison, hydrophobic SiHy silicone-polymer microdomains uptake negligible water. Accordingly, SiHy water content can be directly controlled based on the relative monomer fractions added during synthesis.

Likewise, aqueous-solute partition coefficients in Figs. 2 and 3 rise linearly with increasing solvent-free hydrophilic-phase fraction. When  $v_{hyphil} = 0$ , aqueous-solute partition coefficients are zero. When  $v_{hyphil} = 1$ , aqueous-solute partition coefficients are those of the conventional hydrogels of the same type (i.e., HEMA, MAA, or 10% MAA/90% HEMA). Thus, aqueous-solute partition coefficients are given by

$$k_i = v_{hyphil} \phi_{1,hyphil} E_{i,hyphil} \quad (4)$$

where  $k_i$  is the solute partition coefficient of aqueous solute  $i$  and  $E_{i,hyphil}$  is the overall hydrophilic-phase enhancement factor [14]. In Eq. (4),  $E_{i,hyphil}$  accounts for specific solute adsorption to the polymer strands, electrostatic interaction, and solute hard-sphere size exclusion [15]. Table 2 reports values for  $E_{i,hyphil}$  in the conventional hydrogels that contain no silicone monomer or macromer (i.e., HEMA, MAA, or 10% MAA/90% HEMA). Details on the specific calculation are provided in Dursch et al. [14]. Solid lines in Figs. 2 and 3 are drawn using Eq. (4) with no adjustable constants. For all synthesized SiHys, agreement between theory and experiment is good. The slight discrepancies when  $v_{hyphil} = 1$  are due to errors in accounting precisely for hard-sphere size exclusion, as discussed previously [14]. Eq. (4) re-emphasizes that aqueous solutes are confined to water-filled domains that localize in the SiHy hydrophilic-phase domains. Since silicone microdomains imbibe negligible water, aqueous-solute uptake is negligible. Thus, SiHy aqueous-solute partition coefficients are a volume-fraction weighted average of those in the conventional hydrogels of the same type. This result suggests that the structure of the SiHy hydrophilic-polymer microdomains is similar to that of the conventional hydrogel.

Oleophilic-solute uptake in Fig. 4 likewise shows a linear dependence on  $v_{hyphil}$ . Contrary to water and aqueous-solute uptake, however, oleophilic-solute partition coefficients decrease linearly with  $v_{hyphil}$  owing to strong solute affinity for the silicone-polymer microdomains. Since we find minimal uptake of silicone oil in the SiHy studied, theory for oleophilic-solute partition coefficients is slightly different than that for the hydrophilic solutes where significant amounts of water reside in the



**Fig. 4.** Oleophilic-solute partition coefficients,  $k_i$ , as a function of the solvent-free volume fraction of hydrophilic monomer,  $v_{hyphil}$ , for Nile Red (triangles) and Bodipy Green (diamonds) in HEMA-based SiHys. Filled and open symbols denote TRIS- or M-PDMS-based SiHys, respectively. Typical error bars for Nile Red are shown. Error bars for Bodipy Green are the size of the data points. Lines are drawn according to theory.

hydrophilic domains. We define the partition coefficient of an oleophilic solute distributed between a SiHy and bulk silicone oil by

$$k_i = (1 - v_{hyphil})\phi_{2,hyphob}K_{i,hyphob}, \quad (5)$$

where  $k_i$  is the solute partition coefficient of oleophilic solute  $i$ ,  $\phi_{2,hyphob}$  is the silicone-polymer (i.e., monomer plus macromer) volume fraction of a hypothetical silicone-oil contacted TRIS or M-PDMS homopolymer network, and  $K_{i,hyphob}$  is the Henry's adsorption constant of solute  $i$  between bulk silicone oil and the SiHy hydrophobic microdomains (e.g., TRIS or M-PDMS) [14]. In Eq. (5), the amphiphilic macromer fraction is included in the hydrophobic-phase fraction, since water uptake of a homopolymer macromer hydrogel is minimal (i.e., the macromer hydrogel is primarily hydrophobic). Since our synthesized SiHys imbibe negligible silicone oil,  $\phi_{2,hyphob}$  is unity.

