TITLE:

Three-dimensional Printing of Thermoplastic Materials to Create Automated Syringe Pumps with Feedback Control for Microfluidic Applications

AUTHORS AND AFFILIATIONS:

Ming-Cheng Chen[1] *, John R. Lake[1] *, Keith C. Heyde[2], and Warren C. Ruder[1,2] *

[1]Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A.
[2]Department of Mechanical Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania, U.S.A.

*These authors contributed equally

CORRESPONDING AUTHOR:

Warren C. Ruder
warrenr@pitt.edu

EMAIL ADDRESSES OF CO-AUTHORS:

Ming-Cheng Chen (mic121@pitt.edu)
John R. Lake (jlake@mit.edu)
Keith C. Heyde (kheyde@andrew.cmu.edu)

KEYWORDS:

3D-printing, closed-loop, feedback, control, low-cost, microfluidics, pressure regulation, syringe pumps

SUMMARY:

Here we present a protocol to construct a pressure-controlled syringe pump to be used in microfluidic applications. This syringe pump is made from some additively manufactured body, off-the-shelf hardware, and open-source electronics. The resulting system is low-cost, straightforward to build, and delivers well-regulated fluid flow to enable rapid microfluidic research.

ABSTRACT:

Microfluidics has become a critical tool in research across the biological, chemical, and physical sciences. One important component of microfluidic experimentation is a stable fluid handling system capable of accurately providing an inlet flow rate or inlet pressure. Here, we have developed a syringe pump system capable of controlling and regulating the inlet fluid pressure delivered to a microfluidic device. This system was designed using low-cost materials and additive manufacturing principles, leveraging three-dimensional (3D) printing of thermoplastic materials and off-the-shelf components whenever possible. This system is composed of three main components: a syringe pump, a pressure transducer, and a programmable microcontroller. Within this paper, we detail a set of protocols for fabricating, assembling, and programming this syringe pump system. Furthermore, we have included representative results

that demonstrate high-fidelity, feedback control of inlet pressure using this system. We expect this protocol will allow researchers to fabricate low-cost syringe pump systems, lowering the entry barrier for the use of microfluidics in biomedical, chemical, and materials research.

INTRODUCTION:

Microfluidic tools have become useful for scientists in biological and chemical research. Due to the low volume utilization, rapid measurement capabilities, and well-defined flow profiles, microfluidics has gained traction in genomic and proteomic research, high-throughput screening, medical diagnostics, nanotechnology, and single-cell analysis[1-4]. Furthermore, the flexibility of microfluidic device design readily enables basic science research, such as investigating the spatiotemporal dynamics of cultured bacterial colonies[5].

Many types of fluid injection systems have been developed to accurately deliver flow to microfluidic devices. Examples of such injection systems include peristaltic and recirculation pumps[6], pressure-controller systems[7], and syringe pumps[8]. These injection systems, including syringe pumps, are often composed of expensive precision engineered components. Augmenting these systems with closed-loop feedback control of pressure in the output flow adds to the cost of these systems. In response, we previously developed a robust, low-cost syringe pump system that uses closed-loop feedback control to regulate outputted flow pressure. By using closed-loop pressure control, the need for expensive precision-engineered components is abrogated[9].

The combination of affordable 3D-printing hardware and a significant growth in associated open-source software has made the design and fabrication of microfluidic devices increasingly accessible to researchers from a variety of disciplines[10]. However, the systems used to drive fluid through these devices remain expensive. To address this need for a low-cost fluid control system, we developed a design that can be fabricated by researchers in the lab, requiring only a small number of assembly steps. Despite its low-cost and straightforward assembly, this system can provide precise flow control and provides an alternative to commercially available, closed-loop syringe pump systems, which can be prohibitively expensive.

Here, we provide protocols for the construction and use of the closed-loop controlled syringe pump system we developed (**Figure 1**). The fluid handling system is composed of a physical syringe pump inspired by a previous study[11], a microcontroller, and a piezoresistive pressure sensor. When assembled and programmed with a proportional-integral-derivative (PID) controller, the system is capable of delivering a well-regulated, pressure-driven flow to microfluidic devices. This provides a low-cost and flexible alternative to high-cost commercial products, enabling a broader group of researchers to use microfluidics in their work.

