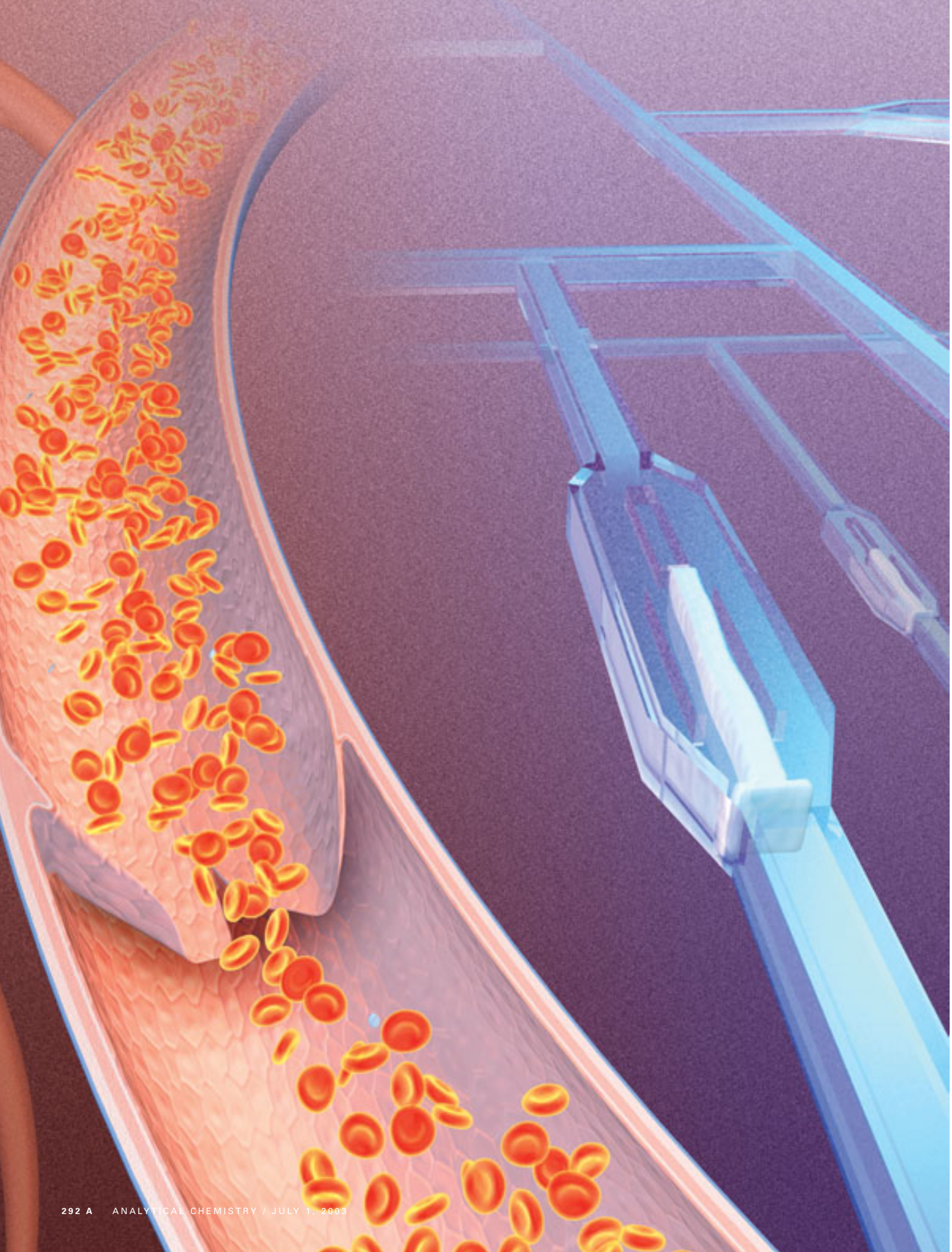


Organic and Biomimetic Designs for Microfluidic Systems

New strategies offer a flexible approach to designing microscale devices.

A microfluidic device typically consists of channels, reservoirs, pumps, and valves. One approach to designing such an integrated system is to fabricate individual components and assemble them to achieve the required system-level functionality. This assembly approach works well when the connectivity of components and their interactions are well understood and the same design can be reused.

In biological or chemical assays, the sequence in which components are connected varies with the type of analysis and analyte. For example, in certain reactions, a separation step precedes a reaction step to remove contaminants, whereas in others, the separation step follows the reaction step to remove byproducts. Thus, a need exists to design microfluidic circuits that are specific to a particular analysis yet versatile enough to be simply and efficiently restructured for another type of analysis. As a step toward flexible system design, we explore the idea of creating a technology platform—microfluidic tectonics—that allows end users to connect different components for a particular application. The platform approach uses liquid-phase photopolymerization to fabricate passive and active microsystem components within a few minutes.

