Published in final edited form as:
Anal Chem. 2002 September 1; 74(17): 4566–4569.

Fabrication of Microchannel Structures in Fluorinated Ethylene Propylene

Eskil Sahlin, **Amy T. Beisler**, **Steven J. Woltman**, and **Stephen G. Weber***
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Abstract

A new technique for fabrication of channel structures with diameters down to 13 μm in fluorinated ethylene propylene (also known as poly(tetrafluoroethylene-*co*-hexafluoropropylene), FEP) is described. The technique is based on the unique property of a dual-layer fluoropolymer tubing consisting of an outer layer of poly(tetrafluoroethylene) (PTFE) and an inner layer of FEP. When heated (>350 °C), the outer PTFE layer shrinks while the inner FEP layer melts, resulting in filling of all empty space inside the tubing with FEP. The channel structures are formed using tungsten wires as templates that are pulled out after completion of the shrinking and melting process. While several analytical devices have been reproducibly prepared and shown to function, this report describes a single example. A microreactor coupled to an electrochemical flow cell detects the biuret complex of the natively electroinactive peptide des-Tyr-Leu-enkephalin.

Microfluidic systems with channel dimensions below 100 μm have received enormous attention in the last twenty years. Different types of separations can be performed in these channels including capillary liquid chromatography,[1] capillary electrophoresis,[2] and capillary electrochromatography.[3] Several types of tubing with minimum diameters between 5 and 100 μm are commercially available in many materials. To combine operations (including, for example, injection, separation, detection, dilution, chemical reactions, cell lysis, and PCR amplification), techniques for fabrication of more complex channel structures on so-called chips have been developed. Initial applications were simple one-dimensional separations with optical detection in glass. More recently, one-dimensional separations have been carried out on polymeric chips[4,5] and glass chips with a polymeric separation medium,[3] multiple separation channels with mass spectrometric detection,[6] two-dimensional separations,[7,8] mixing,[9] adsorption,[10] and electrochemical detection[11,12] have also been carried out on chips. Fabrication techniques for channels with dimensions in the 10–100-μm range include photolithography and wet etching, radiation-induced etching, molding, imprinting, and casting and are applied to materials such as glass, plastics, and polymeric materials.[13–18]

Decreasing the dimensions of channels and reservoirs results in an increase in the wall area-to-solution volume ratio. Hence, interaction between solvents and solutes with the wall surface can be a major problem in miniaturized flow systems. Several types of interactions are possible including, for example, adsorption, absorption, and leakage of compounds from the wall material. In addition, several typical materials used in microfluidic devices are only resistant to a limited number of chemicals.

Fluoropolymers have some unique properties originating from the C–F bond that make them particularly suitable as material for chemical containers.[19] These materials are thermally stable and chemically inert to acids, bases, oxidizing and reducing agents, and most solvents. However, the high inertness of fluoropolymers makes it difficult to fabricate microstructures

---

* Corresponding author. E-mail: sweber@pitt.edu..

in these materials. Existing microfabrication techniques for fluoropolymers include synchrotron radiation direct photoetching,[20,21] low-energy ion beam with a mesh mask[22] or in combination with photolithography,[23] and magnetically controlled reactive ion etching.[24] However, none of these microfabrication techniques have been employed for fabrication of microfluidic devices.

In this article, a new technique for fabrication of microchannel structures in fluorinated ethylene propylene (FEP, also known as poly(tetrafluoroethylene-*co*-hexafluoropropylene)) is introduced. FEP is a copolymer of hexafluoropropylene and tetrafluoroethylene with a typical hexafluoropropylene content of 15–20%.[25] Hence, the properties of FEP are often similar to poly(tetrafluoroethylene) (PTFE),[25] which is well characterized. The critical surface tension of FEP is 17.8 and 18.0 mN/m at 25 °C for hexafluoropropylene contents of 16 and 23%, respectively, and is slightly lower than of PTFE.[26] For comparison, the critical surface tension at 20 °C of PTFE is 18 mN/m, polyethylene 31 mN/m, polystyrene 33 mN/m, and poly(vinyl chloride) 39 mN/m.[27] FEP also has a low refractive index, 1.338 (temperature and exact FEP composition unknown).[28]

