# Probing the Surface Structural Rearrangement of Hydrogels by Sum-Frequency Generation Spectroscopy

Qing Chen, Dan Zhang,† Gabor Somorjai, and Carolyn R. Bertozzi*

*Department of Chemistry*
*University of California at Berkeley*
*Materials Sciences Division*
*Lawrence Berkeley National Laboratory*
*Berkeley, California 94720*

*Received September 2, 1998*

The dynamic behavior of polymer surfaces has drawn significant recent attention, particularly in the field of biomedical materials.[1,2] Theoretical and experimental studies have shown that the surface properties of most polymers change in accordance with the nature of the surrounding medium, the thermodynamic driving force for the restructuring being minimization of interfacial free energy.[1] Surface reorganization is particularly pronounced in hydrogel materials as they transform from a dehydrated state to a hydrated state when immersed in water, or the reverse during dehydration.[3] Attempts to study this process have been impeded by a lack of suitable techniques. Traditional surface analysis techniques such as X-ray photoelectron spectroscopy (XPS) are performed in high vacuum and thus are difficult to operate for hydrated samples.[4] Contact angle measurements, which quantify surface hydrophobicity, have provided indications of water-induced surface restructuring of hydrogel polymers.[3,5] These macroscopic measurements, however, do not provide molecular level information regarding the structure of the interface. Consequently, the structures of polymer/air and polymer/water interfaces and the mechanism by which one interface rearranges to the other have yet to be determined in molecular detail.

IR + visible sum-frequency generation spectroscopy (SFG) has emerged as a powerful tool for studying various surfaces and interfaces.[6−9] SFG generates surface-specific vibrational spectra, providing information regarding the composition and orientation of moieties at the material surface.[9] Most importantly, SFG can be used to study any interface accessible to light, including solid/water interfaces,[8,9] which makes it well suited for biomedical materials research. Here we report the use of SFG to investigate the structural rearrangement of hydrogel surfaces during the transition from a hydrated to a dehydrated state. By recording in real time the changes in the vibrational spectra of moieties on the polymer surface, we were able to directly demonstrate the surface reorientation of polymer-associated functional groups.

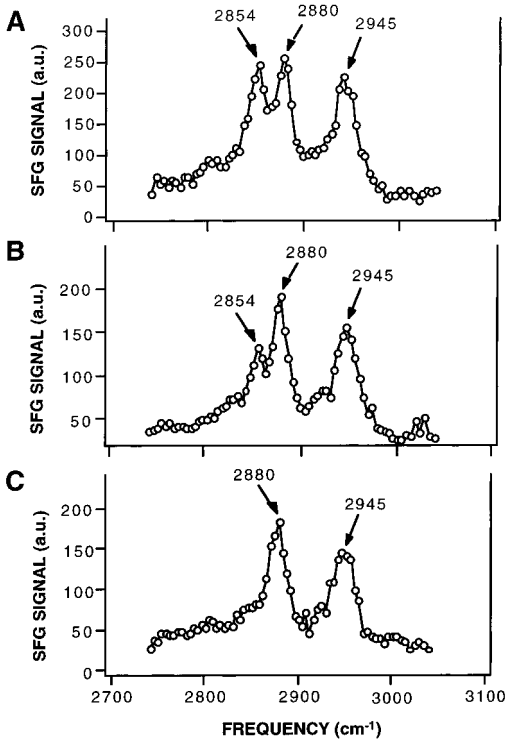


**Figure 1.** SFG spectra of polyHEMA acquired from different interfaces. (A) Hydrated polyHEMA at the water/polymer interface. (B) Hydrated polyHEMA at the air/polymer interface. (C) Dry polyHEMA at the air/polymer interface. The infrared field was p-polarized, and the visible and sum-frequency fields were s-polarized.

We chose cross-linked poly(2-hydroxyethyl)methacrylate (polyHEMA), a widely used biomedical material, for this study since it has been extensively studied with respect to interfacial phenomena.[1−5,10] The SFG spectrum of the surface of hydrated polyHEMA was recorded under water (Figure 1A). After removal from water, the material was again analyzed by SFG in air during which time (∼15 min) the water began to evaporate from the hydrogel (Figure 1B). Finally, the material was dried extensively, and the SFG spectrum of the dehydrated sample was recorded in air (Figure 1C).

The spectrum of the dry polymer in air (Figure 1C) showed two major peaks in the region from 2700 to 3100 $cm^{-1}$ which we assigned to the methyl groups on the polymer backbone.[11] The dominance of these peaks indicates a preponderance of methyl groups at the surface of the material when the polymer is in the dehydrated state. In previously reported spectra of polypropylene surfaces, a weak resonance at 2840 $cm^{-1}$ was ascribed to the backbone $CH_2$ groups of the polymer.[9a] An analogous peak for backbone $CH_2$ groups in the spectra of polyHEMA was not

* To whom correspondence should be addressed.
† Current address: Analytical Sciences Laboratory, Corporate Research, Exxon Research and Engineering Company, Route 22 E., Annandale, NJ 08801.

