High Throughput Measurements of Polymer Fluids for Formulations*

Kathryn L. Beers, João T. Cabral, Howard J. Walls and Eric J. Amis
Polymers Division, National Institute of Standards and Technology
Gaithersburg, MD 20899-8542, USA

ABSTRACT

Rapid prototyping of microfluidic handling devices has gained popularity due to the ability to quickly test and modify new design features several times in one day. At the NIST Combinatorial Methods Center (NCMC), we have modified common microfluidic fabrication techniques to extend their use to organic fluids. Ultraviolet (UV) curable adhesives were used to create molded resins with increased solvent resistance. This has allowed the preparation of new types of combinatorial libraries and development of new measurement methods to complement the small sample sizes of these libraries. Most importantly, it can be used to tie together multiple stages of the formulation process, from the synthesis of polymers to the measurement of complex-fluid properties, in small and inexpensive platforms. Our first demonstrations of this technology are in the areas of emulsions and polymer blends. Measurement techniques include light and x-ray scattering and rheology. Milli-fluidic handling and measurements will increase the dimensions of parameter space that are available to accurate and systematic study of polymer solutions. These capabilities will also enable the generation of new information in the field of polymer formulations, which is presently dominated by empirical knowledge.

INTRODUCTION

Advanced materials development in areas as varied as personal care, construction and tissue engineering require new approaches to quickly acquire large quantities of reliable data on complicated multi-component mixtures. Considerable attention has been placed on generating large sample libraries for testing material properties. Successes in catalyst discovery and polymer synthesis are good examples of the value in this approach. There are problems, however, where high-resolution control of the composition of a mixture is required. For example, in polymer formulation slight changes in the fraction of added compatibilizer or the molecular mass of the copolymer added to a polymer blend have dramatic impact on phase morphologies and kinetics. While existing methods can still be useful in these situations, staggeringly large sample sets would be required to prepare libraries which reflected both the large and small scope problems faced by formulation scientists.

To complement the static library approach, we are interested in developing methods to continuously change and measure fluid composition and properties. Besides combinatorial methods, another technology developed for application in the life sciences has also drawn attention from multiple materials science disciplines: microfluidics, also called lab-on-a-chip or micro-total-analytical-systems (µTAS).[1] These small devices contain channels carved into silicon, glass or polymer platforms, through which fluids are pumped, mixed, reacted and analyzed, often sequentially on the same platform. We are adapting these methods to materials science problems and use similar devices to prepare and measure complex polymer mixtures.
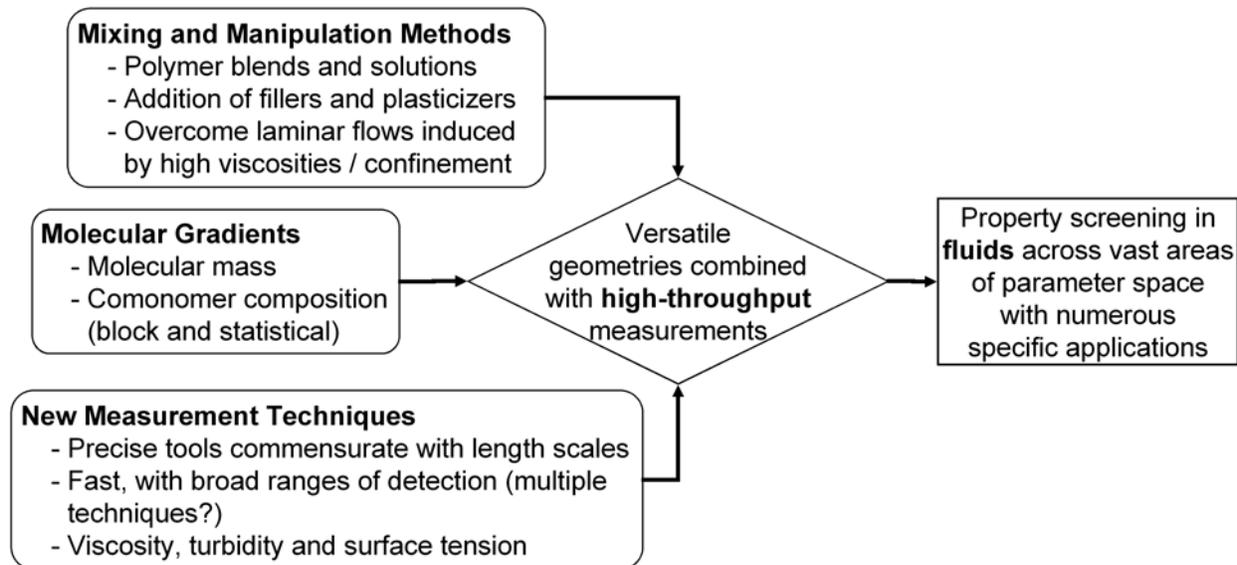
Mixing and Manipulation Methods
- Polymer blends and solutions
- Addition of fillers and plasticizers
- Overcome laminar flows induced
  by high viscosities / confinement

