

Integrated Surface Modification of Fully Polymeric Microfluidic Devices Using Living Radical Photopolymerization Chemistry

ROBERT P. SEBRA,¹ KRISTI S. ANSETH,^{1,2} CHRISTOPHER N. BOWMAN^{1,3}

¹Department of Chemical and Biological Engineering, ECCH 111, CB424, University of Colorado, Boulder, Colorado 80309-0424

²Howard Hughes Medical Institute, University of Colorado, Boulder, Colorado 80309-0424

³Department of Restorative Dentistry, University of Colorado Health Sciences Center, Biomaterials Research Center, Denver, Colorado 80262

Received 2 August 2005; accepted 20 November 2005

DOI: 10.1002/pola.21247

Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Surface modification using living radical polymerization (LRP) chemistry is a powerful technique for surface modification of polymeric substrates. This research demonstrates the ability to use LRP as a polymer substrate surface-modification platform for covalently grafting polymer chains in a spatially and temporally controlled fashion. Specifically, dithiocarbamate functionalities are introduced onto polymer surfaces using tetraethylthiuram disulfide. This technique enables integration of LRP-based grafting for the development of an integrated, covalent surface-modification method for microfluidic device construction. The unique photolithographic method enables construction of devices that are not substrate-limited. To demonstrate the utility of this approach, both controlled fluid flow and cell patterning applications were demonstrated upon modification with various chemical functionalities. Specifically, poly(ethylene glycol) (375) monoacrylate and trifluoroethyl acrylate were grafted to control fluidic flow on a microfluidic device. Before patterning, surface-functionalized samples were characterized with both goniometric and infrared spectroscopy to ensure that photografting was occurring through pendant dithiocarbamate functionalities. Near-infrared results demonstrated conversion of grafted monomers when dithiocarbamate-functionalized surfaces were used, as compared to dormant control surfaces. Furthermore, attenuated total reflectance/infrared spectroscopy results verified the presence of dithiocarbamate functionalities on the substrate surfaces, which were useful in grafting chains of various functionalities whose contact angles ranged from 7 to 86°. © 2006 Wiley Periodicals, Inc. *J Polym Sci Part A: Polym Chem* 44: 1404–1413, 2006

Keywords: graft copolymers; microstructures; photopolymerization

Correspondence to: C. N. Bowman (E-mail: bowmanc@colorado.edu)

Journal of Polymer Science: Part A: Polymer Chemistry, Vol. 44, 1404–1413 (2006)
© 2006 Wiley Periodicals, Inc.

INTRODUCTION

A variety of research endeavors have focused on the development of polymeric microfluidic devices for chemical and biological applications, motivated by device efficiency, throughput, and cost effectiveness. Microfluidic research has greatly affected areas including directed fluid flow, cell patterning, molecular/biological sorting, and bio-detection by introducing efficient, functional microdevices that achieve the same utility as larger, more expensive systems.¹⁻⁸ In particular, the soft lithography technique¹ has become one of the most commonly used fabrication methods for constructing microfluidic devices of this nature. Specifically, research using the soft lithography technique includes the development of flow-controlled devices and gradient microfluidic mixing channels and the patterning of conductive polymeric materials on polydimethylsiloxane-based devices for use as integrated electrodes.^{1,3,4,7} Furthermore, Beebe et al.⁹ recently presented work illustrating the detection of botulinum toxin on a microfluidic device produced with the microfluidic tectonics platform and noncovalently functionalized agarose beads, demonstrating significant progress in microfluidic device applications.

Although techniques including microfluidic tectonics and soft lithography have been successfully developed for the construction of microfluidic devices, these platforms are substrate-limited and deficient in readily available, integrated surface-modification techniques. Further limitations with current techniques include the requirement for physical manipulation or machining to produce a complete device without layer delamination.⁶ Therefore, to eliminate many of these concerns, current microfluidics research would benefit greatly from a general approach for the use of chemistries to covalently functionalize a variety of polymeric substrate materials in three dimensions with integrated spatial and temporal control.

Toward this goal, the surface modification of polymeric device matrices facilitates the incorporation of multiple functionalities and provides the ability to tune and enhance surface properties such as adhesiveness, hydrophobicity, biocompatibility, antifouling, surface hardness, and surface roughness. Through the integration of microfluidic device fabrication methods with surface-modification chemistries, device functionality is dramatically improved while bulk material properties are retained.^{6,10}

Noncovalent modification techniques are commonly used in microfluidic device fabrication methods. Typically, these techniques rely heavily on physisorption and surface adsorption,^{3,8,9,11-14} which lead to low surface density and subsequent desorption of functional moieties. Such shortcomings can be circumvented with covalent attachment methods. The ability to covalently bind a variety of chemistries with control over their graft length, density, and composition provides numerous advantages by increasing the accessibility, density, conformation, and mobility. Successful examples of covalent attachment methods include the modification of surfaces with self-assembled monolayers (SAMs) and direct covalent binding to surface-activated groups.^{2,13-18} Specifically, two-dimensional patterns of functional detection proteins have been introduced with silane-based SAM chemistry on a silicon dioxide surface to facilitate a surface affinity toward specific immunoglobulin proteins.^{13,15,16} Monolayer conjugation chemistries have been used to demonstrate the attachment of chemical and biological functionalities such as proteins, are well characterized, have excellent surface coverage characteristics, and include a variety of surface-attachment chemistries.^{15,16} However, these techniques involve time-intensive chemistry, are substrate-limited, and most often lack temporal control.