(1) (a) Andrade, J. D. *Polymer Surface Dynamics*; Plenum Press: New York, 1988. (b) Carbassi, F.; Morra, M.; Occhiello, E. *Polymer Surfaces from Physics to Technology*; Chichester, New York: Wiley: 1994.
(2) (a) Vogler, E. A. *J. Electron Spectroscopy* **1996**, *81*, 237. (b) Gardella, J. A.; Hernandez de Gatica, N. L. *J. Electron Spectrosc. Relat. Phenom.* **1996**, *81*, 227.
(3) (a) Holly, F. J.; Refojo, M. F. *J. Biomed. Mater. Res.* **1975**, *9*, 315. (b) Holly, F. J.; Refojo, M. F. In *Hydrogels for Medical and Related Applications*; Andrade, J. D., Ed.; ACS Symposium Series, Vol. 31; American Chemical Society: Washington, DC, 1976, pp 252−266.
(4) (a) Ratner, B. D.; Weathersby, P. K.; Hoffman, A. S. *J. Appl. Polym. Sci.* **1978**, *22*, 643. (b) Lewis, K. B.; Ratner, B. D. *J. Colloid Interface Sci.* **1993**, *159*, 77.
(5) (a) Hogt, A. H.; Gregonis, D. E.; Andrade, J. D.; Kim, S. W.; Dankert, J.; Feijen, J. *J. Colloid Interface Sci.* **1985**, *106*, 289. (b) Ko, Y. C.; Ratner, B. D.; Hoffman, A. S. *J. Colloid Interface Sci.* **1981**, *82*, 25. (c) Morra, M.; Occhiello, E.; Garbassi, F. *J. Colloid Interface Sci.* **1992**, *149*, 84.
(6) (a) Shen, Y. R. *Nature* **1989**, *337*, 519. (b) Eisenthal, K. B. *Annu. Rev. Phys. Chem.* **1992**, *43*, 627. (c) Bain, C. D. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 1281.
(7) Johal, M. S.; Ward, R. N.; Davies, P. B. *J. Phys. Chem.* **1996**, *100*, 274.
(8) (a)Walker, R. A.; Gruetzmacher, J. A.; Richmond, G. L. *J. Am. Chem. Soc.* **1998**, *120*, 6991. (b) Bell, G. R.; Bain, C. D.; Li, Z. X.; Thomas, R. K.; Duffy, D. C.; Penfold, J. *J. Am. Chem. Soc.* **1997**, *119*, 10227.
(9) (a) Zhang, D.; Shen, Y. R.; Somorjai, G. A. *Chem. Phys. Lett.* **1997**, *281*, 394. (b) Zhang, D.; Ward, R. S.; Shen, Y. R.; Somorjai, G. A. *J. Phys. Chem. B* **1997**, *101*, 9060.
(10) Hydrogels were prepared essentially as described in Chilkoti, A.; Lopez, G. P.; Ratner, B. D. *Macromolecules* **1993**, *26*, 4825.
(11) The peak at 2880 $cm^{-1}$ was assigned to the symmetric C−H stretch and the peak at 2945 $cm^{-1}$ to the Fermi resonance band between the symmetric stretch and the overtones of the H−C−H bending modes. Similar peaks were observed in the SFG spectrum of polypropylene (ref 9a).

10.1021/ja9831453 CCC: $18.00 
Published on Web 12/30/1998

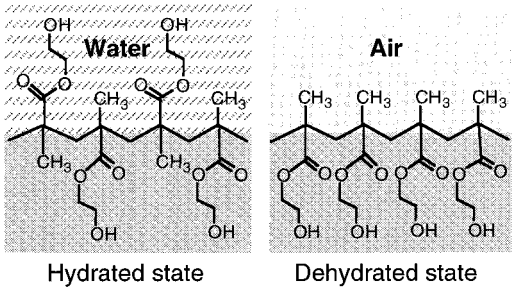


**Figure 2.** A model for reorientation of polymer surface functional groups during dehydration of polyHEMA hydrogels. The proportion of methyl and hydroxyethyl groups depicted at the polymer surface reflect qualitative changes in surface composition.

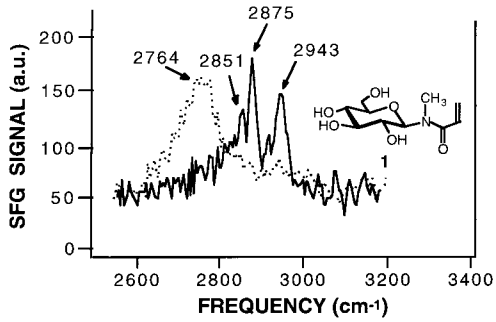


**Figure 3.** SFG spectra of HEMA−carbohydrate copolymers acquired from different interfaces. Solid line: dehydrated copolymer in air. Dotted line: hydrated copolymer under water.

detected, perhaps due to the orientation of these groups. Alternatively, the $CH_2$ groups may not produce an SFG signal for reasons of symmetry.[6a]