In a typical microsystem, components such as valves are modulated by external control signals. However, external control schemes tend to increase the size and complexity of the device. An alternative approach is to activate

Jaisree Moorthy
David J. Beebe
University of Wisconsin–Madison

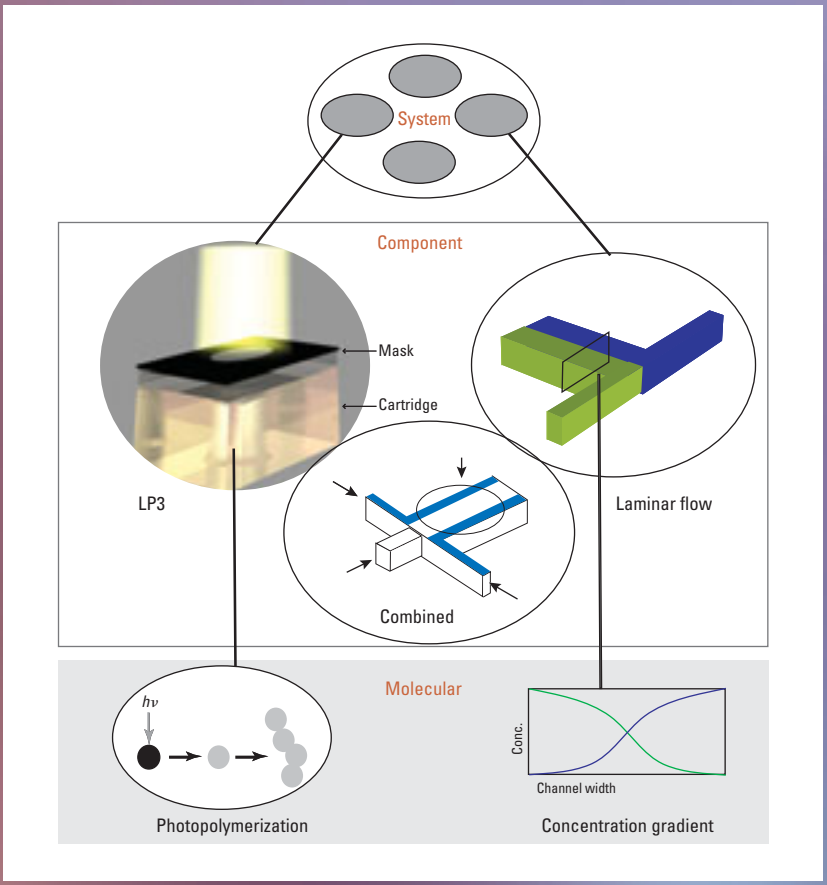


FIGURE 1. Fabricating a μFT platform.

Components are fabricated in situ by LP3, laminar flow, or both. (left) In LP3, a photoinitiator is incorporated in the monomer solution and polymeric structures are fabricated when specific regions are exposed by a photomask. (right) In laminar flow, adjacent streams mix at their interface, creating a structure at the interface of a spatially varying concentration gradient of molecules. This gradient has been used to fabricate inhomogeneous polymeric structures.

the components with internal stimuli, such as temperature, pressure, and chemical agents. A component must possess the appropriate chemical and physical properties to provide the necessary response to achieve internal control, for example, the ability to change its shape or volume depending on the pH of the local environment. Many biological processes are regulated by minute changes in the local environment, and the physiology of organisms is tuned to respond effectively to these changes. The design of devices mimicking such behavior allows autonomous operation. Responsive materials such as hydrogels have been explored to provide functionality to a microsystem that is typically provided by electronic components. In this article, we provide an overview of these materials and discuss the development of such autonomous microfluidic components.

Microfluidic tectonics

Tectonics refers to the science or art of assembling or shaping materials during construction. Microfluidic tectonics (μFT) is the fabrication and assembly of microfluidic components into a universal platform, in which one starts with a "blank slate" (shallow cavity) and proceeds to shape microchannels and components within the cavity by liquid-phase photopolymerization or laminar flow.

Liquid-phase photopolymerization. In μFT, the channel walls and microfluidic components are created from prepolymer solutions. In liquid-phase photopolymerization (LP3), these structures can be fabricated directly inside a shallow cavity or blank slate, which is formed by bonding a polycarbonate film to a glass substrate with an adhesive gasket. We refer to the polycarbonate/gasket/glass system as the "universal cartridge". The universal cartridge is filled with a prepolymer mixture consisting of a monomer, a cross-linker, and a photoinitiator. The type and composition of the prepolymer mixture dictate the physical and chemical properties of the resulting polymeric structure (e.g., the cross-linker concentration influences the rigidity and mechanical strength of the polymer).

A transparent mask is placed on top of the cartridge, which is then irradiated with light of the appropriate wavelength (usually 300–400 nm) to initiate polymerization in the exposed regions and form polymerized structures inside the cartridge (*1*; Figure 1). The polymerization time ranges from 10 s to 5 min, depending on the nature of the prepolymer mixture and channel depth. The unpolymerized mixture is suctioned from the cartridge, leaving an open-channel network or a desired structural component. Photopolymerization allows the components to be fabricated in any location in the microsystem. Moreover, by stacking polycarbonate layers, fabrication of a 3-D channel network is possible, allowing more efficient space utilization and increased functionality (e.g., 3-D chaotic mixer designs and sheath flow) (*2*).

In LP3, a blank slate of any shape and a variety of materials can be used. The main requirements include transparency to polymerizing wavelengths of light and compatibility with prepolymer mixtures. Changes in the placement of components can often be achieved without creating a new mask by making simple positional changes prior to exposure or mixing and matching existing transparency masks (*1*). However, a change in the basic design (e.g., the shape of the component) requires the creation of a new mask.

