

Applying Microfluidic Technology to High Throughput and Combinatorial Polymer Library Synthesis[†]

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Advanced polymeric materials in applications as diverse as tissue engineering, electronics and personal care products require superior control of a wide range of properties. From molecular properties such as molar mass and chain composition, to the properties of complex mixtures, high throughput and combinatorial techniques are providing researchers access to enormous libraries en route to both improved fundamental understanding of structure-property relationships and better products. The appeal of microreactor technology to this scientific community is three-fold: further reduction of scale in expensive specialty applications; faster, less expensive process integration in laboratory-scale investigations of complex, multi-step manufacturing protocols; and potential discovery of new or improved products from the unique microreaction environment.

The technical mission of the NIST Combinatorial Methods Center (NCCM) has two key components: development of new library fabrication techniques and commensurate high throughput and combinatorial measurement methods. Microfluidic technology was initially attractive to the NCCM because it allowed manipulation of polymer solutions at length scales matching several existing measurement methods¹⁻⁵ in the NCCM with the potential to enable fabrication of gradient⁶⁻⁸ polymer libraries with variable molecular properties. The choice of microfluidic device fabrication methods were designed to facilitate rapid redesign and fast in-house production of the chips.^{9,10} Our recent work demonstrates three basic routes to using the micro-environment to prepare both gradient and discrete polymer libraries.

The first is an analog of a continuous reactor for controlled radical polymerization on a chip (CRP chip; Figure 1). CRP, developed in the early 90's, provides access to an unprecedented range of statistical and block copolymers with controlled molecular masses and low polydispersities. This mechanism is used commercially to manufacture a range of specialty materials from photoresists to surfactants, although new applications in nanotechnology and biotechnology are anticipated. Many of the first polymer libraries prepared in parallel reactors, therefore, used CRP chemistries in an effort to map structure-property relationships, particularly in statistical copolymers.

Recently, we demonstrated the application of the CRP chip¹¹ to atom transfer radical polymerization (ATRP).^{12,13} Solutions of monomer containing either initiator or catalyst were mixed at the inlet of the device and the residence time inside the channel (determined by flow rates) was related to

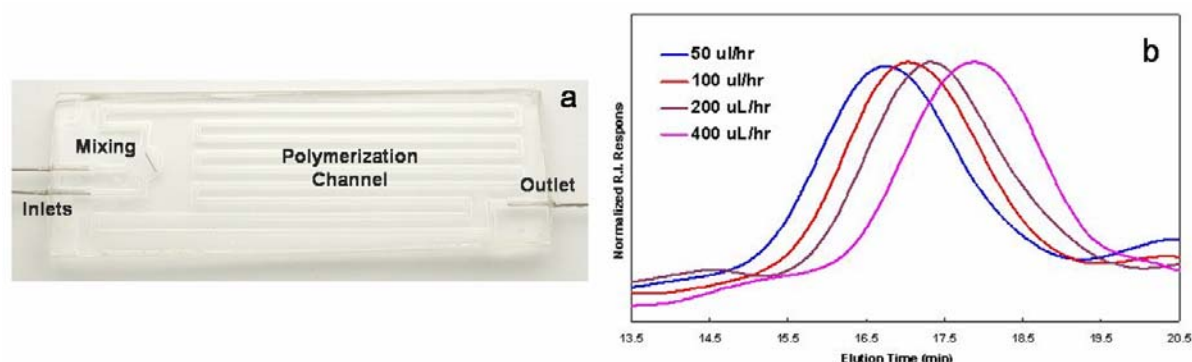


Figure 1. (a) CRP chip for producing well-defined polymeric materials tuned by flow rate and input stoichiometry (b) SEC data for polymers produced at different flow rates.

