

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/5802739>

TOF-SIMS Analysis of a 576 Micropatterned Copolymer Array To Reveal Surface Moieties That Control Wettability

ARTICLE *in* ANALYTICAL CHEMISTRY · FEBRUARY 2008

Impact Factor: 5.64 · DOI: 10.1021/ac071560k · Source: PubMed

CITATIONS

51

READS

46

6 AUTHORS, INCLUDING:



[Andrew Urquhart](#)

Technical University of Denmark

47 PUBLICATIONS 608 CITATIONS

SEE PROFILE



[Morgan Alexander](#)

University of Nottingham

206 PUBLICATIONS 4,106 CITATIONS

SEE PROFILE

TOF-SIMS Analysis of a 576 Micropatterned Copolymer Array To Reveal Surface Moieties That Control Wettability

Andrew J. Urquhart,[†] Michael Taylor,[†] Daniel G. Anderson,[‡] Robert Langer,[‡] Martyn C. Davies,^{*,†} and Morgan R. Alexander^{*,†}

School of Pharmacy, University of Nottingham, Nottingham, NG7 2RD, UK, and Centre for Cancer Research, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139

Time-of-flight secondary ion mass spectrometry (TOF-SIMS) was used in a high-throughput fashion to obtain mass spectra from the surfaces of 576 novel acrylate-based polymers, synthesized using a combinatorial approach and in a micropatterned format. To identify variations in surface chemistry within the library, principal component analysis (PCA) was used. PCA clearly identified surface chemical commonality and differences within the library. The TOF-SIMS spectra were also used to determine the relationship between water contact angle (WCA) and the surface chemistry of the polymer library using partial least-squares regression (PLS). A good correlation between the TOF-SIMS data from the novel polymers and water contact angle was obtained. Examination of the PLS regression vector allowed surface moieties that correlate with high and low WCA to be identified. This in turn provided an insight into molecular structures that significantly influence wettability. This study demonstrates that multivariate analysis can be successfully applied to TOF-SIMS data from a large library of samples and highlights the potential of these techniques for building complex surface property/chemistry models.

High-throughput methods for combinatorial synthesis have risen in prominence within material science over the last 10 years.^{1,2} The development of combinatorial material libraries, particularly in the field of polymeric materials, is beginning to open new opportunities within a wide range of scientific disciplines. The most noteworthy is the biomedical area where libraries have been used to screen for optimal cellular support materials for applications in tissue engineering.^{3–5} The screening, analysis,

and general handling of polymeric libraries can be greatly enhanced when printed in a microarray format onto glass microscope slides. Polymers within libraries can be synthesized in situ during printing³ or prior to printing.⁵ As high-throughput combinatorial approaches have developed in sophistication so have high-throughput analytical procedures.² However, until recently, the surface chemistries and surface properties of combinatorial polymeric libraries remained relatively unstudied.⁶ Material surface properties play a key role in underpinning a number of phenomena ranging from protein adhesion in biomaterials to corrosion prevention in structural engineering. The development of high-throughput surface analysis of microarrayed polymers presents many opportunities for identifying surface property/chemistry relationships from a large number of materials, information that will potentially reduce the time scales required for material development.

Surface analytical techniques can be adapted for the analysis of microarrayed libraries in a high-throughput fashion.⁶ Rapid sample analysis, integral for data acquisition across a large number of samples, can be readily achieved with microarrays given sufficiently small analysis areas and programmable analysis coordinates. One key surface analytical technique that can be used in a high-throughput fashion is time-of-flight secondary ion mass spectrometry (TOF-SIMS). TOF-SIMS⁷ is a surface-sensitive technique that has been successfully applied to a wide range of sample types. A primary ion beam can be focused onto a surface with the resulting impact desorbing both positive and negative secondary ions from the upper ~2 nm of the sample. These secondary ions can be mass analyzed and are usually highly characteristic of the material chemical structure with well-established relationships between fragmentation patterns and polymer structure known.^{8,9} Given the method of generating secondary ions through primary ion impact, it is not unusual for TOF-SIMS data to contain hundreds of secondary ion peaks which hold a wealth of chemical information. It is this degree of

* To whom correspondence should be addressed. E-mail: martyn.davies@nottingham.ac.uk (M.C.D.), morgan.alexander@nottingham.ac.uk (M.R.A.).

[†] University of Nottingham.

[‡] Massachusetts Institute of Technology.

(1) Hubbell, J. A. *Nat. Biotechnol.* **2004**, *22*, 828–829.

(2) Schmatloch, S.; Schubert, U. S. *Macromol. Rapid Commun.* **2004**, *25*, 69–76.

(3) Anderson, D. G.; Levenberg, S.; Langer, R. *Nat. Biotechnol.* **2004**, *22*, 863–866.

(4) Mant, A.; Tourniaire, G.; Diaz-Mochon, J. J.; Elliott, T. J.; Williams, A. P.; Bradley, M. *Biomaterials* **2006**, *27*, 5299–5306.

(5) Tourniaire, G.; Collins, J.; Campbell, S.; Mizomoto, H.; Ogawa, S.; Thaburet, J. F.; Bradley, M. *Chem. Commun.* **2006**, 2118–2120.

(6) Urquhart, A. J.; Anderson, D. G.; Taylor, M.; Alexander, M. R.; Langer, R.; Davies, M. C. *Adv. Mater.* **2007**, *18*, 2486–2491.

(7) Vickerman, J. C.; Briggs, D., Eds. *ToF-SIMS, Surface Analysis by Mass Spectrometry*; IM Publications: Chichester, 2001.

(8) Leeson, A. M.; Alexander, M. R.; Short, R. D.; Briggs, D.; Hearn, M. J. *Surf. Interface Anal.* **1997**, *25*, 261–274.

(9) ION-TOF. *The Munster High Mass Resolution Static SIMS Library*; ION-TOF GmbH: Munster, 2000.

information that sets apart TOF-SIMS from other surface analytical techniques and can make it a favorable choice for polymeric surface analysis. However, the degree of information within TOF-SIMS data can make the comparison and interpretation of more than a handful of new materials a daunting task.

