

Combinatorial Methods for Characterization and Optimization of Polymer Formulations

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Summary

Most applications of polymers involve blends and mixtures of components including solvents, surfactants, copolymers, fillers, organic or inorganic functional additives, and various processing aids. These components provide unique properties of polymeric materials even beyond those tailored into the basic chemical structures. In addition, skillful processing extends the properties for even greater applications. The perennial challenge of polymer science is to understand and exploit the structure-processing-property interplay relationship. We are developing and demonstrating combinatorial methods and high throughput analysis as tools to provide this fundamental understanding.

Introduction

Commercially available combinatorial and high throughput fluid handling and measurement capabilities have enabled tremendous progress in industrial product development; however, the platforms are often costly and time-consuming to implement. The approach adopted by most manufacturers and system suppliers in the area of combinatorial materials science has been to build automated platforms that mimic the development process for a specific material in a narrow application. This greatly increases data acquisition rates, but it is challenging to adapt this system-specific infrastructure to changing needs of scientific research and short time demands of development activities. Our response has been to consider combinatorial libraries in the broadest sense to include diversity in chemical structure, varying compositions of additives to formulations, and manipulation of processing variables as part of the library design.

Our initial approach was to create demonstrations that we refer to as “self-reporting libraries”. The ease of demonstration of this concept for examples in studies of thin films led to the development of a range of applications for blends, biomaterials, scan probe microscopy, and thin film mechanical properties. The work on films also led to a natural focus on applications of gradients of properties (combinatorial library space) rather than the discrete samples common for robotic-based systems of reactor arrays derived from high throughput approaches used by the pharmaceutical industry. In the third stage we have adopted the use of microfluidic technology to show methods for the manipulation and measurement of complex polymeric fluids, thereby providing flexible and inexpensive alternatives to robotics driven instrumentation. The demonstrations of microfluidic tools include examples linked to previous thin film approaches, gradient concepts, and link to recent developments that apply robotic systems to investigate processing variables.

Self-Reporting Libraries

Our concept of a self-reporting library was originally developed as a straightforward example to show how combinatorial methods could be applied to make measurements in materials systems, in contrast to the more common application for “discovery” of new materials. The first example of a self-reporting library derived from studies that showed the effects of film thickness on the kinetics of dewetting behavior. We applied precise orthogonal gradients of film thickness and temperature, and, with the straightforward use of optical and atomic force microscopy, the kinetics of dewetting was studied and compare to results from traditional single sample measurements.

The second, and perhaps the most dramatic example of the concept, was the preparation and visual observation of a complete binary blend phase diagram. Figure 1a shows an optical micrograph of the library that consists of a film of nominal thickness composed of a gradient mixture of polystyrene and polyvinylmethylether. The composition gradient was annealed on a temperature gradient stage with the temperature variation orthogonal to the composition gradient. The phase separation of this LCST system begins almost immediately

at the highest temperature end of the stage and over the course of about one hour spreads to the entire two-phase composition range. Validation data, this time from cloud point measurements of several discrete composition samples, are superimposed on this photograph. As with any new experiment method, validation studies provide confidence in the method and, in the case when they are proceeded by a broad library study the validation studies can be focused on the regions that show particular interest. In the traditional language of combinatorial science these regions may be referred to as “hits”.

The third example of the self-reporting library is derived from the phase diagram library. In this case a polymer blend phase separation library was prepared with two polymers of interest for biocompatibility studies, PCL and PDLA. The base library thus begins with a composition gradient, temperature annealed, phase separated film. The library is further developed by incubation with cell growth media including proteins, buffers, salts, and, in some cases, growth factors. The screening or high-throughput analysis of the library is conducted by plating cells on the library which are then stained for direct observation. Figure 1b shows the self-reported response of cells to this library. Clearly the reporting of the library is limited to what it was designed to show, and the detailed analysis that is necessary to understand the nature of the cell-material interactions requires a new focused library or traditional experiments, both of which can be designed more critically by using the data from this screening library.

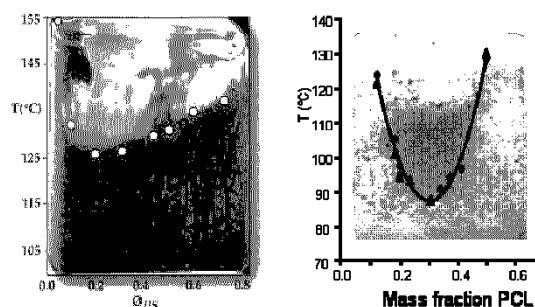


Figure 1: Self-reporting libraries demonstrating (a) phase separation of an LCST polymer blend and (b) preferential cell growth on a similar phase separated blend library of two biocompatible polymers.

Thin Film Properties

Already with the self-reporting libraries we investigated thin film properties to the extent that films are prepared to provide surfaces, for example to control the attachment of cells, or when the thickness of the film modifies stability. In a similar manner, we have prepared and interrogated libraries demonstrating the effect of film thickness and of substrate surface energy on microphase separation behavior of block copolymers. Investigations of adhesion and mechanical properties of polymer films provide a better example of material properties assessment directly applicable to end use applications.

One demonstration of high-throughput investigation of adhesion was shown in a variation on a traditional edge-liftoff or delamination test used to assess strength of interfaces between dissimilar materials. In the traditional test, a coating such as an epoxy adhesive is applied to a metal or ceramic substrate. The bond is then tested by cooling the specimen until delamination occurs by the stress generated from the dissimilar thermal expansion coefficients. The combinatorial approach starts with a gradient or multiple sample discrete library, parses the library into multiple specimens, and tests the delamination of all the samples in the same cooling test, simultaneously.