$K_{i,hyphob}$  reflects the affinity of an oleophilic solute  $i$  for the polymer strands in the SiHy silicone microphases. In all cases, we assume  $K_{i,hyphob}$  is identical for all hydrophobic-polymer strands because the hydrophobic groups of the macromer molecules are nearly identical to those of the silicone monomers. Following Dursch et al. [14],  $K_{i,hyphob}$  was taken as an adjustable constant from best least-squares fits to the partitioning data (with values of 40.4 and 11.4 for Nile Red and Bodipy Green, respectively). Large  $K_{i,hyphob}$  values (i.e., >10) indicate strong interaction between the dye solutes and the silicone-domain polymer. In all cases, Nile Red exhibits stronger interaction with the silicone-domain polymer than does Bodipy Green. Lines in Fig. 4 are drawn according to Eq. (5). Agreement between theory and experiment is excellent, confirming that oleophilic solutes partition primarily into the silicone-polymer microdomains. Consequently, oleophilic-solute partition coefficients can be directly controlled based on the relative amount of silicone monomer added during synthesis.

**Table 2**  
Overall solute enhancement factors,  $E_{i,hyphil}$ , for the conventional hydrogels.

Hydrogel type	Theophylline <sup>a</sup>	Caffeine <sup>a</sup>
HEMA	6.5	6.5
10% MAA/90% HEMA	2.5	2.5
MAA	0.9	0.9

<sup>a</sup> From Dursch et al. [14].

## 5. Discussion

Eqs. (3)–(5) describe SiHys as microphase separated with water and aqueous-solute uptake in the hydrophilic-polymer domains and oleophilic-solute uptake in the silicone-polymer domains. However, phase connectivity of these domains or the specific SiHy phase morphology present cannot be determined from our experiments. Several of the MAA SiHys were translucent, indicating possible macrophase separation. Conversely, all HEMA-based SiHys were transparent; FCLSM images revealed spatially homogeneous partitioning throughout each sample (data not shown), indicating microdomain sizes smaller than the resolution of the microscope ( $\sim 1 \mu\text{m}$ ) [18]. Nevertheless, theory accurately predicts SiHy equilibrium water contents and solute partition coefficients over a wide range of hydrogel compositions and water contents (3–82%).

In determining SiHy equilibrium water contents and solute partition coefficients, the amphiphilic macromer is classified as: (1) hydrophobic (i.e., having negligible water and aqueous-solute uptake), (2) hydrophilic (i.e., having negligible oleophilic-solute uptake), or (3) amphiphilic (i.e., having non-negligible water, aqueous-solute, and oleophilic-solute uptake). Classification is done by measuring the water content and aqueous- and oleophilic-solute partition coefficients of a homopolymer macromer hydrogel. If the macromer is classified as hydrophobic, Eqs. (3)–(5) are used as above. However, when the hydrophobic groups of the macromer molecules are significantly different from those of the silicone monomer, Eq. (5) includes an additive term for oleophilic-solute adsorption to hydrophobic-macromer chains [14]. When the macromer is classified as hydrophilic, water contents of the hydrophilic-monomer/macromer copolymer hydrogel are measured and applied in Eq. (3). Aqueous-solute partition coefficients follow from Eq. (4), but with a second term for aqueous-solute adsorption to hydrophilic-macromer strands [14]. Because hydrophilic macromers uptake negligible oleophilic solutes, oleophilic-solute partitioning prediction uses Eq. (5) as above after replacing  $(1 - v_{hyphil})$  with  $(1 - v_{hyphil} - v_{macromer})$ . When the macromer is classified as amphiphilic, water and aqueous-solute uptake follow that of a hydrophilic-designated macromer, whereas oleophilic-solute uptake follows that of a hydrophobic-designated macromer.

## 6. Conclusions

We report measured and predicted SiHy equilibrium water contents and solute partition coefficients. Fluorescence confocal laser-scanning microscopy and back extraction with UV/Vis-adsorption quantified partition coefficients of two aqueous solutes (i.e., theophylline and caffeine) and two oleophilic solutes (i.e., Nile Red and Bodipy Green) in thirty TRIS- and M-PDMS-based SiHys. Measured SiHy water contents and aqueous-solute partition coefficients increase linearly with the solvent-free hydrophilic-polymer fraction,  $v_{hyphil}$ . Conversely, oleophilic-solute partition coefficients increase linearly with the solvent-free hydrophobic-polymer fraction,  $(1 - v_{hyphil})$ . In all cases, predicted water contents and solute partition coefficients agree well with experiment. Importantly, our new procedure permits a priori estimation of SiHy water contents and solute partition coefficients based solely on properties of the silicone and hydrophilic homopolymer hydrogels, eliminating need for additional mixed-polymer-hydrogel experiments.

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## Appendix A. Figures with essential colour discrimination

Certain figures in this article, particularly Figs. 1–4, are difficult to interpret in black and white. The full colour images can be found in the on-line version, at <http://dx.doi.org/10.1016/j.actbio.2015.02.019>.

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