FLEXIBLE METHODS FOR MICROFLUIDICS

Devices for handling nanoliter quantities of fluids are creating new fabrication challenges and finding new applications in biology, chemistry, and materials science.

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Biotechnology is increasingly about large numbers of experiments, such as analyses of DNA or of drugs, screening of patients, and combinatorial syntheses. All of these procedures require handling fluids. As the number of experiments has grown, the devices used to carry them out have shrunk, and the strategy of "smaller is better" has begun to transform the world of fluidics as it has transformed the world of electronics.

The need in biotechnology applications to manipulate fluids moving in small channels—a process called microfluidics—has stimulated three new areas of research: development of new methods for fabricating fluidic systems, invention of components from which to assemble functionally complex fluidic devices, and examination of the fundamental behavior of fluids in small channels.[1] Developments in microfluidic technology are also contributing to new experiments in fundamental biology, materials science, and physical chemistry.

Interest in microfluidics has been largely motivated by applications, and dimensions and fluids are dictated by these applications. The most mature microfluidic technology is ink-jet printing, which uses orifices less than 100 μm in diameter for the generation of drops of ink. Ink-jet printing is rapidly finding a place in biotechnology for the delivery of reagents to microscopic reactors and for the deposition of DNA into arrays on the surface of biochips. Capillary electrophoresis—a widely used technique for separating different chemical species in aqueous solutions of biological samples—manipulates samples in capillaries that are typically 50 μm in inner diameter. Hand-held systems developed by I-Stat Corp for hospital-based analysis of serum electrolytes were the first commercially developed small analytical systems, and use submillimeter-sized channels. The complex devices now being developed for biological applications—with the analysis of DNA (for genetics and genomics) and proteins (proteomics), and biodefense being the most important—typically involve aqueous solutions and 50- to 100-μm channels. A number of companies are now pursuing the commercialization of microfluidic devices.

Unlike microelectronics, in which the current emphasis is on reducing the size of transistors, microfluidics is focusing on making more complex systems of channels with more sophisticated fluid-handling capabilities, rather than reducing the size of the channels. These systems require the same types of components as larger fluid-handling systems: pumps, valves, mixers, filters, separators, and the like. Although the sizes of channels are large relative to the size of features in microelectronic devices, they are small enough so that flows in them behave quite differently than do the large-scale flows that are familiar from everyday life. The components needed at small scales are therefore often quite different from those used at large scales.

To design the components required for complex microfluidic systems, it is first necessary to understand the properties of fluids flowing in small channels. Fortunately, new, flexible methods of fabricating microchannels, combined with imaging techniques such as confocal microscopy that make it possible to quantify flows in these channels, allow the physics of microflows to be examined at previously unattainable resolution.

The first microfluidic devices, developed by Andreas Manz (now at Imperial College), Jed Harrison (now at the University of Alberta), Michael Ramsey (Oak Ridge National Laboratory), and others in the early 1990s, were fabricated in silicon and glass by conventional, planar fabrication techniques—photolithography and etching—adapted from the microelectronics industry.[2] These methods are precise but expensive, inflexible, and poorly suited to exploratory work. Recently, our laboratory and others have applied soft lithography to the fabrication of microfluidic devices. Described in box 1, these nonphotolithographic microfabrication methods are based on printing and molding organic materials, and are much more straightforward than photolithography for making both prototype devices and special-purpose devices for physical investigations. These methods also make it practical to build three-dimensional (3D) networks of channels and components. They thus offer access to new types of fluidic elements, such as valves and pumps fabricated of elastomeric materials. In addition, they offer the high level of control over the molecular structure of the channel surfaces that is required in biological applications. Perhaps most important, they bring the technology needed to fabricate complex microfluidic devices out of clean rooms and into the laboratories of the biologists and chemists who are the users of these devices.

Flows in microchannels

Laminar flow is the definitive characteristic of microfluidics. Fluids flowing in channels with dimensions on the order of 50 μm and at readily achievable flow speeds are characterized by low Reynolds number, *Re*. As described in box 2, flows in this regime are laminar, not turbulent: The surfaces of constant flow speed are smooth over the typical dimension of the system, and random fluctuations of the flow in time are absent. In the long, narrow geometries of microchannels, flows are also predominantly uniaxial: The entire fluid moves parallel to the local orientation of the walls. The significance of uniaxial laminar flow is that all transport of momentum, mass, and heat in the direction normal to the flow is left to molecular mecha-

