An Approach for Characterizing Scaffold Hydrophobicity

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Statement of Purpose: Surface modifications can critically impact scaffold hydrophobicity, a key modulator of mammalian cell behavior, drug payload release, and medical device fouling.[1-4] Contact angle and protein adsorption measures are two common methods for evaluating scaffold hydrophobicity. However, protein adsorption is a complex phenomenon which is challenging to interpret in terms of scaffold hydrophobicity alone. In addition, the permeability of scaffold surfaces can be problematic for contact angle assessment, since this method can only be strictly applied to smooth, solid, non-permeable surfaces. Therefore, the development of a technique for measuring scaffold hydrophobicity which is simple, sensitive, and independent of variations in scaffold surface permeability would significantly advance the ability to finely tune this variable. The present work develops a method for quantifying scaffold hydrophobicity which exploits their capacity to differentially uptake solvents of distinct polarities. To validate this technique, hydrogels of varying hydrophobicities were prepared by combining hydrophilic poly(ethylene glycol) diacrylate (PEGDA) with either hydrophobic 3-(trimethoxysilyl) propylmethacrylate (TMSPM) or hydrophilic 2-hydroxyethyl methacrylate (HEMA). The ratio of hydrogel swelling in 70% isopropanol to that in water was termed the hydrophobicity index (H-index) and was determined for each gel type, and compared with contact angle and protein absorption measurements.

Methods: ***Hydrogel preparation***. Hybrid hydrogels were prepared by the photopolymerization of aqueous mixtures of 6 kDa PEGDA and varying levels of TMSPM (Sigma) or HEMA (Alfa Aesar). The resulting hydrogel formulations were labeled according to the following sequential nomenclature: 1) the first letter of the primary polymer in the system, 2) the wt% of that polymer, 3) the first letter of the added monomer, and 4) the wt% of that monomer. For instance, a hydrogel containing 22 wt% PEGDA and 8 wt% TMSPM was termed P22T8, whereas a pure 30 wt% PEGDA hydrogel was referred to as P30.
H-Index Hydrophobicity Measures. The H-index for each hydrogel formulation was calculated by $H = \left[\frac{q_{I70}}{q_{diH2O}}\right]$ where q_{I70} and q_{diH2O} are the mass swelling ratio of the hydrogels in 70% Isopropanol and dIH_2O respectively.
Contact Angle and Protein Adsorption. Static contact angle studies were performed on water-swollen gels using a CAM-200 (KSV Instruments) measurement system equipped with an autodispenser, video camera, and drop-shape analysis software. As an indirect assessment of hydrophobicity, hybrid hydrogel adsorption of the serum protein fibrinogen was evaluated.

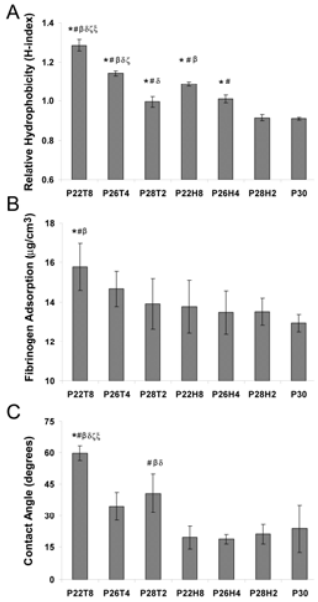

Fig 1. Comparison of the relative hydrogel hydrophobicities as evaluated by (A) H-index, (B) protein adsorption, and (C) contact angle assessments. * significant difference with P30 gels; # significant difference withP28H2 gels; β significant difference with P26H4 gels; δ significant difference with P22H8 gels; ζ significantdifference with P28T2 gels; ξ significant difference with P26T4 gels; $p < 0.05$.

Results and Discussion: The measured hydrogel H-indices reflected known differences in the hydrophobicities of HEMA, TMSPM, and PEGDA (Figure 1). In contrast to contact angle assessments, H-indices also appeared to be independent of variations in hydrogel permeability. In addition, the trend in H-indices agreed well with the trend in protein adsorption across hydrogel formulations, although the H-indices appeared to be able to resolve more subtle differences in hydrogel hydrophobicity than protein adsorption measures.

Conclusions: The present results have shown that H-indices could be used as an alternative method for assessing hydrogel hydrophobicity at higher resolution compared to traditional contact angle and protein absorption measurements. Although this work has focused on validating the H-index method using PEGDA-based hydrogels, this technique can potentially be extended to other scaffold systems, assuming appropriate solvent selection. Thus, the H-index approach has the potential to enable fine-tuning of scaffold hydrophobicity following surface modification and has relevance for tissue regeneration, drug delivery, and medical devices applications.

References:

1. Benoit, D. S. et al. *Nat Mater.* **2008,** 7, (10), 816-23.
2. Lin, M. C. et al. *Optom Vis Sci.* **2010,** 87, (6), 440-7.
3. Monkare, J. et al. *Eur J Pharm Biopharm* **2011,** 22, 22.