



# Engineering Distance Learning: The Promise and Challenges of Microfluidics

Megan Levis<sup>1,2</sup> · Clare Hyland<sup>1</sup> · Jeremiah Zartman<sup>1,2</sup> 

Received: 14 October 2022 / Accepted: 1 June 2023

© The Author(s), under exclusive licence to Biomedical Engineering Society 2023

## Abstract

The recent trend of expanding online education in science and engineering creates the need for remote experiential learning opportunities. Microfluidic devices show great promise in fulfilling that need because they are small, transportable, cheap, and use safe volumes of reagents to complete experiments. The rapid increase of microfluidic devices for point-of-care diagnostics serves as a proof of concept for remote learning applications. This perspective highlights potential scenarios and issues that need to be considered in translating multimodal microfluidics into educational settings. Several educational scenarios are developed, and a Strengths, Weaknesses, Opportunities, and Threats gap analysis highlights the barriers and opportunities for implementing microfluidics in the classroom or in online education formats. Providing students with microfluidic competencies in increasing diverse educational formats will create new opportunities as the microfabrication and diagnostics industries continue to grow.

**Keywords** Biomicrofluidics · Digital learning · Remote educational experiences · Lab classes · Remote learning · Active learning

## Introduction

As the need for experiential learning both inside and outside the classroom continues to increase, microfluidics show promise to advance remote learning opportunities. Microfluidics or Lab-on-a-chip technologies with precise control of nano- or microliters of liquids allow researchers and educators to scale down experiments, moving the domain of experimentation from a lab room to a miniaturized device that can be shipped anywhere [1]. For example, microfluidic devices coupled to smartphones provide a platform for point-of-care DNA analysis [2, 3].

Biochemical and pharmaceutical industries are increasingly utilizing high-throughput systems coupled with machine learning techniques and control systems to create intelligent microfluidic devices [4, 5]. The microfluidics global market size is predicted to grow to \$30–45 billion in

2025 from \$15 billion in 2020 (11–22% compound annual growth) [6–8]. With this growing global microfluidics market, students need training to work in this interdisciplinary field. 3D printed and open-source microfluidic accessories such as flow pumps and microscopes facilitate activities where students build control systems cheaply [9–14]. Therefore, next-generation lab-classes (in-person or remote) will benefit from the addition of microfluidic technologies.

Several challenges have limited the impact of microfluidics outside of dedicated research laboratories to date [1]. First, most microfluidic innovation is communicated in engineering specific publications and are not being communicated to medical and biological researchers interested in specific applications [15]. Second, there are key barriers due to complexity and cost of design and fabrication. In particular, external pumps and pneumatic flow systems often require additional considerations and significant cost. Finally, microfluidic devices must demonstrate a superior solution to the given problem compared to other technologies. Here, we review several microfluidic advances that increase the ease of use of microfluidics. We also highlight low-cost and open-source solutions that can resolve some of the key barriers to microfluidic adoption, particularly for educational needs.

✉ Jeremiah Zartman  
jzartman@nd.edu

<sup>1</sup> Chemical and Biomolecular Engineering Department, The University of Notre Dame, Notre Dame, IN, USA

<sup>2</sup> Bioengineering Graduate Program, The University of Notre Dame, Notre Dame, IN, USA

This short perspective is organized into three main sections. First, we discuss several applications of microfluidics in the classroom. In discussing classroom applications, we present subsections highlighting point-of care microfluidics, microfabrication, and advanced topics on high-throughput devices and microfluidic process controls. Second, we provide a gap analysis, highlighting the unique challenges for the expert teaching of microfabrication versus teaching the applications of microfluidics. Third, we conclude by indicating future directions. In discussing the potential uses of microfluidics as an experiential learning aid, we focus on low-cost and easy to implement solutions to engage students in active learning in the classroom and remote settings.

## Educational Applications of Microfluidics

Multiple courses such as general or analytical chemistry, and transport phenomena have benefited from the use of microfluidics in the classroom [16] (Table 1). For example, molecular interdiffusion, an important topic for advanced chemistry classes, is easily demonstrated with microfluidic mixers [17]. In this activity, students learn concepts of passive diffusion and laminar flow (characterized by low Reynolds numbers). In experiential skill building classes (labs), students learn microfabrication to design and use micromixers with food dye and water. Students then analyze the recorded data using the freely available ImageJ platform [17]. This hands-on experience engages the students while teaching them how to design efficient mixers. Such microfluidic activities teach students about enzyme kinematics.

Concepts related to fluidic properties such as viscosity are naturally demonstrated using microfluidic devices [18]. For example, a two-inlet microfluidic device allows students to calculate the viscosity of fluids with the use of a high-speed camera from a smartphone to measure the relative widths of fluids in a two-inlet device [18]. This technique can enable a modular course activity to illustrate viscosity at the undergraduate and graduate level using only a smartphone, a simple microfluidic device and low volume of liquids. The volume of liquids could be important for safety protocols that require small volumes to be safe. The simple setup of the experiment allows for the experiment to take place while completing coursework remotely.

Overall, microfluidics are very useful for investigating transport phenomena such as laminar flow and the balancing of multiple transport mechanisms such as convection and diffusion (as characterized by the Peclet number, which is the ratio of mass transport due to convection to that of diffusion) [19]. The relative predominance of transport mechanisms are different at the micro level than the macro level, but such a difference can be difficult to understand. Macro transport phenomena are easily demonstrated in a traditional

classroom setting, while microfluidic devices help to more clearly teach transport at a smaller scale (Table 1—Transport) [20].

Analytical chemistry techniques such as chemical and electrophoretic separations are effectively taught in undergraduate laboratories with microfluidic devices [16] (Table 1—Analytical Chemistry). As a second example, students designed and fabricated microfluidic devices to visualize electrophoretic separations and then separated food dyes in the course of a 3-hour undergraduate lab [21]. Photolithography-based fabrication with photomasks printed on transparency sheets was cheap and easy enough that students were able to create multiple backup devices for their separations. In another application of microfluidics, a paper microfluidic utilized colorimetric analysis to quantify amino acid content within a sample [22] (Table 1—Analytical Chemistry). ImageJ software is an ideal software choice to quantify the chemical separations and the colorimetric readings in such analytical microfluidic devices [22, 23]. This is due to the extensive online help documentation, free download, and intuitive interface.

In addition to engineering courses, biology classes also benefit from integration of microfluidics with topics such as binding kinetics and binding affinities (Table 1—Biology) [16, 24]. For example, DNA separations can be demonstrated in undergraduate labs using microfluidics [25]. After extracting DNA and performing PCR, resulting data are analyzed using an Agilent Bioanalyzer.