Molecular Gradients
- Molecular mass
- Comonomer composition
  (block and statistical)

Versatile geometries combined with **high-throughput** measurements

Property screening in **fluids** across vast areas of parameter space with numerous specific applications

New Measurement Techniques
- Precise tools commensurate with length scales
- Fast, with broad ranges of detection (multiple techniques?)
- Viscosity, turbidity and surface tension

Figure 1. General flow diagram representing the methods being developed to address the challenges of formulating polymeric materials.

Here we present our results developing a method to rapidly prototype microfluidic devices in a UV curable resin to form a solvent resistant polymer matrix. Several applications of this technique are demonstrated, including multiple approaches to mixing and preparing sample arrays commensurate with in-house-designed platforms for coating polymer films[2-4] and measuring scattered light.[5]

We are concurrently developing measurement tools that can be scaled down to the length scales of these fluid-handling devices (typically 100 μm to 500 μm). The example described here is the measurement of viscosity, a critical value necessary to understand many behaviors in complex fluids. Figure 1 shows a schematic of our approach to developing an integrated platform for studying the formulation process. By developing a suite of techniques in three basic categories, manipulation, molecular variation and characterization/property measurements, we will create a toolbox through which we hope to bring Lab-on-a-Chip analogues to the formulation scientist's laboratory.

RESULTS

Rapid Prototyping Methods

We recently developed an open-faced rapid prototyping method (Figure 2A) similar to that of Whitesides, et al.[6] with the exception that our methods uses a resin based on multifunctional thiolene monomers with a simpler and faster methodology.[7] In the open face approach, a second step is necessary to cap the device to seal the channels. With our novel closed-face approach, the fully enclosed device can be prepared in one step. These resins form a dense, highly-ordered crosslinked network upon curing,[8] which renders them nearly impermeable to many common organic solvents, for example these devises can manipulate solutions in ethanol, tetrahydrofuran, and toluene, as well as water, unlike many other materials used to quickly and

repeatably prepare microfluidic devices. The cured resin also adheres well to glass and is optically transparent (as purchased, they are marketed as optical adhesives).

Other advantages of using these resins are the curing mechanism and attenuation of these particular formulations and the relationship between the UV dose and the curing depth profile of the resin (Figure 2B). The height of the structures formed is dependent on the liquid-solid transition in the curing cycle. Due to the high attenuation and restricted mass transfer and because the radical curing mechanism behaves like a condensation polymerization, this interface in the bulk material is quite sharp. We recently developed an empirical theory to model this relationship such that the heights of the structures formed in the resin could be controlled by either the time of exposure to the light source or the intensity of the dose.[9] The later has been called gray-scale prototyping and has been demonstrated recently in PDMS to introduce a quasi-3D structure into channel architectures.[10]

Two types of passive mixers can be patterned into the channels using these methods. The first is illustrated in Figure 3. Lateral patterns in the channel walls can be introduced simply by varying the mask structure. These types of patterns can be used to induce a droplet in the channel to rotate and counter-rotate, leading to chaotic mixing of the contents of the droplets through the resulting shear forces.[11] The second mixing method has been demonstrated for mixing compatible inlet streams in a channel, which characteristically mix slowly because the fluids are trapped in a laminar flow regime at these length scales.[12, 13] The layout of the masks used to create these types of geometries in channels is shown in Figure 4. It is the depth dependent curing of the thiolene that makes this type of patterning possible by using a two-step curing process and overlapping masks.

