Reconfigurable microfluidics

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Abstract | Lab-on-a-chip devices leverage microfluidic technologies to enable chemical and biological processes at small scales. However, existing microfluidic channel networks are typically designed for the implementation of a single function or a well-defined protocol and do not allow the flexibility and real-time experimental decision-making essential to many scientific applications. In this Perspective, we highlight that reconfigurability and programmability of microfluidic platforms can support new functionalities that are beyond the reach of current lab-on-a-chip systems. We describe the ideal fully reconfigurable microfluidic device that can change its shape and function dynamically, which would allow researchers to tune a microscale experiment with the capacity to make real-time decisions. We review existing technologies that can dynamically control microscale flows, suggest additional physical mechanisms that could be leveraged towards the goal of reconfigurable microfluidics and highlight the importance of these efforts for the broad scientific community.

The field of lab-on-a-chip seeks to take large-scale chemical and biochemical laboratories and reduce them to the size of a small microfluidic chip. While examples of chemical analysis on microfabricated wafer-based substrates date as far back as the late 1970s, the birth of the field is largely attributed to developments in the early 1990s, where the maturity of microfabrication techniques lowered the technological barriers for the creation of such devices, which paved the way to an explosion in research on the use of microscale systems for biological and chemical analysis (FIG. 1). During these times, Manz, Graber and Widmer published their seminal vision of integrating multiple laboratory steps in devices on the micrometre to millimetre scale, coining the term ‘miniaturized total chemical analysis systems’ (µTAS), now commonly referred to as lab-on-a-chip. Compared with traditional large-scale systems, lab-on-a-chip systems have clear advantages, such as compact size and portability, small sample and reagent volumes, as well as new potential functionalities enabled by the microscale.

Lab-on-a-chip devices are commonly divided into two main families: continuous phase devices and discrete phase devices (see BOX 1). Various physical mechanisms, such as electrowetting\(^1{}\), dielectrophoresis\(^2{}\) and thermocapillary\(^3{}\), are available to precisely control two-phase systems on a large scale. For example, in digital microfluidics\(^4{}\), individual droplets can be manipulated (merged, split or mixed) in real time and on demand, enabling a high degree of programmable functionality. However, many processes, including chromatographic and electrophoretic separations, as well as live cell assays and organs-on-chips, rely on continuous phase flows, whose control remains a substantial challenge\(^5{}\). To date, continuous phase microfluidic chips are largely single-purpose ‘protocols-on-chips’ — they do not allow the flexibility and real-time experimental decision-making essential to many scientific applications. For instance, after carrying out a predetermined protocol, it is rarely possible to perform unplanned follow-up experiments based on the obtained results on the same sample or on the same system.

We believe that the ability to make real-time experimental decisions, in which the observations from the current step can directly influence the subsequent steps in the experiment, can unlock new avenues in numerous fields, including single-cell analysis, chemical synthesis and separation sciences. In this Perspective, we describe our vision to create continuous phase microfluidic systems that are reconfigurable, allowing for dynamic real-time changes to the flow field, and discuss actuation mechanisms that could be leveraged to develop such functionality.

We acknowledge that real-time experimental decision-making cannot be achieved solely by relying on the development of reconfigurable microfluidic systems and will require equal efforts to integrate sensors for rapid feedback and design appropriate control algorithms.

First, we introduce the concept of a reconfigurable microfluidic platform and its potential as a tool for scientific advancement across different fields. We then present the state of the art in reconfigurable microfluidics, discuss actuation mechanisms that have the potential to enable reconfigurable microfluidics and outline future challenges in their implementation.

Reconfigurable microfluidic devices

Microfluidic devices can be classified by their configurability, as described in BOX 2. Traditionally, continuous flow microfluidic devices consist of static microfluidic networks, in which fluids are pumped through channels actively (for example, by pressure gradients or electroosmotic flow) or passively (for example, via capillary-driven flows), which limits them to a predefined functionality. These devices are produced using techniques such as lithography, micromilling, laser ablation and injection moulding. Configurable systems rely on the assembly of a device from existing subunits or on a physical actuation mechanism that transforms a device from a baseline state to a desired functional state. Examples include modular assembly\(^6{}-^{11}\), oleophilic/hydrophobic boundaries\(^12{}-^{13}\) and paraffin structuring\(^14\). In contrast, a reconfigurable system enables multiple transitions between a large number of states and can do so during its operation in real time. Configurable devices are undoubtedly useful, but real-time decision-making in experiments will only be possible with reconfigurable systems.