The analysis of TOF-SIMS data from novel copolymer libraries proves very difficult using conventional spectral comparison approaches. These libraries not only have the complications of a huge sample set but also have the added difficulty of being novel materials without there necessarily being previous analytical work available or the user's knowledge of the system to identify characteristic ion fragments of key importance. Therefore, approaches to data interpretation have to be considered that will accommodate not only the novelty of the samples but also sample number. One such method in the multivariate analysis arsenal, which has shown previous successes with spectrometric data, is principal component analysis (PCA).

PCA is a multivariate statistical technique that can be viewed as a method for reducing a large data matrix (i.e., a series of samples with varying secondary ion peaks) to a few key combinations of variables that describe the most significant trends in the data. Detailed descriptions of PCA can be found elsewhere.^{10,11} As with all multivariate analytical approaches, a critical issue with PCA is the preprocessing of raw data prior to conversion into a data matrix. The established methodology with preprocessing TOF-SIMS raw data is the normalization of each spectrum to the total ion count followed by mean centering of the data,^{10,12,13} and it is this methodology that has been used for data preprocessing within this paper.

The driving force behind our investigation and development of high-throughput surface analysis is to provide data toward an understanding between the surface chemistries and resulting surface properties across a range of materials within a library. In order to do this, equal investigative value has to be given to all materials within a library and not—as is often the case for high-throughput screening—to only the materials that show the desired properties. We chose to investigate the relationship between polymer surface chemistry and wettability. Wettability is an important material property,¹⁴ and to date, no investigations exist that correlate polymer surface chemistry, as inferred by TOF-SIMS data, with wettability across a library of samples. To achieve a correlation between polymer surface functionality and wettability, high-throughput water contact angle (WCA) measurements were made on all polymers within the library and related to TOF-SIMS data via the use of partial least-squares regression (PLS), a multivariate regression technique.^{15,16} PLS takes two distinct experimentally determined sets of data, i.e., X and Y , and builds a predictive model of Y from these sets. The values of predicted

Y either positively correlate or negatively correlate with information from X . By plotting predicted Y against experimental Y , the degree of the model's accuracy can be determined in the form of the linear regression factor R^2 . PLS regression has been successfully used before in determining relationships between univariate data (i.e., cell growth) and TOF-SIMS data.^{13,17}

In this study, we show for the first time how PCA can be successfully applied to both positive and negative ion TOF-SIMS data from a combinatorial library comprising 576 novel polymers in order to highlight similarities and differences within the surface chemistries of the polymers. We also present the first PLS model of polymer wettability with regard to surface chemistry using both the positive and negative secondary ion data.

EXPERIMENTAL SECTION

Time-of-Flight Secondary Ion Mass Spectrometry. TOF-SIMS was performed with an ION-TOF ToF-SIMS IV instrument using a monoisotopic $^{69}\text{Ga}^+$ primary ion source operated at 25 kV and in “bunched mode”. The target current of the primary ion beam was typically 1 pA and with a pulse width of 24 ns before bunching. Secondary ions were sampled from a $100 \times 100 \mu\text{m}$ area of each polymer spot on the array with a 60-s acquisition window for each sample. Ion masses were determined by a time-of-flight analyzer with a mass resolution of five significant figures allowing very accurate mass assignment. Data acquisition for each polymer spot and mass calibration of every spectrum were automated via the design of a specific software batch operations using ION-TOF ToF-Bat software to allow unattended operation. Data acquisition was taken from a total of three microarrays printed onto the same glass slide. Given that the acquisition time of both the positive and negative ion spectra for all 576 polymers in the library can be achieved within 24 h, and since this time frame is easily within the time frame for the screening of a library with biological material (~ 2 – 10 days³), we have designated the acquisition of TOF-SIMS data from a copolymer library as high throughput.⁶

Water Contact Angle Measurement. Measurements were performed using ultrapure water on a Krüss DSA 100 apparatus fitted with a piezodoser head. The piezodoser allowed small ultrapure water droplets (110 pL) to be deposited onto the polymer spots.¹⁸ Sample positions and data acquisition were automated, with droplet side profiles being recorded (a dual camera system was used, one to record a spot's side profile and the other to record a bird's eye view to ensure that the water droplet was deposited at the center of each spot) for data analysis. WCA calculations were performed using a circle segment function as required for small water droplets. Again, data acquisition was taken from a total of three microarrays printed onto the same glass slide.

Data Preprocessing. Given the novel nature of the polymers analyzed, assumptions were not made regarding the integration of spectral regions. Instead, the automated peak search facility within the instrument software was used to fit the positive ion spectra of all polymers comprising 100% of each of the 24 monomers. These generated “peak lists” were then combined into one peak list, which was then applied to all 576 positive ion

(10) Belu, A. M.; Graham, D. J.; Castner, D. G. *Biomaterials* **2003**, *24*, 3635–3653.

(11) Graham, D. J.; Wagner, M. S.; Castner, D. G. *Appl. Surf. Sci.* **2006**, *252*, 6860–6868.

(12) Berman, E. S. F.; Kulp, K. S.; Knize, M. G.; Wu, L. G.; Nelson, E. J.; Nelson, D. O.; Wu, K. J. *Anal. Chem.* **2006**, *78*, 6497–6503.

(13) Yang, L.; Lua, Y. Y.; Jiang, G. L.; Tyler, B. J.; Linford, M. R. *Anal. Chem.* **2005**, *77*, 4654–4661.

(14) Garbassi, F.; Morra, M.; Occhiello, E. *Polymer Surfaces: From Physics to Technology*; John Wiley & Sons Ltd.: Chichester, 1998.

(15) Lorber, A.; Wangen, L. E.; Kowalski, B. R. *J. Chemom.* **1987**, *1*, 19–31.

(16) Manne, R. *Chemom. Intell. Lab. Syst.* **1987**, *2*, 187–197.

(17) Chilkoti, A.; Schmiere, A. E.; Perezluna, V.; Ratner, B. D. *Anal. Chem.* **1995**, *67*, 2883–2891.

(18) Taylor, M.; Urquhart, A. J.; Zelzer, M.; Davies, M. C.; Alexander, M. R. *Langmuir* **2007**, *23*, 6875–6878.