Undergraduate general chemistry experiments performed with microfluidics provide students with experience with reactor configurations that are relevant to many industrial processes (Table 1—General Chemistry) [20, 26]. In many traditional synthetic chemistry labs, reactions are run in batches in a beaker or other container. In many industrial processes, however, most chemical syntheses are performed in a continuous process. Microfluidic devices allow students to simulate continuous reactions on a small scale. The reduction in reagent volume decreases safety hazards of running continuous processes [26]. For example, acid base titrations can be performed in microfluidic devices [27]. Microfluidics allow lab instructors to reach the same results of traditional experiments with lower overhead cost [28]. In addition to titration experiments, students can also design pH detecting and monitoring devices that can be adapted to students of varying educational stages [29, 30].

Microfluidic experiments can also be used to teach chemistry to high school students. For example, microfluidic devices can be created using Shrinky Dinks and can be used to study acid base chemistry [30]. Experiments with such devices introduce students to acid-base neutralization through mixing in a device with curved channels and the design process for microfluidic systems. Implementing microfluidics in the classroom requires an

**Table 1** Examples of microfluidics implemented in educational settings with corresponding techniques involved and associated learning outcomes

		Educational level	Source/made by	Key components	Learning goals
Transport	Laminar Flow [16]	Upper Undergraduate	Purchased	Pump, Imaging	Visualize laminar flow at a microscale and apply the Navier-Stokes equation <sup>a</sup>
	Viscosity [18]	Upper Undergraduate	Instructor	Pressure Sensor, Pump, Imaging	Measure viscosity of different fluids using viscosity equations and linear regression
	Peclet Number [19]	Upper Undergraduate	Instructor	Pump, Imaging	Determine Peclet numbers and demonstrate their significance <sup>a</sup>
	Micromixers [17]	Undergraduate	Students	Imaging, Process Controls	Understand molecular interdiffusion using Reynolds, Peclet and Fourier Numbers
Biology	Binding Kinetics	Undergraduate	Purchased	Pump, Process Controls	Determine binding kinetics in undergraduate biology labs
	Nucleic Acid Detection [2]	Upper Undergraduate	Instructor	Imaging	Understand how to perform diagnostic techniques such as PCR <sup>a</sup>
	Microfluidics for Microbial Ecology [31]	Graduate	Student	Pump, Imaging,	Glucose detection, Viscometer, Flow in a porous medium, droplet formation
	Separations	Undergraduate	Students	Pump, Imaging, Process Controls	Test reproducibility of chemical separations
Analytical chemistry	Colorimetry [22]	Undergraduate	Students	Imaging, Process Controls	Design microfluidics for colorimetric analysis in analytical chemistry labs
	Quantification [22, 32]	Undergraduate	Purchased	Pump, Imaging	Quantify relevant chemical compounds in analytical chemistry labs
	Titration	Highschool/ Undergraduate	Students	N/A	Perform a titration, evaluate and present results
General chemistry	Continuous Reactions	Upper Undergraduate	Students	Pump	Design a microfluidic device for a continuous organic synthesis reaction and assess the product

Microfluidics modules have been implemented at a variety of educational levels from high school to graduate level courses. Device fabrication does not always happen within the classroom and can be constructed by the instructor or purchased online [16] (Fintschenko et al. [16] includes a table of online resources to purchase microfluidics for education). Some devices require additional accessories for the implementation and collection of data from within the device. Finally, each module had a variety of learning outcomes, the significant ones are outlined above. Examples of implemented microfluidics modules spanned across general chemistry, analytical chemistry, biology, and transport courses

<sup>a</sup>Designates methodologies that may be easily implemented for remote learning.

upfront investment of the instructor's time to adapt the mode of learning, but that time can yield a return in terms of student engagement and adaptability due to the small, modular nature of such devices. There are opportunities

for further educational research into the benefits of including a hands-on microfluidic component with a class versus the potential consequences of costing extra lecture time. This cost is likely worth the investment to include active

learning pedagogical approaches that microfluidics afford regardless of synchronicity (something that accompanying videos can facilitate).

### Adapting Biosensing Point-of-Care Microfluidics for Educational Activities

The portability of microfluidics also can enable remote education opportunities. For instance, point-of-care (POC) diagnostic microfluidic devices [33] and wearable real-time biosensors [34] can be adapted for biology and bioengineering wet lab courses that are taught remotely. As an example, the advent and development of isothermal PCR-like amplification have been integrated with smartphone-coupled microfluidic devices [2, 35]. Devices that are developed for use in the field hold promise for instructional data collection with remote learning (Fig 1). Such devices reduce the need for specific lab-designated space/machinery and can replace traditional PCR methods [36].

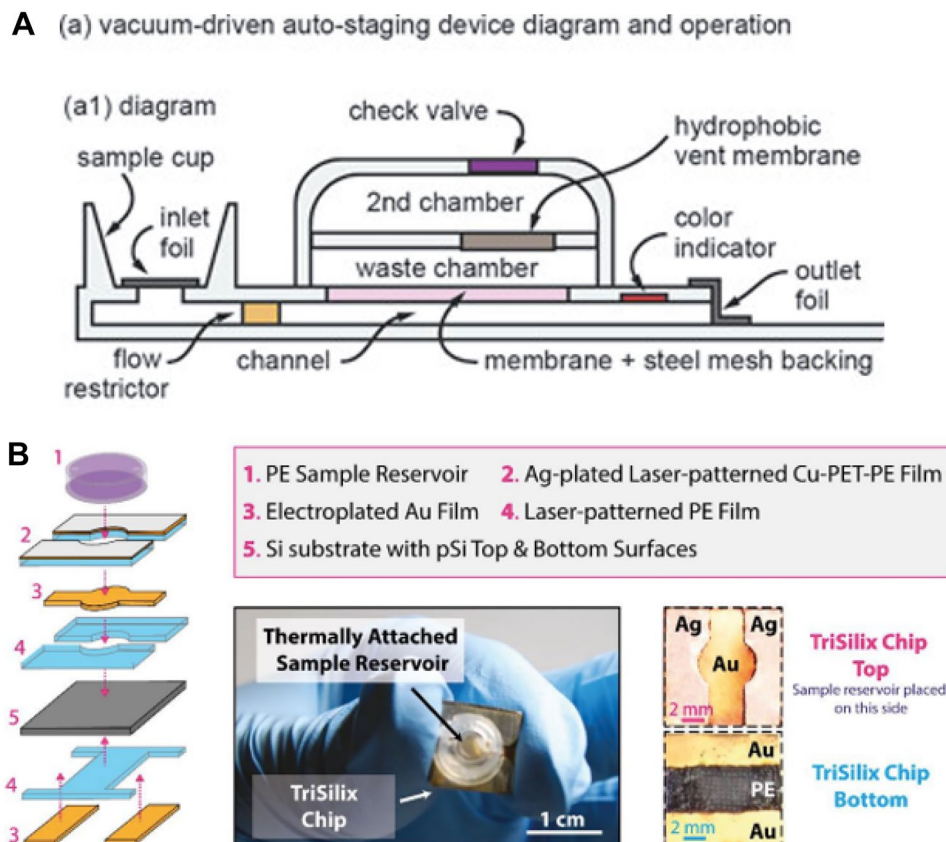
Furthermore, there are a number of commercially available isothermal nucleic acid detection (LAMP) kits that have been coupled with microfluidics for nucleic acid detection [37]. One example is a smartphone-based multiplex 30-minute viral nucleic acid test that uses a nasal swab specimen to quickly ( $\sim 30$  min) detect viral DNA with loop-mediated isothermal amplification (LAMP) [2]. This method has a