Living radical polymerization (LRP) techniques, such as atom transfer radical polymerization (ATRP) and iniferter-based chemistries, allow for additional control in the surface-modification process.^{5,10,15,19-32} In comparison with monolayer chemistries as well as living/controlled surface-modification chemistries such as ATRP, iniferter-based LRP chemistries provide a more efficient grafting approach and also offer both temporal (the grafted polymer chain length increases as a function of time) and spatial control over grafted chains. The controlled nature of LRP systems that are based on photolabile, dithiocarbamate (DTC)-based, surface-initiating moieties, pioneered by Otsu, are especially efficient.^{22-27,33-35}

Previous research using LRP chemistry includes the preparation of well-defined diblock and triblock copolymers.³³ Upon exposure to UV light, the DTC-based molecules cleave into a reactive carbon-based radical and a less reactive sulfur-based DTC radical. In the presence of (meth)acrylate monomers, the reactive carbon-based radical initiates a radical polymerization, allowing the propagation of (meth)acrylate polymer chains. This research illustrates the ability to use LRP as

a surface-modification platform for covalently grafting these polymer chains of controlled length, composition, and surface density onto polymeric microfluidic devices. The grafted polymer chains may further contain pendant moieties for a variety of applications ranging from hydrophobicity control to biological detection. Because the reactive groups are covalently grafted into polymer chains, the chemical conformation and chain mobility are tailored by proper selection of the surface-grafting monomer composition and polymerization conditions. To date, LRP-based grafting has not been integrated into a scheme for the development of functional polymeric devices. In this research, we illustrate the ability to integrate LRP surface chemistry with a photolithographic method⁶ for constructing microfluidic devices that are not substrate-limited. With integrated surface-modification techniques, we can begin to approach applications that are otherwise restricted because of a lack of the appropriate surface chemistries. Here, covalent surface modification is integrated onto a microfluidic device platform to demonstrate spatially and temporally controlled chemical functionalization, which subsequently controls fluid flow and cellular attachment.

EXPERIMENTAL

Materials

The photoinitiator, 2,2-dimethoxy-2-phenylacetophenone (DMPA), was purchased from Ciba-Geigy (Hawthorne, NY). The photoiniferter precursor, tetraethylthiuram disulfide (*N,N*-diethyl dithiocarbamate; TED), was purchased from Sigma-Aldrich. The monomers *tert*-butyl acrylate, *N*-octyl acrylate, hydroxyethyl methacrylate, [poly(ethylene glycol) 375 monoacrylate (PEG (375) monoacrylate)], and trifluoroethyl acrylate (TFEA) were purchased from Sigma-Aldrich. The monomer triethylene glycol diacrylate (TEGDA) was purchased from Sartomer. An aromatic urethane diacrylate (UDA; Ebecryl 4827) was donated by UCB Chemicals (Smyrna, GA). All graft monomers were purified with Aldrich deinhbit columns (product 30,631-2), and the photoiniferters and photoinitiator were used as received.

Methods and Instrumentation

Substrate Preparation

The monomeric substrate material used in these experiments consisted of 48.75 wt % aromatic

UDA and 48.75 wt % TEGDA that was mixed with 1 wt % TED by sonication for 45 min and purged with argon gas for 2 min before photopolymerization with 1.5 wt % DMPA as an initiator. The polymeric substrate layers ($\sim 300 \mu\text{m}$ per layer) were photopolymerized by exposure to a 45 mW/cm^2 intensity, collimated, broad-range UV light for 500 s. The aforementioned exposure conditions yielded a polymeric network with over 90% double-bond conversion, as observed with near-infrared (near-IR) spectroscopy when the acrylate double-bond absorbance peak at 6164 cm^{-1} was monitored. Once photopolymerization was completed, the substrates were washed with copious amounts of methanol to remove any unreacted monomer from the polymerized substrate matrix material.

LRP-Based Photografting

Monomers including PEG (375) monoacrylate, hydroxyethyl methacrylate, TFEA, *N*-octyl acrylate, fluorescein monoacrylate, and *tert*-butyl acrylate were covalently grafted to polymeric substrate surfaces with the LRP surface chemistry. This surface-modification scheme was achieved after each of these monomers was purified with Aldrich deinhbit columns and purging with argon gas for 5 min to remove any dissolved oxygen associated with oxygen inhibition. Any patterned regions of grafted acrylate were formed upon exposure to 45 mW/cm^2 intensity UV light for 900 s with photolithographic techniques previously published.⁶ The resultant patterns were washed in pure methanol for 1 h before being analyzed by Fourier transform infrared (FTIR), attenuated total reflectance (ATR), and optical microscopy or before being tested for application on microfluidic device surfaces.