Mechanical testing of thin film libraries has been demonstrated with the development of a new test capable of rapid measurement of modulus. The method uses libraries of thin films that are attached to a softer substrate of known modulus. From the theory of laminate beam buckling and knowledge of the thicknesses of the layers, the modulus of the library film can be rapidly interrogated. Figure 2a shows an AFM of the buckling pattern in a nanoporous glassy thin film applied to a substrate of PDMS. Figure 2b shows the modulus measured by this method, compared with nanoindentation for the validate study, as a function of porosity. A recent extension of the method has been to reverse the technique by using a thin film layer with known properties as a sensor to measure a library sample of the soft substrate, such as a hydrogel of varying crosslink density. We have not yet fully exploited the method’s speed and simplicity for combinatorial analysis.

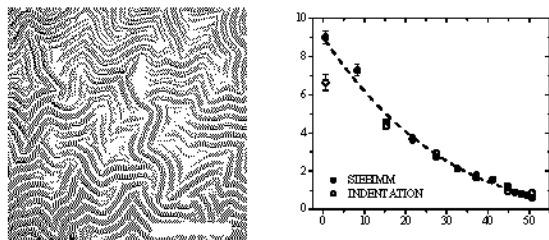


Figure 2: Thin film modulus measurement from bilayer buckling instability where (a) shows an AFM of the buckling in a nanoporous glass which yields (b) the modulus as a function of porosity.

Microfluidics for Polymer Formulations

Although films represent an excellent workspace for demonstrating library methods and they have broad applicability in paints, coatings, electronics, optics, biomaterials, etc., formulations are prepared as suspensions, solutions, blends, and melts. We have adopted the use of microfluidic technology to manipulate and measure complex polymeric fluids. A major goal is to demonstrate flexible and inexpensive alternatives to robotics driven instrumentation. Our microfluidic tools include examples linked to previous thin film work, they retain transferable concepts from the gradient method approaches, and they link to recent developments that apply robotic systems to investigate processing variables. To improve the versatility for this high throughput formulations testing, we needed to build a toolset for microfluidic devices that was complementary for library fabrication and test method development. Our preparation of devices is designed to be fast and modular, allowing for rapid prototype development and increased flexibility. Our fabrication method, an extension of typical procedures, is improved by use of an optical resin with good solvent resistance that obeys a frontal polymerization mechanism. This enables preparation of quasi-three-dimensional channel structures.

We have demonstrated the use of microfluidic chips for the synthesis, mixing and measurements of a variety of systems. Synthetic techniques include controlled radical polymerization on a chip, and organic phase droplets as polymerization microreactors. Microarray libraries have been produced from sequences of droplets with varying co-monomer compositions. Measurements and methods include polymer shrinkage, interfacial tension, on-line fiber-optic Raman spectroscopy, and static and dynamic light scattering. These new approaches enable rapid, often real-time, evaluation of solution properties as composition is systematically varied. The methods have been applied to challenges in dental composite formulation, a variety of 2-phase fluids, and surfactant solutions.

Figure 3 shows an example of using microfluidics to prepare surfactant-stabilized droplets, deforming them in an extensional flow gradient, and from their deformation as a function of shear rate, the interfacial tension is measured. This rapid measurement becomes a tool for high-throughput combinatorial materials investigations when the input to the deformation device is a series of droplets prepared with slightly varying surfactant composition, flow or mixing history, or even aging of the interface itself.

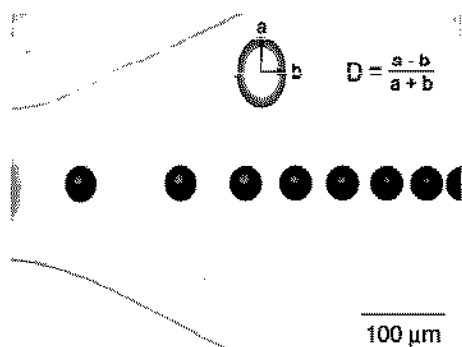


Figure 3: Image of drops flowing left to right in extensional flow gradient. Analysis of deformation yields interfacial tension.

Figure 4 shows another example where a library of discrete droplets each with containing a mixture with slightly varying compositions of monomer and crosslinker. The composition variations between these droplets are so slight that the library can be considered a continuous gradient for all practical purposes. These photopolymerizable mixtures are first characterized for composition (by Raman spectroscopy) and size (optical microscopy with image analysis). The polymerization reaction is initiated and progresses to the desired extent. Raman and optical microscopy are used again to provide extent of reaction and size. The critical issue of shrinkage in dental composites is thus amenable to combinatorial and high-throughput analysis.

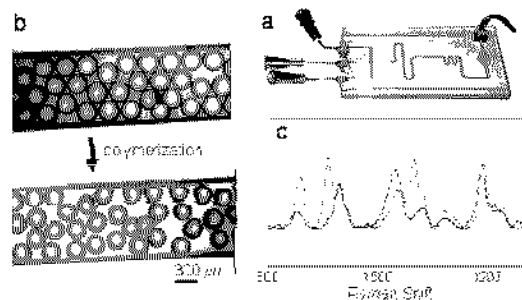


Figure 4: (a) Microfluidic device used to create, mix, polymerize, and characterize monomer droplets; (b) Images of monomer droplets and polymerized particles; (c) Raman spectra of monomer and polymer.

Conclusions

Appropriate design of a combinatorial library, coupled with high-throughput or parallel measurement methods, can be used to provide new tools for analysis of polymeric materials. The applications are obvious for polymer synthesis and the discovery of new materials but it is likely that the more powerful application will be in exploring fundamental understanding of polymer formulations.

References

NIST publications demonstrating the application of combinatorial and high-throughput analysis of polymer materials are available from <http://www.nist.gov/polymers> and <http://www.nist.gov/combi>.