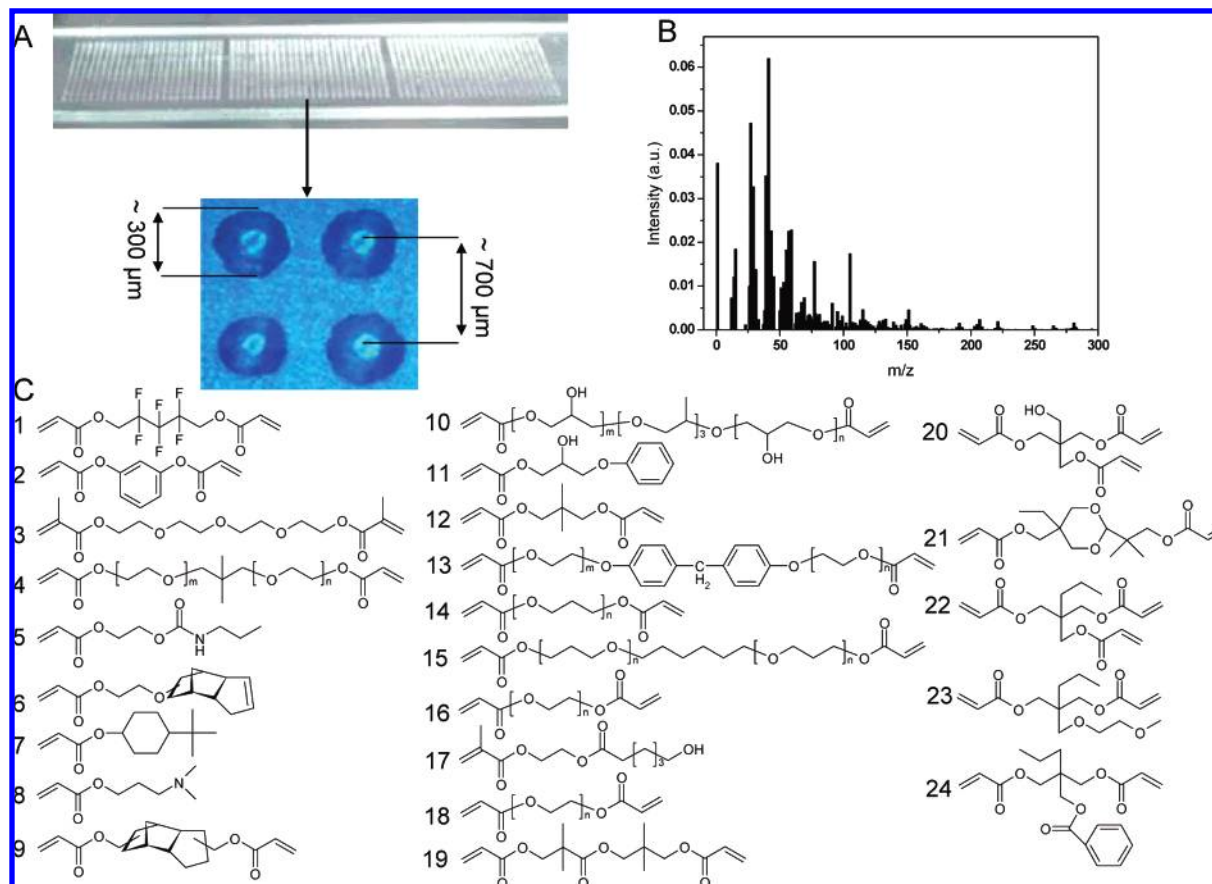


Figure 1. Library layout and chemistry. (A) Photograph showing microarrays printed in triplicate onto a glass microscope slide with microscopic image of four polymer spots to show spot dimensions. (B) Example positive ion TOF-SIMS spectrum from a polymer spot. (c) Structures of the 24 monomers that were used in the polymer array. Monomers were mixed pair wise in a 70:30 ratio to create the 576 polymers.

TOF-SIMS data. This process was repeated for the negative ion TOF-SIMS data. In most spectra, trace sodium and silicon contamination was observed although accounting for less than ~1.5% of the total ion count. The silicon peaks originated from the silicone species poly(dimethylsiloxane).⁹ Peaks associated with silicon and sodium contamination were removed from the data sets. Trace solvent retention was observed for the polymers with key *N,N*-dimethylformamide peaks ($m/z = 30$ and 74 , CH_4N^+ , and $\text{C}_3\text{H}_8\text{NO}^+$) accounting for less than ~0.5% of the total ion count. Solvent retention in polymer films has been previously reported for tetrahydrofuran and hexane solvents.⁸ While adventitious carbonaceous contamination is likely to be present on any number of polymer spots, it is apparent from the results presented here that polymers can be separated by PCA based on monomer composition, which would indicate that adventitious carbon contamination is negligible. It is also impossible to elucidate the presence of adventitious carbonaceous contamination given its variability and the absence of copolymer spectra acquired without previous exposure to the atmosphere. The poly(hydroxyethyl methacrylate) (PHEMA)-coated substrate was not detected in the TOF-SIMS analysis¹⁹ from the copolymer spots. After peak integration using instrument software, the data were exported into OriginPro 7.5, normalized, and arranged into three data matrices: positive ions, negative ions, and concatenated (i.e., a linked

positive and negative ion matrix). Concatenation followed standard procedures as described in refs 13, 20, and 21.

Multivariate Statistics. Data matrices were exported into eigenvector PLS_Toolbox 3.5 for Matlab. For PCA, the TOF-SIMS data matrices were preprocessed by mean-centering. For PLS, both TOF-SIMS and WCA data matrices were also preprocessed by mean-centering. The SIMPLS algorithm²² was used in the PLS analysis rather than the NIPALS algorithm due to it being a faster calculation to perform for the computer processing, a significant factor to take into consideration when handling large data sets. SIMPLS has been previously shown to produce identical PLS results to NIPALS when modeling univariate data.²³ The PLS model was determined using six latent variables and cross-validated using the leave-one-out approach.

Materials. Epoxy-coated glass slides (Xenopore) were dip coated in 4% (w/v) PHEMA (Aldrich) solution in ethanol. Monomers were purchased from Aldrich and Scientific Polymers (see Figure 1 for structures). Stock solutions were prepared at a ratio of 75% (v/v) monomer, 25% (v/v) dimethyl formamide, and 1% (w/v) 2,2-dimethoxy-2-phenylacetophenone (photoinitiator).