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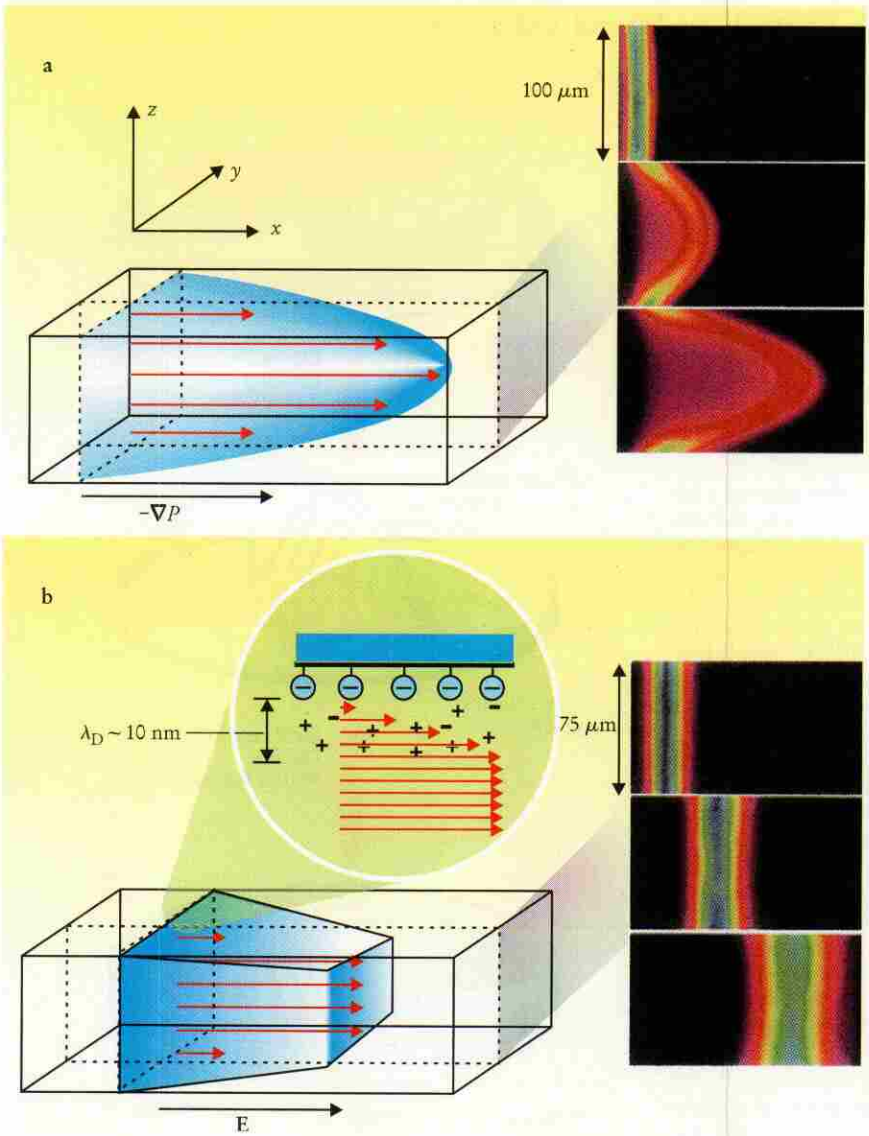


FIGURE 1. FLOW PROFILES IN microchannels. **(a)** A pressure gradient, $-\nabla P$, along a channel generates a parabolic or Poiseuille flow profile in the channel. The velocity of the flow varies across the entire cross-sectional area of the channel. On the right is an experimental measurement of the distortion of a volume of fluid in a Poiseuille flow. The frames show the state of the volume of fluid 0, 66, and 165 ms after the creation of a fluorescent molecule. **(b)** In electroosmotic (EO) flow in a channel, motion is induced by an applied electric field **E**. The flow speed only varies within the so-called Debye screening layer, of thickness λ_D. On the right is an experimental measurement of the distortion of a volume of fluid in an EO flow. The frames show the state of the fluorescent volume of fluid 0, 66, and 165 ms after the creation of a fluorescent molecule.[3]

nisms: molecular viscosity, molecular diffusivity, and thermal conductivity.

Pumping in microfluidic systems is accomplished using either pressure or, for water and other very polar solvents, electric fields. Pressure-driven motion, termed Poiseuille flow, is well understood but has two disadvantages. First, designing and fabricating reliable mechanical pumps in the traditional materials of silicon and glass has been difficult: These devices require multiple levels of fabrication, and are easily damaged by particles of dust and contaminants in the fluid. Second, as illustrated in figure 1a, Poiseuille flow is characterized by a parabolic velocity profile over the cross section of the channel, with zero velocity at the walls and a maximum at the channel's center. This nonuniformity in flow speed occurs because the imposed pressure exerts a uniform force over the cross-sectional area of the channel, but momentum leaves the flow, due to interactions with the solid boundary, only at the walls (see box 2). The parabolic flow profile distorts a volume of fluid as it flows down the channel. When used to separate different molecules in solution, such a flow spatially broadens the bands of distinct species.[3]