detection limit close to commercial thermocyclers,  $5.5 \times 10^4$  copies per mL, i.e.,  $\sim 18$  copies/cycle [2]. This smartphone device could be extended by integrating an assay similar to the assay developed for SARS-CoV-2 and HIV to be used for COVID or HIV/AIDs investigations [38]. These devices functionalities can also be adapted for educational experiences to train the next generation of scientists and engineers. Specifically, such a lab course activity could be designed in which students isolate and conduct nucleic acid testing of bacteria such as *E. coli* within prefabricated, 3-D printed devices. The reagents for such detection devices are provided by Sun et al. [2], the protocol to create such a device is provided by Chen et al. [3], and a portable COVID-19 specific detection device is described in Ganguli et al. [39]. Such approaches integrated within college sophomore/junior-level biology labs would allow remote students to complete lab-type data collection for nucleic acid testing outside of a traditional classroom setting. Additional options include adapting current educational PCR labs, such as miniPCR, toward the remote microfluidics platform [40].

### Democratization of Microfabrication for a Broad Spectrum of Research and Teaching Labs

Simple and cost-effective methods of microfabrication allow researchers and educators to incorporate microfluidics into

**Fig. 1** Examples of bio-microfluidic devices developed for point-of-care diagnostics. **A** Analysis of pressure-driven membrane preconcentration for point-of-care assays [41]. Reproduced from Ref. [41] with permission from AIP. **B** Disposable silicon-based all-in-one micro-qPCR for rapid on-site detection of pathogens [35]. PE film is polyethylene film. Reproduced from Ref. [35] under Creative Commons License.



**Table 2** Overview of fabrication techniques and associated costs and challenges to implement.

Fabrication technique	Listed resolution	Technical limitations	Capital cost (approx. 2021 costs)	Reagent/supply cost (approx.)	Time to fabricate device	Barriers to implement in class	Suggested implementation
Etched tape and glass cover slips [44]	~ 1 mm	Low resolution, and limited applications	\$10	\$0.50	1 hour	Too simple for many applications	Individual student fabrication
Pasta/PDMS [42]	~ 1 mm	Low resolution	\$20	\$5	1 day	Multiple day process	In-class or remote individual fabrication <sup>a</sup>
3D printing [10, 45, 46]	10 $\mu$ m	Limited channel shapes	\$400–4000	\$25	2 days	More challenging design process	Designs submitted to an instructor for remote printing <sup>a</sup>
Paper microfluidics (ink jet printing) [43]	5 $\mu$ m	Some expensive equipment and materials	\$30,000	\$0.10	5 hours	High initial cost	Asynchronous or instructor fabricated device <sup>a</sup>
Xurography [14, 47]	25 $\mu$ m	Requires alignment of layers by hand	\$400	\$1	2 hours	Low yield	Design submitted to instructor or group fabrication <sup>a</sup>
Photolithography	15 nm	Expensive and significant training	\$1000–10,000	\$50	1 week	Multi-day fabrication process	Highest level—graduate focused class

<sup>a</sup>Designates methodologies that may be easily implemented for remote learning.

their workflow and curricula. Traditionally, microfluidic devices have been created with photolithography, a technique that requires multi-million-dollar clean rooms and extensive training (Table 2). This presents a high entry barrier to develop and utilize microfluidics, thus limiting this approach to users that can afford the cost of time in a clean room [10]. Three dimensional (3D) printing and laser cutting have also been used to produce microfluidics, but these methods require specialized equipment that some schools and universities do not have (Table 2) [42]. 3D printing often lacks the resolution required for biosensing and cell separation applications. Sensing often requires very small amounts of fluids, and 3D printers lack the resolution to create devices with such small channels. Inkjet printing provides a resolution of ~ 5  $\mu$ m as an alternative to traditionally 3D printed microfluidics [43]. The devices as described by Su et al. (2016) are fabricated via inkjet printing on paper. Paper-printed devices have applications in electronics, and the microfluidic devices can be printed onto virtually any substrate (Table 2). This technique allows for rapid fabrication with low cost and high precision. While there have been great advances in developing new methods of fluidic fabrication that enable educational tools for remote educational experiences, there remains a need for low-cost prefabricated microfluidics kits available at scale.

Traditional 3D printing techniques make certain configurations such as serpentine channels difficult to fabricate. The

layer-by-layer deposition requires support structures beneath each feature, which must be removed before use [46]. A new technique of 3D printing using DLP/SLA (digital light processing/stereolithography apparatus) resin instead of PDMS (Polydimethylsiloxane), which is used in traditional photolithography, can create more complex microchannels and intersections of channels [46]. As a test case, the 3D printing method led to the creation of a device containing spiral microchannel with right-angled triangular cross-section for cell separation which was technically impossible to fabricate using standard lithography. In addition to the complex structure of these microfluidic devices, DLP/SLA 3D printed devices are capable of withstanding much higher amounts of pressure (up to 150 psi) as compared to PDMS, which can withstand pressures of ~ 50 psi [46]. Furthermore, for cell culture applications, it can be difficult to fabricate devices using polystyrene (PS), the standard substrate of choice for many protocols. A new method of fabrication without the previously necessary toxic reagents was used to make high strength bonds of PDMS and PS to create leak free and toxin free microfluidics for cell culture [48]. In addition to the developments of microfabrication techniques, there have also been optimization of microfluidic devices for delicate applications, such as tissue dissociation [49]. Such microfluidic devices need to be highly optimized for disassociation techniques. Certain materials such as PDMS are not optimal for the high-flow and high-pressure requirements of tissue



dissociation [50]; rather polyimide film is preferred. Both the shape of the microchambers and device materials influence the relative success of cell retrieval from dissociation. Materials such as PDMS are affordable. However, the techniques of fabrication and associated required machinery still limit affordability and access.