PROTOCOL:

1. 3D-printing and assembly of syringe pump

1.1. Prepare and 3D-print the syringe pump components.

1.1.1. Download the .STL design files from the **Supplemental Files** of this paper.

NOTE: There are six .STL files, titled 'JoVE_Syringe_Clamp_10mL_Size.stl', 'JoVE_Syringe_Platform.stl', 'JoVE_Syringe_Plunger_Connectors.stl', 'JoVE_Syringe_Pump_End_Stop.stl', 'JoVE_Syringe_Pump_Motor_Connector.stl', and 'JoVE_Syringe_Pump_Traveler_Push.stl', in the **Supplemental Files**. These files correspond to the 3D-printed components of the syringe pump.

1.1.2. Prepare these files for printing by opening them in a software package dedicated to the conversion of .STL model files to executable instruction sets for the 3D-printer being used. Ensure that the proper software is being used as some printers will require proprietary software, whereas others may be able to print directly from the .STL file.

1.1.3. Print the plastic components using acrylonitrile butadiene styrene (ABS) with a high-quality 3D-printer setting. If other common 3D-printing materials are being used, such as polylactic acid (PLA) or other thermoplastic elastomers, make sure that the finished mechanical properties (e.g. elasticity, yield strength) are comparable to ABS.

1.1.4. Detach the printed parts from the printing platform of the 3D-printer. Remove the printed supporting structure from the finished parts.

NOTE: The supporting structure is designed by the printer-specific software used to convert the .STL model files to the executable instruction set for the 3D-printer. The amount and the structure of the supporting material may vary based on the software used.

1.1.5. Smooth the printed components by sanding any rough edges using sandpaper. For best results, use sandpaper with a grit size below 220. Make sure all components are smooth before assembling.

1.1.6. Ensure that all seven parts have been printed.

NOTE: These parts have been named the following: (I) Motor Connector, (II) Traveler Push, (III) End Stop, (IV) Syringe Platform, (V) Syringe Clamp, (VI) Syringe Plunger Male Connector and (VII) Syringe Plunger Female Connector. The Roman numeral for each component is referred to in **Figure 2A**. A detailed list of the mechanical parts for the assembly is found in the **Table of Materials.**

1.2. Assemble the syringe pump (**Figure 2**).

1.2.1. Fasten the stepper motor to a threaded rod using a motor shaft Z-axis flexible coupler with set screws. Before continuing, make sure that rotating the stepper motor shaft drives the threaded rod without slippage.

1.2.2. Connect the syringe platform to the motor connector by firmly pressing the syringe platform's connection pegs into the mating holes on top of the motor connector.

1.2.3. Attach the assembled part in step 1.2.1 with the part in step 1.2.2 by fastening four 16 mm screws through the motor connector.

1.2.4. Insert two linear ball bearings and a 0.8 mm hex nut into the openings located on the bottom of the traveler push.

1.2.5. Align the threaded rod on the motor connector through the 0.8 mm hex nut in the traveler push.

1.2.6. Insert the two linear shafts through the traveler push and the motor connector.

1.2.7. Place two hex nuts in the hexagonal spaces of the motor connector piece, and then use two 16 mm screws to tighten the connections, securing the linear shafts from moving.

1.2.8. Insert the ball bearing into the middle opening of the end stop.

1.2.9. Connect the end stop with the assembled components from step 1.2.7.

1.2.10. Place two hex nuts in the hexagonal spaces of the end stop piece, and then use two 16 mm screws to tighten the connections to affix the end stop to the assembly.

1.2.11. Attach the syringe plunger female connector piece to the traveler push piece using two steel lock nuts and two 16 mm screws.

1.2.12. Place a 10 mL syringe on the top of the pump. Ensure the head of the plunger is aligned into the notch of the syringe plunger female connector piece and the top of the syringe barrel is fixed into the slot of the motor connector.

1.2.13. Insert the syringe plunger male connector piece into the syringe plunger female connector. Ensure that there is a tight fit between the male and female components, securing the plunger in place.

1.2.14. Connect the syringe clamp to the syringe platform using two hex nuts and two 35 mm screws, ensuring the syringe barrel is fixed into the slot of the syringe clamp.

2. Microfluidic device preparation

2.1. Fabricate master molds using photolithography.

NOTE: A procedure detailing the design and fabrication of master molds for microfluidic device fabrication may be found in previous literature[12].