FIGURE 2 illustrates our vision of a reconfigurable microfluidic platform in...
which the flow field can be arbitrarily controlled in real time by the user. This tunability could be achieved either by shaping physical boundaries in the chip and forcing the liquid through the resulting networks or by directly manipulating the liquid using body or surface forces. Both approaches would allow the microchip to be configured to drive fluids along ad hoc fluidic networks and provide a variety of desired functionalities, including mixing, splitting, merging, confining, stagnating, shearing and pumping. The physical boundaries approach would also enable the formation of structural elements such as chambers, traps and posts. The ability to control the geometry and functionality of a microfluidic chip in real time could afford new capabilities for a variety of applications. Below, we expand on three potential applications that could be advanced and improved by using such a reconfigurable platform. The potential benefits that a reconfigurable microfluidic platform could provide to these fields are summarized in Table 1.

## Chemical synthesis

A fully automated synthesis platform capable of independently planning and executing its own synthetic route to produce a wide range of molecules for various applications such as drug discovery has been a long-standing goal across the chemistry community. Significant progress has been made on artificial intelligence approaches for synthesis and robotics-enabled automated pipetting for its execution. The use of automated chemical synthesizers for reactions with very small volumes could enable the production of valuable compounds. Microfluidic platforms are a good match for such syntheses, as they provide efficient handling of small volumes with shortened transport times of mass and heat. As no two syntheses are identical, covering the range of desired processes would require several different microfluidic chips. However, a reconfigurable microfluidic platform could tune its functionality to suit the desired synthesis protocol. Moreover, such a platform could adapt itself in real time to correct for any deviations during the synthesis based on feedback from on-chip sensors, such as pH meters, conductivity detectors, absorbance imaging or by interfacing with off-chip techniques, such as mass spectrometry or liquid chromatography.

## Single-cell analysis

The interaction and communication between individual cells plays a central role across biology, for instance, the cooperative work of cells in the immune system, the differentiation of stem cells and the proliferation of cancer cells. Over the past decade, there has been considerable development in high-throughput methods of single-cell analysis. Tools developed include various microfluidic chips for individual or paired cell capture and analysis, droplet microfluidics, digital microfluidics, fluorescence-activated cell sorting (FACS) and microFACS and on-chip pneumatic valves. These tools have reduced the time necessary for hands-on work and allowed for studies at previously unattainable single-cell scales, enabling fundamental biological discoveries. However, existing high-throughput single-cell analysis technologies are not well suited for studying cell interactions for which the ability to dynamically join, separate or reconfigure cells is important. As a result, important questions in cellular behaviour and, in particular, single-cell systems, such as evaluating communication between multiple cells, remain beyond the reach of existing tools. A reconfigurable microfluidic platform capable of real-time modification of the experimental conditions can, thus, be a valuable tool for answering such questions.

## Analytical separations

Capillary-based separation techniques are a standard in the majority of chemical and biological laboratories, with the most prominent approaches being liquid chromatography (for example, reverse phase liquid chromatography and size-exclusion chromatography). The re-emergence of microfluidics has enabled new capabilities for a variety of applications that could be advanced and improved by using such a reconfigurable platform. The potential benefits that a reconfigurable microfluidic platform could provide to these fields are summarized in Table 1.
liquid chromatography) and electrokinetics (for example, capillary electrophoresis and isoelectric focusing). Compared with their column and gel counterparts, capillary-based systems allow the use of smaller volumes and provide higher resolution and faster analysis times. Most of these techniques have been migrated to microfluidic chips, which provide additional capabilities by enabling more complex geometries, direct visualization and multidimensional separations. However, one disadvantage that both capillaries and microfluidic chips share is the difficulty to access the separated fractions. For example, an isoelectric focusing separation would produce a series of bands corresponding to proteins with different isoelectric points; often, it is desirable to retrieve these bands for further analysis using capillary electrophoresis or mass spectrometry. In contrast to open platforms such as gel slabs, where the band can be cut out of the gel, capillaries and on-chip approaches have rigid walls, preventing such access. One could envision a fully reconfigurable microfluidic platform with a separation channel that partitions into segments, with each capturing a separated fragment. These segments could then be manipulated on the chip and, for example, merged with other microchannels to enable a reaction, and then be introduced into another formed channel for a second separation. Finally, separation products could be delivered to the chip outlet for interfacing with off-chip instrumentation.