Because developing a new mask can take a day or two, a faster method has been devised using micromirror arrays for maskless fabrication. Micromirrors are light reflectors that can be actuated using electrostatics; such arrays are used in a liquid-crystal display light projector. When fabrication is conducted with micro-

mirrors, specific regions on the device can be exposed to light by controlling the orientation of the mirrors through a computer interface. The fabrication of a channel network or component inside a universal cartridge is now limited only by the time required to draw the layout on the computer, essentially allowing real-time μFT.

Laminar flow. Another way to fabricate microfluidic components in situ takes advantage of the flow profile of fluids. Laminar flow occurs inside micrometer-sized channels, in which the viscous properties of the fluid dominate; for example, the flow of water through a microchannel is analogous to the flow of a viscous fluid such as honey through a significantly larger channel (*3*). Laminar flow is smooth, steady, and predictable. Two or more streams flowing adjacent to each other mix at their interface mainly by diffusion. Because diffusion is inversely proportional to the size of the molecules, mixing can be time-consuming for large molecules such as proteins. Therefore, the development of micromixers for efficient mixing is an active research field (*4*, *5*).

However, slow mixing can be an advantage. For example, size-based separation can be achieved between adjacent streams (*6*) because large molecules diffuse more slowly than smaller molecules. Slow mixing provides a well-defined interface that can be used for in situ fabrication. As the reactants flow past each other in adjacent streams, the structure develops at the interface as the product is formed (Figure 1). Whitesides and coworkers have fabricated silver and gold wires by electrodeless laminar flow deposition of the metals (*7*). Recently, Zhao and colleagues fabricated nylon membranes inside microchannels by flowing reactants in adjacent streams (*8*).

The two approaches can be combined to integrate each of their capabilities—laminar flow to control geometry (by confining the streams) and LP3 to create polymeric structures (*9*). As the molecules diffuse between the laminar flow streams, a spatial gradient in their concentration develops (Figure 1). This concentration gradient has been used to spatially vary the monomer composition prior to LP3 for the purpose of creating polymeric structures with inhomogeneous properties (*10*). Thus, creating components with asymmetric material properties is possible with these two approaches.

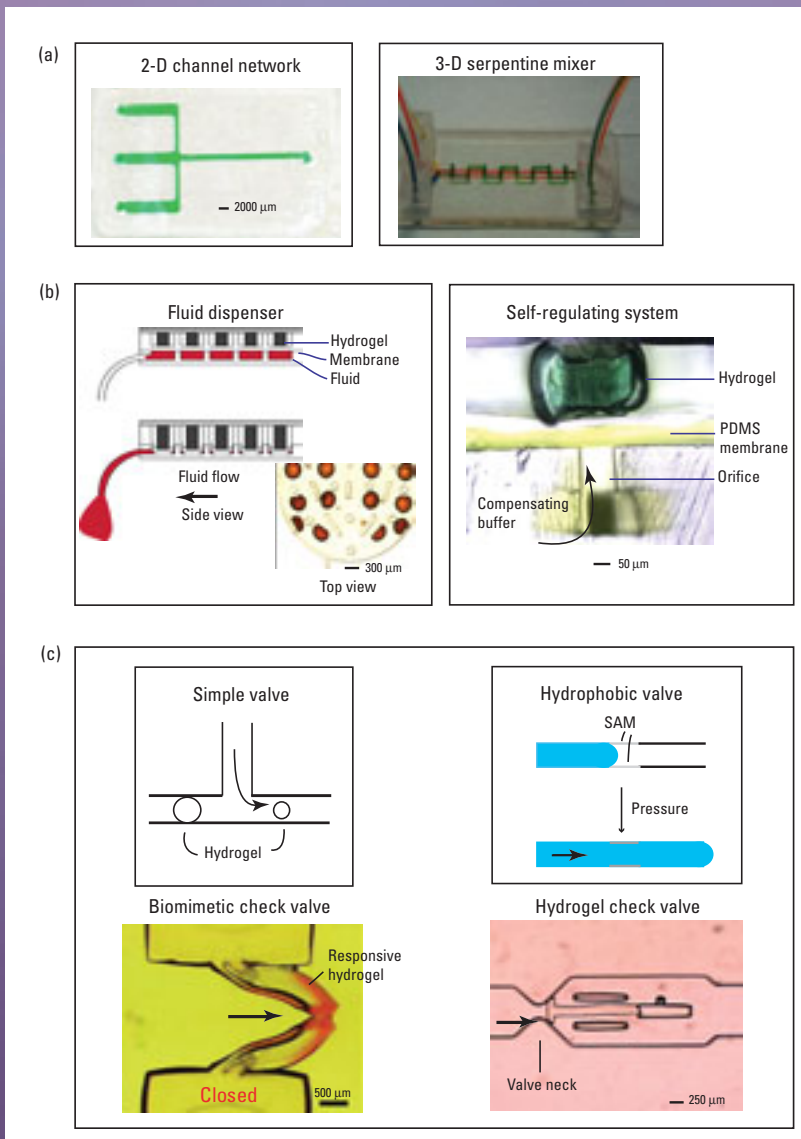


FIGURE 2. Channel network and microfuidic components prepared by μFT methods.

(a) Microchannels have been fabricated in both 2-D and 3-D in a universal cartridge. The 3-D serpentine network (green) can also function as a chaotic mixer. (Adapted with permission from Ref. 1.) (b) Fluid dispensers and flow regulators have been fabricated by combining hydrogels with elastomeric materials. (c) Active and passive valves are created using responsive materials. (Adapted with permission from Refs. 14 and 25.)