Electrically driven flow, known as electroosmosis, offers a useful alternative to pressure-driven flow of water, but has its own weaknesses: sensitivity to impurities that adsorb on the wall of the channel, ohmic generation of heat in the fluid, and the need for high voltages (on the order of kilovolts). In electroosmosis, illustrated in figure 1b, an electric field generates a net force on the fluid near the interface of the fluid with its solid boundaries, where a small separation of charge occurs due to the equilibrium adsorption and desorption of ions. For water in contact with silica, the ionization of silanol groups ($Si–OH \rightleftharpoons Si–O^- + H^+$) leads to about one negative charge per 16 nm^2 of the silica surface. The excess cations are localized near the interface by Coulombic interactions. This charged region near the interface, called the Debye screening layer, has a thickness λ_D that is typically less than 10 nm for aqueous buffers used in biochemistry. As the fluid in the Debye layer moves toward the oppositely charged electrode, it carries with it the bulk of the liquid in the channel. As a result, the velocity profile is essentially flat across the channel.[3] This type of flow is ideal for separations based on the charge-to-size ratio of the molecular components of biological samples in solution, since broadening of the separated bands of differing species occurs only by diffusion, not as a result of the differences in flow velocity across the channel. Because of this tendency to separate species, electroosmotic flow is usually not well suited for transporting multicomponent solutions when separation is not desired.

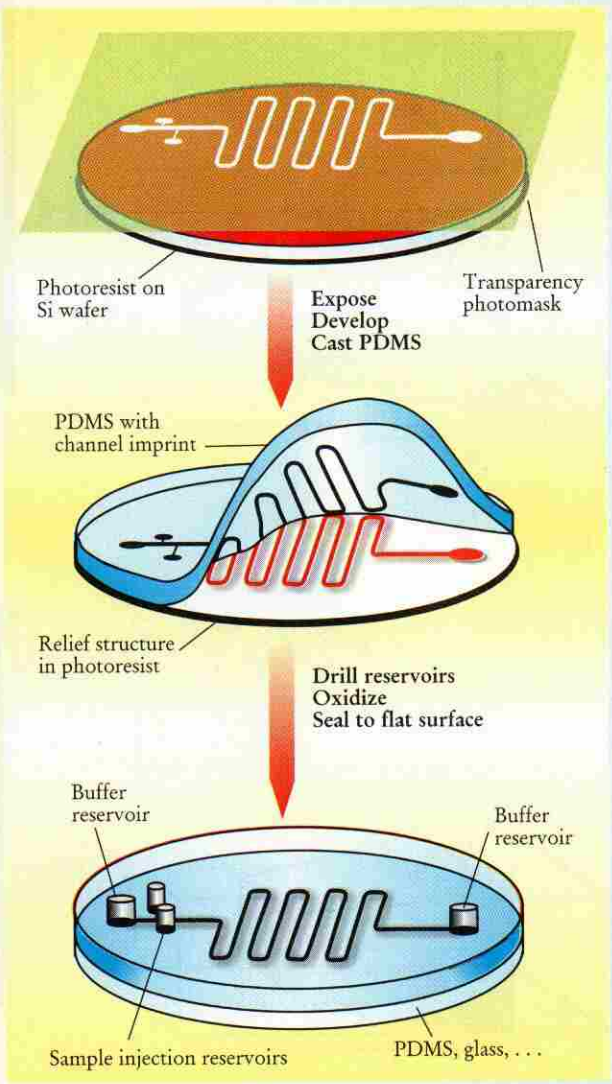
In the laminar flows generated by these pumping schemes, adjacent streams of fluids with different chemical composition remain distinct except for diffusive mixing at their interface. We have studied this diffusion process in Poiseuille flows using fluorescence confocal microscopy. The confocal microscope allows us to visualize the 3D shape of the diffusively mixed region between streams of solutions that contain molecules that become fluorescent when they react with one another. We found

Box 1. Fabricating Microfluidic Devices

The standard methods for fabricating microfluidic devices were inherited from the microelectronics industry. Patterns of etch resists are defined on rigid, planar substrates such as silicon with photolithography or electron-beam lithography, and relief structures are then created with reactive-ion or wet etching.[2,6] The advantages of this methodology are high spatial resolution (about 100 nm) and parallel processing—photolithography and etching create all features in a single step. The highly developed methods of photolithography, however, have disadvantages for the fabrication of microfluidic devices: They are expensive, they require inconvenient methods for the sealing of channel structures, and they provide no simple method of interconnecting channel systems (such as for sample collection, introduction, and analysis).

Organic polymers offer an alternative technology for the fabrication of microfluidic systems. These materials are especially useful for biological applications, in which aqueous solutions are almost universally used and the highest temperatures required (about 120°C for sterilization) are easily tolerated by many polymers. Molding and printing are the technologies most commonly used to fabricate microstructures from polymers. We and others have developed a set of methods for the rapid prototyping of microfluidic devices based on soft lithography. We commonly make the microfluidic devices out of the silicone elastomer PDMS (polydimethylsiloxane). PDMS has a number of useful properties, including low cost, low toxicity, and commercial availability; transparency from the visible into the near ultraviolet; chemical inertness; versatile surface chemistry; and mechanical flexibility and durability. Sealing can be achieved by oxidizing the PDMS surface; adhesives are not required.