EXPERIMENTAL SECTION

Materials and Tools

Heat shrink/melt tubing, consisting of an outer PTFE and an inner layer of FEP, with an inner diameter of 0.036 in. was obtained from Small Parts, Inc. (Miami Lakes, FL). Tungsten wires (13-, 25-, and 50-μm diameter) were purchased from Goodfellow Corp. (Berwyn, PA). Heating of the heat shrink/melt tubing was achieved with a heat gun with a variable-temperature range of 100–600 °C) and equipped with a reduction nozzle. Fused-silica capillaries were obtained from Polymicro Technologies, Inc. (Phoenix, AZ), and carbon fibers (30-μm diameter) were obtained from World Precision Instruments, Inc. (Sarasota, FL). Silver-containing epoxy used for electrical contacts with the carbon fibers was obtained from Epoxy Technology, Inc. (Billerica, MA). A pair of tapered stainless steel forceps was used to keep the original alignment of objects inside the heat shrink/melt tubing during heating.

Instrumentation for Flow Injection Analysis

A Waters 600 E Multisolvent Delivery System (Milford, MA) with a flow splitter tee giving flow rates in the 1–3 μL/min range was used to pump the mobile phase consisting of 3% 1-propanol and 0.1% trifluoroacetic acid in water. Injection of 1.0-μL samples was performed using a microinjection valve (Upchurch Scientific, Oak Harbor, WA)). The biuret reagent, consisting of 0.6 M sodium carbonate, 0.6 M sodium bicarbonate, 30 mM sodium tartrate, and 5.0 mM copper sulfate, pH 9.80, was delivered with an Isco model 100 DM syringe pump (Lincoln, NE) at a flow rate of 1 μL/min and mixed with the mobile phase using a laboratory-made Y-connector. The Y-connector consisted of two 50-μm-i.d. fused-silica capillaries (the two arms of the Y) and one 75-μm-i.d. fused-silica capillary (the foot of the Y) and is further described below. The Y-connector was connected such that the 75-μm-i.d. fused-silica capillary delivered the biuret reagent. Reagent and analyte mixed by diffusion during passage through 23.7 cm of 50-μm-i.d. fused-silica capillary following the “Y”.

Amperometric detection was performed using a BAS CV-27 potentiostat (Bioanalytical Systems, Inc., West Lafayette, IN) with a Keithley 427 current amplifier (Keithley Instruments, Inc., Cleveland, OH) at 10^{11} V/A gain with a rise time of 300 ms. All electrochemical measurements were performed in a Faraday cage with an Ag/AgCl (3 M NaCl) electrode located in the outlet reservoir as a combined reference and auxiliary electrode. Data were collected at 12.5 Hz using Ezchrom chromatographic software (Scientific Software, Inc., San Ramon, CA).

Chemicals

[des-Tyr] Leu-enkephalin was obtained from American Peptide Co., Inc. (Sunnyvale, CA). Trifluoroacetic acid was obtained from Fisher Scientific (Pittsburgh, PA). 1-Propanol was obtained from J.T. Baker (Phillipsburg, NJ). ACS-grade copper sulfate pentahydrate (J.T. Baker) and ACS-grade sodium tartrate (Fisher Scientific) were recrystallized from water before use. All other chemicals were of analytical grade. All solutions were prepared using MilliQ-water from a Millipore system.

RESULTS AND DISCUSSION

Fabrication Technique

Heating is achieved by a heat gun. The channel structures are formed by incorporating objects resistant to the heat into the FEP material. By removing objects after completion of the shrinking and melting process, empty space such as channels and reservoirs can be created in the FEP material. Removal of objects can be achieved by pulling out the objects or by etching or dissolving the objects. For objects that should be pulled out, it is necessary to move the objects by pulling them a short distance after completion of the shrinking and melting process while the FEP material is still hot. This prevents the FEP material from sticking to the objects. When the tubing is cooled to room temperature, the object is pulled out. Objects that are not moved while the FEP material is hot will adhere tightly to the FEP material. This is used to integrate electrodes with the channels. Contact between different objects in the tube's lumen is achieved by pressing them together with forceps during heating and subsequent cooling to room temperature.