Traditionally, microfluidic devices are fabricated in a clean room on equipment that require extensive training to use [51–53]. Alternative methods of fabrication such as xurography or razor cutting take advantage of low cost desktop cutting plotters, and microfluidic devices are able to be created with a large number of design possibilities and high precision with intuitive consumer software [54]. Xurography exhibits lower feature resolution ( $\geq 25\ \mu\text{m}$ ) than photolithography ( $\geq 15\ \text{nm}$ ) but the conceptualization to completed fabrication time can be reduced to a few minutes, which allows for rapid prototyping [55]. Xurography-based microfluidic devices lend themselves to introduce microfluidic fabrication in undergraduate classes [56].

Fabrication is a hurdle for most undergraduate classes because many traditional techniques require a long-time frame (multiple days/weeks) and significant expertise because they involve training on delicate expensive machinery, which precludes many applications in the undergraduate class setting or in remote learning scenarios. To overcome this barrier, fabrication methods are needed at low cost and high iterability to integrate well into an educational setting. One proposed solution uses easily accessible affordable items such as pasta, petroleum jelly and PDMS to create microfluidics for a class [42]. In this technique, pasta is molded into different shapes after soaking and dried into a variety of 2D and 3D configurations. The desired pasta shape is then placed in petroleum jelly and PDMS is poured over the top of the pasta in the petroleum jelly and allowed to cure. The PDMS then is peeled away from the pasta and petroleum jelly to reveal the channels with the defined geometry. This novel technique lowers the barrier to entry for microfluidic study in undergraduate labs and research labs interested in working with microfluidics, because students can create microfluidic devices without training on any equipment or software. This is an example of a simplified microfabrication technique that introduces students to microfluidics and microfabrication. A potential drawback of this method is that there is no computer automated design aspect, and the physical mold is the only ‘copy’ of any design and is not repeatable at scale.

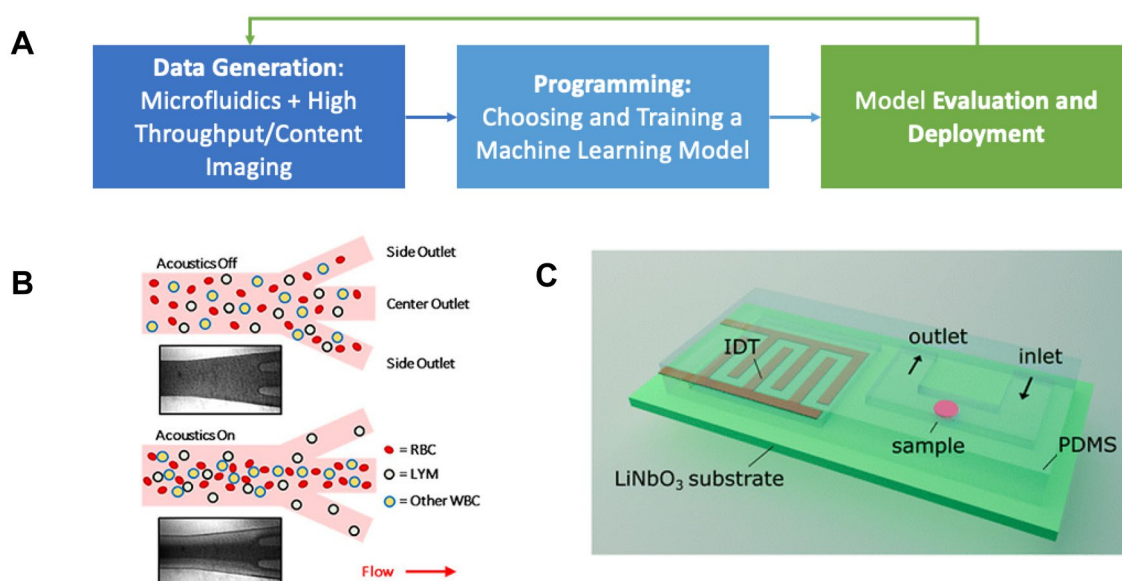
Recently, the Crone and Carpick groups at University of Wisconsin used microfluidic devices to conduct an undergraduate lab in micro- and nano-scale mechanics [56]. Simple glass coverslip microfluidic devices were tested and optimized in the labs. These classroom activities highlight how low-cost microfluidics are powerful tools for diagnostics and research in the developing world. For example, paper-based

microfluidic devices enable the diagnosis of patients without a trained expert, access to power, or expensive tests [57]. Advantages of these low-cost devices include providing more analytical power to areas with limited access to important chemical reagents, power, and highly trained personnel. Additionally, microfluidic device fabrication allows students to gain experience with the iterative engineering design process. Due to limited access to pre-designed kits, the use and fabrication of microfluidics are primarily do-it-yourself (DIY). Microfluidics integrated with traditional learning requires a time commitment from instructors that may involve significant troubleshooting. Despite this potential use of time the use of microfluidics increases the possibility of active learning.

### Advanced Topics: Educational Opportunities Utilizing High-Throughput Devices

Recently, high throughput devices have synergized with machine learning techniques, including AI, for a host of data-driven observation and modeling applications (Fig 2A) [4]. For example, microfluidic devices allow for the scale-up of organ/organism culture throughput. Microfluidics can control the chemical, mechanical, and electrical environment of culture chambers [58]. Frequently used model systems include *C. elegans*, *Drosophila*, and zebrafish, which share several complementary features that make them amenable to studies in microfluidic devices [59–62]. However, these organisms are larger than micro-scale cells (or small particles). These meso-scale samples require a specific toolkit to sort and manipulate whole-organism sized samples for high throughput experimental assays.

Recently, an acoustofluidic device was created that automates label-free blood sample sorting (Fig 2B) [63]. Notable advances include the use of low-cost polystyrene (as opposed to glass or silicone), which allow for twelve parallel channels to sort blood samples, while maintaining the sensitive discrimination of cell types that had been previously developed in single-channel devices. This sample sorting is extended to automated sorting of *C. elegans* and other whole-animal samples [59, 64]. Differences in size and fluorescence allow for imaging, analysis, and autonomous sorting of samples without requiring immobilization or physical contact. The continuous sorting was able to reach nearly 100% efficacy sorting worms at different ages with minimal toxicity. Companies such as Carolina Biological Supply Company allow educators to purchase such model organisms for study [65]. Additionally, mechanical actuation and pressure flow actuated devices have been created to automate controlled perturbations on living systems (reviewed in detail here [66]). Specifically, Fig 2C shows another acoustofluidic device for probing quantitative cell mechanical properties, which is coupled with a computational mechanical model. A



**Fig. 2** High throughput microfluidics, synergies with AI, and developments in acoustofluidics. **A** High throughput microfluidic devices paired with high content imaging on microscopes are particularly synergistic with artificial intelligence. Figure panel summarizes Ref. [4]. **B** Scalable high-throughput acoustophoresis in arrayed plastic

microchannels demonstrates the use for blood sorting [63]. Reprint from Ref. [63] with permission from AIP. **C** Acoustic erythrocytometer for mechanically probing cell viscoelasticity [67]. Reproduced from Ref. [67] under Creative Commons License.