The SFG spectrum of the hydrated polymer recorded under water revealed a peak at 2854 $cm^{-1}$ (Figure 1A). This resonance is characteristic of the symmetric stretch of C−H bonds adjacent to the oxygen atoms in the ethylene glycol group ($-OCH_2CH_2$-OH), the hydrophilic component of the polymer.[12] The intensity of this peak varied from moderate to weak as the hydrogel transformed from the hydrated state to the dehydrated state (Figure 1B). Since acquisition of the SFG spectrum takes 10−15 min, Figure 1B represents a time-averaged account of the surface structures that were exposed during that interval after removal from water. In the fully dehydrated sample (Figure 1C), the vibrational contribution of the $CH_2$ groups within the ethylene glycol moieties could not be detected.

It has been proposed that massive reorientation of the backbone of cross-linked hydrogel polymers is restricted by the presence of the cross-links.[3,5] Side groups, on the other hand, when exposed to different environments, can rotate along the axis of the polymer chains to minimize the surface free energy. Thus, the reversible reorientation of side groups should account for the majority of movement at the outermost surface between 5 and 10 Å, a depth profile that is exactly within the scope of the SFG technique. The data shown in Figure 1 provide the first direct structural evidence in support of this model and suggest that polyHEMA hydrogels can adopt two discrete surface states as illustrated in Figure 2. When the hydrogel is exposed to air, polar side chains are buried in the bulk, and nonpolar methyl groups orient toward the surface to form a "hydrophobic conformation". In water, polar ethylene glycol groups migrate to the surface and coexist with methyl groups at the surface, creating a "hydrophilic conformation". It should be noted that relative peak amplitudes are not direct quantitative measures of chromophore abundance at the surface because the chromophores have different nonlinear polarizabilities. Nonetheless, the prominent peaks at 2945 and 2880 $cm^{-1}$ in the fully hydrated material (Figure 1A) indicate that some proportion of hydrophobic methyl groups remain at the surface despite the surrounding polar mileu.

Copolymers of HEMA with synthetic monomers[13] or biomolecules[14] are well-appreciated as biocompatible materials. The surface properties of these polyHEMA-based copolymers are of paramount importance for their performance *in vivo*, which prompted us to pursue SFG analysis of hydrogels comprising HEMA and a synthetic carbohydrate, glucose acrylamide **1** (20 wt %) (Figure 3). The SFG spectrum of the HEMA−carbohydrate copolymers in the dehydrated state revealed two major peaks at 2875 and 2943 $cm^{-1}$ which were assigned to the backbone-pendant methyl groups (Figure 3).[13] The weak resonance at 2851 $cm^{-1}$ can be accounted for by $-CH_2OH$ groups from ethylene glycol moieties or sugar residues. When the copolymer was fully hydrated, a broad peak emerged at 2764 $cm^{-1}$ which may reflect the *N*-methyl C−H stretch from exposed carbohydrates in concert with other obscured resonances.[15] The dramatic difference between the SFG spectra of the dehydrated and hydrated surfaces may result from increased exposure of hydrophilic carbohydrate moieties at the polymer surface.

In summary, SFG is well-suited for probing the dynamics of hydrogel surface rearrangements in various enviroments, provided the process occurs on a time scale greater than several minutes. Different polymer systems are thought to undergo surface structural reorientations on time scales ranging from minutes to months,[1,3] and many of these processes are therefore amenable to analysis by SFG.

**Acknowledgment.** This research was supported by the Laboratory Technology Research Partnership Program, Office of Energy Research, U.S. Department of Energy under a Cooperative Research and Development Agreement (CRADA) between Lawrence Berkeley National Laboratory and Sunsoft (Contract No. DE-AC03-76SF00098) and by the Director, Office of Energy Research, Office of Basic Energy Sciences and Materials Sciences Division of the U.S. Department of Energy (Contract No. DE-AC03-76SF00098).

**Supporting Information Available:** Synthetic procedures and spectral data for compound **1** and details for SFG spectra aquisition and peak assignments (3 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA9831453

(12) Roeges, N. P. G. *A Guide to the Complete Interpretation of Infrared Spectra of Organic Structures*; John Wiley & Sons: Chichester, England, 1994.

(13) (a) Blanco, M. D.; Trigo, R. M.; Garcia, O.; Teijon, J. M. *J. Biomater. Sci., Polym. Ed.* **1997**, *8*, 709 and references therein. (b) Quinn, C. P.; Pathak, C. P.; Heller, A.; Hubbell, J. A. *Biomaterials* **1995**, *16*, 389.

(14) (a) Gorham, S. D. In *Biomaterials*: *Novel Materials from Biological Sources*; Byrom, D., Ed.; Stockton Press: New York, 1991.

(15) Peak assignments were based on previous reports that the lone pair of electrons of a nitrogen atom weakens the C−H bond parallel to the axis of this orbital, resulting in a lower frequency for the symmetric stretch (ref 12).