This technology is presently being used to develop high-throughput and combinatorial measurements of emulsions and colloidal suspensions.
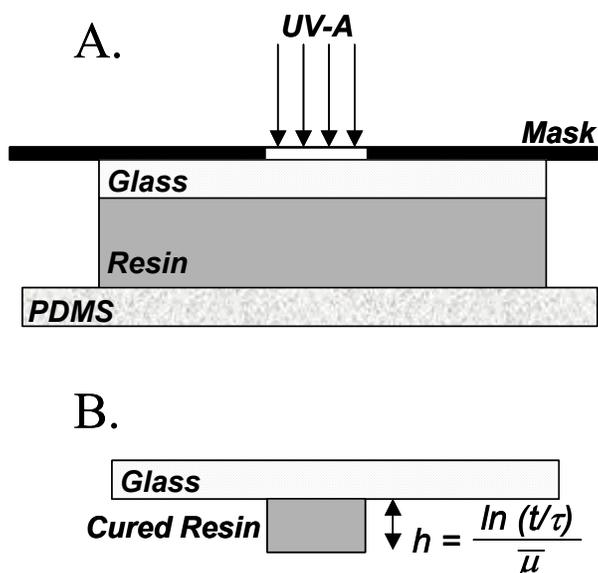

Figure 2. A. Stacking of elements in the fabrication process to prepare open-faced structures from the thiolene resin. B. Schematic of resulting structures on glass where the height of the structures (h) depend on the time of exposure (t), weighted average attenuation in the medium (μ-bar) and a characteristic induction time (τ) determined in part by the intensity of the light source and the rate of conversion of the monomer.
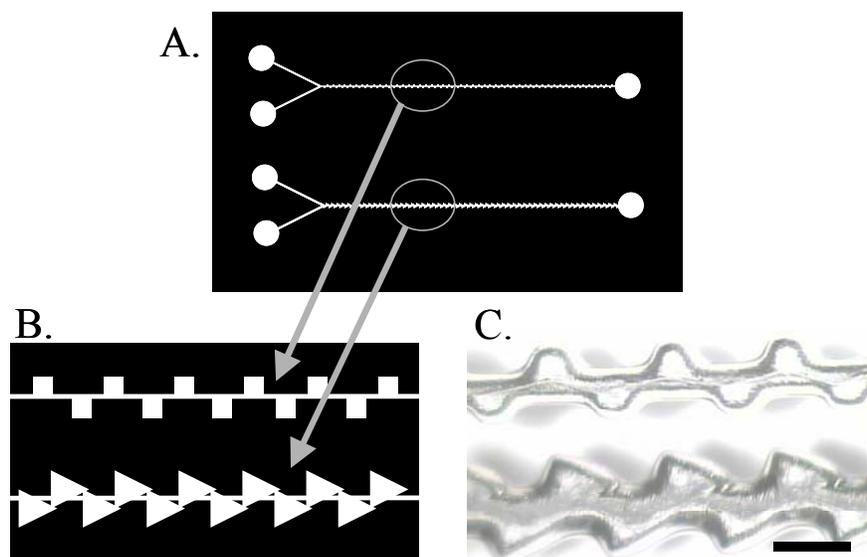
Figure 3. A. Powerpoint image printed on transparency to serve as masks in rapid prototyping procedure. B. 1200× magnification of main channels showing patterns incorporated into the channel walls. C. Replicated structures in PDMS from the corresponding masters prepared from mask A. Scale bar 300 μm
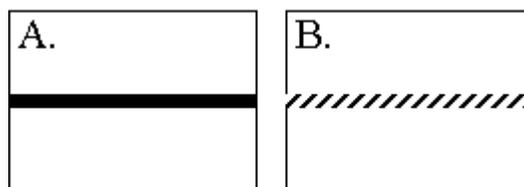

Figure 4. Layout of masks for creating mixing patterns in channel beds similar to those found in reference 11. The two masks are stacked, A over B, and mask A is removed prior to complete curing to leave a patterned channel in the cured resin. Inverted masks can also be used to create a master for prototyping in PDMS as in Figure 3.

Viscosity and Rheology Measurement Tools

We have developed two high-throughput tools to measure rheological properties. The first is a small capillary viscometer based on the prototyping technique described above. The device has several channels each of different size (taking advantage of the length scale versatility of our technique) allowing viscosity measurements at several different shear rates simultaneously.[14] An equation similar to the Poiseuille's law for flow in a capillary is used for data analysis along with tracking the travel time of the fluid (or tracer particle) through each channel of known dimensions. The apparent viscosity is the result. Drawbacks to this method include that it is not a dynamic measurement hence the complex modulus (G^*) or complex viscosity (η^*) cannot be

measured. Secondly, fluids of widely different viscosities, or densities, or surface tensions are difficult to measure successively in this device.