Materials

A typical lab-on-a-chip microsystem consists of analytical process-

es connected by fluidic pathways or channel networks. The channel walls form the skeleton of the microsystem and are therefore fabricated from mechanically strong hydrophobic polymers, such as poly(isobornyl acrylate) (*9*). These materials can be fabricated using LP3 or laminar flow, display minimal change (5–10%) in volume after polymerization, and show high tolerance to common organic solvents. These materials are also used to form "pillars" or "posts" that can provide mechanical support for other microfluidic components. The channel network can also be designed to function as a passive component. For example, a 3-D serpentine channel network was used to improve the extent of mixing between laminar flow streams (*2*; Figure 2a).

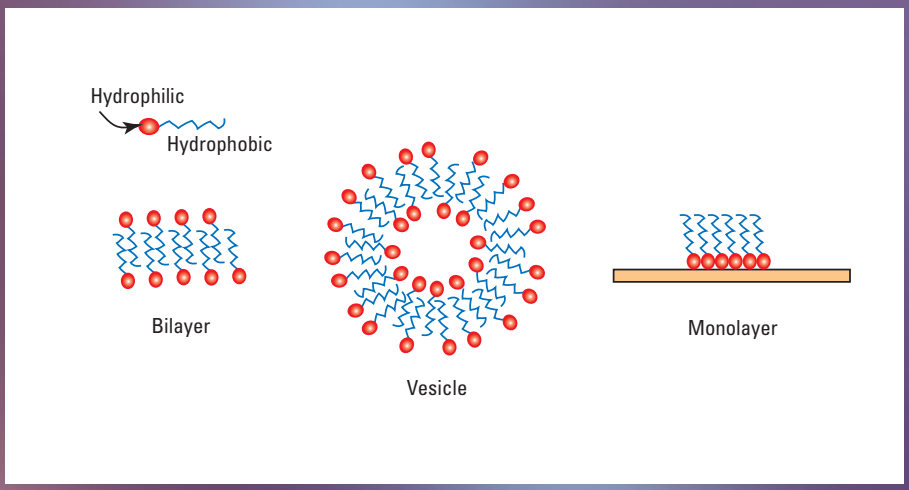


FIGURE 3. Amphiphilic molecules self-assemble in aqueous solution to form bilayers or vesicles and on surfaces to form SAMs.

As vesicles, these materials have been used as containers, and as SAMs they have been used to alter the surface properties of channel walls.

Hydrogels have been around for ~50 years and have recently been extensively studied for use in pharmaceutical drug delivery and as tissue scaffolds (*11*). Hydrogels are a class of cross-linked polymers that have the ability to "absorb" water. Responsive hydrogels can undergo phase transitions, wherein an external stimulus, such as pH, chemical or biological agents (*12*), temperature, or an electric field (*13*) leads to large volume changes. The stimulus changes the polymer backbone, which then affects the movement of water and ions into and out of the polymer matrix.

In the temperature-sensitive hydrogel poly(*N*-isopropyl acrylamide), the movement of water is initiated by a change in the hydropathy of the backbone, whereas in the pH-sensitive hydrogel poly(2-hydroxyethyl methylacrylate-*co*-acrylic acid), the movement of water is initiated by ionization of the backbone. Although the exact mechanism of swelling is still an active area of study, models and experiments suggest that the movement of ions or molecules and water into the hydrogel is mainly by diffusion. Therefore, the time scales for the volume change will depend on the distance traveled by or the initial size of the hydrogel. Earlier studies with thick hydrogel slabs—on the order of millimeters and centimeters—reported response times ranging from a few hours to a few days. By scaling down the size to micrometers, the volume changed in a few minutes (*14*). The response time was further reduced to a few seconds by increasing the porosity of the material (*15*). These quicker response times indicate that components that function in real time can be fabricated. The volume change can provide a mechanical force, thus transducing a chemical stimulus into a mechanical action, as in muscles. The factors affecting the force are the dimension of the hydrogel structure, the chemical composition of the polymer matrix, and the environmental conditions (*16*).

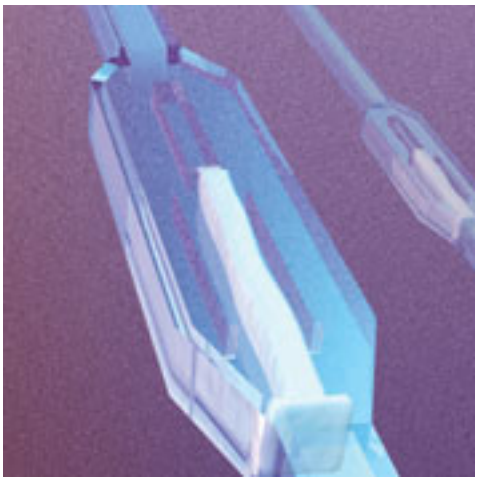
Responsive hydrogels have been explored for use as sensors and actuators. Valves, pumps, and detection components have been developed within microfluidic channels via μFT using stimuli-responsive hydrogels. Chemical groups define the type of stimulus to which the hydrogel responds, and the physical properties (e.g., size or porosity) determine the response time. With a wide range of chemical and physical properties, hydrogels can be tuned to the application.