Straight Channels

Straight channels are fabricated by heating a heat shrink/melt tubing with a tungsten wire going through the tubing. After completion of the shrinking and melting process, the tungsten wire is pulled out. The fabrication technique is further illustrated in Figure 1, showing a channel shaped by a 50-μm-diameter tungsten wire. The tungsten wire is only partly removed to demonstrate that the FEP material has filled all empty space around the wire during the shrinking and melting process. Typically, heating, shrinking, melting, and movement of the tungsten wire is performed for 3–4-cm-long segments. By repeating this process segment after segment, longer channels can be created. For instance, 50-μm-diameter channels can be created with a length up to 50 cm.

Figure 2 shows SEM pictures of the cross sections of channels with diameters equal to 13, 25, and 50 μm. The 13-μm-diameter channel outlet was partly blocked when the tubing was cut with a razor blade. All channel cross sections are circular with a diameter equal to the diameter of the tungsten wire used as template.

Channels Connected to Fused-Silica Capillaries

Channels connected to fused-silica capillaries (in series) with zero dead volume can be achieved by threading a tungsten wire into a fused-silica capillary prior to heating. Fused-silica capillaries can then further be connected to, for example, other tubing, injector valves, and pumps with commercially available fittings.

Y-Connectors

Channels connected in a Y-configuration can be achieved by threading two tungsten wires (25-μm diameter) into two 50-μm-i.d. fused-silica capillaries (one wire into each capillary). Next, both tungsten wires are threaded into one 75-μm-i.d. fused-silica capillary. The capillaries are then aligned in a piece of heat shrink/melt tubing so that the two 50-μm-i.d. fused-silica capillaries are pointing out at one end of the tubing and the 75-μm-i.d. fused-silica capillary is pointing out at the other end of the tubing. Subsequent to heating and melting of the tubing, the tungsten wires are pulled out. In this way, a Y-connector with two short 25-μm channels connecting two 50-μm fluid conduits (the two arms of the Y) with one 75-μm conduit (the foot of the Y) is fabricated. A microscopic photograph of a Y-connector is shown in Figure 3a.

Channels with Integrated Electrodes

Channels with an integrated carbon fiber electrode can be fabricated by inserting a carbon fiber through a hole in the heat shrink/melt tubing so that it is aligned perpendicular to the tungsten wire. During heating and subsequent cooling to room temperature, the carbon fiber and the tungsten wire are pressed together with forceps. After removal of the tungsten wire, a channel is formed where an electrode (the carbon fiber) is tangentially in contact with the channel. A microscopic photograph of a 25-μm-diameter channel with a 30-μm-diameter carbon fiber is shown in Figure 3b. Electrical contact with the carbon fiber is achieved with conducting silver epoxy.

Flow Injection Analysis with Amperometric Detection of a Redox-Active Compound Formed by Mixing Two Flow Streams Using a Y-Connector

We have developed the biuret reagent for peptide derivatization.[29,30] With this reagent, copper-(II) forms an electroactive complex with the peptide backbone that is easily and reversibly detected at an electrochemical detector.[31] Since this derivatization technique is most easily achieved postcolumn, the necessity for an efficient, small-volume reactor is apparent. The utility of the fabricated Y-connector for this purpose was investigated using flow injection techniques by connecting the aforementioned electrochemical cell downstream from a fabricated Y-connector to form an integrated reactor/detector unit. One of the 50-μm fluid conduits was used to deliver the peptide solution while the other was used for “mixing” this solution with the biuret reagent, which was delivered through the 75-μm conduit. The time the fluid streams have to combine or “mix” is determined by two factors: length of tubing and flow rate. When used postcolumn, it is necessary to achieve efficient mixing of the fluid streams in minimal time so that band broadening resulting from the reactor does not become significant. Using the described device for combining streams flowing at 1–2 μL/min allows ~10 s for reaction (23.7 cm of 50-μm tubing) before the analyte arrives at the electrochemical detector. Figure 4 show the signal from oxidation of copper(II)-complexed [des-Tyr] Leu-enkephalin (GGFL) at +700 mV after injection of 1.0 μL of 50 μM GGFL. Also included in Figure 4 is a trace from an injection of GGFL with the biuret stream blocked. There is no signal from GGFL in the absence of the copper(II) stream.