One method of measuring rheology on very small (pL to µL) sized samples is particle tracking micro-rheology. This technique requires small tracer particles (sub-micron) be present in the sample of interest. The Brownian displacement of the particles is tracked over a short period of time and then a generalized form of the Stokes-Einstein equation is used to fit the data and back out the viscosity. Advantages are the small sample size and short acquisition times. However, by its very nature the technique explores the nano-scale rather than the bulk rheology of a sample. Although this is interesting and useful, there is a practical need for bulk rheology measurements for the understanding and development of complex formulations. Furthermore, inherent to this technique is that only very small stresses and strains are accessible; therefore, shear thinning cannot be measured by this technique.

We are developing milli-fluidics devices that incorporate small magnetic particles (of order 500 µm) that will be oscillated and their displacement tracked relative to an applied magnetic field. These flow-through devices would then measure the dynamic rheology of a gradient sample on a milli-fluidic device within channels with cross-sectional areas on the order of a few millimeters. The relatively large size of the magnetic probe particle compared to the polymer (or fluid) structural length scale enables bulk rheology measurement (unlike particle tracking micro-rheology) while the actively driven nature of the systems should enable measurement of shear thinning properties as well as measurement of the complex modulus (G*) or the complex viscosity (η*).

The second high-throughput rheology device that we have developed is a scaled intermediary between a typical stress rheometer with multiple Couette (cup-and-bob) cells and the microscale version described above. One cell of this new multi sample rheometer (or combi-rheometer) is shown in schematic in Figure 5. Four test cells hold discrete samples to be tested. Each test cell has a rotor with a small magnet embedded in it. The array of rotors align with a static B_0 magnetic field in a 2-axis Helmholtz coil. A second B_1 magnetic field oscillates orthogonal to the B_0 field such that the rotors in each test cell respond to this field in amplitude and phase in proportion to the viscosity and viscoelasticity of the sample in the test cell. This
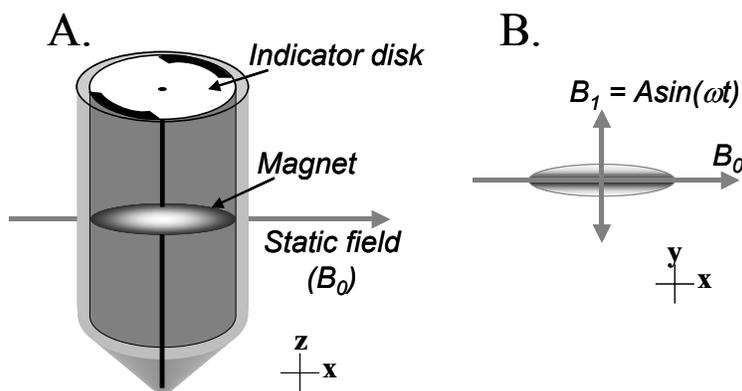

Figure 5. One cell of the combi-rheometer illustrating the basic design and mode of operation. Typical sample volumes are about 1.5 mL.
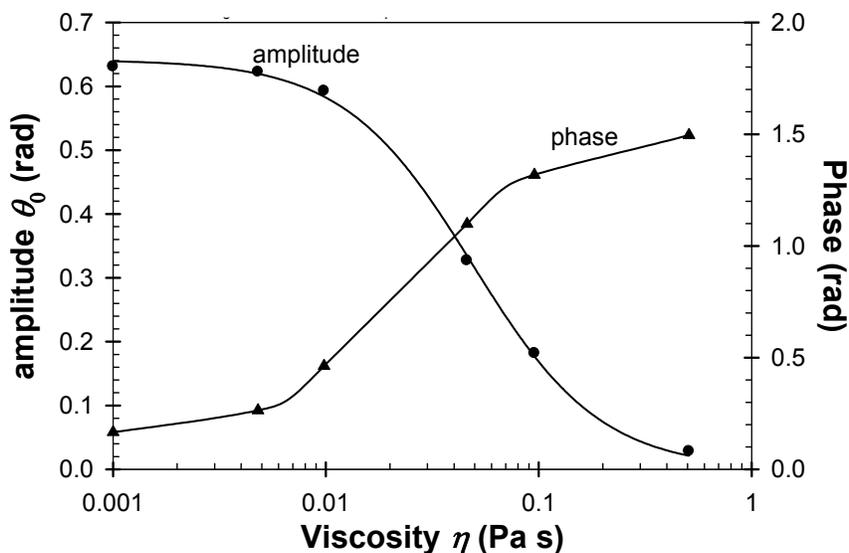
Figure 6. Calibration curve for zero shear viscosities constructed with a fixed, low frequency.
$B_0 = 13$ Gauss; $B_1 = 5.5 \times \sin(\omega t)$ Gauss, $\omega = 0.7$ Hz

combi-rheometer has been demonstrated to simultaneously measure the zero shear (or Newtonian) viscosity of four samples, Figure 6. By sweeping the frequency of the B_1 field and use of an appropriate model for an oscillating body in a viscous fluid [15, 16] we expect to simultaneously measure the complex viscosity of four samples (still under development).