**Existing reconfigurable systems**

The first reconfigurable systems, developed in the early 2000s, were based on a fixed microfluidic network supplemented by on-chip valves controlling the flow paths. Among the large number of valve actuation mechanisms, including electrostatic, magnetic, piezoelectric and thermal, the best-known example is the pneumatic valve, which is composed of a flexible membrane that deflects under pneumatic actuation to close or open a fluidic channel. Routing fluid in a predefined fluidic network could also be achieved by subjecting the fluid itself to surface or body forces that direct its path through the network. For example, electroosmotic flow has been used to direct the flow, either by controlling the electric field distribution in the network or by controlling the surface potential in different branches.

### Discontinuous phase microfluidics

Discontinuous phase microfluidics utilizes immiscible phases to partition a liquid of interest into discrete volumes, such as water in oil. There are two common approaches in which discrete microfluidics is implemented: droplet microfluidics relies on a continuous injection of one phase into another, providing high-throughput production of droplets with limited ability to individually manipulate each one; digital microfluidics utilizes electrode arrays for control of individual droplets, thus enabling a high level of reconfigurability and operational flexibility.

### Continuous phase microfluidics

Continuous phase microfluidics relies on the manipulation of a single liquid — one phase, or molecules within this phase, provide functional processes such as transport, mixing and separation. To date, the level of flow reconfigurability is limited, as it is dictated by the fixed device geometry.

### Alternative actuation mechanisms

In addition to the systems discussed, a large number of actuation mechanisms have the potential to create powerful reconfigurable systems, but have yet to be fully explored. Some of these mechanisms have been used to route liquid through a pre-existing network, while others have only been applied for basic fluid transport. Despite the utility of devices that route liquids through pre-existing networks for a variety of applications, they do not represent the ultimate reconfigurable system, as they have channels with preset dimensions in which they can only offer a finite number of fluidic routes. Here, we present what we consider the most advanced form of reconfigurability — the dynamic shaping of boundaries, either through manipulation.
of physical boundaries (liquid or solid) or through the application of forces to the liquid itself (virtual boundaries). A fundamental difference between the two approaches is their effect on diffusive mass transport: physical boundaries that are solid (mechanical actuators) or semipermeable (hydrogels) completely eliminate or significantly diminish diffusive transport through them. Therefore, they are appropriate for cases where sample confinement is desired. In contrast, virtual channels are implemented in an open chamber, which allows for unobstructed diffusive mass transport between different regions of the flow field. Diffusive transport may be a disadvantage if one seeks to isolate one region from another, but could also be leveraged to create useful diffusion–advection interactions, such as in the case of bidirectional flow. Here, we provide a brief review of relevant physical and chemical mechanisms and speculate how they could be further developed for reconfigurable systems.

**Physical boundaries**

Electrowetting has been reported as an effective method for the dynamic creation of microfluidic channels. Although demonstrations have, so far, been limited to few channels (1 to 5), this approach could likely be scaled up based on the infrastructure developed for droplet microfluidics, where fairly large arrays of electrodes have been developed. However, flow within liquid boundaries is inherently limited to relatively low pressures, dictated by the Laplace pressure that can be sustained by the interface. Also, from a practical perspective, handling two phases adds an additional level of complexity over single phases. As an alternative, we envision a reconfigurable system in which none of the physical boundaries are fixed. Instead, the ceiling and/or floor of the chip is deformed arbitrarily, thus defining the fluidic path. Such deformations could potentially be achieved by responsive materials or by mechanical actuations.

**Phase-transition hydrogels.** Volume phase transition is a process in which hydrogels shrink or expand in response to a certain stimulus, either physical (for example, temperature, electric/magnetic fields, light or pressure) or chemical (for example, pH or salt concentration). The change in volume is usually reversible and the extent of this change, which can vary by more than an order of magnitude, depends on the hydrogel characteristics, such as chemical composition and degrees of cross-linkage, as well as on the intensity of the external stimulus.