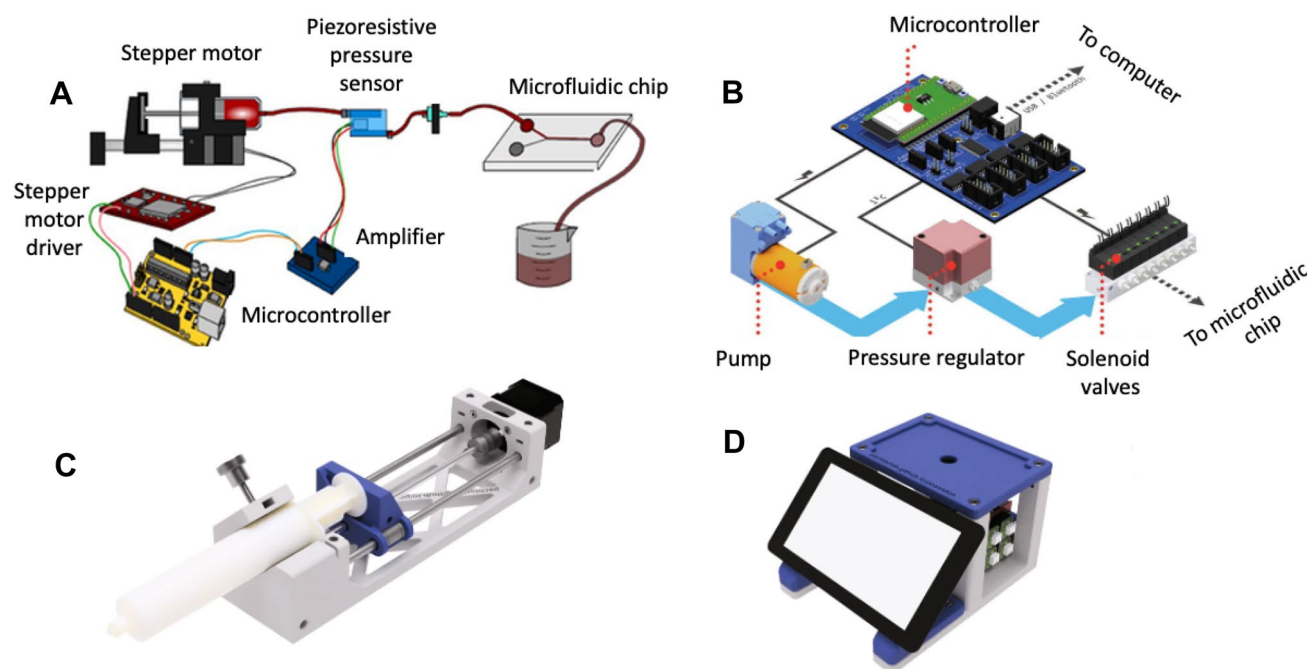
LiNbO<sub>3</sub> ferroelectric/piezoelectric substrate is used to generate the surface acoustic waves for contact free perturbations and associated measurements within the device [67]. These devices provide many examples of the diversity of novel microfluidic devices that can be translated to provide cutting-edge hands-on educational experiences that combine biology and engineering. For example, blood sorting with acoustofluidics can be mimicked for remote learning with the use of sorting microspheres. These can be imaged with an iPhone and analyzed with FIJI or other free software. Thresholds can be adjusted and measurements of efficacy sorting due to size or fluorescence sorting can be quantified. Speakers from a smartphone can induce flow disturbances in microfluidic devices [68]. Due to the flexible resolution requirements for creating channels and features that are needed for larger living organisms, these devices can be adapted using low-cost microfluidics [14, 61].

### Advanced Topics: Syringe Pumps and Process Controls are Key to Microfluidic Usage

A key issue for low cost and transportable microfluidics is the controlled regulation of fluid flow. Generally syringe pumps, as opposed to peristaltic or recirculation pumps are used, because of their ability to reliably perfuse incredibly small volumes [69]. These pumps cost on the order of thousands of dollars for a commercial model (e.g., Harvard Apparatus Pump 11 Elite infuse-only single syringe pump).

A lower end syringe pump can cost in the range of a few hundred dollars (e.g., New Era Pump Systems NE-300 Just Infusion Syringe Pump) [70]. These lower cost pumps are limited in their use for infusing small volumes, the user must know the dimensions of their syringes (pre-programming and programmability not included), and target volumes cannot be set. A commercial syringe pump (Harvard Apparatus) is standard for research purposes and was used for example, in the microfluidic viscometer described in the section on “Educational Applications of Microfluidics.” For microfluidic experiments to be fully cost effective for remote learning applications, their accessories must also be cost effective as well. To this end, a number of research groups have designed DIY solutions that reduce the cost of said pumps tenfold to hundreds of dollars [11–13, 69]. This cost could still be prohibitive for some classes and requires more development to lower costs or would require avoiding class projects that require fluidic pumps (See Table 1—Components).

Such DIY pumps are controlled by microchips such as an Arduino and made from a combination of 3D printed parts and off-the-shelf hardware. The designs are available free online through sites such as GitHub [71]. Another key advantage is that these devices can be assembled in under an hour, thus enabling the use of these syringe pumps for a classroom or remote learning situation [11]. These syringe pumps are becoming increasingly sophisticated in that they contain control systems capable of maintaining constant pressure throughout time with either PID (proportional,



**Fig. 3** Open source and low-cost flow pumps, control systems, and microscopes for use with microfluidic devices. **A** A low-cost (\$110) feedback-controlled syringe pressure pump for use with microfluidic devices using PID and Bang-Bang methods to regulate pump pressure [69]. The liquid containing syringe is held in place by the 3D printed syringe pump parts, shown in black. These parts connect to a stepper motor, depicted with gray and black stripes. When this stepper motor is actuated, the syringe pushes liquid through Tygon tubing, which passes through a piezoresistive pressure sensor before entering a microfluidic channel. The electrical signal from the sensor is passed to an instrumentation amplifier, shown with the dark blue rectangle,

before being transmitted and received by analog pins on an Arduino microcontroller. In response to these signals, the Arduino actuates the syringe pump via a stepper motor driver, closing the feedback loop. Reproduced from Ref. [69] under Creative Commons License. **B** All-in-one automated microfluidics control system with integrated pressure control and solenoid valves [72]. Reproduced from Ref. [72] under Creative Commons License. **C** and **D** Poseidon System syringe pump (C) and microscope (D) are open source and made from 3D printed and consumer parts [11]. Reproduced from Ref. [11] under Creative Commons License.

integral, and derivative error) or bang-bang control methods (Fig 3A) [69]. Even more recently these pumps have been integrated with more functionality to control both pressure and valve opening/closing within the platform (Fig 3B) [72]. The Patcher Lab even includes designs of a corresponding DIY microscope to replace the need for purchasing a traditional light microscope (Fig 3C, D) [11]. These examples of open source and low-cost pumps and integrated microfluidic platforms lay the foundation for increased accessibility and adoption of microfluidic technologies. Recently, reinforced latex balloons have also been incorporated into microfluidic devices to provide pressure driven flow [73]. Despite the advantages of DIY microfluidic control systems, they still require time and training to build, so there is still a need for commercially available low-cost pumps to allow microfluidic control systems to be financially conducive to classroom settings.