Other materials can self-assemble in various geometries; one such class of materials is amphiphilic molecules. Amphiphiles, such as lipid molecules, are versatile building blocks in any biological organism. The molecules consist of hydrophobic and hydrophilic regions and, depending on their relative length, they can self-assemble to form micelles and bilayers in aqueous solutions (*17*; Figure 3). Both arrangements are found in nature in the form of cell and organelle membranes and vesicles. Over the past 30–40 years, vesicles have found applications as "containers" in the cosmetic and drug industries and as cleaning agents in detergents. Amphiphiles are also widely used to pattern solid surfaces. Depending on the interfacial energy, the hydrophobic or hydrophilic end of the molecules makes direct contact with the surface and self-assembles to form a monolayer, or SAM. In microchannels, where the surface area to volume ratio is very large, fluid flow can be manipulated by controlling the surface properties (*18*, *19*).

Fluid control and manipulation

Fluids are typically transported inside microchannels using a syringe pump or pressure head for physically driven flows or an electric field for electrokinetic flows. All these methods require an external force or instrumentation. To develop a truly self-contained autonomous microscale system, the driving force to move the fluid must come from within the device.

When a responsive hydrogel undergoes a phase transition, it exerts a force on the channel wall, which when applied to an elastic membrane, "squeezes out" or dispenses fluid from a channel (or chamber) adjacent to the membrane (*20*; Figure 2b). In addition, the flow rate through an orifice can be dynamically controlled by coupling the change in volume of a hydrogel post to the size of the orifice (*21*; Figure 2b). A feedback mechanism can be engineered into the component by using a pH-sensitive hydrogel. The result is that a constant output pH is maintained, despite perturbations of the input flow rate through autonomous control of the flow rate of a compensating buffer through an orifice. Such a self-regulated system is important for reactions and assays that are sensitive to environmental conditions and holds promise for intelligent drug delivery.



Valves, pumps, and detection components have been developed within microfluidic channels using stimuli-responsive hydrogels.

Valves direct flow in a microchannel and can be either actively or passively operated. A conventional active valve consists of a diaphragm coupled to an actuator that externally controls the diaphragm to open or close the channel. This approach is challenging to construct because the diaphragm must be flexible and integrable with the actuator and because of unfavorable forces at this small scale for some actuation methods. A simpler valve was designed by using a responsive hydrogel as the active control. A cylindrical post slightly smaller than the channel width was fabricated by LP3 (Figure 2c). The cylinder swelled to block the channel completely when the structure was subjected to an appropriate stimulus. Researchers have explored hydrogel materials that are sensitive to glucose (*22*), temperature (*23*), and pH (*14*) for this purpose.

A passive valve does not require an actuator and is usually directly controlled by the pressure of the fluid. These valves are typically closed and cannot distinguish the direction of fluid flow. When pressure exerted by the fluid reaches a threshold value, the valve opens, and the fluid flows past. In the conventional design, a flexible diaphragm is fabricated, which can be displaced by the fluid's internal pressure. However, incorporating the membrane can be labor-intensive, and the pressure required to move the diaphragm can be very large, which may be impractical for an autonomous or portable system. Mastrangelo and others have demonstrated that a fluid can be controlled inside a microchannel by patterning a patch of SAMs perpendicular to the direction of flow so that they change the surface energy of the channel walls (*24*; Figure 2c). Because the pressure required to initiate flow through a hydrophobic channel is larger than that needed for a hydrophilic channel, the fluid can be stopped at a desired location below a certain threshold pressure.

Another class of valves, referred to as check valves, allows flow in only one direction and is important in systems where backflow and contamination between fluids must be prevented. Natural valves in the heart and veins are different forms of check valves; they are soft and deformable. In one direction, the deformation favors blood flow, while in the other direction, the fluid flow forces the valves to close. This bio-inspired design is seen in a check valve consisting of two strips of hydrogel, each composed of a responsive and nonresponsive part fabricated sequentially using LP3 (*25*; Figure 2c) In the presence of the stimulus, only the responsive part of the strips swell, causing them to bend. The shape of the valve in its swollen or activated state is similar to the valves in veins. The activated valve is normally closed, but upon exerting pressure, the valve deforms, favoring flow only in one direction.

An in situ polymerized hydrogel plug was used to create a "mobile" valve inside a microchannel (*26*). The materials for the channel and plug were chosen so that there was minimal adhesion between them. When high pressure was applied to the hydrogel plug, it moved in the microchannel to close specific channels. Although high external pressure is required to move the plug, this approach gives the user freedom to open or close channels on the basis of the application.

Another check valve design takes advantage of the spring force of the swelling hydrogel (Figure 2c). In this design, a hydrogel piston was anchored at one end while the "head" was allowed to move into a constricted region or "valve neck". This movement is brought about by the spring force generated in the piston during swelling and allows for the valve to assemble into its active form. Once assembled, the valve allows fluid flow in only one direction.