(19) Maldonado-Codina, C.; Morgan, P. B.; Efron, N.; Canry, J. C. *Opt. Vision Sci.* **2004**, *81*, 455–460.

(20) Canteri, R.; Speranza, G.; Anderle, M.; Turri, S.; Radice, S. *Surf. Interface Anal.* **2003**, *35*, 318–326.

(21) Smentkowski, V. S.; Keenan, M. R.; Ohlhausen, J. A.; Kotula, P. G. *Anal. Chem.* **2005**, *77*, 1530–1536.

(22) de Jong, S. *Chemom. Intell. Lab. Syst.* **1993**, *18*, 251–263.

(23) Xu, Q. S.; de Jong, S.; Lewi, P.; Massart, D. L. *Chemom. Intell. Lab. Syst.* **2004**, *71*, 21–31.

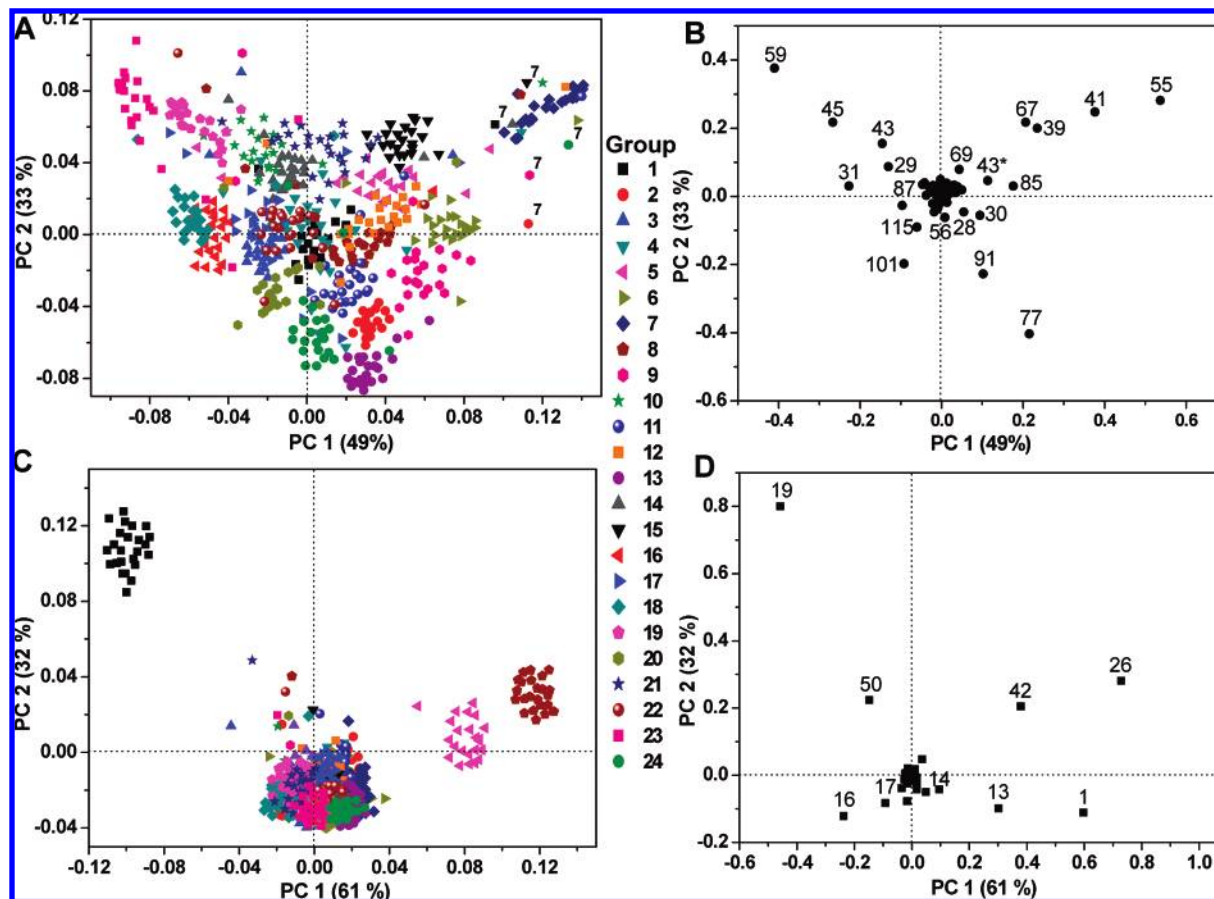


Figure 2. PCA of polymer library. (A) Scores plot for PC 1 and 2 using positive ion spectra from all 576 polymers. Polymers grouped by major monomer constituent. Polymers designated with a superscript 7 are example outliers where the minor constituent is monomer 7. (B) Loadings plot for PC 1 and 2 to show ion fragments associated with positive ion scores discrimination. (C) Scores plot for PC 1 and 2 using negative ion spectra from all polymers. (D) Loadings plot for PC 1 and 2 to show ion fragments associated with negative ion scores plot. The key denotes polymers grouped by major monomer constituent.

Solutions were mixed in a 70:30 ratio (v/v) and then printed onto the glass slides using a robotic fluid handling system. Polymerization involved using long-wave UV radiation in an argon environment. Full details on microarray synthesis can be found elsewhere³ (see Figure 1A and C for average polymer spot dimensions and monomers used respectively).

RESULTS AND DISCUSSION

TOF-SIMS analysis of microarrays has been previously successful for molecular,²⁴ genomic,^{25,26} and proteomic²⁷ systems. To achieve TOF-SIMS analysis of a combinatorial polymer library, both positive and negative ion TOF-SIMS data were automatically obtained for all 576 combinatorial polymers over the course of 24 h. Each spectrum obtained showed good quality with many ions being pertinent toward the surface molecular structure of the polymers (e.g., Figure 1B). Three replicates of the microarray were investigated with the mean of each polymer spot being shown in each figure to increase clarity.