The figure shows how we use a transparency printed on a high-resolution printer as a mask for photolithography. A printer using about 5000 dots per inch generates smooth 50-μm features, and 20-μm features with substantial edge roughness. With a single structure defined in photoresist by photolithography, we can generate many replicas in PDMS by molding. To form a sealed channel structure, we oxidize the surface of the PDMS replica in a low-temperature plasma and bring it into contact with clean glass, silica, or another piece of surface-activated PDMS. This seal can withstand pressures up to 5 bars. Without oxidation, PDMS will also form a watertight, noncovalent seal when pressed against itself, glass, or most other smooth surfaces; these reversible seals are useful when a demountable fluidic device is required.[14]



Variations on these soft lithographic methods have been developed recently by Steve Quake's group at Caltech and David Beebe's group at the University of Wisconsin.[15]

that the width of the intermixed region grows as $(D\tau)^{1/2}$ near the center of the channel, where the flow speed is almost uniform, and as $(D\tau)^{1/3}$ near the top and bottom walls, where the flow speed is changing rapidly as a function of the distance from the wall. Here, D is the molecular diffusivity and τ is the time that the two streams have been in contact. These results agree with dimensional scaling arguments that extend the classic result in transport theory, known as the Lévêque problem, for diffusion perpendicular to the walls.[4]

More complicated, nonuniaxial fluid motion can be generated by creating patterns along the walls of microchannels. The dependence of the speed and direction of electroosmotic flow on the charge of a channel's walls means that flows can be tailored by controlling surface properties. Figure 2 shows an example in which an applied field parallel to a surface patterned with regions of positive and negative charge generates convection rolls inside a microchannel.[5] Armand Ajdari of ESPCI in Paris has modeled a variety of effects related to electroosmosis in the presence of nonuniform distributions of surface charge and variable channel geometry.

Another pumping scheme that involves patterning the properties of the walls of a microchannel uses surface tension to move drops of a fluid surrounded by air. Spatial variations in the temperature of the walls of the channel create gradients in the tension of the liquid–vapor interface of the drop: The surface tension decreases as the temperature increases. By building resistive heating elements into the microchannel wall, the group of Mark Burns at the University of Michigan can move drops of fluid in a channel by heating the wall near the rear of the drop. The decrease in the surface tension from the front to the back of the drop pulls the drop through the channel. The advantage of moving independent drops of solution in microchannels is that the contents of each drop may be

kept separate from that of neighboring drops.[6] (See also PHYSICS TODAY, January 2000, page 9.)

Microfluidic components

Pumps, valves, and mixers are some of the basic building blocks of any integrated microfluidic system. There is still no broad agreement on the best designs for these components or even on the materials to be used for their construction; the technology is still a work in progress. Ultimately, most bioanalytical systems will probably be made of polymers because these materials are inexpensive. Applications involving organic solvents or high temperatures may require glass.

Figure 3a shows an example from our group of a valve that exploits the elastomeric character of polydimethylsiloxane (PDMS). This passive check valve is a fluidic rectifier: Pressure in one side of the device prevents fluid from flowing through the device; pressure in the other side opens a flap and allows the fluid to flow.

Figure 3b shows a mixer designed by David Beebe's group at the University of Wisconsin (formerly at the University of Illinois) and illustrates the types of new devices that must be developed to perform familiar functions when turbulence is no longer available as an aid. This 3D serpentine channel acts as a passive mixer for laminarly flowing fluids based on a type of chaotic flow known as chaotic advection. Chaotic advection appears in certain steady 3D flows and time-dependent 2D flows, and mixes the fluid by continuously stretching different volumes of the fluid and folding them into one another. In a qualitative sense, the path taken by a given fluid element in the flow depends in a sensitive way on its encounters with a series of weak secondary flows or eddies, present even at low *Re* in the corners of channels, that transport the element across the flow.[7]

The integration of components into a functional device is facilitated by the use of soft lithography. Steve Quake and coworkers at Caltech[8] have integrated pumps and valves to generate a micro flow cytometer, a device that sorts biological cells using a T-junction with pumps and valves in the arms controlled based on the signal from a fluorescence microscope (see figure 4). A similar T-junction channel system can measure the size of individual, fluorescently labeled DNA fragments and sort them based on their size. The small detection volume (less than 1 pL) in these microfabricated sorters increases the sensitivity of the device for the detection of single cells or molecules by decreasing the background signal due to the carrier fluid.