Contact-Angle Measurement

A variety of mono(meth)acrylated functionalities including PEG (375) monoacrylate and TFEA were photografted onto DTC-incorporated substrates via UV-induced radical photopolymerization. After modification, substrate samples were washed with copious amounts of methanol and water to remove any unreacted monomer. Then, with a $10\text{-}\mu\text{L}$ distilled water drop size and the sessile drop goniometric technique,^{36,37} contact angles of modified surfaces were collected in triplicate for analysis. In addition, PEG (375) monoacrylate was photografted for various UV-light

exposure times ranging from 0 to 900 s. The dependence of the UV exposure time on the surface contact angle was determined after samples were grafted at the appropriate time and further cleaned with methanol before contact-angle measurements were performed in triplicate.

Attenuated Total Reflectance/Infrared Spectroscopy (ATR-IR)

ATR-IR studies were conducted with a Nicolet Nexus 670 ESP FTIR spectrometer with a Smart-Ark ATR accessory equipped with a ZnSe crystal, a KBR beam splitter, and a deuterated triglycine sulfate (DTGS) detector. The ATR accessory was used to provide FTIR data based on the analysis of the material's surface that was placed into contact with the ZnSe crystal. All ATR samples consisted of methanol-washed, prepolymerized substrate samples. These samples were then clamped in full contact with the isopropyl alcohol cleaned ATR crystal for surface analysis to detect the presence of DTC groups on the surface of the UDA/TEGDA substrate material. Various samples were then analyzed on the basis of mid-infrared absorbance bands present at the surface of these substrates. The appropriate control, consisting of a polymer substrate that did not contain any TED for the incorporation of DTC onto substrate surfaces, was used to provide a control spectrum for analysis.

Near-Fourier Transform Infrared (Near-FTIR) Spectroscopy

Near-FTIR studies were conducted with a Nicolet 750 Magna FTIR spectrometer with a KBr beam splitter and a DTGS detector. Initially, the infrared (IR) specimen mold containing the sample was placed in a horizontal transmission apparatus,¹⁰ which was continuously purged with dry air. Then, a series of scans were recorded, with spectra taken at the rate of approximately 2 scans per second. Samples were irradiated with UV light until the reaction was complete, as indicated by the functional group absorption spectra no longer decreasing. With this near-IR technique, relatively thick samples can be monitored, as absorptivities in the near-IR region are low.^{38,39} In this research, PEG (375) monoacrylate was used as a grafting monomer for the near-FTIR results presented.

The IR specimen mold was prepared with a substrate-coated glass slide (UDA/TEGDA poly-

mer coated slide at complete conversion) and a clean glass slide, with a metal spacer between them. The mold was clamped together, and the monomer solution was carefully pipetted from the open sides of the specimen mold to avoid bubble formation. Furthermore, metal spacers (thickness = 50 μm) were used to control the thickness of the monomer solution on top of the substrate. Surface initiation kinetics of purified and purged PEG (375) monoacrylate monomer grafting solutions were monitored with near-FTIR as the chamber was purged with dry air. The substrate and PEG (375) monoacrylate conversions were monitored with the carbon-carbon double-bond absorption peak at 6164 cm^{-1} . The conversions were calculated from the ratio of the peak areas before and after photopolymerization.

Illumination Sources

To monitor the photopolymerization kinetics of monomers with FTIR, initiation was performed via an EXFO Acticure light source (EXFO, Mississauga, Ontario) with a 320–500-nm filter and peak emission centered at 365 nm. For micropattern fabrication and for the formation of reactive substrates that were used for measuring the surface kinetics, an optical mask alignment system (Optical Associates, Inc., San Jose, CA), coupled to a 5-cm collimated flood exposure source that generated 45 mW/cm^2 of 365-nm radiation, was employed. Irradiation intensities were measured with an International Light, Inc. (Newburyport, MA), model IL1400A radiometer.

Three-Dimensional (3D) Microfluidic Device Construction and Modification

With this LRP grafting approach,⁶ 3D microfluidic devices with multiple channel-grafted functionalities were constructed with the base substrate formulations. First, the base layer was polymerized for 500 s. Then, a high-resolution photomask was placed in contact with an argon-purged, monomeric matrix solution. The layer thickness was adjusted to 300 μm before collimated UV-light exposure, and this led to a spatially controlled photopolymerization that formed the next device layer atop the previous.⁶ Upon the completion of layer exposure, unreacted monomer was removed via a methanol wash solution, and the polymerized trenches were filled with molten wax to prepare a level surface for further polymerization of sequential layers needed within the device. Each 400- μm

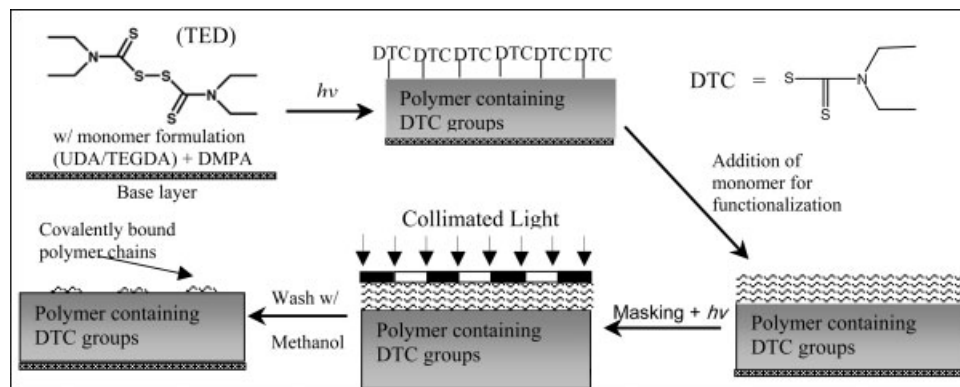


Figure 1. Controlled/living radical photopolymerization grafting chemistry with the DTC surface functionality.

channel was covalently and spatially surface-modified with either PEG (375) monoacrylate or TFEA after photografting for 900 s. Finally, the device top was covalently attached through LRP photopolymerization chemistry, and the whole device was removed from the polycarbonate base substrate. After removal, the channel regions were washed, and this resulted in a fully polymeric microfluidic device modified with various surface chemistries for controlled-fluid-flow purposes.