PCA of TOF-SIMS Data from All 576 Copolymers within the Library. To investigate chemical variance within the surface

region of all polymers, PCA was performed on both the positive and negative ion TOF-SIMS data sets. The first two principal components show the best overall discrimination between copolymer surface chemistry within the library and therefore it is these two principal components that will be focused on throughout this section.

Figure 2A shows the PCA scores plot for the positive ion spectra of all polymers in the library. Grouping polymers together based on major monomer composition produces clusters with varying degrees of divergence. The degree to which polymers cluster for one major monomer constituent reflects the contribution of said major monomer to a polymer's surface. Thus, groups with tight clustering reflect polymer surfaces where the major monomer constituent is the dominant surface component compared to the minor monomer constituent. Tight clustering is observed within groups such as 13 and 18 while groups such as 9 and 21 show, in comparison, greater separation.

In some instances, certain minor monomer constituents affect the surface chemistry of some polymers to a greater degree than major monomer constituents. As an example, it can be seen in Figure 2A that there are a number of outliers (i.e., samples that surround a major monomer cluster but are not associated with it) from various polymer groups surrounding the group 7 cluster. These outliers are polymers where monomer 7 is the minor

(24) Xu, J. Y.; Braun, R. M.; Winograd, N. *Appl. Surf. Sci.* **2003**, *203*, 201–204.

(25) Cheran, L. E.; Vukovich, D.; Thompson, M. *Analyst* **2003**, *128*, 126–129.

(26) May, C. J.; Canavan, H. E.; Castner, D. G. *Anal. Chem.* **2004**, *76*, 1114–1122.

(27) Belu, A. M.; Yang, Z. P.; Aslami, R.; Chilkoti, A. *Anal. Chem.* **2001**, *73*, 143–150.

constituent and reflect surface chemistries where monomer 7 is dominant rather than the major monomer. This phenomenon can be seen for other minor constituents such as the outliers around groups 19 and 23. Polymers can also be pulled, to a varying degree, toward the general position of the minor monomer constituent. A good example of this is the polymer from the major monomer 23 group that can be found located within the group 21 cluster. The minor constituent of this polymer is in fact monomer 7 and not monomer 21. It is apparent from the PCA that this polymer has to some degree a similar surface chemistry (in terms of secondary ions associated with principal components 1 and 2) as the group 21 polymers; the polymer is however made up of two different monomers. This phenomenon can most likely be explained by neither monomer being foremost at the surface of the polymer. The location of this polymer within the scores plot indicates that it produces similar secondary ions (associated with principal components 1 and 2) at similar intensities as the group 21 polymers.

The representation of major and minor monomer constituents at the surface of the copolymers is difficult to explain purely on monomer chemistry. It is not chemically intuitive—based on monomer molecular structure—why certain monomers, e.g., monomers 7, 19, and 23, are more prominent at the surface than other monomers, e.g., monomers 10, 12, and 21. However, from the results presented here, it is apparent that certain monomers will dominate the surface chemistry of a polymer more so than others. The results also show that the polymer surface chemistries within the library do not reflect the 70:30 major to minor monomer ratio associated with bulk polymer chemistry. This is an important point if correlations are to be made between material chemistry and results from screening procedures. Screening procedures that rely on surface phenomena are governed by material surface chemistry and not the bulk. It is critical that material surface chemistries are not assumed to reflect bulk chemistries and that surface analytical data are used instead.

The loadings plot (Figure 2B) contains the mass peak information used to produce the scores plot (Table 1 shows proposed ion structure assignments while Figures S-1a and b (Supporting Information, SI) represent the breakdown of the loadings plot into PC 1 and 2, respectively). Interestingly, even though the mass peaks detected for the polymers ranged from 1 to 800 m/z , the peaks that appear to drive the scores plot (Figure 2A) fall within a narrow region (30–150 m/z) reflecting the propensity of the acrylate-based polymers to form key ion fragments of low m/z .^{9,28} Though intact monomeric units (e.g., for monomer 2, $m/z = 147$ corresponds to the $[M + H]^+$ ion) were detected for the majority of the monomers used, they have little effect on the most significant principal components in the analysis. The differentiation between the surface chemistry of the polymers within the library (Figure 2A) is governed by a series of polymeric fragments, and although it is possible to discuss this in detail for all the polymers investigated, here we shall just emphasize a number of examples associated with principal component 1 (PC 1).

Positive PC 1 values are strongly associated with nonoxygenated hydrocarbon fragments (see Figure 2B, Table 1, and Figure S-1a, SI), e.g., $m/z = 41, 55,$ and 67 are $C_3H_5^+$, $C_4H_7^+$, and $C_5H_7^+$,

Table 1. Ion Fragments (m/z) and Structural Assignment for Positive Ion Spectra and Negative Ion Spectra PCA Loadings

m/z	positive ion structure	m/z	negative ion structure
28	CH_2N^+	1	H^-
29	CHO^+	13	CH^-
30	CH_4N^+	14	CH_2^-
31	CH_3O^+	16	O^-
39	$C_3H_3^+$	17	OH^-
41	$C_3H_5^+$	19	F^-
43	$C_2H_3O^+$	26	CN^-
43*	$C_3H_7^+$	42	CNO^-
45	$C_2H_5O^+$	50	CF_2^-
55	$C_4H_7^+$		
56	$C_3H_6N^+$		
59	$C_3H_7O^+$		
67	$C_6H_7^+$		
69	$C_5H_9^+$		
77	$C_6H_5^+$		
85	$C_6H_{13}^+$		
87	$C_4H_7O_2^+$		
91	$C_7H_7^+$		
101	$C_6H_9O_2^+$		
115	$C_6H_{11}O_2^+$		

respectively. Given that positive loading on PC 1 is dominated by hydrocarbon secondary ions, it can be seen that group 7 polymers and its surrounding outliers (see Figure 2A) are strongly associated with these ions, particularly the $C_4H_7^+$ ion ($m/z = 55$). Monomer 7 is a 4-butylcyclohexyl acrylate, and it is likely that the propensity to form the $C_4H_7^+$ ions reflects fragmentation of the butyl species into a $(CH_3)_2C=CH^+$ structure. This suggests that the butyl capped cyclohexyl group preferentially orientates at the polymer surface. Certain hydrocarbon fragments are associated with cyclic positive ions, e.g., $C_6H_5^+$ and $C_7H_7^+$ ($m/z = 77$ and 91), predominantly associated with aromatics. The major monomer 2, 11, 13, and 24 clusters (see Figure 2A) all comprise major monomers that contain phenyl groups. These polymers are localized within the same area of the scores plot due to these cyclic fragments. Interestingly, groups 6 and 9 both contain nonaromatic tricyclic ring structures and sit between the polymer clusters dominated by more linear fragments (e.g., group 7) and those dominated by cyclic ones (e.g., group 13). This indicates that the tricyclic structure has some propensity to fragment into both linear and cyclic ions while for the butyl capped cyclohexyl structure in monomer 7 it is apparent that fragmentation favors linear ions.