An early and elegant incorporation of hydrogels within microfluidics was demonstrated using a self-regulated valving system, where the opening/closing of the valve was governed by the pH of the solution. The hydrogels were fabricated in situ, within the microfluidic networks, by polymerizing the basic constituents using local illumination. This principle was then expanded to achieve self-regulation based on other stimuli, including chemical concentrations and temperature. A first implementation of an actively controlled valve was achieved by using an external heating element to control the temperature of a temperature-sensitive hydrogel (poly(N-isopropylacrylamide)), which expands at room temperature and shrinks at temperatures above ~33°C. This mechanism was also used for controlling individual valves within a pre-existing microfluidic network. The use of temperature-responsive hydrogels enabled the creation of artificial skin to a large-scale array of 65 × 65 hydrogel pixels, each of which had a 300 μm × 300 μm footprint that was individually addressed by a temperature field dynamically controlled by a light projection system. However, this particular implementation was never explored in the context of reconfigurable microfluidics. By using a light-controlled hydrogel, its structures could be individually controlled and have an arbitrary shape based on the projected light pattern; this could significantly expand previous works in which only a predefined array of traps can be turned on or off at the same time. Thus, the entire channel network could be formed and modified in real time and a variety of functional elements, beyond traps, could be implemented using this approach.

Having recently fuelled the enormous progress in soft robotics and biomaterials, advances in hydrogels can contribute to the development of novel, dynamically controlled physical boundaries. Using hydrogels as 'walls' can block advective flows while still allowing diffusion...
of chemical species through them because of their inherent nanosized porous structure. This unique feature can be leveraged towards integrating flow routing with applications requiring mass transport with zero net flow; examples include the delivery of reagents to cells without shearing them, separations such as microdialysis and chromatography, the creation of chemical gradients and biosensing.

Mechanical deformations. As an alternative approach, one could imagine, for example, a device consisting of a rigid ceiling and a soft elastic floor, placed on top of an array of individually addressable mechanical actuators. Upon actuation of the array according to an arbitrary pattern imposed by the user, the floor would deform locally, pressing onto the ceiling, thus defining the fluid path. The challenge lies in obtaining a system capable of providing enough displacement, while sustaining large enough pressures and providing sufficient spatiotemporal resolution. A digital micromirror device is a well-established technology that can provide deformation of individual (~10-µm) pixels over a high-resolution array. However, micromirrors need only enough force to redirect light and not to push on a fluidic system. These silicon microelectromechanical systems were not designed to generate enough force to create substantial deformations. However, despite the number of technologies for single ~100-µm-scale actuators that can generate the required force, creating and controlling compact arrays of such actuators remain challenging.

To date, one of the most advanced platforms implementing the concept of mechanical deformations of a membrane was made using an array of hydrogel ‘pixels’ individually addressable by optothermal actuation, to arbitrarily deform a membrane attached to it. However, this work was presented in the context of its application to artificial skins. Based on previous work done on hydrogel actuation and its ability to sustain sufficient forces when used as a valve, we believe that this technology has great potential for reconfigurable microfluidics. For instance, the fluid can be placed on top of the membrane and the microfluidic network can be modified by actuating the hydrogel array. The use of these hydrogel pixels highlights that technologies that can enable the creation of high-resolution devices exist and will have to be adapted to realize their applicability to reconfigurable microfluidics.

In addition to using an array of discrete mechanical actuators, the actuation of the deformable surface could be achieved by creating pressure with an underlying layer of fluid. For example, an elastic sheet suspended on top of a thin liquid film can be deformed by subjecting the liquid to non-uniform electroosmotic flow, but the pressures that such a system can produce are fairly low, ranging from tens to hundreds of pascals. Although the pressure could increase by as much as two orders of magnitude using non-Newtonian fluids, the viscosity of which is dependent on the applied stresses, this modification has not yet been demonstrated in practice. Many of the fluidic mechanisms that will be discussed in the next section, such as acoustic and magnetohydrodynamic, could likely be used to create such pressure distributions resulting in the desired deformations, and they should be further studied in the context of their ability to provide sufficient resolution, force and displacement.

Virtual boundaries
Hydrodynamic control is likely the clearest implementation of virtual-boundaries-based actuation. In this approach, streamlines are shaped by the injection of fluid at multiple locations within a fluidic chamber, resulting in an internal pressure distribution, which

| Table 1 | Benefits of a reconfigurable microfluidic system to representative on-chip applications |
| --- | --- |
| Application type | Potential beneficial features |
| Chemical synthesis | Adapt functions to fit desired synthesis protocol | Adjust the flow fields to correct for deviations in synthesis in real time |
| Single-cell analysis | Dynamically manipulate individual cells | Make real-time decisions based on experimental observations |
| Analytical separations | Modify geometry to capture and manipulate specific analytes | Couple different separation techniques on demand |