2.1.1. Using the preferred computer-aided design (CAD) software, create the required drawings for a photomask and print it onto a glass or quartz plate.

NOTE: Other materials may be acceptable based on the requirements of the mask aligner used. The printing of these photomasks is typically completed by a third-party vendor.

2.1.2. Use photolithography methods to create a master mold from the photomask. Perform this procedure in a cleanroom environment.

2.1.3. Expose the fabricated master mold to a fluorosilane vapor in a vacuum desiccator.

NOTE: This process facilitates the release of polydimethylsiloxane (PDMS) from the master mold when fabricating microfluidic devices. To treat the master mold, add three drops of fluorosilane to a beaker and place the beaker in a vacuum chamber.

2.1.4. Apply a vacuum for 1 min. Close the vacuum chamber but keep the master mold in the chamber for 30 min to allow for the deposition of fluorosilane. As a safety precaution, perform this procedure in a fume hood to limit exposure to the hazardous fluorosilane vapor.

2.2. Fabricate PDMS devices.

2.2.1. Weigh the PDMS pre-polymer in a weigh boat. Although the desired thickness of the final PDMS device may vary, 30 g of pre-polymer works well for a master mold of 100 mm in diameter.

2.2.2. Measure and add a curing agent in a 1:10 ratio to the pre-polymer. For a master mold of 100 mm in diameter, add 3 g of a curing agent.

2.2.3. Mix the pre-polymer and curing agent vigorously by hand using a disposable spatula. After 30 s, check that there are small, regularly separated air bubbles in the solution, indicating the pre-polymer and curing agents are well-mixed.

2.2.4. Place the master mold in a culture plate and carefully pour the PDMS mixture on top of the master mold.

NOTE: The desired thickness of the PDMS device may vary depending on its application.

2.2.5. Degas the mixture in a vacuum desiccator for 1 hr. Ensure that no bubbles are observable within the mixture. If there are any bubbles present, release the vacuum pressure quickly, and then reapply a vacuum. Allow the mixture to sit for at least 10 min after this procedure.

2.2.6. Move the PDMS mixture to an oven set at 90 °C. Allow the mixture to cure for 30 min.

2.2.7. Remove the PDMS from the master mold. Cut the PDMS into the desired dimensions using a razor blade. Wear gloves to limit the PDMS exposure to contaminants.

2.2.8. Punch holes for inlet and outlet ports with a 23 G dispensing needle. To facilitate this process, file the needle with a metal file or sandpaper to sharpen the blunt ends. Ensure that the punctuated cylinder of PDMS is removed from the needle after every puncture.

NOTE: Needles with different sizes can be used for punching holes. Ensure the size is slightly bigger than the needles used in step 3 of this protocol.

2.2.9. Wash the PDMS with filtered deionized water and air-dry the PDMS using an air or nitrogen source fitted with a 0.2 µm filter.

NOTE: The exact pressure is not critical, and a pressurized gas source from a building's central system works well for this step.

2.2.10. Clean a No. 1 borosilicate cover glass substrate with a surfactant, such as a powdered detergent, and air-dry it using a pressurized air source fitted with a 0.2 µm filter. Clean it thoroughly as cover glass is often coated with a hydrophobic lubricant and is unable to bind to PDMS unless it is properly cleaned.

2.2.11. Using pressure-sensitive tape, lightly touch the PDMS to remove any residual dust. To ensure the molded features are not compromised, do not press with large amounts of force on the tape.

2.2.12. Place the PDMS device and a cleaned cover glass into an oxygen plasma cleaner for 1 min. Ensure the color from the plasma cleaner chamber is bright magenta during the process. Make sure that the PDMS device has its molded features exposed, face-up, in the plasma cleaner.

2.2.13. Take the PDMS and the cover glass from the plasma cleaner and place the cover glass, face-down, onto the PDMS device.

NOTE: This will cause the cover glass and the PDMS to bond almost immediately. If the binding is not visible, gently press the cover glass to the PDMS in a section of PDMS devoid of molded features. This should cause bonding to occur between the PDMS and the cover glass.

2.2.14. Put the PDMS device in an oven at 90 °C for at least 12 h to ensure the PDMS and the cover glass are well-bonded.