CONCLUSIONS

Fluoropolymers including FEP are known to be resistant to acids, bases, oxidizing and reducing agents, and almost all solvents, and they have generally low surface energies. Hence, they are particularly well-suited as materials in microfluidic devices. The fabricated microfluidic devices presented here can find applications in microscale separation techniques including capillary electrophoresis, capillary liquid chromatography, and capillary electrochromatography. Aside from separation techniques, FEP channels will also be an excellent choice as material in several rapidly growing fields such as microscale variants of drug screening, organic synthesis, and immunoassays.

The technique presented here is the only technique today for fabrication of microfluidic devices in fluoropolymer materials. The technique is relatively inexpensive and results in channel structures with circular channel cross sections and with channel diameters down to 13 μm in

FEP. Different objects such as electrodes and fused-silica capillaries can be integrated with the channels.

We recognize that the approach suffers in comparison to photolithographic and imprinting approaches if the basis for the comparison is the ease of production of thousands of similar devices. While this is certainly true today, it must be remembered that there are many tools in analytical chemistry that are not mass produced. Further, in comparison to photolithographically created items, the FEP devices described here are flexible (both conceptually and literally), chemically inert, inexpensive, and fast to prototype and they interface well with standard fused silica.

Acknowledgements

NIH is acknowledged for financial support through Grant GM 44842

References

1. Ericson C, Holm J, Ericson T, Hjertén S. Anal Chem 2000;72:81–87. [PubMed: 10655638]
2. Schasfoort RBM, Schlautmann S, Hendrikse J, Van Den Berg A. Science 1999;286:942–945. [PubMed: 10542145]
3. Throckmorton DJ, Shepodd TJ, Singh AK. Anal Chem 2002;74:784–789. [PubMed: 11866058]
4. Mizukami Y, Rajniak D, Rajniak A, Nishimura M. Sens Actuators, B 2002;B81:202–209.
5. Wang SC, Perso CE, Morris MD. Anal Chem 2000;72:1704–1706. [PubMed: 10763272]
6. Li J, Tremblay TL, Thibault P, Wang C, Attiya S, Harrison DJ. Eur J Mass Spectrom 2001;7:143–155.
7. Gottschlich N, Jacobson SC, Culbertson CT, Ramsey JM. Anal Chem 2001;73:2669–2674. [PubMed: 11403315]
8. Rocklin RD, Ramsey RS, Ramsey JM. Anal Chem 2000;72:5244–5249. [PubMed: 11080871]
9. He B, Burke BJ, Zhang X, Zhang R, Regnier FE. Anal Chem 2001;73:1942–1947. [PubMed: 11354474]
10. Kutter JP, Jacobson SC, Ramsey JM. J Microcolumn Sep 2000;12:93–97.
11. Niwa O, Kurita R, Liu Z, Horiuchi T, Torimitsu K. Anal Chem 2000;72:949–955. [PubMed: 10739197]
12. Woolley AT, Lao KQ, Glazer AN, Mathies RA. Anal Chem 1998;70:684–688. [PubMed: 9491753]
13. Soper SA, Ford SM, Qi S, McCarley RL, Kelly K, Murphy MC. Anal Chem 2000;72:643A–651A.
14. Bousse L, Cohen C, Nikiforov T, Chow A, Kopf-Sill AR, Dubrow R, Parce JW. Annu Rev Biophys Biomol Struct 2000;29:155–181. [PubMed: 10940246]
15. Becker H, Gärtner C. Electrophoresis 2000;21:12–26. [PubMed: 10634467]
16. Dolník V, Liu S, Jovanovich S. Electrophoresis :41–54.
17. Jakeway SC, de Mello AJ, Russell EL. Fresenius J Anal Chem 2000;366:525–539. [PubMed: 11225765]
18. McCreedy T. Trends Anal Chem 2000;19:396–401.
19. Thomas, R. R. In Fluoropolymers 2 Properties; Hougham, G., Cassidy, P. E., Johns, K., Davidson, T., Eds.; Kluwer Academic/Plenum Publishers: New York, 1999; pp 47–67.
20. Katoh T, Zhang Y. Microsyst Technol 1998;4:135.
21. Kato T, Nishi N, Fukagawa M, Ueno H, Sugiyama S. Sens Actuators, A 2001;89:10–15.
22. Garner CE, Gabriel SB, Kuo YS. Thin Solid Films 1982;95:351–362.
23. Lee LP, Berger SA, Liepmann D, Pruitt L. Sens Actuators, A 1998;71:144–149.
24. Furuya A, Shimokawa F, Matsuura T, Sawada R. J Micromech Microeng 1996;6:310–319.
25. Bur, A. J. In Fluoropolymers; Wall, L. A., Ed.; John Wiley & Sons: New York, 1972; pp 475–505.
26. Bernett MK, Zisman WA. J Phys Chem 1960;64:1292–1294.
27. Shafrin EG, Zisman WA. J Phys Chem :519–524.