Fig. 2 | Our vision of a reconfigurable microfluidic platform. The user will be able to draw any desired microfluidic configuration on a computer and this design will be instantaneously implemented on the reconfigurable chip. The ideal reconfigurable system would be able to rapidly switch between a large number of states and functionalities, thus allowing the user to dynamically interact with the on-chip experiment. The ability to reconfigure a chip in real time will open the door to a wide range of applications in chemical and biological analysis, such as chemical synthesis, medical diagnostics and single-cell research.
guides the streamline. The number of degrees of freedom can be increased by having additional actuation sources, but this strategy is not scalable, owing to the size and cost of pumping systems. Furthermore, hydrodynamic control is based on the injection of momentum together with mass, where the latter is not always desired. Additional physical mechanisms that allow injection of pure momentum into the flow and are potentially more amenable to scaling are discussed below.

**Electrically driven flows.** Electrically driven flows result from the interaction of electric fields with electrolyte solutions and can be roughly divided into electrokinetic flows, in which charges arise in the diffused electric double layer (EDL) formed at liquid–solid or liquid–liquid interfaces, and electrohydrodynamic flows, in which a gradient of the liquid electrical properties, such as conductivity and permittivity, afford net charges in the fluid bulk. The most widely used form of electrokinetic flows is electroosmotic flow. In its simplest form, a direct current (DC) electric field is applied parallel to a surface, which applies a body force to the fluid through its interaction with the net charge in the EDL, dragging the liquid bulk through viscous forces. Non-uniformities in either of these elements, that is, the EDL or the electric field, give rise to pressure gradients that affect the flow. Dynamically modulating the charge distribution in a microfluidic chamber, by using gate electrodes, for example, enables a certain level of flow reconfigurability. However, other electroosmosis-based mechanisms that are commonly used to pump fluids could also be implemented for this purpose. A good candidate is induced-charge electroosmosis, which occurs when an electric field acts on the induced EDL on a polarizable surface, such as an electrode. Net flow can be generated when using a linear array of electrodes either by having directional asymmetry of the electrodes (alternating current (AC) electroosmosis) or by activating the electrodes sequentially (travelling wave electroosmosis). Complex flow patterns could potentially be shaped in real time by using a 2D array of electrodes that can be individually addressed with a dedicated AC signal. AC electroosmosis and travelling wave electroosmosis often use exposed electrodes that are susceptible to degradation over time and might cause faradaic reactions, leading to a device failure. However, these set-ups require only a few volts and no external electric field along the channel and are, thus, more suitable for being integrated in solid-state platforms compared with electroosmotic flow.

![States of the art in reconfigurable microfluidic systems](https://creativecommons.org/licenses/by/4.0/). Panel a | Pneumatic valves utilize a thin elastic membrane that can be deflected using pressurized gas to close or open channels in the fluidic network. Panel b,c | Electroosmotic valves rely on inducing electroosmotic flow (EOF) in desired branches of a microfluidic network by controlling either the electric field or the surface charge. Panel d | Magnetohydrodynamic valves also rely on selective activation of the flow in specific branches, by controlling the local electric current. For dynamic boundaries (right), the dynamic manipulation of boundaries can be further classified to physical boundaries (liquid or solid) and to virtual boundaries, where the fluid is directly manipulated.
Mechanical deformations of a deformable elastic sheet, gels, such as phase-transition hydrogels, pulsating physical boundaries. Such boundaries can be solids, as in the case of a deformable elastic sheet, gels, such as phase-transition hydrogels, or immiscible liquids, such as water-in-oil channels, as in the case of electrowetting. An alternative form of reconfiguration is by applying surface or body forces to the liquid itself, thus forming virtual boundaries. Such forces can arise through the interaction of ions with electric and/or magnetic fields, as in the case of electrodynamics or magnetohydrodynamics, through non-uniform surface tension, as in the case of thermocapillary flows, or through transfer of momentum with or without mass, as in hydrodynamics and surface acoustic waves.