Negative values along PC 1 are strongly associated with oxygenated hydrocarbon ions, such as CH_3O^+ , $C_2H_5O^+$, and $C_3H_7O^+$ ($m/z = 31, 45,$ and 59), as seen in Figure 2B, Table 1, and Figure S-1a (SI). Polymers where monomer 23 is the major constituent (group 23) show the greatest degree of fragmentation into these ions, i.e., the largest negative loading value on PC 1. Monomer 23 contains a 1,2 dimethoxyethane side chain, which could easily fragment into $C_3H_7O^+$, thus contributing to the differentiation observed. Interestingly, TOF-SIMS imaging of microarrays has previously shown a high intensity with $C_3H_7O^+$ ions for polymers containing monomer 23.⁶ Focusing on the three ethylene glycol backboned monomers (3, 16, 18), it can be seen that there is strong differentiation in PC 1 between the three groups. This can be attributed to the difference in the number of

(28) Briggs, D.; Fletcher, I. W.; Goncalves, N. M. *Surf. Interface Anal.* **2000**, *29*, 303–309.

ethylene glycol units that comprise the monomer backbone; thus, monomer 3 contains three discrete ethylene glycol units while monomer 16 contains ~ 7 and monomer 18 ~ 10 units. It is consistent with previous PCA work on molecular hydrocarbons that has shown that alkyl chain lengths can be separated to individual carbon atoms using PCA.¹³ We could continue this type of analysis to investigate the relationships between various polymer clusters across the library, but it is beyond the scope of this publication.

PCA using the negative ion TOF-SIMS data from the combinatorial library shows poor separation between the polymers based on a major monomer constituent within the scores plot, Figure 2C. This is primarily due to the relatively limited information that can be obtained from the negative ion spectra of acrylate polymers, due to the high probability of atomic fragment (e.g., O^-) formation over molecular fragments in comparison to positive ion spectra.⁹ Previous work on acrylate polymers has shown unique negative ion peaks associated with $CH_2=C(R)CO_2^-$ ion formation, where R reflects the acrylate, i.e., $CH_2=C(CH_3)CO_2^-$ for methacrylate or $CH_2=CHCO_2^-$ for acrylate.^{9,29} For this library, all monomers are acrylates except monomers 3 and 17, which are methacrylates. PCA of the negative ion spectra from this library does not separate the methacrylate monomers from the acrylate monomers.

It has also been observed for acrylate homopolymers that side-chain groups can be detected through the formation of AO^- ions, where A denotes the side chain (i.e., AO^- would be detected in $(CH_2CH)_nCO_2A$).²⁹ In this library, side-chain ions do not separate out the polymers in the PCA of the negative ion spectra. This is mainly due to the monomers used to produce the library, which are predominantly non-side-chain-containing di- and triacrylates (e.g., monomers 1, 2, 3, etc). Seven of the 24 monomers used do not fall into this category. Monomers 5, 17, 23, and 24 are not separated by AO^- ion formation, even though they do have side chains, most likely due to the chemical structure of their side chains. These side chains connect to the carboxyl functionality via the carbon atom ($A-C=O$) rather than the oxygen atom ($AO-C=O$) that would generate the AO^- ion. Finally, monomers 6, 7, and 8 have the correct side-chain structure for the formation of acrylic AO^- ions. Monomer 6 is unlikely to form a side-chain AO^- ion due to the presence of the $C=C$ bond within the tricyclic ring. This creates another possible site for polymerization, which would turn the side chain into a backbone structure with some similarity to monomer 9. Monomers 7 and 8 are not separated by AO^- ion formation in the PCA; however, they can be separated by other ions with both PCA plots.

Instead, only the polymers that produce unique atomic or low molecular weight negative ions, e.g., F^- and CN^- , are separated to any considerable degree. Polymers do cluster based on the major monomer constituent; however, only three polymer groups differentiate significantly from the majority of the polymers in the library and these contain monomers 1, 5, and 8. Unsurprisingly, the chemical structures of monomers 1, 5, and 8 contain species that produce distinct anions from fluorinated and also nitrogen-containing polymers, e.g., F^- , C_2F^- , CN^- , and CNO^- ($m/z = 19, 50, 26$, and 42) (see Figure 2D). It is worth noting that the separation of major monomer 5 and 8 copolymers is likely to

depend on amide fragmentation into CNO^- in monomer 5 (see monomer 5 structure in Figure 1C). The outliers that project from the main polymer cluster represent polymers where monomer 1, the fluorinated monomer, is the minor constituent.

To present an indication of the statistical significance of polymer separation, ellipses with a confidence limit of 95%³⁰ were drawn around the homopolymers within the library (see Supporting Information Figures S-3 and S-4). Each library contains one polymer made entirely from one monomer. It can be seen that there is relatively good separation between homopolymers in the positive ion PCA scores. For the negative ion, PCA of the homopolymers shows considerable ellipse overlap with the three exceptions of the homopolymers comprised of monomers 1, 5, and 8.

Overall PCA of positive ion TOF-SIMS data produce the most significant differentiation between polymer surface chemistry within this combinatorial library. PCA of the negative ion TOF-SIMS data only differentiates polymers that have surfaces that comprise certain atoms, e.g., F, N, S, etc. PCA of combinatorial polymeric libraries should use both positive and negative ion TOF-SIMS data to elucidate surface chemical differences within the novel polymers.