28. Seferis, J. C. In Polymer Handbook, 4th ed.; Brandrup, J., Immergut, E. H., Grulke, E. A., Eds.; John Wiley & Sons: New York, 1999; pp VI/574–VI/578.
29. Chen JG, Vinski E, Colizza K, Weber SG. J Chromatogr, A 1995;705:171–184. [PubMed: 7640768]
30. Chen JG, Woltman SJ, Weber SG. J Chromatogr, A 1995;691:301–315. [PubMed: 7894655]
31. Chen JG, Logman M, Weber SG. Electroanalysis 1999;11:331–336.

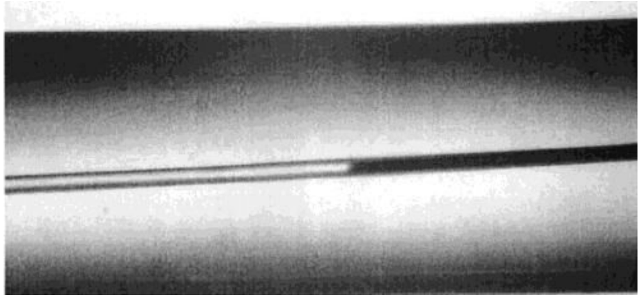

Figure 1.
Microscopic photograph of a 50-μm-diameter channel in FEP with a tungsten wire not completely pulled out.