3. Feedback-controlled syringe pump system assembly

3.1. Remove 80% of the length of the wire insulation and shielding from a pressure sensor's electrical cable using a razor. Be gentle when cutting to ensure the wires are not compromised

above the desired length. Once the insulation and shielding are removed, connect the wires to male rectangular connectors.

3.2. Using a similar approach to the previous step, remove 1 - 2 cm of the wire insulation from a stepper motor's leads and connect the wires to male rectangular connectors.

3.3. Affix the syringe onto the inlet side of the pressure sensor. Connect a 22 G dispensing needle onto the outlet side of the pressure sensor.

3.4. Slide one end of 0.51 cm diameter tubing over the 22 G dispensing needle attached to the pressure sensor.

3.5. Slide the other end of 0.51 cm diameter tubing over a 22 G dispensing needle that can be connected to the microfluidic device. Connect the needle to the inlet port of the microfluidic device.

3.6. Connect the outlet port of a microfluidic device to a waste disposal reservoir using a 22 G needle and 0.51 cm diameter tubing, similar to the inlet port's connection.

3.7. Assemble the electronic circuit on a prototyping breadboard according to the diagram in **Figure 3**.

NOTE: This breadboard serves to condition the signal from the pressure sensor to be monitored by a microcontroller. Other compatible microcontrollers may be used to monitor the pressure sensor signal.

3.8. Connect the wires from the stepper motor with the stepper motor driver. Connect the wires from the pressure sensor and the stepper motor driver with the breadboard according to the schematic in **Figure 3**.

3.9. Connect the output signal from the breadboard with the analog input pin on the microcontroller.

3.10. Connect the logic input pins from the stepper motor driver with the digital pins on the microcontroller. The STEP input on the stepper motor driver is connected with a pulse width modulated (PWM) port of digital pins on the microcontroller, denoted by a '~' sign.

3.11. Connect the power supply with the breadboard according to the diagram in **Figure 3**. Set the power supply to 10 V for the breadboard and the stepper motor driver.

4. Pressure sensor calibration

NOTE: Based on the amplifier chosen in this paper, the formula to calculate the gain is $G = 5 + (200k/R_G)$ with $R_G = R1$ and G = amplifier gain. The amplifier gain here is approximately 606. This

value can be changed by changing the resistance used for R1. In addition, as the logic level of the microcontroller board is 5 V and the instrumentation is powered with 10 V, a simple voltage divider circuit, R2 and R3, is used to safeguard the output signal to be no more than 5 V.

4.1. Download and install the appropriate integrated development environment (IDE) for the microcontroller.

4.2. Download the controller code titled 'Pressure_Sensing.ino' from the **Supplemental Files**. Use this code is to acquire the pressure signal from dual pressure sensors.

NOTE: The microcontroller and controller code used in this paper include analog input pins with a 10-bit resolution which read the analog signals from the pressure sensor every 200 ms to actuate the stepper motors. The number in the bracket of analogRead() corresponds to the analog input pin connected to the output signal from the voltage divider circuit in the pressure sensor circuit in **Figure 3**. The delay variable represents the interval at which the signal is reevaluated and the output accordingly, in ms.

4.3. Apply known pressures to the inlet of the sensor with the outlet capped and measure the resulting output signal.

NOTE: A simple method to calibrate the pressure sensor uses a reservoir with water held at varying heights. The resulting gravitational pressure detected will allow one to calibrate the pressure sensor.

4.4. Plot the diagram with the calibration pressure applied (Pa) on the x-axis and the pressure signal (V) on the y-axis to get a numerical value of the y-intercept.

4.5. Apply this numerical value in the controller code, such as the sensor1Offset and sensor2Offset variables in the 'Dual_Pump_PID_Control.ino' code of the **Supplemental Files**, to calibrate the pressure value in the feedback control system.

5. Capturing images from the microfluidic device

5.1. Connect a microcontroller to an open-source single-board computer via a serial interface so that the image captured by the microcomputer triggers pressure measurements to be taken by the microcontroller.

5.2. Connect a camera module made for the single-board computer to one of the eye-pieces of a stereomicroscope. Here, a 20X magnification is used to image the microfluidic devices.

6. Controlling syringe pressure pumps

6.1. Open the IDE for the open-source microcontroller. Download the Timer.h[13] and AccelStepper.h[14] libraries to the microcontroller's IDE library directory.