Microfluidics in the laboratory

With the availability of simple techniques for fabrication and basic designs for components, microfluidic devices become versatile tools. One problem addressed by these devices is that of delivering reagents to the surface of a cell with subcellular accuracy. The strategy we have used is to allow the cell to attach to the floor of a Y-shaped microchannel system and then to deliver reagents to it in streams of laminarly flowing buffer, as shown in figure 5a. The cell lies downstream from the Y. Two different aqueous streams are pumped into the two arms of the Y. One is an aqueous buffer solution of trypsin, an enzyme that cleaves proteins, commonly used in biology to disconnect an attached cell from its substrate by cleaving the proteins that connect the two. The second stream contains buffer alone. Because trypsin has a high molecular weight (about 35 000 atomic mass units) and thus a low diffusivity (about 10^{-6} cm^2/s), blurring of the interface between the two streams is relatively slow. The position of the interface in the channel can be controlled with an accuracy of a few microns by controlling the rate at which liquid flows into the two arms of the Y. In this experiment, the interface between the streams was centered over a cell. The trypsin released half of the cell from the substrate; the half exposed only to buffer was unaffected. This ability to treat a portion of a cell selectively with a reagent present in a stream of flowing buffer provides new capabilities to cell biology. For example, scientists can conduct experiments on one part of a cell and use the other part as a control, or they can label part of the cell surface (or, in some cases, the cell interior) and monitor the

Box 2. Fluid Mechanics in Microchannels

The first step in modeling a flow is to predict if the flow will be laminar or turbulent based on the Reynolds number, *Re*. The Reynolds number is the ratio of the inertial forces to the viscous forces acting on a small element of fluid. In microchannel flow, the Reynolds number can be written as the ratio of the kinetic energy of a volume of liquid in the flow to the energy dissipated by that volume in the shear caused by interactions with its solid boundaries: $Re = \rho U^2 V/\mu US = \rho UL/\mu$, where μ is the viscosity, ρ is the density, and U is the average flow speed of the fluid. The characteristic linear dimension L is the ratio of the volume V of the fluid to the surface area S of the walls that bound it. For example, for a microchannel that is 1 cm long, 1 mm wide, and 100 μm deep, L is 50 μm. It is found empirically that in pipes (for which L is the diameter) with smooth walls, flows are laminar for $Re < 2000$. Taking $L = 50$ μm for a microchannel and $\rho = 1$ g/cm^3 and $\mu = 0.01$ g/(cm s) for water, we find that flows in microchannels should be laminar for flow speeds less than 10 m/s. Standard flow speeds in microfluidic applications are 1 cm/s or less, giving $Re \leq 1$, so we can be confident in applying low-*Re* models to microfluidic flows.

At low *Re*, the infamous nonlinearities associated with the Navier–Stokes equation are absent. A uniaxial, incompressible flow at low *Re* is governed by

$$\frac{\partial u_x}{\partial t} = \frac{\mu}{\rho}\nabla^2 u_x - \frac{1}{\rho}\frac{dp}{dx} + \frac{1}{\rho}f_b. \qquad (1)$$

Here, the coordinates are as defined in figure 1a, u_x is the velocity field along the channel, p is the pressure, and f_b is the net force per unit volume acting on the fluid, known as the body force (due, for instance, to gravity or electromagnetic interactions). The boundary condition at a solid interface is $u_x = 0$. (Recent experiments have cast doubt on the universal validity of this no-slip condition, but for most cases, slip is negligible.[12])

Note the similarity of this equation to the diffusion equation ($\partial c/\partial t = D\nabla^2 c$) for the temporal evolution of the concentration of chemical species in a fluid, and the heat equation ($\partial T/\partial t = \alpha\nabla^2 T$) for the temporal evolution of distributions of temperature. In equation 1, we see that pressure gradients and body forces act as sources or sinks of fluid motion, and this motion spreads across the fluid diffusively with an effective diffusion constant of $\nu = \mu/\rho$, called the kinematic viscosity. Like the molecular diffusivity D and thermal diffusivity α, ν has its origins in the dynamics and interactions of molecules that transfer motion (coherent flowing motion in the case of ν) through the fluid.