RESULTS AND DISCUSSION

DTC functionality has been readily incorporated into polymeric substrates for controlled-surface-grafting purposes.^{28–30} One significant incorporation mechanism requires TED cleavage into two DTC radicals upon exposure to UV light, contributing primarily to termination of both bulk- and surface-initiated polymer chains within our polymer substrate. Upon sequential exposure to UV light, the DTC functionalities are then used to create surface-attached carbon radicals that facilitate surface modification through the controlled LRP-based photografting mechanism, as illustrated in Figure 1. In general, the DTC radicals do not readily initiate the formation of polymer chains but do recombine with surface and bulk propagating chains to reform DTC end-capped groups. Ultimately, this LRP-based chemistry provides a means for spatially and temporally controlled surface modification of DTC-incorporated surfaces, where the surface-graft length is dependent on the UV exposure time. Previous work has demonstrated the synthesis and incorporation of iniferter chemistries that make use of DTC groups for grafting acrylate monomers from

surfaces over a period of up to 5 h.^{28–30} This research expands LRP-based photografting, making use of TED as another mechanism for introducing DTC functionality into the polymeric substrates used in making integrated microfluidic devices. Also, this method allows for the facile introduction of dense functional tethers with the ability to control fluid flow and biological function on a polymeric microfluidic platform. Furthermore, this LRP modification platform offers a covalent, controlled surface-modification scheme for quickly (5–15 min) incorporating a variety of functionalities into polymeric microfluidic devices, without time-consuming additional steps in the development of a functional device. This chemistry has also been previously shown to

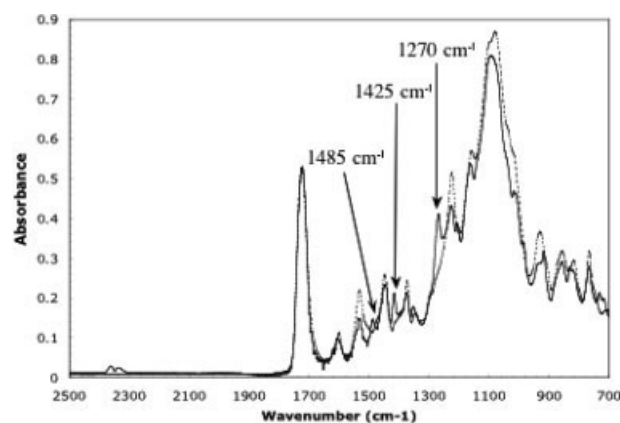


Figure 2. ATR-FTIR results showing peaks at 1270, 1485, and 1425 cm^{-1} that are associated with the DTC functionality introduced into the substrate through the inclusion of 3% TED (—) into the substrate material. A control sample that did not include DTC groups on the surface of the substrate material did not yield these absorbance peaks (---).

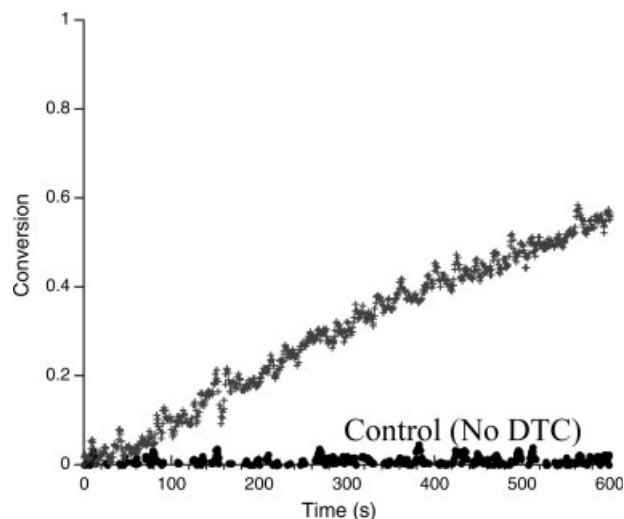


Figure 3. Conversion kinetics of PEG (375) monoacrylate photografted on substrates made (+) in the presence and (●) in the absence of DTC. There was no significant conversion on the polymer substrate that was not DTC-functionalized.

increase covalent bonding between multiple layers in 3D microfluidic devices.⁶

Spectroscopic Analysis of LRP-Based Grafting

ATR-FTIR spectroscopy has been used to evaluate the incorporation of DTC groups within the UDA/TEGDA polymeric substrate that is used to construct microfluidic devices. ATR-FTIR results shown in Figure 2 illustrate this effect, showing peaks at 1270, 1485, and 1425 cm^{-1} . These peaks have further been shown to be associated with the DTC functionality²⁹ introduced into the substrate material through the inclusion of TED. Control samples that do not include DTC groups on the surface of the substrate material do not yield these absorbance peaks. This result suggests that DTC functionalities are introduced onto the surface of the matrix material for further grafting, as demonstrated in this research.

