Spectroscopic Monitoring of Polymerization in Microfluidic Channels[†]

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INTRODUCTION

Over the last decade there have been significant advances in the use of microfluidic devices for conducting chemical analysis driven by the many advantages that these methods have over conventional macro-scale analysis routines. These advantages include increased efficiency, reduced mixing times, low consumption of reagents and rapid chemical analysis.[1]

The small sample volumes present within microfluidic channels require the application of sensitive analytical techniques for on-chip monitoring of chemical reactions. A range of spectroscopic techniques have been applied for on-chip detection of laminar flows including fluorescence microscopy,[2] ultraviolet (UV) absorption[3] and, to a lesser extent, Raman microscopy.[2,4-5] However these techniques have been largely limited to aqueous solutions and aqueous based chemical reactions.

At NIST Combinatorial Methods Center (NCMC) we are interested in the construction of material libraries that explore a range of polymer chemistries and properties. To this end, we have developed a thiolene based microfluidic fabrication technology stable to a number of organic solvents and monomer systems.[6] In this study we extend on-chip application of spectroscopic techniques to the analysis of monomer and polymeric systems. We have applied Raman and fluorescence spectroscopic techniques for high-throughput, combinatorial analysis of polymer droplets in microfluidic devices in order to establish a library of data to assess degree of polymerization and constituent concentration (Figure 1).

EXPERIMENTAL[7]

Materials. Dodecane diol dimethacrylate cross-linker (Esstech), decyl methacrylate monomer (Esstech) and Irgacure 819 photoinitiator (Ciba Specialty Chemicals) were used as received. For fluorescence analysis 10^{-5} mass fraction of a fluorescent dye, Bis-pyrene propane (BPP Molecular Probes), was doped into the organic phase droplets

Device Fabrication and Droplet Formulation. Microfluidic devices were constructed of thiolene-based resin by rapid photolithography as described elsewhere.[6] Flow focusing devices[8] were used to generate organic phase droplets in a matrix of 8 mmol/l sodium doceclysulfate solution. Droplet arrays with gradients of monomer and photoinitiator concentrations were formulated in devices. The droplets formed were in the range of 250 μm to 500 μm in diameter. A Novacure 2100 UV source or a diode laser at 407 nm (Power Technology) was used to initiate polymerization of the droplets in the device.

On-Chip Analysis Techniques. On-chip spectroscopic analysis was conducted on static arrays of droplets as well as in real-time on flowing droplets. Raman spectra were acquired using a Raman systems R2001 spectrometer with CCD detector and 785 nm laser. On-chip data were obtained by interfacing the microfluidic device with a fiber optic probe (300 μm focal size) allowing spectra to be acquired from individual monomer droplets. All spectral manipulation including baseline correction and peak intensity measurements were conducted using Grams AI (Galactic Industries). All spectra were pre-treated by background subtraction of the Raman scattering of the empty channel. Spectral acquisition times were varied from 30 s to 240 s to optimize the signal-to-noise ratio.

Fluorescence measurements were acquired at an excitation wavelength of 350 nm using a xenon arc lamp source. Spectra were obtained using a remote fiber optic sensor connected to a LabView controlled CCD spectrometer (Ocean Optics). The optical sensor consists of a bundle of seven 200 μm core diameter optical fibers. The central fiber illuminates the sample while the six surrounding fibers transmit fluorescence to the CCD array. Acquisition times were varied in the range of 200 ms for real-time analysis to 2 s for analysis of static droplet arrays.
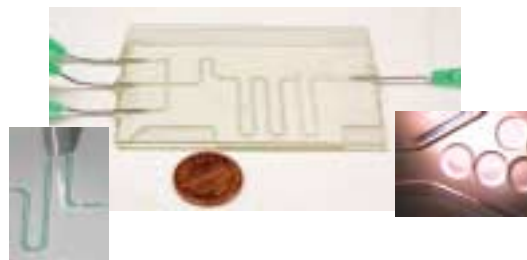

Figure 1. Typical microfluidic device with insets showing images of organic phase droplets (right) and the optical probe utilized for on-chip Raman analysis (left).