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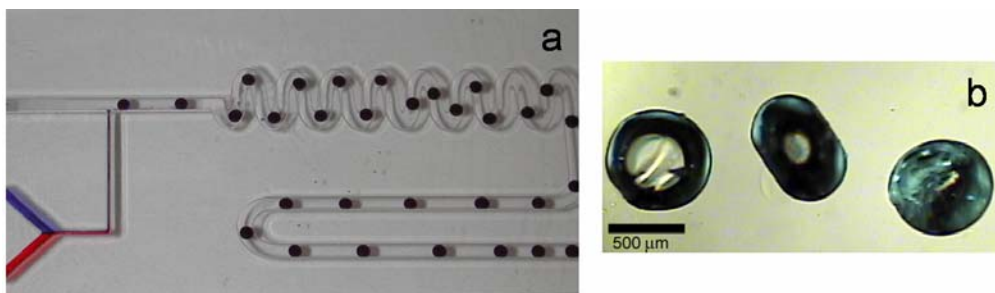


Figure 2. One goal is a device that produces, polymerizes and characterizes polymer microspheres. (a) This device shows two-component toluene droplets suspended in an aqueous continuous phase. (b) Asymmetric particles produced from droplet-phase microreactors in a microfluidic device.

reaction time and, therefore, conversion and molecular mass of the resulting polymer. When the data were represented as semi-logarithmic conversion vs. time, as would data collected from batch reactions, results similar to those in the literature were obtained.¹⁴ More recent work includes the preparation of block copolymers using the CRP Chip¹⁵ and demonstration of a new high throughput approach to evaluation of rate behavior and, possibly, kinetic rate constants using the CRP chip.¹⁶

Although the materials prepared by the CRP chip are primarily low molecular mass (< 30,000 g/mol), and are often in solution, many desired libraries require high molecular mass polymer, or crosslinked systems. Our second route to preparing polymer libraries uses organic phase droplets in a microfluidic device¹⁷ to enable the synthesis of high molar mass materials and crosslinked particles while using a lower viscosity continuous phase to drive flow through the device. The result is near monodisperse polymer particles when the composition and flow rates are held constant, and a discrete array of compositions when the contents of the droplets are varied systematically over time (Figure 2).

Our third and final route has a goal which is fundamentally different from the first two. Microchannel confined surface initiated polymerization (μ SIP; Figure 3)¹⁸ employs a shallow channel (between 90 nm and 300 μ m deep), formed through a patterned polydimethylsiloxane (PDMS) stamp, to confine a solution of monomer and catalyst over an initiator-functionalized silicon substrate. The result is a polymer grafted surface (brush) with geometry determined by the channel design and a gradient in molecular properties determined by the solution flow rate(s). These surface functional specimens are designed to create gradients for mapping the directed self-assembly at interfaces of a variety of materials including block copolymers, conducting polymers and living cells.

Several key features of μ SIP illustrate its utility for combinatorial library fabrication. The surface in contact with the PDMS stamp retains initiating capacity after the stamp has been removed, as do grafted polymers synthesized through an ATRP route. Accordingly, complex graft copolymer libraries can be

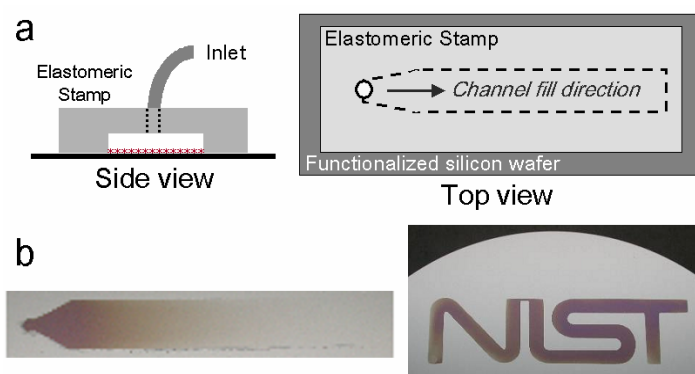


Figure 3. (a) Schematic of microchannel confined surface initiated polymerization (μ SIP) used to produce surface grafted polymer gradients. (b) Image of a grafted polymer molecular mass gradient and a patterned substrate prepared using μ SIP.

built through sequential iterations of μ SIP. Utilizing multiple channels, it is possible to pattern the same surface with multiple brush configurations, as flow and stoichiometry conditions can be varied from channel to channel. Confined gradients formed inside microchannels enable fabrication of grafted libraries of both statistical copolymers and gradient (tapered) block copolymers. The specimens produced will be useful for mapping directed self assembly of a variety of materials on gradient surfaces.¹⁹⁻²¹

These three basic synthetic strategies will be discussed along with some examples of measurement tools which complement the libraries prepared by them.

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