Once DTC was demonstrated to be on the substrate surface, it was important to demonstrate spatially and temporally controlled grafting of acrylate monomers in two dimensions before this chemistry was applied in three dimensions with a microfluidic device. To illustrate LRP-based grafting, the near-FTIR technique was used to monitor the photografting of PEG (375) monoacrylate on the UDA/TEGDA substrate prepared in the presence of 1 wt % TED with the conversion kinetics of PEG (375) monoacrylate on the same substrate

prepared in the presence of the DMPA photoinitiator (but in the absence of TED). The formulation with 1 wt % TED was chosen because a high conversion of the substrate material could still be achieved while the ability to incorporate enough DTC functionality on the surface for photografting was retained. Increasing the concentration of TED in the polymer substrate would increase the surface DTC concentration, facilitating denser grafting, but the substrate conversion decreased to $\sim 80\%$ when 1.5 wt % TED was used. Also, although no polymerization occurs on a substrate prepared in the absence of TED, polymerization readily occurs on a substrate containing DTC groups. The conversion of PEG (375) monoacrylate on substrates polymerized in the presence or absence of TED is shown in Figure 3. Furthermore, curing studies of PEG (375) monoacrylate between two clean glass slides (results not shown here) indicate that PEG (375) monoacrylate does not undergo any significant polymerization under the same irradiation conditions, even after extended periods of exposure up to 60 min.

Photografting of a Variety of Functionalities with the LRP-Based Mechanism

Overall, microfluidic devices rely heavily on methods to control surface hydrophobicity for both directing fluid flow and for various biological applications. The applications and results shown in this article rely heavily on the use of photografted PEG to facilitate a variety of applications on microfluidic devices, but a variety of surface properties can be achieved with DTC-based modification chemistry. In Table 1, we present substrate contact-angle measurements of a selection of modified polymeric surfaces, using standard goniometric techniques. Controlling the surface contact angle through changes in the surface functionality, while retaining the original bulk material properties, is useful for many applica-

Table 1. Contact Angles of Monomers Photografted for 900 s on DTC-Incorporated Substrates

Grafted Monomer	Contact Angle
Control (UDA/TEGDA substrate)	$46 \pm 2^\circ$
TFEA	$86 \pm 4^\circ$
<i>tert</i> -Butyl acrylate	$72 \pm 2^\circ$
<i>N</i> -Octyl acrylate	$65 \pm 1^\circ$
2-Hydroxyethyl methacrylate	$43 \pm 3^\circ$
PEG (375) monoacrylate	$7 \pm 2^\circ$

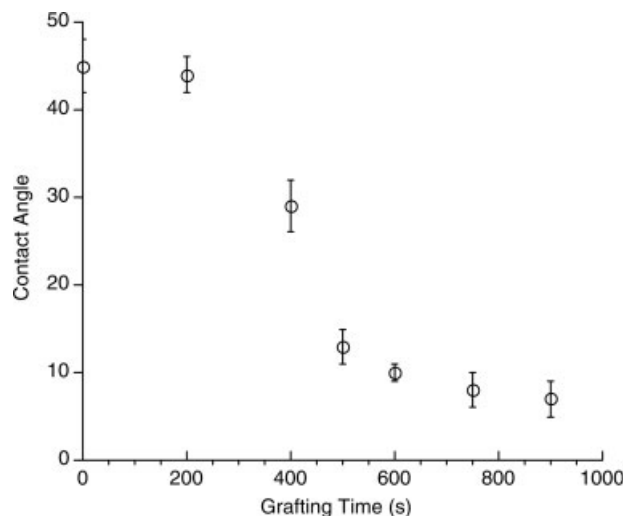


Figure 4. Plot of the water contact angle of PEG monoacrylate grafted substrates after exposure to UV light as a function of the grafting exposure time, showing a decrease in the contact angle with the UV-light exposure time when hydrophilic PEG-functionalized chains were grafted from the substrate surface.

tions, including flow control and cell patterning. A variety of mono(meth)acrylated functionalities, including PEG (375) monoacrylate, TFEA, *tert*-butyl acrylate, *N*-octyl acrylate, and hydroxyethyl methacrylate, were photografted onto UDA/TEGDA sub-

strates via UV patterning for 15 min. After modification, substrate samples were washed with copious amounts of methanol and water to remove any unreacted monomer. Then, with the sessile drop goniometric technique,^{36,39} the contact angles of the modified surfaces ranged from 7° with PEG (375) monoacrylate to 86° with TFEA, as shown in Table 1. The urethane/TEGDA substrate has a contact angle of 50°. Thus, a variety of surface properties ranging from hydrophobic to hydrophilic can be achieved on a single device surface through the use of photolithographic patterning with this DTC-based surface chemistry.