Electrically driven pumping was also demonstrated by leveraging the interaction of an electric field with induced gradients of conductivity and permittivity in the fluid bulk, also known as induction electrophoretic flows. A convenient way to form such gradients is by an imposed thermal gradient, usually produced by strong illumination or Joule heating. Similar to the electrokinetic techniques described, we believe that such electothermal flows could also be leveraged to implement reconfigurable flow. For instance, one could create arbitrary conductivity gradients that would drive the desired flow by having localized and individually addressable heat sources at the bottom of a microfluidic channel, such as patterned resistors or patterned light. In contrast to other electrokinetic techniques, electrophoretic flows can generate stronger microflows (>100 μm s⁻¹) for fluids with higher conductivities (>1 S m⁻¹). Therefore, these mechanisms have been shown to work robustly in biological applications that involve high-conductivity biofluids (>0.7 S m⁻¹), such as saliva, blood and urine.

Thermocapillary flows. Marangoni flow is obtained at fluid–fluid interfaces — between two immiscible liquids or between a liquid and a gas — that are subjected to a non-uniform surface tension. Such non-uniformities give rise to tangential stresses that drive the fluid along the interface, away from lower-surface-tension regions, and carry the rest of the fluid through viscous interactions. Thermocapillary flows are a subset of Marangoni flows, wherein surface tension variations are driven by temperature gradients. They have been the subject of active study in the fluid mechanics community for the past several decades. In contrast to other Marangoni flow mechanisms, such as chemical gradients, thermocapillary flows can be dynamically controlled because heat can be added and removed from the system by using external means and small temperature gradients (a few degrees over centimetre scales) can yield significant flows. Furthermore, thermocapillary flow has the potential to serve as an effective method for the control and manipulation of liquids in microfluidic devices, because, at the microscale, surface tension effects become dominant over body forces, such as density gradients and gravitational forces.

A major challenge in using thermocapillary flows for large-scale flow patterning lies in the need for an interface between two immiscible fluids, which hinders its use for configurations containing free surfaces. Consequently, both evaporation and contamination pose difficulties for practical implementation. However, designing a microfluidic channel with only a few openings can help minimize these undesired effects because only a limited free surface region is exposed. To this end, placing a free surface region as a segment within a microfluidic channel afforded a pressure gradient that drove the flow through the rest of the microchannel. An alternative approach involves creating air pockets on one of the microfluidic chamber walls; this would limit the evaporation and create a large area of water–air interface. In addition, theoretical studies suggest that thermocapillary flows can be achieved on superhydrophobic surfaces, wherein liquid–air interfaces are formed between pillars on which the fluid is suspended. This last approach can certainly enable the fabrication of closed configurations, but the introduction of superhydrophobic surfaces introduces new practical challenges, namely, superhydrophobic surfaces are more susceptible to instability triggered by various factors, such as external pressure, condensation and electrowetting, and efforts to create stable superhydrophobic structures that allow operation over long periods of time without collapsing are required.

Similar to the case of electothermal flows and hydrogel actuation, a considerable challenge is the large-scale control of the temperature field. Potential solutions include local heating of the bulk liquid electrically or optically or heating only the interface, which could be through the local heating of particles placed at the interface. The latter strategy would provide both a higher spatial resolution and faster response time compared with heat transfer through the liquid film because the process is governed by the interface.
Surface acoustic waves. Acoustic waves result from pressure oscillations that propagate through matter and can move fluids through the transfer of energy into the volume and manipulate particles through acoustic radiation from the surrounding liquid.

The most common implementation of acoustic waves in microfluidics is through surface acoustic waves (SAWs). SAW sources can be integrated on the same chip as the fluidic components and are typically made of piezoelectric materials. In addition, SAWs are not very sensitive to the composition of the fluid, enabling their use across different applications, including those that involve biological samples, spanning a range of pH and ionic strength values. To date, several efforts have displayed how SAWs can serve as a pumping element in microfluidic channels; for example, a SAW-driven device capable of pulling liquid from a droplet reservoir into a microchannel, leveraging the liquid–air interface. This concept was extended to a microchannel grid in which the liquid is driven by activating multiple transducers located at the entry/exit points of the grid. SAW-driven pumps have also been developed in an entirely filled closed-loop channel without the need for a liquid–air interface, providing a good potential driving mechanism for reconfigurable systems. However, in contrast to electrical or thermal forces, which can directly act on the entire area of the fluidic chamber, effective energy coupling in SAWs occurs at liquid–air interfaces. Therefore, SAW actuation would be based on an array of actuators located at the circumference of the chamber. Although this mechanism has some resemblance to hydrodynamic flow manipulation through injection of fluids at the boundaries, the momentum for SAW actuation is injected through the forces on the boundaries of the channel, rather than through the injection of mass. To date, only a few SAW sources have been used to implement SAW fluid actuation. Thus, overcoming technological challenges such as the scaling and integration of a large array of individual SAW sources, with emphasis on the thermal management of dense, high-energy actuators, can enable an expansion in this space.