In a microsystem, a filter is useful in sample preparation and

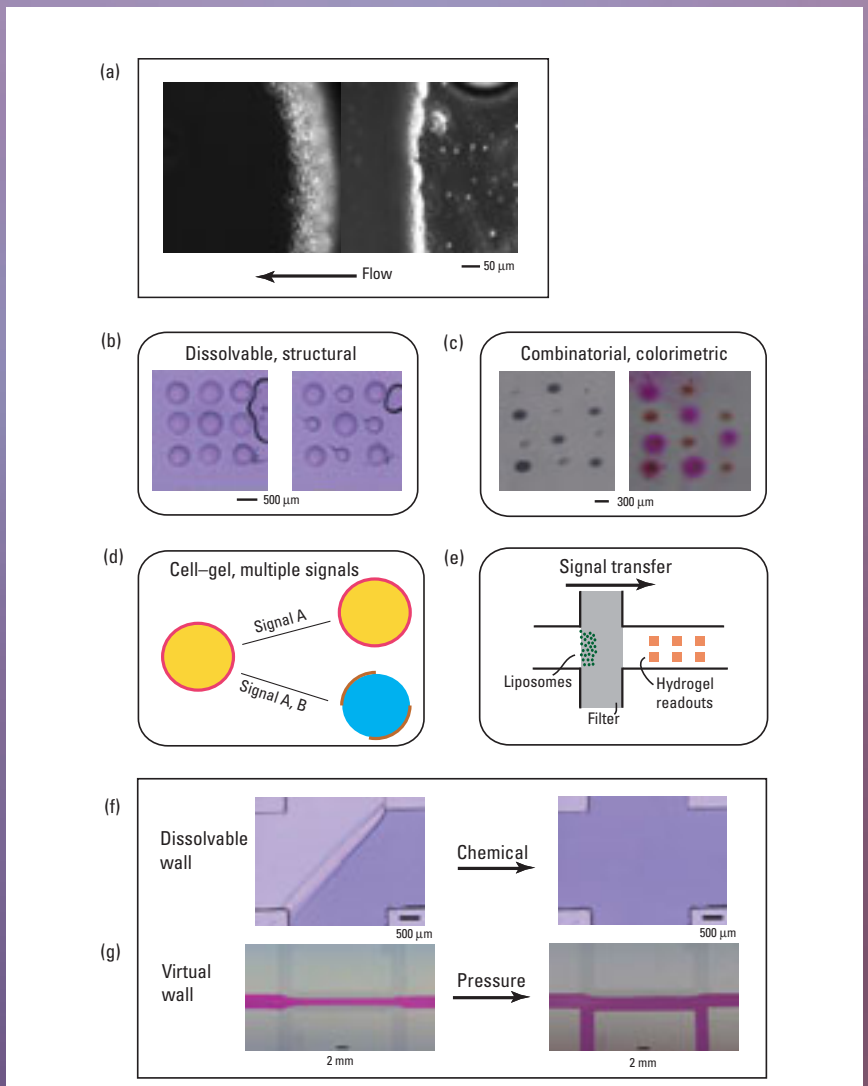


FIGURE 4. Hydrogel-based microfluidic components fabricated using μFT methods for performing specific processes in the microsystem.

(a) Porous filters have been fabricated in situ using emulsion photopolymerization. Separation efficiency of blood cells was comparable to centrifuging. The sensing capability of hydrogels offers various detection schemes such as the (b) structural and (c) color changes that can be seen by the human eye. (d) Combining hydrogels with amphiphilic molecules forms a cell–gel sensor. (e) Combining liposomes and responsive hydrogel structures generates signal transfer schemes. (f) Physical and (g) virtual walls have been created inside microchannels to form temporary compartments for isolating reagents or fabrication processes. The physical wall was removed by flowing chemicals, and the virtual wall was broken when the fluid pressure inside the microchannel was increased. [(a), (c), and (g) adapted with permission from Refs. 30, 33, and 34, respectively.]

purification. Filters made of porous materials also provide a large area where a surface-catalyzed reaction (*27*) or sample detection may be carried out. Another function of a filter can be to provide docking stations to hold a cell (e.g., ova or embryo [*28*]) or other objects (e.g., bead or vesicle [*29*]) in a known section of the microchannel.

A porous filter was prepared inside the microchannel by "emulsion photopolymerization" of a mixture of monomer, porogen (e.g., water or salts), a cross-linker, and a photoinitiator by using μFT methods. An emulsion consisting of monomer droplets was formed by agitating the mixture. A contiguous polymer network surrounded by interconnected paths or pores was formed upon polymerization and drying to remove the water. The size and distribution of pores and the mechanical properties of the filter depend on numerous factors, including the composition of the prepolymer mixture, the polymerization technique, and the surface energy of the channel walls. This variability allows a filter's properties to be adjusted to fit an application.

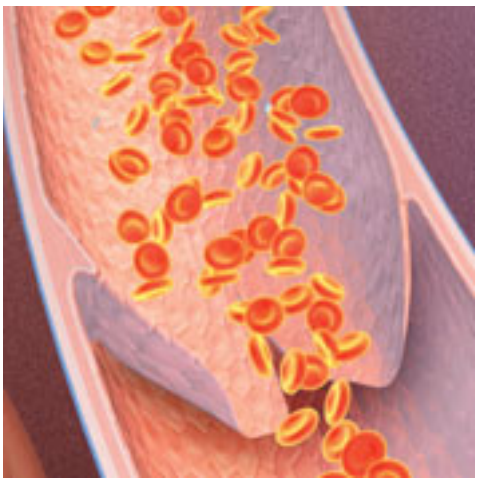
A fabricated filter was used to prepare whole-blood samples for diagnostic studies (Figure 4a). Cell separation from whole blood is often required when the microsystem is used as a diagnostic device for assaying body fluid directly from a patient or end user. The current methodology for separation is centrifugation, which is difficult to use for nanoliter and microliter sample volumes because the inertial forces diminish with sample size. Moreover, centrifugation requires external power, which could be impractical in a portable diagnostic device. Separation by a porous filter is as efficient as centrifugation and retains the advantage of using small volumes (*30*).