6.2. Download the controller code titled 'Dual_Pump_PID_Control.ino' from the **Supplemental Files**. This code is used to control the feedback-controlled syringe pump system with two pumps.

6.3. Program the controller code so that it fits the experiment being conducted. Modify the control parameters or the timing parameters to fit the desired response and duration of the experiment. Compile and upload the code to the microcontroller before running the experiment.

NOTE: In the controller code, setPoint1/2 values are used to change the pressure level and stepper1/2Out values are used to adjust the pump speed. The last two values in the AccelStepper stepper1/2 column correspond to the port number on the microcontroller. The milliTiming variable dictates the frequency of reading the analog signal from the pressure sensors and the printTiming variable dictates the frequency of outputting speed and pressure values to a serial monitor for inspection. All units are in ms. The maxError variable is determined from the logic level of the microcontroller board. A value of 5 is used here as the microcontroller in this protocol is 5 V.

6.4. Turn on the power supply for the syringe pumps system. Set the voltage to 10 V for the stepper motor power supply.

7. Tuning the PID Controller parameters

NOTE: The ideal controller parameter values may vary depending on the application and the microfluidic device geometry. For example, for long-term studies (hours), a lower proportional constant (Kp) may be preferable to minimize overshoot at the expense of response time. These tradeoffs depend on experimental conditions and objectives.

7.1. Tune the controller, using a manual approach, by first adjusting the proportional constant (Kp) to improve the response time of a step function.

NOTE: Although algorithmic approaches may be used, manual tuning works for the microfluidic applications shown in this paper.

7.2. Next, alter the integral (Ki) and differential (Kd) parameters to minimize the overshoot and ensure a set-point stability.

7.3. Set the PID values for the Kp, Ki, and Kd variables in the controller code of the **Supplemental Files**.

REPRESENTATIVE RESULTS:

Here, we present a protocol for the construction of a feedback-controlled syringe pump system and demonstrate its potential uses for microfluidic applications. **Figure 1** shows the connected

system of the syringe pump, pressure sensor, microfluidic device, microcontroller, pressure sensor circuit, and stepper motor driver. Detailed callouts for the syringe pump assembly are shown in **Figure 2** and the electronic circuit schematic for pressure sensing is presented in **Figure 3**. The process of tuning the controlling parameters is shown in **Figure 4.** Finally, a representative result of controlling inlet pressure in a two-inlet Y-shaped microfluidic device is shown in **Figure 5**.

FIGURE AND TABLE LEGENDS:

Figure 1: Setup of the feedback-controlled syringe pump system. This image shows the setup of the syringe pump system. The syringe contains the solution for injection and is actuated by the 3D-printed syringe pump. As (**A**) the piezoresistive pressure sensor is connected with (**B**) the syringe pump and (**C**) the microfluidic device, the pressure from the device is detected and converted into an electrical signal to (**D**) the pressure sensor circuit with instrumentation amplifier once the liquid is delivered through the tubing. The signal from the pressure sensor is read by (**E**) the open-source microcontroller board which then transmits the necessary signal to (**F**) the stepper motor driver to control the actuation of the syringe pump. (**G**) A power supply and (**H**) a laptop is needed to operate and program the system.

Figure 2: Assembly photo for the 3D-printed syringe pump. This figure shows the step-by-step instructions for the 3D-printed syringe pump assembly, with photos corresponding to the procedure in step 1.2 of the protocol. (**A**) This image shows the materials for the syringe pump assembly. (**B**) This image shows how the stepper motor is connected to the threaded rod (step 1.2.1). (**C**) This image shows how the part from step 1.2.1 of the protocol is connected to the part from step 1.2.2 of the protocol (step 1.2.3). (**D**) This image shows the assembly of the traveler push piece (step 1.2.5). (**E**) This image shows how the end stop is connected (step 1.2.10). (**F**) This image shows how the syringe plunger female connector piece is connected to the assembled components (step 1.2.11). (**G**) This image shows the assembly of the syringe plunger male connector piece (step 1.2.13). (**H**) This image shows how the syringe clamp is connected (step 1.2.14).