PLS Analysis of TOF-SIMS Data versus WCA To Determine Relationships between Polymer Surface Chemistry and Wettability. PLS analysis was performed to investigate the relationship between polymer surface chemistry and corresponding wettability for all polymers within the library. PLS analysis of data allows the development of multivariate statistical models that can be used to determine relationships between surface chemical spectroscopic information (e.g., secondary ions) and a surface property.¹⁷ By interrogating the model, it is possible to elucidate the surface chemistry (e.g., functional groups, pendent chains off polymer backbones, etc.) that is implicated with a particular surface property, i.e., wettability.

To build the most accurate model to represent the effects of surface chemistry, the TOF-SIMS data of both the positive and negative ion spectra of each polymer were concatenated (i.e., linked). As shown with the PCA data, positive and negative ion spectra can hold different information in terms of chemical surface species; therefore, to accurately reflect the fragmentation pattern of a polymer, the two spectral data sets were combined. PLS models were also built using only the positive or negative ion spectra. These models showed less accuracy within the linear regression, i.e., poorer R^2 values, especially the model deriving from the negative ion spectra due to the limited mass spectral information provided. To build the PLS model from the triplicate of both the TOF-SIMS and the WCA data sets, the mean of both sets was taken rather than build three separate models.

Figure 3A shows the predicted WCA against the measured WCA of all polymers within the library using the concatenated TOF-SIMS data set. The model shows good agreement between the experimental and predicted values ($R^2 = 0.94$) with values ranging between 47° and 93° . The majority of polymers within the library fall into a WCA range of 60° – 80° , which is within the WCA values of more common acrylate-based polymers (e.g., poly(methyl methacrylate) has a value of $\sim 70^\circ$ ¹⁸). Polymers where either monomer 7 or 8 as the major constituent form two distinct

(29) Briggs, D.; Brown, A.; Vickerman, J. C. *Handbook of Static Secondary Ion Mass Spectrometry (SIMS)*; John Wiley & Sons: Chichester, 1989.

(30) Wagner, M. S.; Castner, D. G. *Langmuir* **2001**, *17*, 4649–4660.

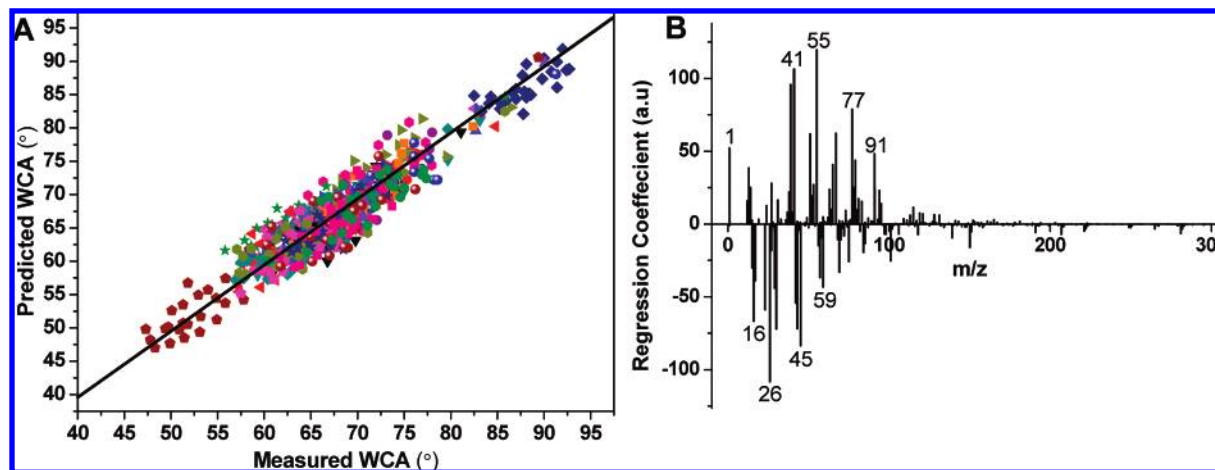


Figure 3. PLS (with six latent variables) model (A) of predicted WCA against measured WCA for all 576 polymers in the library (linear fit is shown, $R^2 = 0.94$). Polymer groupings follow the same labeling system as used in Figure 2. (B) Regression vector plotted as regression coefficient versus peak m/z for the concatenated data set (see Table 2 for ion structural assignment).

groups which fall outside the WCA range of the majority of polymers. Group 7 polymers are the most hydrophobic set of the entire library (82° – 93°) and have surface chemistries dominated by the *tert*-butylcyclohexyl pendent chain of monomer 7. The *tert*-butylcyclohexyl species is a nonoxygenated hydrocarbon structure and is thus a hydrophobic species.

Conversely, group 8 polymers show the most hydrophilic WCA values (see Figure 3A). Previous work on tertiary amine-containing polymers³¹ and SAMs³² has shown that these materials have positive surface charges within water (pH 7.4). This can represent either protonation of the tertiary amine to form a trimethylaminium species (i.e., R_3NH^+) or the formation of a quaternary salt species with trace impurities in the water (e.g., $R_3NH^+Cl^-$). A similar phenomenon is likely to occur for polymer surfaces that are dominated by monomer 8, which contains a tertiary amine pendent chain. Positively charged surfaces will have a greater polar component of surface energy and will thus be more hydrophilic. This indicates that monomer 8 as a major monomer constituent produces generally the most polar polymer surfaces except where monomer 7 is a minor constituent. Surprisingly, monomer 17, a hydroxyl-terminated pendent chain monoacrylate, does not produce the most polar polymer surfaces when a major constituent. This proves difficult to explain but could be attributed to a lower number of hydroxyl terminated pendent chains at the surfaces of polymers, where monomer 17 is the major constituent, in comparison to tertiary amine pendent chains at the surfaces of polymers where monomer 8 is the major constituent. Previous work has shown similar WCA values for combinatorial polymers where monomer 17 is the major constituent.⁶

The degree to which a secondary ion (either positive or negative) affects the PLS model is determined by its regression coefficient value. Secondary ions with positive regression coefficients positively correlate with WCA, while those with negative coefficients negatively correlate with the WCA. Figure 3B shows the regression vector plotted as the regression coefficients versus ion m/z , while Table 2 shows the secondary ions with the largest