While micrometer-scale structures are small enough to ensure low-*Re* behavior, they are not so small that molecular graininess of fluids becomes important. Even for gases in microchannels, many billions of molecules occupy a characteristic volume element of the flow in a microchannel with volume L^3; the fluid behaves like a continuum, and the Navier–Stokes equation gives an accurate description of the flow.[16]

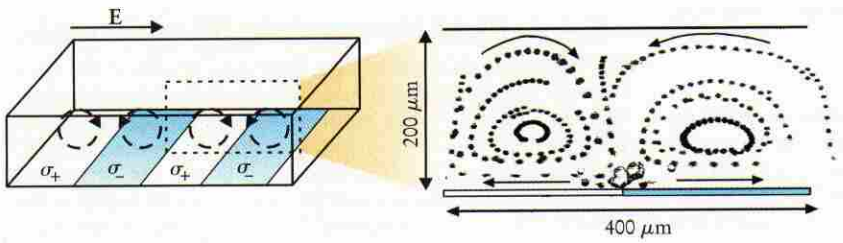
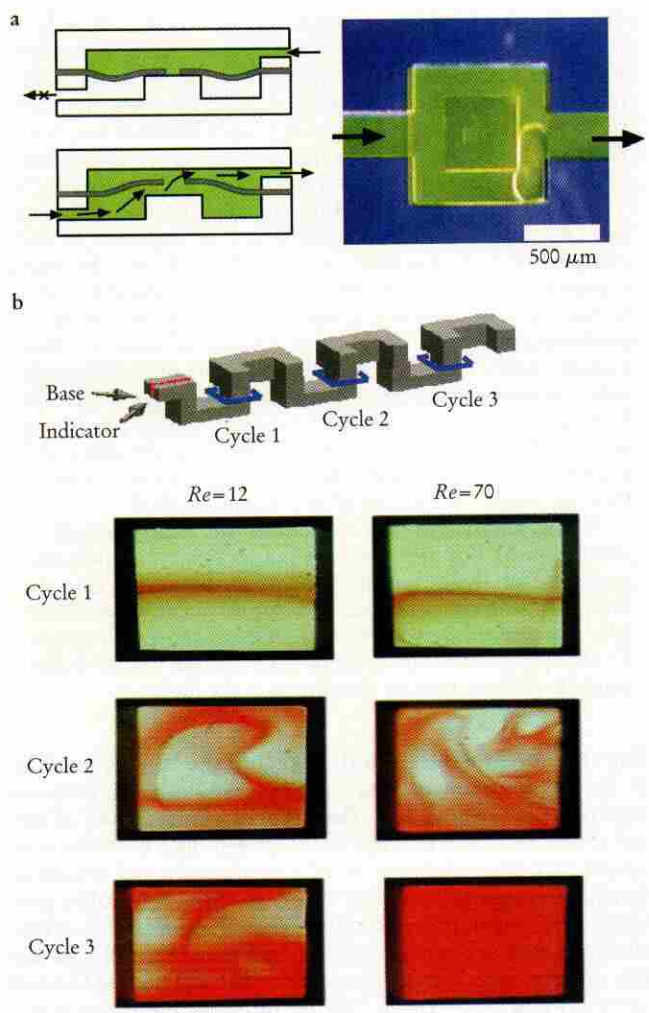


FIGURE 2. PATTERNING THE SURFACE can produce nonaxial flows in microchannels. Here, the bottom of the channel was patterned with regions of positive (σ_+) and negative (σ_-) surface charges, and fluid flow was driven by an applied electric field **E**. In the panel at the right, the trajectories of electrically neutral fluorescent beads (black dots) in two adjacent rolls reveal the streamlines of the flow. The black arrows indicate the direction of flow.[5]

evolution of the cell's position, structure, or environment.[9]

A second problem of broad interest in cell biology is that of observing the behavior of cells in gradients (see PHYSICS TODAY, January 2000, page 24). How does a cell sense the gradient and how does it respond to it? The network of channels in figure 5b forms gradients in the concentration of molecules present in a stream of buffer. The strategy is to start with a small number of fluid streams and then to allow them to divide and mix into multiple streams carrying the gradient. Recombination of these multiple streams into a single stream, under conditions of laminar flow, allows the gradient to be propagated along the length of the larger channel with only diffusional broadening of the gradient profile. In the microfluidic system shown, a linear gradient from red to green with three gradations is transformed into a linear gradient with nine gradations. The horizontal channels with serpentine profile allow the two streams flowing laminarly through them to mix their composition completely by diffusion. The serpentine form keeps the device compact; it does not influence mixing (unlike the chaotic advection mixer of figure 3b). By changing the number of input channels and the order in which the different initial solutions are injected, one can generate a variety of smooth gradients over relatively broad channels (up to millimeters) with a limited number of initial solutions.[10]

A third problem that can be addressed using laminar flows in microchannels is the measurement of the kinetics of chemical reactions that are initiated by mixing two or more components. The strategy used is to inject the reaction component solutions into adjacent streams flowing laminarly in a single channel. At the interface between the streams, the components mix by diffusion, which initiates the reaction. For steady injection of solutions of constant composition, the flow, the degree of mixing, and the state of reaction reach a steady state in the stationary frame of the laboratory; observing the state of the reaction at different distances downstream from the point of injection allows the temporal evolution of the reaction to be monitored. Figure 5c shows how controlled mixing between adjacent laminar flows has been used to study the early stages of protein folding. An advantage of this method is that the width of the mixing volume can be reduced, by hydrodynamic focusing, to lower the mixing time (which scales as the square of the width of the mixing volume). The experiments achieved submillisecond resolution for the measurement of the initial collapse of the protein.[11] (See also PHYSICS TODAY, June 1998, page 9.)