To recapitulate the claim that the surface-graft amount is temporally controlled by the UV-light exposure time, a decrease in the contact angle with time during the grafting of hydrophilic PEG (375) is shown in Figure 4. Grafted substrate samples with UV-light exposure times ranging from 0 to 900 s resulted in contact angles that decreased from 50 to 7°. This result suggests that an increase in the surface functionality is occurring with time after 400 s of exposure time, and it is hypothesized to be a result of an increased density of grafted chains with time and/or an increase in the graft chain length with time. Also, the observation that the contact angle does not significantly change between exposure times of

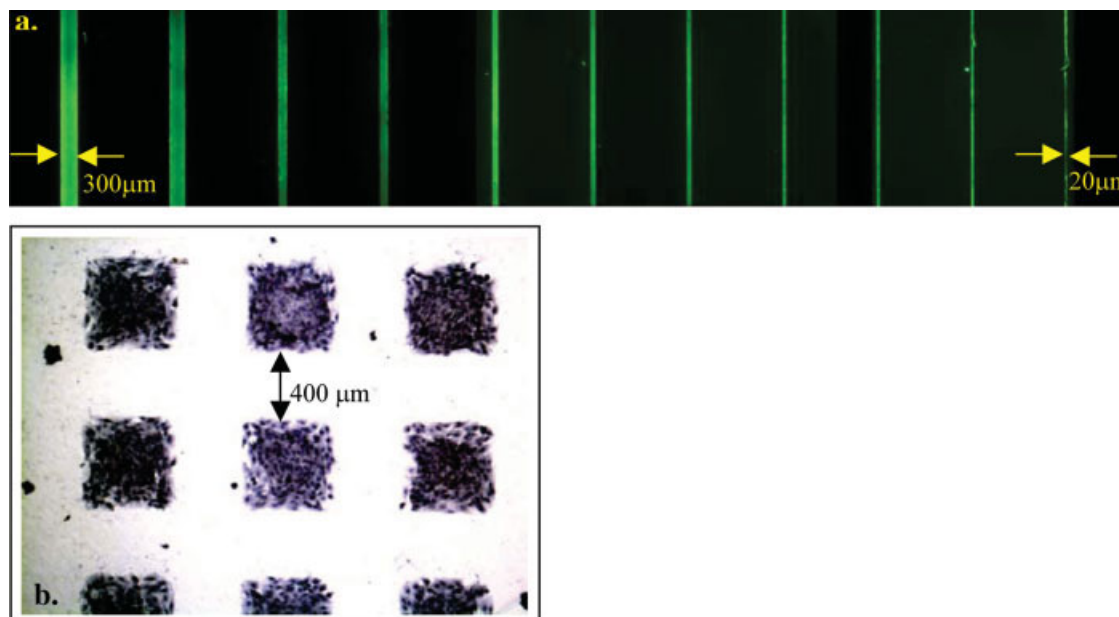


Figure 5. (a) Spatially resolved, fluorescently labeled PEG acrylate photografted (900 s) on a UDA/TEGDA substrate in patterned stripes ranging from 300 to 20 μm in width and (b) cell patterning in which islands of 3T3 fibroblasts voluntarily seed around a PEG-grafted substrate (white regions are PEG-modified, and cell islands are stained purple with hematoxylin staining).

0 and 200 s verifies that the contact angle is not changing simply because of residual or adsorbed monomer.

Aside from using controlled surface hydrophobicity for directed fluid flow, a variety of biological applications are greatly impacted by surface properties and functionality. One area that can benefit from surface-modification technologies is that of cellular patterning. Cell species respond differently to a variety of factors, including the surface charge and hydrophobicity. Controlled modification of cell scaffold materials is a useful means of retaining bulk properties of a material that otherwise does not support cellular adhesion and vice versa.

Using this LRP-based surface chemistry to graft antifouling materials such as PEG is useful as a means of facilitating these applications. As shown in Figure 5(a), PEG (375) is grafted in the presence of 1 mg/mL fluorescein acrylate to illustrate spatially controlled grafting of the PEG functionality on the surface of the substrate material. In this case, the spatial resolution of the fluorescent patterns ranges from 300 to 20 μm in width.

Because of the surface charge and functionality associated with UDA/TEGDA, this substrate material supports nonspecific cellular adhesion without requiring any further modification. To demonstrate the utility of LRP surface modification for cell patterning, PEG (375) was grafted from the polymeric substrate material in a high-resolution pattern, and then 3T3 fibroblasts were seeded at 100,000 cells/mL for 24 h to demonstrate spatial adhesion control. As shown in Figure 5(b), 3T3 fibroblasts only adhered to the regions that were not patterned with PEG (375) because of the difference in hydrophobicity and charge. Cellular adhesion only in regions unmodified with PEG (375) was expected because PEG has been shown to reduce protein adhesion that is frequently associated with cell adhesion. This result highlights the cytocompatibility of the base substrate, while also illustrating that control over surface chemistry is useful to control cell adhesion on scaffold materials and prevent biofouling in microfluidic devices.