## Challenges and Emerging Opportunities for Microfluidics in Education

Translating low-cost microfluidic fabrication techniques and open-source devices can enhance course learning outcomes, both in traditional and remote learning modalities. Microfluidic approaches increase the ways in which students learn both basic and advanced topics by providing visual and interactive examples of several topics on a small scale. As experiential tools, microfluidics lower barriers to demonstrating key concepts in chemistry, biology, physics, and engineering. Microfluidic modules can increase student involvement and thus motivation through active learning pedagogy [74]. Additionally, hands-on experience with microfluidic devices correspondingly leads to new opportunities for employment, commercialization, and entrepreneurship in the growing microfabrication industry [8].

While promising to enhance learning experiences, implementation of microfluidics into courses still requires significant work. There are two potential educational thrusts



for microfluidics in education. First, microfluidics/micro-fabrication experts may seek to incorporate microfluidics into courses via design and implementation projects or fabrication labs. Second, instructors without specific expertise in microfluidics/microfabrication may want to incorporate demonstrations of key topics in the courses they teach. Each of these educational objectives will have distinct barriers to implementation (Fig. 4).

### Gap Analysis: Teaching Microfabrication Remotely/Online

A subset of instructors may already use microfluidics in their research or perform micro-fabrication in their graduate-level courses. For this expert population, the open source and 3D-printable microfluidic systems may provide a route to introducing microfluidics into lower-level courses or in remote teaching scenarios. Here, we highlight a variety of microfluidic applications that inspire extensions for existing lab or design course. In many cases, microfabrication does not require a clean or semi-clean room. A variety of materials can be used at equally diverse price points. Examples

like the PETL system demonstrate how students can design microfluidic devices on their laptops and then submit for fabrication [14]. Subsequently, they will receive the commercially fabricated product in the mail. The key barriers to implementation for this scenario are how best to simplify microfabrication utilized in research for course activities. The highlighted examples of microfluidics provide a resource to encourage the translation of microfabrication in the classroom.

### Gap Analysis: Teaching Microfluidic Applications Remotely/Online

Many educators are seeking tools and experiential (active learning) opportunities for general science and engineering courses, including remote/hybrid lab courses. Here, the need is to continue to advance course instruction in line with industry needs and pedagogical standards. For instructors who want to incorporate microfluidics in their classes, the greatest challenge to implementation is to identify out-of-the-box prefabricated tools. Here, a solution from the

**Fig. 4** Strengths, Weaknesses, Opportunities, and Threats (SWOT) Analysis for the implementation of microfluidics into courses.



microfluidic ChipShop, Lab Smith, or the PETL Fluidics company provide prepared educational kits that can be used by instructors or students themselves to show key concepts or to learn about microfluidic control systems (see Table 1, “Purchased” microfluidic chips) [75–77]. In each case, the key challenges to overcome are the time and cost required for implementation. Further advancements through “hackable” microfluidic systems will lead to creative, and cheaper solutions.

## Future Directions

There are both benefits and challenges in using microfluidics as educational tools. All classes are limited in terms of the content that can be covered. Introducing a microfluidics component necessarily reduces time for discussion of other topics. Most microfluidic modules are still DIY as many microfluidic technologies are still emerging. Multiple researchers have noted the quiescent promise of microfluidics (see Beebe 2002; Sackman 2014) [1, 15]. Microfluidics are rounding the corner of mass appeal/interest and are accelerating in research, industry and market size [6, 8, 9]. 3-D printing took off when there was a surge in open-source technologies that allowed for ‘hackability’ that drove the prices down from the increased innovation. Similarly, microfluidics are now moving into the space of open-source and low-cost options. Even though several low-cost research devices have been developed, it can still be expensive and time consuming to incorporate microfluidic exercises within a class. Due to the existing constraints and lack of commercial kit options, many class environments are not presently suited to include microfluidics. However, low cost and open-source microfluidics are advancing at a rapid rate that will only decrease barriers to implementation in and out of the classroom [9]. Overall, these factors suggest that microfluidic labs have significant potential to provide students with remote experiential learning opportunities with strong learning outcomes.

**Acknowledgements** We thank Professor Fernando Ontiveros (St. John Fischer College), Mayesha Sahir Mim (Notre Dame), Victoria Goodrich (Notre Dame) and the 2020-21 Notre Dame Institute for Advanced Study (NDIAS) Graduate Fellows for feedback on early versions of the manuscript.

**Funding** JZ was supported in part by NIH R35GM124935, NSF CBET-1553826, and NSF DBI-2120200. ML was supported by NIH R35GM124935, NSF CBET-1553826 and Notre Dame’s Technology Ethics Center.

**Data Availability** Data sharing is not applicable to this article as no new data were created or analyzed in this study.

**Code Availability** Code sharing is not applicable to this article as no new code were created in this study.

## Declarations

**Conflict of interest** The authors indicate no conflicts of interest.

**Ethical Approval** No ethics approval is required since no data was collected.

**Consent to Participate** No participation consent is required since no data was collected.

**Consent for Publication** Figures from this paper have been previously published and have been accessed under creatives commons licenses and through approval as indicated in the figure captions.