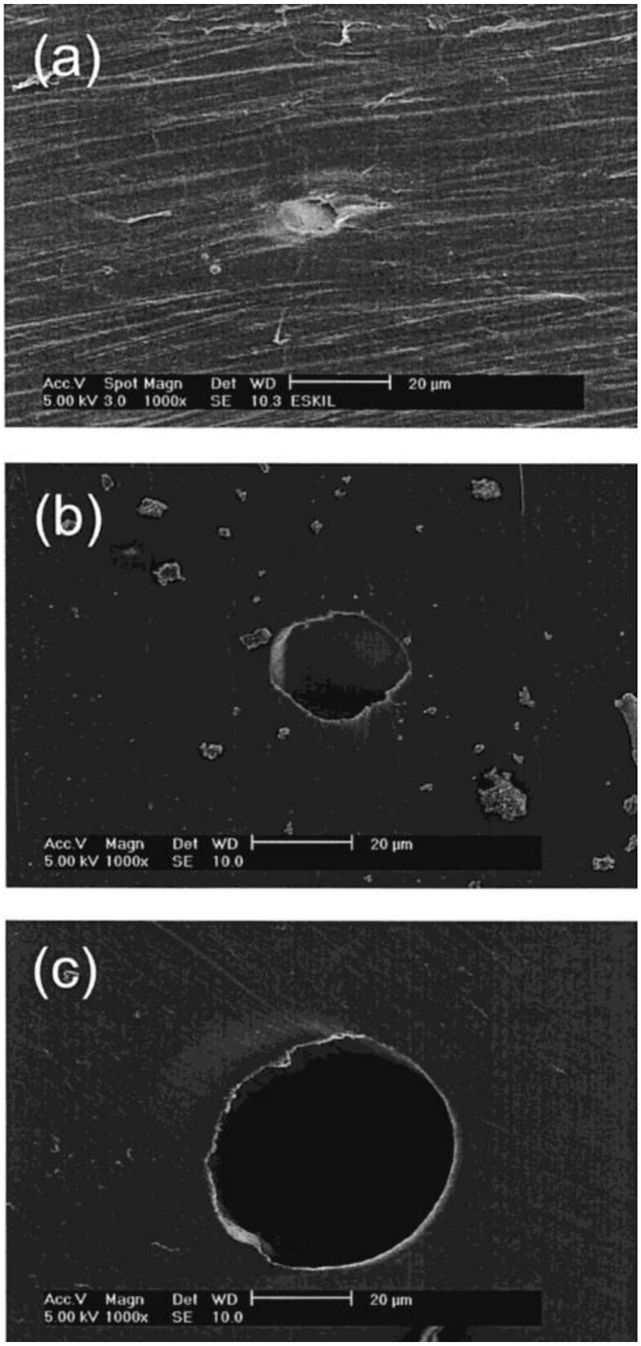

Figure 2.

SEM pictures of channel cross sections of (a) 13-, (b) 25-, and (c) 50-µm-diameter channels.

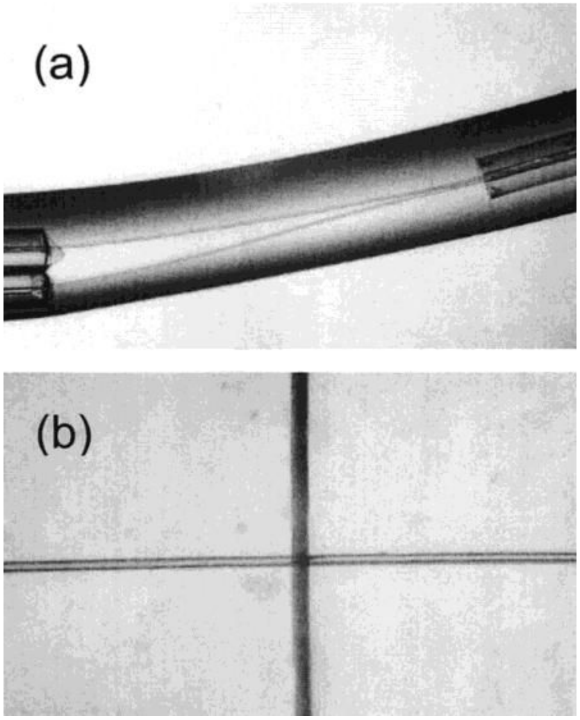

Figure 3.
Microscopic photographs of (a) Y-connection consisting of two 50-μm-i.d. and one 75-μm-i.d. fused-silica capillaries with 25-μm-diameter channels and (b) of a 25-μm-diameter channel with a 30-μm-diameter carbon fiber tangentially in contact with the channel.

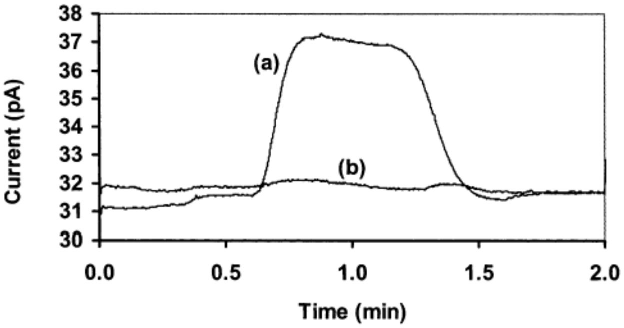

Figure 4.
Flow injection analysis of (a) 50 μM GGFL and (b) a blank at +700 mV following mixing with biuret reagent. Flow injection analysis was performed in a mobile phase composed of 3.0% 1-propanol and 0.10% trifluoroacetic acid with an injection volume of 1.0 μL and with a biuret reagent composition of 0.6 M sodium carbonate, 0.6 M sodium bicarbonate, 30 mM sodium tartrate, and 5.0 mM copper sulfate, pH 9.80.