Detection

A typical detector consists of a sensor to test the sample and a display unit to present the results to the user. Researchers have explored several methods, such as conductivity and UV–vis and fluorescence spectroscopies, to detect and monitor the environment inside micrometer-sized devices (*31*). These techniques are usually associated with complex instrumentation and power requirements, making fabrication and portability of the system difficult. The ability to provide readout or display capabilities in

an autonomous manner would be beneficial, particularly for low-cost disposable diagnostic applications. One advantage of using responsive hydrogels is that environmental conditions are reflected in their physical properties, which can be perceived by the human eye and interpreted intelligently, without the need for external instruments or computation.

The phase transition in a responsive hydrogel is brought about by changes in specific groups on the polymer backbone. In a pH-responsive hydrogel, this change is the ionization of a chemical group. Another way to engineer responsiveness is to incorporate a cross-linker that can be cleaved by chemical or enzymatic reactions, resulting in a volume change or disintegration of the hydrogel. Yu et al. have demonstrated a chemoresponsive hydrogel in the μFT platform (*10*). The cross-linker (*N*,*N*′-cystamine-bisacrylamide) contains disulfide bonds, which were broken in the presence of a reducing agent, leading to disintegration of the hydrogel.



Patterning hydrophobic and hydrophilic regions can create temporary compartments.

Another detection scheme, which is based on structural changes, is to create hydrogels in which the matrix is held by a specific interaction (Figure 4b). For example, Miyata and co-workers developed a bioresponsive hydrogel in which the cross-linkers were formed by antigen–antibody interaction (*32*). In the presence of a free antigen, the cross-linkers were dissolved, resulting in volumetric expansion of the structure and thus recognition of the specific antigen. The detection selectivity thus depends on the type of cross-linker, and the sensitivity will depend on the density of cross-linkers in the polymer matrix. The disappearance or volume change in the hydrogel sensor can be easily visualized without other instrumentation. An unaided eye can detect the disappearance of a 100-μm circle or a similar change in the diameter of a post within a microchannel.

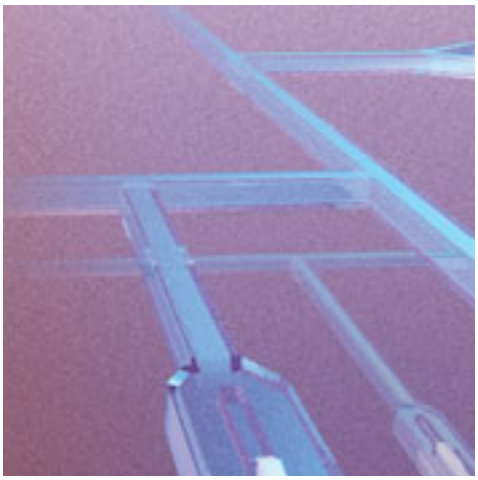
Alternatively, the action (dissolution or volume change) can be used to trigger a color-producing reaction. The eye easily perceives color change, and this simple detection mechanism can be exploited by entrapping ion-sensitive dyes in a hydrogel matrix (*33*). Both the dye and the hydrogel have a specific response function to the local environment, changes which are reflected in the color and size of the readout structure. A combinatorial readout display consisting of a layout of different dyes was fabricated using LP3 and tested to display pH changes inside the microchannel (Figure 4c). The basic colorimetric format was extended to include biomolecule detection and chemical reactions by entrapping proteins in the polymer. One advantage of using the dye–immobilized-gel construct is that the high volume support of the hydrogel provides sufficient color signal intensity for perception by the naked eye, unlike surface-immobilized dyes that typically require optical or electronic detection because of low intensities. The wide availability of dyes sensitive to both chemical and biological agents will be extended to many applications, such as rapid screening of combinatorial libraries. Moreover, polymer matrixes responsive to other stimuli, such as temperature, can provide readouts that are sensitive to multiple stimuli.

Researchers are exploring cells as potential biosensors for the recognition of pathogens. However, using cells comes with a cost, namely, maintenance of appropriate environments and a supply of nutrients. To produce sensors with similar capabilities, researchers have developed "artificial" cells in the μFT platform by overlaying a monolayer of amphiphilic molecules onto a responsive hydrogel (*9*). The lipid molecules protect the hydrogel from the external environment just as a cell would. When the monolayer is disrupted because of mechanical stress or chemical molecules, the hydrogel is exposed to the environment. If the environment favors a phase transition or a color change, a response can be detected.

The cell–gel system can be modified to detect specific molecules by embedding surface receptors in the lipid layer so that upon recognition, the monolayer is disrupted. As the lipid layer and the hydrogel respond to different stimuli, cell–gel sensors are activated only in the presence of both stimuli (Figure 4d). This mechanism may help minimize false positives. Moreover, this construct provides flexibility because various combinations of stimuli-sensitive materials can be engineered into the component. A similar mechanism can be found in many biological processes, where at least two signals are required to elicit a response. For example, simultaneous recognition of two signals is required to activate T cells (in the immune system) against a tumor or virus-infected cells.