## References

1. Beebe DJ, Mensing GA, Walker GM. Physics and applications of microfluidics in biology. *Annu Rev Biomed Eng.* 2002;4:261–86.
2. Sun F, et al. Smartphone-based multiplex 30-minute nucleic acid test of live virus from nasal swab extract. *Lab Chip.* 2020;20:1621–7.
3. Chen W, et al. Mobile platform for multiplexed detection and differentiation of disease-specific nucleic acid sequences, using microfluidic loop-mediated isothermal amplification and smartphone detection. *Anal Chem.* 2017;89:11219–26.
4. Isozaki A, et al. AI on a chip. *Lab Chip.* 2020;20:3074–90.
5. Galan EA, et al. Intelligent microfluidics: the convergence of machine learning and microfluidics in materials science and biomedicine. *Matter.* 2020;3:1893–922.
6. Microfluidics market size to reach US\$ 32.97 billion by 2027. GlobeNewswire News Room. 2020. <http://www.globenewswire.com/news-release/2020/11/10/2124073/0/en/Microfluidics-Market-Size-to-Reach-US-32-97-Billion-by-2027.html>.
7. Itd R M. Microfluidics Market by Product (Devices, Components (Chips, Sensors, Pump, Valves, and Needles), Application (IVD [POC, Clinical, Veterinary], Research, Manufacturing, Therapeutics), End User and Region - Global Forecast to 2025. <https://www.researchandmarkets.com/reports/5031311/microfluidics-market-by-product-devices>.
8. Global Microfluidics Industry (2020 to 2025) - Expanding Applications of Drug Delivery Technologies Presents Opportunities - ResearchAndMarkets.com. 2020. <https://www.businesswire.com/news/home/20200527005431/en/Global-Microfluidics-Industry-2020-to-2025---Expanding-Applications-of-Drug-Delivery-Technologies-Presents-Opportunities---ResearchAndMarkets.com>.
9. Researchers open up low-cost open-source microfluidics 3D printing. 3D Printing Industry. 2021. <https://3dprintingindustry.com/news/researchers-open-up-low-cost-open-source-microfluidics-3d-printing-184761/>.
10. Ho CMB, Ng SH, Li KHH, Yoon Y-J. 3D printed microfluidics for biological applications. *Lab Chip.* 2015;15:3627–37.
11. Boeshaghi AS, da Beltrame EV, Bannon D, Gehring J, Pachter L. Principles of open source bioinstrumentation applied to the poseidon syringe pump system. *Sci Rep.* 2019;9:12385.
12. Klar V, Pearce JM, Kärki P, Kuosmanen P. Ystruder: open source multifunction extruder with sensing and monitoring capabilities. *HardwareX.* 2019;6: e00080.
13. Wijnen B, Hunt EJ, Anzalone GC, Pearce JM. Open-source syringe pump library. *PLoS ONE.* 2014;9: e107216.

14. Levis M, et al. Microfluidics on the fly: Inexpensive rapid fabrication of thermally laminated microfluidic devices for live imaging and multimodal perturbations of multicellular systems. *Biomicrofluidics*. 2019;13: 024111.
15. Sackmann EK, Fulton AL, Beebe DJ. The present and future role of microfluidics in biomedical research. *Nature*. 2014;507:181–9.
16. Fintschenko Y. Education: a modular approach to microfluidics in the teaching laboratory. *Lab Chip*. 2011;11:3394–400.
17. Archer S. Microfluidics and microfabrication in a chemical engineering lab. *Chem Eng Educ*. 2011;45:285–9.
18. Kim S, Kim KC, Yeom E. Microfluidic method for measuring viscosity using images from smartphone. *Opt Lasers Eng*. 2018;104:237–43.
19. Piunno PAE, et al. A comprehensive microfluidics device construction and characterization module for the advanced undergraduate analytical chemistry laboratory. *J Chem Educ*. 2014;91:902–7.
20. Rackus DG, Riedel-Kruse IH, Pamme N. “Learning on a chip:” microfluidics for formal and informal science education. *Biomicrofluidics*. 2019;13: 041501.
21. Teerasong S, McClain RL. A student-made microfluidic device for electrophoretic separation of food dyes. *J Chem Educ*. 2011;88:465–7.
22. Cai L, Wu Y, Xu C, Chen Z. A simple paper-based microfluidic device for the determination of the total amino acid content in a tea leaf extract. *J Chem Educ*. 2013;90:232–4.
23. Schindelin J, et al. Fiji: an open-source platform for biological-image analysis. *Nat Methods*. 2012;9:676–82.
24. Merrin J. Frontiers in microfluidics, a teaching resource review. *Bioengineering (Basel)*. 2019;6:E109.
25. Chao T-C, Bhattacharya S, Ros A. Microfluidic gel electrophoresis in the undergraduate laboratory applied to food analysis. *J Chem Educ*. 2012;89:125–9.
26. Feng ZV, Edelman KR, Swanson BP. Student-fabricated microfluidic devices as flow reactors for organic and inorganic synthesis. *J Chem Educ*. 2015;92:723–7.
27. Cai L, Ouyang Z, Huang X, Xu C. Comprehensive training of undergraduates majoring in chemical education by designing and implementing a simple thread-based microfluidic experiment. *J Chem Educ*. 2020. <https://doi.org/10.1021/acs.jchemed.9b01201>.
28. Kapoor A, Balasubramanian S, Vaishampayan V, Ghosh R. Lab-on-a-chip: a potential tool for enhancing teaching-learning in developing countries using paper microfluidics. In: International conference on transforming engineering education (ICTEE), pp. 1–7. 2017. <https://doi.org/10.1109/ICTEED.2017.8586151>.
29. Greener J, Tumarkin E, Debono M, Dicks AP, Kumacheva E. Education: a microfluidic platform for university-level analytical chemistry laboratories. *Lab Chip*. 2012;12:696–701.
30. Hemling M, et al. Microfluidics for high school chemistry students. *J Chem Educ*. 2014;91:112–5.
31. Salek MM, et al. An interdisciplinary and application-oriented approach to teach microfluidics. *Biomicrofluidics*. 2021;15: 014104.
32. Giri B, Peesara RR, Yanagisawa N, Dutta D. Undergraduate laboratory module for implementing ELISA on the high performance microfluidic platform. *J Chem Educ*. 2015;92:728–32.
33. Nasserli B, et al. Point-of-care microfluidic devices for pathogen detection. *Biosens Bioelectron*. 2018;117:112–28.
34. Koh A, et al. A soft, wearable microfluidic device for the capture, storage, and colorimetric sensing of sweat. *Sci Transl Med*. 2016;8:366ra165.
35. Nunez-Bajo E, et al. Disposable silicon-based all-in-one micro-qPCR for rapid on-site detection of pathogens. *Nat Commun*. 2020;11:6176.
36. Keikha M. LAMP method as one of the best candidates for replacing with PCR method. *Malays J Med Sci*. 2018;25:121–3.
37. Mori Y, Notomi T. Loop-mediated isothermal amplification (LAMP): a rapid, accurate, and cost-effective diagnostic method for infectious diseases. *J Infect Chemother*. 2009;15:62–9.
38. Ding X, Yin K, Li Z, Liu C. All-in-One Dual CRISPR-Cas12a (AIO-DCRISPR) Assay: A Case for Rapid, Ultrasensitive and Visual Detection of Novel Coronavirus SARS-CoV-2 and HIV virus. 2020. <https://doi.org/10.1101/2020.03.19.998724>.
39. Ganguli A, et al. Rapid isothermal amplification and portable detection system for SARS-CoV-2. *PNAS*. 2020;117:22727–35.
40. miniPCR Sleep Lab™ - Lark or Owl? miniPCR. <https://www.minipcr.com/product/minipcr-sleep-lab/>.
41. Drexelius A, et al. Analysis of pressure-driven membrane pre-concentration for point-of-care assays. *Biomicrofluidics*. 2020;14: 054101.
42. Nguyen N, et al. “Do-it-in-classroom” fabrication of microfluidic systems by replica moulding of pasta structures. *Biomicrofluidics*. 2018;12: 044115.
43. Su W, Cook BS, Fang Y, Tentzeris MM. Fully inkjet-printed microfluidics: a solution to low-cost rapid three-dimensional microfluidics fabrication with numerous electrical and sensing applications. *Sci Rep*. 2016;6:35111.
44. Greer J, Sundberg SO, Wittwer CT, Gale BK. Comparison of glass etching to xurography prototyping of microfluidic channels for DNA melting analysis. *J Micromech Microeng*. 2007;17:2407.
45. Yuen PK, Goral VN. Low-cost rapid prototyping of flexible microfluidic devices using a desktop digital craft cutter. *Lab Chip*. 2010;10:384–7.
46. RazaviBazaz S, et al. 3D printing of inertial microfluidic devices. *Sci Rep*. 2020;10:5929.
47. Bartholomeusz DA, Boutte RW, Andrade JD. Xurography: rapid prototyping of microstructures using a cutting plotter. *J Microelectromech Syst*. 2005;14:1364–74.
48. Song K-Y, Zhang H, Zhang W-J, Teixeira A. Enhancement of the surface free energy of PDMS for reversible and leakage-free bonding of PDMS–PS microfluidic cell-culture systems. *Microfluid Nanofluid*. 2018;22:135.
49. Qiu X, et al. Microfluidic channel optimization to improve hydrodynamic dissociation of cell aggregates and tissue. *Sci Rep*. 2018;8:2774.
50. Hardy BS, Uechi K, Zhen J, Kavehpour HP. The deformation of flexible PDMS microchannels under a pressure driven flow. *Lab Chip*. 2009;9:935–8.
51. Berlanda SF, Breitfeld M, Dietsche CL, Dittrich PS. Recent advances in microfluidic technology for bioanalysis and diagnostics. *Anal Chem*. 2021;93:311–31.
52. Paik S, et al. Near-field sub-diffraction photolithography with an elastomeric photomask. *Nat Commun*. 2020;11:805.
53. Ito T, Okazaki S. Pushing the limits of lithography. *Nature*. 2000;406:1027–31.
54. Islam M, Natu R, Martinez-Duarte R. A study on the limits and advantages of using a desktop cutter plotter to fabricate microfluidic networks. *Microfluid Nanofluid*. 2015;19:973–85.
55. Cosson S, Aeberli LG, Brandenburg N, Lutolf MP. Ultra-rapid prototyping of flexible, multi-layered microfluidic devices via razor writing. *Lab Chip*. 2014;15:72–6.
56. Crone WC, Carpick RW, Lux KW. Incorporating nanotechnology into undergraduate education. 6.
57. Martinez AW, Phillips ST, Whitesides GM, Carrilho E. Diagnostics for the developing world: microfluidic paper-based analytical devices. *Anal Chem*. 2010;82:3–10.
58. Levario TJ, Zhao C, Rouse T, Shvartsman SY, Lu H. An integrated platform for large-scale data collection and precise perturbation of live *Drosophila* embryos. *Sci Rep*. 2016;6:21366.