What's downstream

What's next for microfluidics? Perhaps nanofluidics; perhaps unusual fluids; certainly applications. Some work on nanometer-scale fluidic systems has already begun. The group of Harold Craighead at Cornell University has demonstrated that high-molecular-weight DNA can be

FIGURE 3. MICROFLUIDIC COMPONENTS. **(a)** A passive check valve in a multilayer structure of polydimethylsiloxane (PDMS). The upper schematic shows the valve in the closed position: Pressure applied from the right presses the flexible diaphragm against a post, blocking flow through the hole in the center of the diaphragm. The lower schematic shows the valve in the open position: Pressure applied from the left lifts the diaphragm off the post and allows flow through the diaphragm hole. The image on the right shows flow of a fluorescent fluid through the valve. **(b)** The design of this chaotic advection mixer exploits the character of laminar flow in a three-dimensional serpentine channel to mix adjacent streams in a single flow. A solution of pH indicator runs adjacent to a stream of basic solution and reveals the progress of mixing. As the two solutions mix, the indicator becomes red. Mixing is efficient even at low Reynolds numbers: Although the flow is laminar, there are weak eddies in the corners.[7]

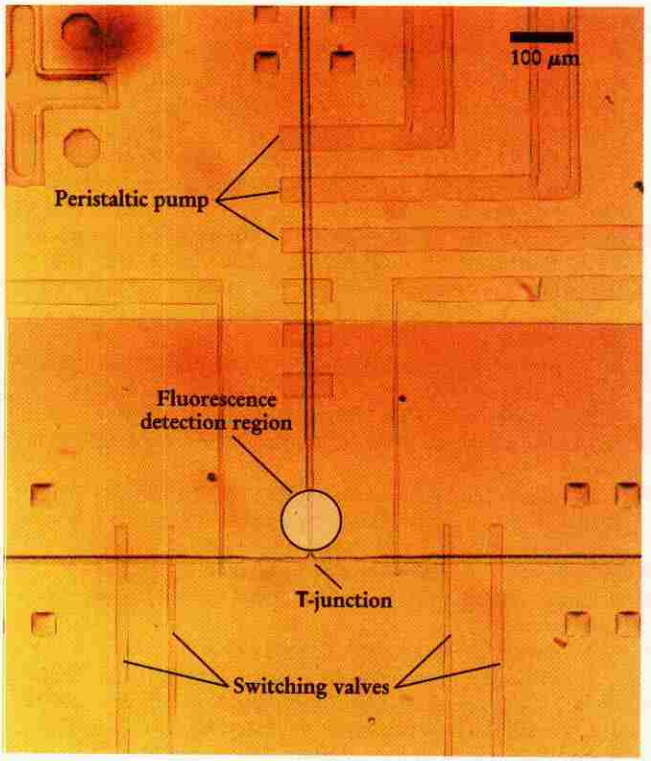


FIGURE 4. PRESSURE-DRIVEN CELL SORTER is one example of an integrated microfluidic device. The fluidic chip contains two layers of channels separated by a thin, flexible membrane of PDMS. Channels in the lower layer carry liquid samples for analysis; channels in the upper layer carry air. Valves are formed at the crossing points between channels in the two layers. Raising the air pressure in an upper channel deforms the interlayer membrane at the crossing point and closes the lower channel. Neighboring valves can be activated sequentially to act as a peristaltic pump. Such a three-valve arrangement, viewed here from above, pumps in a solution containing cells toward the T-junction. Double valves on each branch of the T direct the flow based on the signal from a fluorescence detector just upstream of the T. The cross pattern in the top left of the image is an alignment mark used in the fabrication of the multilayer polymer device.[8]

separated by electrophoresis in the absence of a gel in a microchannel about 50 μm wide and 10 cm long with a depth that alternates between 0.1 and 1 μm along its length. The thick sections of the channel retard the progress of small fragments more than large fragments. This trend is the opposite of what happens in standard gel electrophoresis, in which the small fragments travel more quickly than the larger ones.

Transport phenomena in nanoscopic channels are not well understood. Work in porous materials, theory, and simulations all suggest that qualitatively new behavior—such as slip at the liquid–solid interface or inhomogeneity of transport coefficients—will emerge as the size of channels shrinks.[12] There will be ways to exploit these phenomena in the design of new fluidic components.