Drawbacks to the new combi-rheometer include sample size. In its current form this device requires approximately 1.5 mL of discrete sample. Our goal, as mentioned above, is the development of μL sample sizes and [continuous] gradients in sample composition. However, the basic concepts developed and demonstrated in the new combi-rheometer are being scaled down and adapted for a fluidic-type device.

For scaling the concepts of the combi-rheometer down to a fluidics device the changes may seem large but are in fact fairly superficial. Instead of the Couette cell with a rotating bob as the shear device, a sphere or cylinder that rolls or undergoes linear rather than rotational translation will be used. However, what remains the same is the moving of a test piece with a magnetic field and tracking its displacement in amplitude and phase with respect to the driving ac B_1 field. Test probe tracking will be done by centroid tracking, much as the centroid of each mark on the indicator disk is tracked now. Data fitting and phase shift will also follow nearly identical algorithms. The Helmholtz coil setup may either be the current one or an adaptation of the current one with the B_0 and B_1 fields being linear and the B_0 field being changed to a linear gradient. These details are still under design and preliminary testing. Nonetheless, the same electronics and a similar data acquisition and analysis setup will be used.

CONCLUSION

We are in the early stages of developing a toolkit of methods that will be used to build a modular, high throughput platform for constructing and measuring complex fluids, typically requiring 100's μL of sample. The ability to rapidly prototype fluidic devices that can tolerate organic and aqueous solution environments has been demonstrated and used to prepare several alternative passive mixing devices. An instrument to measure rheology of complex fluids has

also been developed with the goal of reducing the sample volumes necessary to perform the measurement to size scales commensurate with the fluid handling devices. The methods use applied magnetic fields to manipulate a probe in the sample. Having built the hardware for the instrument and validated the approach, only the sample preparation method and probe will need to be modified to scale down the measurement.

EXPERIMENTAL DETAILS [17]

Prototyping

The thiolene-based optical adhesive was patterned on one or between two glass slides (1 mm thick; Corning Microslides, 75 mm $\times$ 50 mm, Model 2947). Polydimethylsiloxane (PDMS; 10:1 mass ratio base to curing agent ; Sylgard 184, Dow Corning) and the thiolene resin (Norland adhesives #61, 68 and 81) were used as received. The light source was a Spectroline SB-100P flood lamp optimized for 365 nm with a Spectroline DRC-100X digital radiometer with a DIX-365A UV-A sensor. Masks were designed using a variety of graphics programs (Powerpoint, Canvas or Photoshop) and printed on transparencies (3M, model CG3300) with a 1500 dpi laser printer (Hewlett Packard, model 8000N).[6]

Rheology

The combi-rheometer is composed of Couette cells, a 2-axis, Helmholtz coil, function generator and amplifiers to drive the coils, and image acquisition hardware and software. The 2-axis Helmholtz coil is of square design permitting ease of construction and sample placement, as well as simplifying the computations needed to design the instrument.[18] Typically the B_0 field is 13.7 Gauss while a typical value for the B_1 field is around 5 Gauss (i.e., $5 \times \sin(\omega t)$ where ω is frequency). Bandwidth limitations are not expected over the frequency range (0.1 Hz to 5 Hz) typically used. In house written image analysis software was developed using Interactive Data Language (IDL, Research Systems Inc.). The program extracts the angular displacement of the rotors (via indicator disks) and the applied B_1 field via the LED. Amplitude and phase shift (relative to the ac signal in the B_1 coil) is then determined in the program via fits of the collected data. Testing and calibration of the instrument was done using viscosity standard spanning nearly 3 decades in viscosity. For viscosities greater than 1 mPa s, polydimethly siloxane (silicone oil) Newtonian standards were used. Water was used as the 1 mPa s standard.

ACKNOWLEDGMENT

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