59. Zhang J, et al. Fluorescence-based sorting of *Caenorhabditis elegans* via acoustofluidics. *Lab Chip*. 2020;20:1729–39.
60. Narciso C, Zartman J. Reverse-engineering organogenesis through feedback loops between model systems. *Curr Opin Biotechnol*. 2018;52:1–8.
61. Levis M, Ontiveros F, Juan J, Kavanagh A, Zartman JJ. Rapid fabrication of custom microfluidic devices for research and educational applications. *JoVE J Vis Exp*. 2019. <https://doi.org/10.3791/60307>.
62. Mondal S, Ahlawat S, Koushika SP. Simple microfluidic devices for in vivo imaging of *C. elegans* *Drosophila* and Zebrafish. *J Vis Exp*. 2012. <https://doi.org/10.3791/3780>.
63. Dubay R, et al. Scalable high-throughput acoustophoresis in arrayed plastic microchannels. *Biomicrofluidics*. 2019;13:034105.
64. Afzal M, et al. Acoustomicrofluidic separation of tardigrades from raw cultures for sample preparation. *Zool J Linn Soc*. 2020;188:809–19.
65. Carolina® Science Distance Learning: Principles of Biology Kit. Carolina.com. <https://www.carolina.com/distance-learning-science-kits-solutions/carolina-science-distance-learning-principles-of-biology-kit/581001.pr>.
66. Zabihisari A, Hilliker AJ, Rezai P. Fly-on-a-chip: microfluidics for *Drosophila melanogaster* studies. *Int Bio (Cam)*. 2019;11:425–43.
67. Link A, Franke T. Acoustic erythrocytometer for mechanically probing cell viscoelasticity. *Lab Chip*. 2020;20:1991–8.
68. Thurgood P, et al. Generation of programmable dynamic flow patterns in microfluidics using audio signals. *Lab Chip*. 2021;21:4672–84.
69. Lake JR, Heyde KC, Ruder WC. Low-cost feedback-controlled syringe pressure pumps for microfluidics applications. *PLoS ONE*. 2017;12: e0175089.
70. SyringePump.com - NE-300 Just Infusion Syringe Pump. [http://www.syringepump.com/NE-300.php?gclid=Cj0KCQjw0caCBhCIAARIsAGAfMxHWqVRJt0pVMvbt3wt6HVXpuEF81bXJLTc20B6RpnEr1rI-v1\\_0-YaAoNqEALw\\_wcB](http://www.syringepump.com/NE-300.php?gclid=Cj0KCQjw0caCBhCIAARIsAGAfMxHWqVRJt0pVMvbt3wt6HVXpuEF81bXJLTc20B6RpnEr1rI-v1_0-YaAoNqEALw_wcB).
71. <https://pachterlab.github.io/poseidon/> (2019).
72. Watson C, Senyo S. All-in-one automated microfluidics control system. *HardwareX*. 2019;5: e00063.
73. Thurgood P, et al. Self-sufficient, low-cost microfluidic pumps utilising reinforced balloons. *Lab Chip*. 2019;19:2885–96.
74. Active Learning. Vanderbilt University. <https://cft.vanderbilt.edu/guides-sub-pages/active-learning/>.
75. Education. PetlFluidics. <https://www.petlfluidics.com/education>.
76. Microfluidic Starter Kits. microfluidic ChipShop. <https://www.microfluidic-chipshop.com/catalogue/microfluidic-kits/microfluidic-starter-kits/>.
77. Microfluidic Education Kit. LabSmith. <https://labsmith.com/product/education-kit/>.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.