Integration of LRP Grafting Chemistry onto a Fully Polymeric Microfluidic Device

Of great interest is the integration of this photografting chemistry onto a microfluidic device, overcoming the limitations associated with sur-

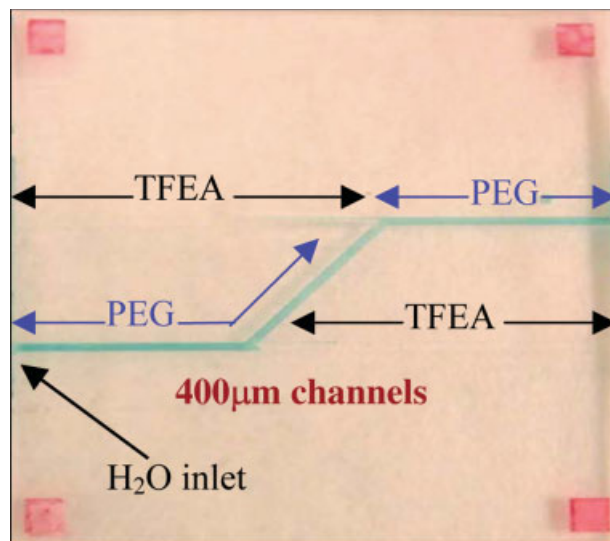


Figure 6. Microfluidic device illustrating directed H_2O flow via modification with hydrophilic PEG (375) monoacrylate and hydrophobic TFEA. The water contains a blue dye for visualization purposes and flows from one channel to another, as indicated by the arrows.

face modification in current microfabrication schemes. This integration impacts microfluidic applications ranging from integrated cell sorting and biological microassay device development to directed fluid flow on a lab-on-a-chip device.

The device shown in Figure 6 was constructed with the photolithographic techniques described previously in this text. The 400- μm -wide channels of this device were surface-modified with LRP-based grafting to introduce functionality on all sides of each polymer channel for the purpose of directing fluid flow on the basis of surface hydrophilicity. Furthermore, the device consisted of three layers that were covalently attached because of the incorporation of DTC groups on each (300 μm thick) polymer layer. Surface modification was achieved in sequential UV exposures. First, a channel was surface-modified with photolithographic techniques to graft PEG (375) acrylate from the channel surface. After washing with methanol, additional UV exposure was performed in different channel regions to yield modification with TFEA. This technique facilitated the design of regions that were modified hydrophobically and hydrophilically on the same device layer. As shown, the channels were spatially modified with PEG (375) and TFEA on the same device. When it was fully constructed, water flowed through the device and followed the channels modified with PEG (375) because of the

hydrophilic nature of PEG in comparison with TFEA. The channels modified with hydrophobic TFEA repelled water flow, demonstrating fluid flow control on this polymeric microfluidic device. This result demonstrates that fluid flow is readily directed in a microfluidic device simply by the modification of the channel surfaces with photografted functionalities.

CONCLUSIONS

The DTC-mediated LRP chemistry demonstrated in this research can be used to obtain a variety of surface chemistries on polymeric substrate surfaces, including in a fully integrated polymeric microfluidic device. A variety of grafted functionalities were demonstrated, ranging from hydrophilic PEG (375) monoacrylate modified surfaces with a contact angle of 7° to hydrophobic surface modification with TFEA, which yielded a contact angle of 86° . The photolithographically controlled grafting also enabled the patterning of multiple surface chemistries on a single surface with spatial and temporal control over surface properties such as hydrophobicity, graft location, graft density, and graft length. Although FTIR and goniometric techniques were used to conclude that surface functionality does increase with UV exposure time, allowing for tailored surface chemistries, the development of more extensive techniques facilitating the characterization of these grafted chains on polymeric surfaces may be of great interest.

Moreover, the DTC-incorporated UDA/TEGDA substrate provides a route for rapid fabrication of surfaces that are readily grafted with controlled LRP chemistry. Furthermore, this chemistry offers a way of surface-modifying substrates for applications varying from directed fluid flow to surface-assisted cell patterning. Examples were demonstrated, including controlled fluid flow and patterning of 3T3 fibroblasts on the same substrate material, modified with PEG (375). Although these applications are fully dependent on surface functionality implemented through an LRP photografting technique, other applications requiring biological detection, protein attachment, drug delivery, sensory responses, or surface fluorescence, among others, benefit from this chemistry.

The authors are grateful for financial support for this research from the Defense Advanced Research Projects Agency Symbiosys program, the Air Force Office of Sci-

entific Research, and the Howard Hughes Medical Institute. R. P. Sebra was also supported by a fellowship from the Department of Education Graduate Assistance in Areas of National Need program.