Figure 3: Illustration for the microcontroller and pressure sensor circuit. The circuit allows the microcontroller board to measure amplified pressure signals from the pressure sensor. (**A**) This is the assembly photo for the circuit. (**B**) This figure shows the circuit board layouts.

Figure 4: Tuning of control parameters. The PID controller used to regulate the syringe pump fluid pressure may be tuned by modifying the proportional (Kp), integral (Ki), and differential (Kd) parameters. Here, we show how tuning (using Kp) will help to reduce the response time. Further tuning (using Ki and Kd) can help to ensure a setpoint stability and reduce overshoot. In this protocol, controllers are primarily tuned using a manual trial-and-error approach.

Figure 5: Control of inlet pressure for a laminar flow microfluidic device. A Y-shaped microfluidic device is fabricated following the procedure detailed in step 2 of this protocol. The device features two inlet ports and one outlet port. Two syringe pump systems are assembled

to control the inlet pressures. One of the syringes is loaded with a blue dye and the other is loaded with water. (**A**) These images of the fluid flow resulting from the same pressure provided by both pumps are captured using the approach detailed in step 6 of this protocol. (**B**)**.** This figure shows how the inlet pressures are monitored and controlled using the PID controller tuned in **Figure 4**. Close adherence to the set point can be observed. Shorter (s) and longer (h) experiments have demonstrated similar results.

DISCUSSION:

Here, we presented a new design for a syringe pump system with closed-loop pressure control. This was accomplished by integrating a 3D-printed syringe pump with a piezoresistive pressure sensor and an open-source microcontroller. By employing a PID controller, we were able to precisely control the inlet pressure and provide fast response times while simultaneously maintaining the stability about a set point.

Many experiments using microfluidic devices require a precise fluidic control and exploit a well-characterized laminar flow profile. Examples where a stable flow profile is important include experiments that explore temporal and spatial concentration gradients[15] and generate precise fluidic encapsulations for further analysis[16]**.** By using a PID controller to maintain the high-performance response, the system described in this protocol produces the flow regulation and long-term stability necessary to study such laminar flow experiments.

However, it is important to recognize that microfluidic devices and experiments involving them have subtle variations and differences. For instance, different microfluidic geometries (channel width and height) may necessitate different flow profiles. As a result, the parameters for the PID controllers must be tuned accordingly. Additionally, some experiments may require a tight regulation of the pressure ranges. In these cases, the pressure overshoot may not be acceptable. As such, the PID control parameters must be tuned so that the overshoot is minimized, usually at the expense of response time.

Due to the low-cost production of this syringe pump system, researchers should be able to rapidly develop microfluidic experiments. The estimated cost for a 3D-printed syringe pump, microcontroller, and pressure sensor circuit is approximately US$130. In contrast to commercially available alternatives, such as peristaltic and recirculation pumps, this syringe pump system provides a flexible and straightforward platform that may be adapted to a variety of laboratory uses. Although not discussed here, simpler control strategies, such as the bang-bang controller, may be used for long-term microfluidic studies. Additionally, the syringe pump systems may be used to apply a vacuum pressure to a control volume.

One potential limitation of this syringe pump system using a PID controller is the reliance on a constant power supply. Because the PID control method requires the constant energization of the stepper motor, there is a relatively large power requirement. In contrast, the bang-bang controller only energizes the stepper motor when necessary, using substantially less power. This power requirement may be mitigated by developing a hybrid control structure that implements a PID controller to initially reach a set-point range, and then de-energizes the

stepper motor coils once the pressure value is within a given set-point range. Alternatively, a simple bang-bang controller may be used as well.

Additionally, this syringe pump system allows for a flexible performance and control by altering the size of both the stepper motor and the syringe itself. In previous experiments, we have used syringes of 1 mL, 5 mL, 10 mL, and 30 mL. Naturally, each syringe pump may necessitate slightly different PID controller parameters and would, therefore, require individualized parameter tuning. However, this flexibility allows the syringe pump system described in this protocol to be used in a range of applications.

It should be noted that a common area of microdevice failure is an inability to effectively bond the PDMS to the cover glass. For the microfluidic device fabrication, the power of the plasma cleaner should be optimized if the binding is ineffective. Also, any lubricants or impurities on the cover glass' surface should be removed prior to the bonding to ensure a strong bond with the PDMS. Thoroughly washing and removing any dust from the PDMS component should help to ensure a good seal is formed between the PDMS and the glass.