Magnetohydrodynamics. MHD describes the motion of a conductive liquid subjected simultaneously to an electric field and a perpendicular magnetic field component, giving rise to a Lorentz body force that acts on the liquid. Recognized as an effective method for fluidic pumping, the most common implementation of MHD makes use of a magnetic field produced by a magnet (permanent or electric) external to the chip, with an electric field produced by sets of electrodes located on opposite walls of the fluidic channel.

MHD could be implemented using DC or AC fields. DC actuation allows the use of permanent magnets with zero power consumption, but has practical challenges related to bubble generation and degradation of the electrodes by electrolysis. Methods for avoiding or reducing these effects include placing the electrodes in open reservoirs far from the controlled channel or using redox species to minimize faradaic reactions. AC actuation essentially eliminates bubble generation but requires the use of electromagnets that are synchronized with the electric field and need high power to produce significant magnetic fields. Furthermore, alternating magnetic fields induce parasitic currents in the channel electrodes, giving rise to Joule heating. For the most part, MHD has been used on dimensions larger than 100 μm, because MHD actuation relies on a volumetric force to drive the fluid, which does not scale favourably as the channel dimensions decrease. Controlling pairs of electrodes in different branches of the network was a significant step towards reconfigurability, which demonstrated the ability to control the flow within a fluidic network. At present, demonstrations have been limited to a relatively small number of controllable channels, but such a platform could be used as a truly reconfigurable system by having a very large number of individually controlled branches. Furthermore, one could envision creating virtual channels by using an array of electrodes to create localized flows within an unobstructed chamber. Importantly though, MHD electrodes in such a chamber could be operated by voltages on the order of tens of volts or less (resulting in few milliamperes across micrometre-sized channels), which is lower than the voltage levels required in other electrokinetic techniques (typically requiring hundreds of volts). This lower required voltage can potentially enable an easier implementation of large arrays using standard microelectronic controllers. Yet, fabricating such a large array would require overcoming problems associated with Joule heating, electrolysis and individual electrode control in large arrays.

Future challenges
Reconfigurable microfluidics has the potential to enhance the capabilities of microfluidic platforms. However, reconfigurability cannot overcome the fundamental limitations associated with microfluidics, such as the limited volumes that could be processed using microscale devices, and is not a necessity for every on-chip application. For instance, although the development of a diagnostic chip could benefit from a reconfigurable system that would allow various assay configurations to be quickly tested, the final design could be 'frozen' and implemented as a static microfluidic chip, allowing mass production at a low cost.

For those applications that could benefit from reconfigurability, the choice of actuation mechanisms is paramount for their successful implementation. For example, confining cells is typically required for single-cell applications and, therefore, mechanisms allowing reconfigurable physical boundaries will be more suitable. Analytical separation applications would benefit from mechanisms with fast response time and high spatial resolution, to allow rapid capturing of analytes with minimal dispersion. Chemical synthesis should work with a wide range of liquids, likely excluding mechanisms that depend on the liquid properties, such as electrokinetic or magnetohydrodynamic ones. Regardless of the specific selected mechanism, some common challenges must be overcome to develop a reconfigurable platform.

Individual actuator control
For single-cell analysis, spatial resolution on the order of a cell size (10 μm) would be required. Other applications may be less demanding and could already benefit from devices with a spatial resolution on the order of 100 μm. For such scales, arrays with a density of 10,000–1,000,000 actuators cm⁻² would be required. Given that typical dimensions for microfluidic devices are on the order of 1–10 cm, the total number of actuators may range between 10,000 and 100,000,000. One of the greatest challenges is the ability to address each actuator individually. In displays, this is typically done by scanning over the rows and columns of the display matrix and using per-pixel circuitry to maintain the pixel active until it is addressed again. Unfortunately, this methodology cannot be directly applied to the majority of microfluidic actuation mechanisms, as those rely on substantially higher power per pixel, which is not supported by standard microelectronics. Thus, a significant effort of the community is required to integrate specialized high-power complementary metal–oxide–semiconductor processes.
with microfluidics in tandem with the development and miniaturization of the actuators. Alternatively, the unique and diverse physical mechanisms that could be used in reconfigurable microfluidics also provide opportunities for other large-scale control approaches. For example, using photosensitive materials on-chip may allow for decoupling the control layer from the chip itself and the use of an external light-projection system, which is inherently high resolution, to project a desired configuration onto the chip. The photosensitive materials could trigger any number of subsequent physical mechanisms, from conductivity changes for implementing switches to heating for inducing phase changes and changing mechanical properties to drive direct deformations.