Relying completely on the responsive hydrogel can limit the types of signals and molecules that may be detected. For each type of signal, the raw materials for the hydrogel must be created individually, which can be both difficult and time-consuming. A more efficient method would be to use a signal transfer mechanism commonly seen in signaling cascades of biological systems. In this mechanism, the sensitivity of one interaction initiates a common cascade, and, in most cases, the signal is amplified during the transfer. For example, although various receptors in

the cell membrane are sensitive to specific molecules, the binding events in cells are relayed to the nucleus via a common kinase pathway. A similar strategy has been developed using the μFT platform, wherein functional liposomes (lipid vesicles) were used in conjugation with a responsive hydrogel (*29*). The liposome contained the stimulus for the hydrogel and was held by a porous filter, upstream from the hydrogel. In the presence of an external chemical or biological signal, specific reactions were initiated at the liposome's surface, leading to its lysis and subsequent spilling of the contents, thus relaying the signal to the hydrogel (Figure 4e).



The scale at which these devices operate will aid studies directed toward understanding biological phenomena and processes at the cellular level.

Compartmentalization and integration

In a broad sense, the construction of channel networks creates compartments. Our focus is on temporary compartments, wherein the walls can be removed by an external stimulus. Temporary isolation will prevent contamination from another process or reactant. The compartments can be formed by either fabricating a polymeric structure (a physical wall; Figure 4f) or changing the surface energy of an existing channel wall (a virtual wall; Figure 4g). Dissolvable physical walls have been fabricated by LP3 using chemoresponsive hydrogels that contain disulfide cross-linkers, which were cleaved in the presence of a reducing agent.

Because the surface energy of the channel walls influences the flow profile inside the microchannels, patterning hydrophobic and hydrophilic regions can create temporary compartments. At low pressures, aqueous fluids are confined to hydrophilic regions because the interfaces between the patterns act as virtual walls. However, the walls break down when the pressure is increased past a certain threshold, allowing fluid flow through the channel. Such virtual walls have been built by patterning hydrophobic regions with SAMs using laminar flow. The threshold pressure to break the walls depends on surface hydrophobicity, therefore multiple compartments with different threshold pressures can be constructed by patterning the channel walls with SAMs with different chemical structures (*34*).

A microsystem containing a built-in storage facility (a cavity in a polymer) for reagents would be a useful component in a portable device or personalized diagnostic kit. Such reservoirs have been constructed using elastomeric materials or swollen hydrogels. In the presence of a stimulus, the hydrogel shrinks, spilling out the reagents. Such schemes have been explored for developing stimuli-specific drug carriers and can be easily incorporated into the μFT platform (*35*).

μFT provides the end user with the flexibility to design and fabricate microsystems on an ad hoc basis to accommodate the various process step sequences among assays. The connectivity between the analytical processes can be improved by incorporating a decision mechanism, wherein an end or byproduct of a preceding process activates a subsequent component or process. For example, a physical wall separating two reagents can be dissolved by the end product of a preceding reaction step, initiating the next step of the assay. Furthermore, because the components are fabricated in situ, the integration process is part of the –design and fabrication. Therefore, the tasks for developing a microsystem are reduced to designing the component layout, choosing appropriate materials, and fabricating it—all of which can be performed by the end user. However, because most of the components are created from monomer solutions and require solvents to remove unpolymerized materials, compatibility between polymerized structures and monomer solutions of the next component (or solvent) to be fabricated must be addressed. By judiciously choosing the sequence in which the components are fabricated, such compatibility issues can be averted (*29*).

Merging technologies

The scale at which these devices operate will aid studies directed toward understanding biological phenomena and processes at the cellular level (*36*). However, the potential of microfluidic devices is yet to be wholly realized. One of the impediments we see is the availability of a platform that truly mimics the laboratory workspace in the sense of offering containers in various shapes and sizes, choices in material properties, freedom to arrange the process steps and rearrange them when the reaction fails, and the ability to interface with electronics or existing instrumentation.

The μFT approach described provides a flexible fabrication platform, offering the end user the freedom in choosing the apparatuses and dictating the reaction sequence. However, traditional fabrication approaches, such as deposition, will be required to interface electronics to the microsystem. Moreover, because hydrogels are also responsive to electric fields, the properties of the components could be fine-tuned once interfaced. For example, platinum electrodes were patterned and

used to control the extent of hydrogel swelling via an electric stimulus (*37*).

Traditional approaches to system design can benefit from the μFT platform. For example, in collaboration with Sohn's group at Princeton University, we have used the flexibility inherent in μFT to design and construct an opposing electrode configuration that is normally difficult to achieve by traditional microfabrication approaches. The resulting microfluidic sensing device performs high-frequency impedance measurements of cells and molecules. Thus, the strengths of both approaches can and should be coupled to produce integrated microsystems that may be used for diagnosis, to perform reactions, and as sensors in engineering applications.

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Jaisree Moorthy is a graduate research assistant and David J. Beebe is a professor at the University of Wisconsin–Madison. Moorthy's research interests include development of microfluidic platforms for studying interactions between biolmolecules. Beebe's research interests include development of organic microfabrication methods to facilitate advances in medicine and biology and the study of the effects of microenvironments on living systems. Address correspondence about this article to Beebe at Department of Biomedical Engineering, University of Wisconsin–Madison, Madison, WI 53706 (dbeebe@engr.wisc.edu).

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