The low-cost, feedback-controlled syringe pump system presented here allows researchers to manipulate the fluid profile with a high degree of stability in a flexible manner. By integrating the pressure sensing module with simple PID control methods, the system is able to provide high-performance pressure-driven flow control. This tool can be broadly applied across many research fields where microfluidics tools are in use.

ACKNOWLEDGMENTS:
The authors acknowledge support from the Office of Naval Research awards N00014-17-12306 and N00014-15-1-2502, as well as from the Air Force Office of Scientific Research award FA9550-13-1-0108 and the National Science Foundation Grant No. 1709238.

DISCLOSURES:
The authors have nothing to disclose.

REFERENCES:
1. Sackmann, E. K., Fulton, A. L., Beebe, D. J. The present and future role of microfluidics in biomedical research. *Nature.* **507** (7491), 181-189, doi:10.1038/nature13118 (2014).

2. Duncombe, T. A., Tentori, A. M., Herr, A. E. Microfluidics: reframing biological enquiry. *Nature Reviews Molecular Cell Biology.* **16** (9), 554-567, doi:10.1038/nrm4041 (2015).

3. Prakadan, S. M., Shalek, A. K., Weitz, D. A. Scaling by shrinking: empowering single-cell 'omics' with microfluidic devices. *Nature Reviews Genetics.* **18** (6), doi:10.1038/nrg.2017.15 (2017).

4. Kim, Y., Langer, R. Microfluidics in nanomedicine. *Reviews in Cell Biology and Molecular Medicine.* **1**, 127–152 (2015).

5. Rusconi, R., Garren, M., Stocker, R. Microfluidics expanding the frontiers of microbial ecology. *Annual Review of Biophysics.* **43**, 65-91, doi:10.1146/annurev-biophys-051013-022916 (2014).

6. Skafte-Pedersen, P., Sabourin, D., Dufva, M., Snakenborg, D. Multi-channel peristaltic pump for microfluidic applications featuring monolithic PDMS inlay. *Lab on a Chip.* **9** (20), 3003-3006, doi:10.1039/b906156h (2009).

7. Heo, Y. J., Kang, J., Kim, M. J., Chung, W. K. Tuning-free controller to accurately regulate flow rates in a microfluidic network. *Scientific Reports.* **6** 23273, doi:10.1038/srep23273 (2016).

8. Kuczenski, B., LeDuc, P. R., Messner, W. C. Pressure-driven spatiotemporal control of the laminar flow interface in a microfluidic network. *Lab on a Chip.* **7** (5), 647-649, doi:10.1039/b617065j (2007).

9. Lake, J. R., Heyde, K. C., Ruder, W. C. Low-cost feedback-controlled syringe pressure pumps for microfluidics applications. *PLoS One.* **12** (4), e0175089, doi:10.1371/journal.pone.0175089 (2017).

10. Kong, D. S. et al. Open-source, community-driven microfluidics with metafluidics. *Nature Biotechnology.* **35** (6), 523-529, doi:10.1038/nbt.3873 (2017).

11. Wijnen, B., Hunt, E. J., Anzalone, G. C., Pearce, J. M. Open-source syringe pump library. *PLoS One.* **9** (9), e107216, doi:10.1371/journal.pone.0107216 (2014).

12. Ferry, M. S., Razinkov, I. A., Hasty, J. Microfluidics for synthetic biology: from design to execution. *Methods in Enzymology.* **497**, 295-372, doi:10.1016/B978-0-12-385075-1.00014-7 (2011).

13. Christensen, J. *Arduino Libraries for Timer.h*, <https://github.com/JChristensen/Timer>.

14. Adafruit Industries, *Arduino Libraries for AccelStepper.h*, <https://github.com/adafruit/AccelStepper>.

15. Lin, F. et al. Generation of dynamic temporal and spatial concentration gradients using microfluidic devices. *Lab on a Chip.* **4** (3), 164-167, doi:10.1039/b313600k (2004).

16. Korczyk, P. M., Cybulski, O., Makulska, S., Garstecki, P. Effects of unsteadiness of the rates of flow on the dynamics of formation of droplets in microfluidic systems. *Lab on a Chip.* **11** (1), 173-175, doi:10.1039/c0lc00088d (2011).