DISCUSSION

Study of material libraries is greatly enhanced by the application of molecular specific analytical techniques for on-chip analysis. Such techniques can provide rapid, accurate measurements using small volumes of sample. Spectroscopic detection methods such as Raman and fluorescence provide means to monitor chemical species without disturbing the chemical reaction. Both fluorescence and Raman techniques employ the use of a single probe allowing easy interface of the measurement system with the microfluidic device.

Our first study applying these spectroscopic techniques for analysis of polymer libraries has involved the generation of droplets of reagents for application as 'microreactors'. Each droplet is treated as a discrete element in the array of samples created in the device. Gradients of droplets were produced containing a range of monomer and photoinitiator concentrations by varying the relative flow rates of the organic input streams. The spectroscopic probes were focused onto a number of individual droplets within the device to acquire the necessary data.

Raman spectroscopy was applied for measurement of the monomer / cross-linker concentration gradients constructed within the device by calculating the peak intensity ratio of the bands in the C=C stretching region of the spectra (1700 cm^{-1} to 1550 cm^{-1}). To determine the composition of the droplets on-chip data were correlated to a series of calibration spectra. Raman data were also acquired for measurement of the final degree of monomer conversion following polymerization by analysis of the depletion in the intensity of the stretching vibration of the methacrylic double bond after 24 h of cure.

On-chip fluorescence measurements were combined with Raman data to gain comprehensive assessment of material composition and conversion.
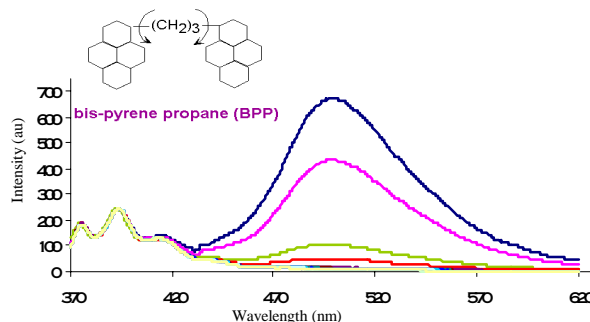

Figure 2. Change in fluorecence emision spectra observed during polymerization of organic droplets on a microfluidic device.

The emission intensity of the fluorescent dye, incorporated into the monomer at low concentrations was used as a molecular viscosity probe to monitor changes in droplet viscosity. The relative uncertainty of the fluorescence intensity measurements was 0.5 %.

The rapid acquisition times of this technique allowed real-time monitoring of droplet polymerization. Upon excitation at 350 nm, BPP decays with monomer fluorescence bands at 377 nm, 395 nm and 415 nm, and a broad excited state dimer (excimer) band extending from 470 nm to 570 nm (Figure 2). At a given temperature, the rate at which excimer fluorescence is generated depends on resin viscosity that inhibits intramolecular motion.[9] Thus, the ratio of excimer to monomer emission intensities can be utilized to probe local rotational viscosity. These data are used to provide kinetic information on the extent of material conversion at a range of component compositions and irradiation intensities.

CONCLUSIONS

The research presented here demonstrates the development of an integrated microfluidic platform combining gradient polymerization of methacrylic polymer systems and on-line spectroscopy. We show that Raman and fluorescence spectroscopy are suitable and sensitive techniques for monitoring the composition and degree of conversion of polymer libraries formulated in organic phase droplets on microfluidic devices. Combinatorial gradients can be formulated and measured in real-time on both flowing and static arrays.

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7. Certain equipment, instruments or materials are identified in this paper in order to adequately specify the experimental details. Such identification does not imply recommendation by the National Institute of Standards and Technology nor does it imply the materials are necessarily the best available for the purpose.
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