The use of non-Newtonian fluids, for which the viscosity depends on the shear rate, is another promising direction for the development of microfluidics devices. Colloidal suspensions and concentrated polymer solutions, which include many biological fluids, are common

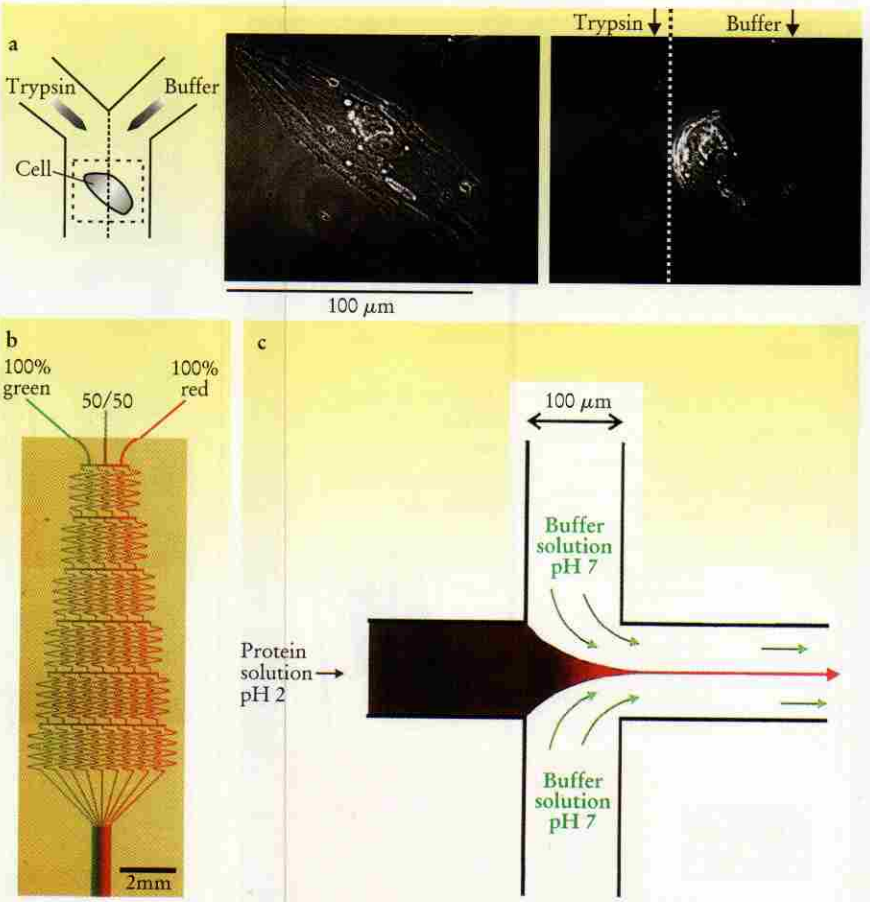


FIGURE 5. APPLICATION EXAMPLES. (a) Patterned flow of the protein-cleaving enzyme trypsin over a cell from the capillary wall of a cow. As shown at left, a stream containing a trypsin solution is injected beside a stream just containing buffer solution. The middle panel shows that the full cell is attached to the floor of the microchannel before treatment with trypsin. As seen at right, after the treatment, the half of the cell exposed to trypsin has become detached.[9] (b) Gradient formation by a network of microchannels. Three input dye solutions (100% green, 50% green/50% red, and 100% red) are transformed into nine output solutions with a linear gradient.[10] (c) Mixing of laminar flows in a microchannel makes possible the study of protein folding. A solution of a denatured protein (cytochrome c) at pH 2 is injected at a low flow rate between two rapidly flowing streams of buffer at pH 7. The width of the stream of protein solution narrows as it climbs to the speed of the neighboring streams. Diffusive mixing of the side streams into the protein solution raises the pH, which induces folding. The radius of gyration can be measured at different stages of folding by shining an x-ray beam at various positions along the channel.[11]

examples of non-Newtonian fluids. In such fluids, the viscosity either grows (shear thickening) or decreases (shear thinning) with increasing shear rate. There are examples of turbulentlike instabilities in flows of non-Newtonian fluids at low Reynolds number. These instabilities, named "elastic turbulence," could perhaps be generated in microfluidic channels to act as efficient mixers.[13]

While microfluidic devices are beginning to be commercialized, there is still no standard for even the simplest components such as pumps, valves, and mixers; the field remains open for exploration. This exploration is facilitated by the move toward simple fabrication methods—rapid prototyping based on the molding of elastomers—that reduce costs and delays. These methods also allow the mechanical properties of the flexible substrate to play a role in the function of the device.

Current microfluidic devices are usually attached to a thoroughly macroscopic box that contains power supplies, optical elements, and fluidic interfaces for the introduction and extraction of samples. An open challenge is the chip-scale integration of multiple fluidic components with electrical and optical controls into fully functional devices.

There also remains plenty of room for the invention of new applications of microfluidics, both in and out of the laboratory. Imagine a T-shirt made from a fabric of microchannels, carrying coolants and monitoring vital signs, and entirely powered by the body heat of the wearer. It's not impossible!

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