**Temporal control**

In addition to the required spatial resolution, the ideal reconfigurable microfluidic device should be able to switch from one configuration to another sufficiently quickly. For cellular studies, the required timescales are relatively long, posing no particular challenges to the response time. However, applications in separation, sorting or synthesis, particularly at a high-throughput scale, require fast response times — ideally in the millisecond range. For methods relying on electric or magnetic fields, the response time is typically on the order of tens of milliseconds. However, the response time is significantly longer for many other mechanisms, at different timescales, for example, using photosensitive materials or temperature gradients, on the order of tens of milliseconds. However, the response time is typically on the order of hundreds of milliseconds to seconds. The lack of fast, responsive hydrogels presents an opportunity for chemists and materials scientists to contribute to the development of new types of responsive materials.

**Design and automation**

The field of lab-on-a-chip has made a tremendous impact on chemical and biological analysis; however, the high level of expertise required for the microfabrication and the operation of the devices prevents non-experts from using them. The ideal reconfigurable platform should be a standard tool in the hands of practitioners in other fields and, thus, it should be easy to use without having knowledge of the underlying actuation mechanism. For this ease of utility, the building hardware blocks of the platform should be augmented with a dedicated software with an intuitive user interface. Ideally, the user should draw only the desired configuration and the software should translate it to the required commands to the hardware, based on the physics of the mechanism.

**Materials compatibility**

The choice of materials should be tailored to the desired actuation mechanism and the target application. Commonly, microfluidic chips are made out of crystalline silicon, amorphous oxides (SiO₂, SiON), thermoplastics (poly(methyl methacrylate) (PMMA), cyclic olefin copolymer (COC), cyclic olefin polymer (COP) or organic elastomers (polydimethylsiloxane (PDMS)). Although silicon and oxides offer very good chemical compatibility, they are rigid and, therefore, not suitable for mechanisms requiring boundary deformations. Conversely, elastomers commonly used in microfluidics are suitable for applications in aqueous environments, such as single-cell and biochemical separation, but are poorly suited for applications requiring solvents or where they are subject to swelling or decomposition, such as organic chemistry. Therefore, one goal that the materials community should strive to overcome involves the development of elastic materials that can be integrated in microfluidic systems and are also chemically resistant to a large spectrum of common organic solvents.

For mechanisms relying on liquid–surface interactions, such as electrokinetic actuations, surface properties are of paramount importance. As an example, the chemical nature of the surface is a main parameter in designing electroosmotic-flow-driven mechanisms, which are currently limited to work with electrolytes with low ionic strength, within a specific pH range and are sensitive to undesired absorption of biomolecules onto the surface. Materials or coatings that render the surface less sensitive to the electrolyte properties could enable making electrokinetic methods more versatile for reconfigurable microfluidics.

**Concluding remarks**

The concept of lab-on-a-chip is often presented in analogy to microelectronics, aiming to revolutionize chemical and biological analysis in the same way that microelectronics has revolutionized information technology. However, in contrast to microfluidics, microelectronics evolved with a strong emphasis on reconfigurability and scalability, in which a single chip is capable of changing its function. One of the most important aspects in reconfigurability is that it allows users to define the functionality of the chip and create novel applications and uses, without having to possess expert knowledge about the underlying hardware or physical mechanism driving it.

In this Perspective, we reviewed some of the technologies that we believe can serve as the baseline for reconfigurable platforms. It is by no means an exhaustive list and we are aware that it is very likely that many other mechanisms, at different stages of development, could be equally relevant. We do not know from what particular field or discipline the ‘solution’ for reconfigurable microfluidics will arise. It is as likely to come from engineering disciplines, such as micromechanics or microelectronics, from physics, such as fluid mechanics or photonics, or from chemistry, such as stimulus-responsive materials or zeta potential manipulation. At the same time, the most significant impact for such a platform is clearly in the biosciences. Regardless of the choice of mechanism, a reconfigurable microfluidic platform will likely provide ample opportunities for innovation to researchers in a variety of disciplines. We, thus, call on the community to join us in this effort.
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Competing interests
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