REFERENCES AND NOTES

- Xia, Y. N.; Whitesides, G. M. *Angew Chem Int Ed* 1998, 37, 551–575.
- Yakovleva, J.; Davidsson, R.; Lobanova, A.; Bengtsson, M.; Eremin, S.; Laurell, T.; Emneus, J. *Anal Chem* 2002, 74, 2994–3004.
- Sia, S. K.; Whitesides, G. M. *Electrophoresis* 2003, 24, 3563–3576.
- Ostuni, E.; Chen, C. S.; Ingber, D. E.; Whitesides, G. M. *Langmuir* 2001, 17, 2828–2834.
- Simms, H. M. B. C.; Good, B. T.; Davis, R. H.; Anseth, K. S.; Bowman, C. N. *Lab Chip* 2005, 5(2), 151–157.
- Hutchison, J. B. H. K.; Good, B. T.; Sebra, R. P.; Luo, N.; Anseth, K. S.; Bowman, C. N. *Lab Chip* 2004, 4, 658–662.
- Chen, C. S.; Jiang, X. Y.; Whitesides, G. M. *MRS Bull* 2005, 30, 194–201.
- Beebe, D. J.; Moore, J. S.; Bauer, J. M.; Yu, Q.; Liu, R. H.; Devadoss, C.; Jo, B. H. *Proc Natl Acad Sci* 2000, 404, 588.
- Moorthy, J. M. G.; Kim, D.; Mohanty, S.; Eddington, D. T.; Tepp, W. H.; Johnson, E. A.; Beebe, D. J. *Electrophoresis* 2004, 25, 1705–1713.
- Reddy, S. S. R.; Anseth, K.; Bowman, C. N. *J Polym Sci Part A: Polym Chem* 2005, 43, 2143–2144.
- Mayer, M. Y. J.; Gitlin, I.; Gracias, D. H.; Whitesides, G. M. *Proteomics* 2004, 4, 2366–2376.
- Angenendt, P.; Glokler, J.; Konthur, Z.; Lehrach, H.; Cahill, D. J. *Anal Chem* 2003, 75, 4368–4372.
- Delamar, E.; Bernard, A.; Schmid, H.; Michel, B.; Biebuyck, H. *Langmuir* 1997, 276, 779–781.
- Yakovleva, J.; Davidsson, R.; Bengtsson, M.; Laurell, T.; Emneus, J. *Biosens Bioelectron* 2003, 19, 21–34.
- Schwarz, A.; Rossier, J. S.; Roulet, E.; Mermoud, N.; Roberts, M. A.; Girault, H. H. *Langmuir* 1998, 14, 5526–5531.
- Delamar, E.; Sundarababu, G.; Biebuyck, H.; Michel, B.; Gerber, C.; Sigrist, H.; Wolf, H.; Ringsdorf, H.; Xanthopoulos, N.; Mathieu, H. J. *Langmuir* 1996, 12, 1997–2006.
- de Wildt, R. M. T.; Mundy, C. R.; Gorick, B. D.; Tomlinson, I. M. *Nat Biotech* 2000, 18, 989–994.
- Sirringhaus, H.; Kawase, T.; Friend, R. H.; Shimoda, T.; Inbasekaran, M.; Wu, W.; Woo, E. P. *Science* 2000, 290, 2123–2126.
- Ward, J. H.; Peppas, N. A. *Macromolecules* 2000, 33, 5137–5142.
- Ward, J. H.; Shahar, A.; Peppas, N. A. *Polymer* 2002, 43, 1745–1752.

21. Sebra, R. P.; Hutchison, J. B.; Haraldsson, K. T.; Anseth, K. S.; Bowman, C. N. *Abstr Pap Am Chem Soc* 2003, 225, U578–U578.
22. Otsu, T.; Yoshida, M. *Makromol Chem Rapid Commun* 1982, 3, 127–132.
23. Otsu, T.; Matsumoto, A. *Microencapsulation–Microgels–Iniferters*; Springer-Verlag GmbH: New York, 1998; pp 75–137.
24. (a) Otsu, T. *J Polym Sci Part A: Polym Chem* 2000, 38, 2121–2136; (b) Nakayama, Y.; Anderson, J. M.; Matsuda, T. *J Biomed Mater Res* 2000, 53, 584–591.
25. Nakayama, Y.; Matsuda, T. *Macromolecules* 1999, 32, 5405–5410.
26. Matsuda, T.; Sugawara, T. *J Polym Sci Part A: Polym Chem* 1996, 32, 165–173.
27. Luo, N.; Metters, A. T.; Hutchison, J. B.; Bowman, C. N.; Anseth, K. S. *Macromolecules* 2003, 36, 6739–6745.
28. Luo, N.; Hutchison, J. B.; Anseth, K. S.; Bowman, C. N. *Macromolecules* 2002, 35, 2487–2493.
29. Luo, N.; Hutchison, J. B.; Anseth, K. S.; Bowman, C. N. *J Polym Sci Part A: Polym Chem* 2002, 40, 1885–1891.
30. Hutchison, J. B.; Haraldsson, K. T.; Hawker, C. J.; Bowman, C. N.; Anseth, K. S. *Abstr Pap Am Chem Soc* 2002, 224, U489–U489.
31. Patten, T. E.; Xia, J.; Abernathy, T.; Martyjaszewski, K. *Science* 1996, 272.
32. Otsu, T.; Kuriyama, A. *Polym J* 1985, 17, 97–104.
33. Nakayama, Y.; Matsuda, T. *Langmuir* 1999, 15, 5560–5566.
34. Nakayama, Y.; Matsuda, T. *Macromolecules* 1996, 29, 8622–8630.
35. Cassie, A. B. D. *Discuss Faraday Soc* 1952, 75, 5041.
36. Bain, C.; Whitesides, G. A. *Langmuir* 1989, 5, 1370–1378.
37. Stansbury, J. W.; Dickens, S. H. *Dent Mater* 2001, 17, 71–79.
38. Lovell, L. G.; Lu, H.; Elliott, J. E.; Stansbury, J. W.; Bowman, C. N. *Dent Mater* 2001, 17, 504–511.
39. Cassie, A. B. *Discuss Faraday Soc* 1952, 75, 5041.