Table 2. Shows Ion Structural Assignment for the Ions with the Largest Regression Coefficients for the PLS Wettability Model

m/z	ion structure	positive corr (au)	m/z	ion structure	negative corr (au)
1	H^-	52	15	NH^-	-30
13	CH^-	39	16	O^-	-67
14	CH_2^-	25	17	OH^-	-39
27	$C_2H_3^+$	28	23	Na^+	-59
39	$C_3H_3^+$	96	26	CN^-	-108
41	$C_3H_5^+$	106	29	CHO^+	-44
51	$C_4H_3^+$	62	30	CH_4N^+	-72
53	$C_4H_5^+$	27	42	CNO^-	-54
55	$C_4H_7^+$	120	43	$C_2H_3O^+$	-72
65	$C_5H_5^+$	41	45	$C_2H_5O^+$	-83
67	$C_5H_7^+$	62	57	$C_3H_5O^+$	-37
77	$C_6H_5^+$	79	59	$C_3H_7O^+$	-27
78	$C_6H_6^+$	25	59	$C_2H_3O_2^+$	-43
79	$C_6H_7^+$	44	69	$C_4H_5O^+$	-33
91	$C_7H_7^+$	48	75	$C_3H_7O_2^+$	-26

regression coefficients (≥ 3 , i.e., those ions that are the most significant in describing WCA for the library). Ions with large positive regression coefficients, e.g., $C_nH_m(\pm)$, are associated with nonoxygenated hydrocarbon chemical structures. Hydrocarbons are nonpolar species and therefore hydrophobic. Polymers where the major constituent has a significant hydrocarbon proportion (e.g., monomers 6, 7, 9, etc.) show relatively high WCAs, reflecting the nonpolar nature of the surfaces of these polymers. The ion fragment with the largest positive regression coefficient, $C_4H_7^+$ ($m/z = 55$), is strongly associated with monomer 7 and in this monomer's case is likely to derive from the cleavage of the tertiary butyl group into $(CH_3)_2C=CH^+$. Ions with large negative regression coefficients are associated with linear oxygenated hydrocarbon fragments (e.g., $C_nH_mO^+$) and amine/amide fragments (e.g., CN^- , CNO^- , and CH_4N^+). The PLS model for low WCA values splits into two groups of polymers, those associated with amine/amide functionality (e.g., monomers 5 and 8) and those associated with ethylene glycol backbone functionality (e.g., monomer 3, 16, and 18).

Polymers where monomer 8 is the major constituent show the lowest WCA values, and this is reflected in the model with the regression coefficient values of the CN^- and CH_4N^+ ions. The

(31) Wei, X. Z.; Zhu, B. K.; Xiao, L.; Xu, Y. Y.; Geckeler, K. E. *Macromol. Rapid Commun.* **2005**, *26*, 1224–1227.

(32) Shyue, J. J.; De Guire, M. R.; Nakanishi, T.; Masuda, Y.; Kuomoto, K.; Sukenik, C. N. *Langmuir* **2004**, *20*, 8693–8698.

polymers that comprise major monomers with ethylene glycol backbones (monomers 3, 16, and 18) also show relatively low WCAs. Water molecules have been shown to strongly hydrogen bond to the O atom of the ethylene glycol units in poly(ethylene glycol) (PEG).^{33,34} This observation is likely to explain the relatively low WCA values (range of $\sim 57^\circ$ – 67°) observed for these polymers. The WCA value of a pure PEG film is $\sim 59^\circ$.³⁵ The regression coefficients of two key ethylene glycol structured ions, $\text{C}_2\text{H}_3\text{O}^+$ and $\text{C}_2\text{H}_5\text{O}^+$, also corroborate the observation of ethylene glycol units having a hydrophilic nature.

Overall the PLS model shows good correlation between both the predicted and measured WCAs within the library. Deviations away from the model do exist, but all samples fall within a $\pm 10\%$ band from the linear regression line (see Figure 3A). Given the sheer volume of samples, degrees of experimental error, and potential surface roughness effects on WCA, the accuracy of the PLS model seems very acceptable. The regression vector shows major regression coefficients (secondary ions) that follow conventional understanding with regard to the interaction between a given surface chemistry and a water droplet, thus providing confidence in the accuracy of the PLS model.

CONCLUSIONS

The work here has demonstrated that PCA can be applied to TOF-SIMS data from large combinatorial libraries with successful differentiation of polymer surface chemistries. The differentiation of polymers based on surface chemistry holds significant value to a number of disciplines where surface interactions are critical. In micropatterned combinatorial material libraries, the ability to determine whether a major or minor constituent is surface

dominant is of critical importance if correlations are to be made between library chemistry and a screening process. It is imperative that the surface chemistry of a combinatorial material is not assumed to equate to the material's bulk chemistry in screening processes where surface chemistry is a controlling factor.

The PLS model correlating wettability with surface chemistry across the entire library has successfully shown that PLS analysis can be used to build models that correlate surface chemistry with a surface property for a large number of materials. The ability to correlate large volumes of data from a large library of samples allows for more accurate and relevant models to be produced. The ultimate goal in determining correlations between surface chemistry and surface properties is to move one step closer to rational material design, where a material can be engineered to produce a desired response. For example, combinatorial materials, where hydrophobicity was an important parameter, might consider the use of 4-butylcyclohexyl acrylate (monomer 7) given its hydrophobicity and surface segregation properties. The applicability of multivariate statistics to combinatorial libraries will hopefully advance material design and discovery for a range of scientific fields.

ACKNOWLEDGMENT

This work was funded by the BBSRC (project grant BBC5163791) and the National Institutes of Health (grant R01 DE016516).

SUPPORTING INFORMATION AVAILABLE

Additional information as noted in text. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(33) Dreesen, L.; Humbert, C.; Hollander, P.; Mani, A. A.; Ataka, K.; Thiry, P. A.; Peremans, A. *Chem. Phys. Lett.* **2001**, *333*, 327–331.

(34) Ide, M.; Yoshikawa, D.; Maeda, Y.; Kitano, H. *Langmuir* **1999**, *15*, 926–929.

(35) Suh, K. Y.; Jon, S. *Langmuir* **2005**, *21*, 6836–6841.

Received for review July 24, 2007. Accepted October 1, 2007.

AC071560K