

3D-Printable Micropipette

Martin D. Brennan¹, Fahad F. Bokhari¹, David T. Eddington^{1,*},

1 Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, USA

* dte@uic.edu

Abstract

Open source development of lab equipment is being facilitated, in part, by growing availability of 3D printing which allows the production of simple lab tools. We developed 3D-printable parts that, along with a disposable syringe, form a micropipette. Once assembled the pipette requires no calibration or validation with a scale. Our printed micropipette is assessed in comparison to a commercial pipette demonstrating comparable performance in accuracy and precision and approaches ISO standard.

Introduction

The open source development model, initially applied to software, is thriving in the development of open source scientific equipment due in part to increasing access of 3D printing [1,2]. Open design 3D-printable lab equipment is an attractive idea because, like open source software, it allows free access to technology that is otherwise inaccessible due to proprietary and/or financial barriers. Open design tools create opportunity for scientists and educational programs in remote or resource limited areas to participate with inexpensive and easy to make tools [1]. Open source development also enables the development of custom solutions to meet unique applications not met by commercial products that are shared freely and are user modifiable [3,4]. Some advanced, noteworthy open-source scientific equipment include a PCR device [5], and a two-photon microscope [6] although even simple tools are impactful especially if the fabrication is simplified by 3D printing.

3D printing as a form of additive manufacturing has existed for decades although the recent availability of inexpensive desktop printers [?, 7] have made it feasible for consumers to design and print prototypes and even functional parts, and consumer goods [3]. Proliferation of free CAD software [OpenSCAD, Blender, SketchUp] and design sharing sites [?, 7–9] have also supported the growth and popularity of open designed parts and projects. Some simple and clever printable parts that have emerged are ones that give a new function to a ubiquitous existing device such as drill bit attachment designed to hold centrifuge tubes, turning the drill into a centrifuge [10]. Although this may make a rather crude centrifuge it may be an adequate method that only costs pennies compared to commercially available centrifuges. Other examples of open-design research tools that utilize 3D printed parts include optics equipment [11], microscopes [12,13], syringe pumps [14], and reactionware [15] to name a few.

There are a few open design printable micropipettes including a popular one which uses parts scavenged from a retractable pen in addition to the printed parts [16]. An air displacement pipette uses a piston operating principle to draw liquid into the pipette.

Figure 1. CAD rendering of printable parts. Three parts are printed: the body, plunger shaft, and luer-lock adapter for pipette tips.

Figure 2. CAD rendering of printable parts. Three parts are printed: the body, plunger shaft, and luer-lock adapter for pipette tips.

In a typical commercial pipette the piston is made gas-tight with a gasketed plunger inside a smooth barrel. Consumer grade fused deposition modeling (FDM) printers are unable to form a smooth surface do to the formation of ridges that occur as each layer that is deposited. The ridges formed by FDM make it impractical to form a gas-tight seal between moving parts, even with a gasket. Printable open-design micropipettes get around this limitation by stretching a membrane over one end of a printed tube, which when pressed causes the displacement. The displacement membrane can be made from any elastic material such as a latex glove. After assembly this design requires the user to validate the volumes dispensed with a high precision scale. Without verification with a scale the volumes dispensed can only be estimated based on theoretical displacement intended by the design. There is no built-in feature such as a digital readout for the user to set the displacement to a desired volume. The pipette can be calibrated to a specific volume with a set screw but if a new volume is desired it has to be re-adjusted and validated with a scale.

We present a new open design 3D-printable micropipette that works by actuating a 1 mL syringe to a user adjustable set-point. This allows the user to set the pipette to a volume a priori by reading the graduations of the syringe barrel. The scale marks on the syringe can be used to adjust the dispensed volume accurately without calibrating with a scale. Our pipette also offers a simplified assembly requiring no glue, tape or permanent connections.

Materials and Methods

Design

Our printed pipette is designed to actuate a 1 mL syringe to a user set displacement. The core of the design is two printed parts, the body and the plunger. A 1 mL BD syringe twists to lock in the body part and is held into place by the syringe flanges. The plunger part slides freely in the body part and actuates the syringe by pushing the thumb press. The pipette is spring loaded towards a set point which is adjustable by a set-screw. When the plunger is depressed the system locks when it reaches the ready point, where it is ready to draw in fluid. The plunger is held in place with a notch and groove design which is then released with a lever drawing in fluid. The displacement is directly readable with the syringe graduations and is equal to the distance between the set and the ready point. The pipette can also be pressed past the ready point to purge the transferred fluid completely from the pipette tip. An additional printed part adapts standard micropipette tips to the luer fitting of the pipette. Additional materials required for assembly include a spring, a nut and bolt and washers.

Our printed pipette mimics commercial pipettes's design, function, and user operation, making it intuitive to use. It also can reach to the bottom of a 15 mL conical tube.

Figure 3. Photos of pipette. The pipette is composed of three printed parts, a 1 mL syringe and some additional hardware.

Validation

The pipette was validated and compared to a commercial pipette. The pipette was tested to see if the set point would drift between during use for example small, incremental movements of the screw or other parts causing the pipetted volume to drift. To test the pipette the same volume was pipetted 50 times without moving or re-adjusting the set point. The printed pipette's accuracy and precision was characterized and compared to a commercial pipette. The printed pipette and a series of commercial pipettes were tested at volumes of 20 μL 50 μL and 200 μL . The printed pipette was adjusted to the the target volume by eye from the syringe graduations, and the resulting volume was measured and repeated 5 times to account for variability. Measurements were taken from the commercial pipette in a similar way.

To test user friendliness and feasibility for using the pipette without verifying with a scale, data was also gathered from novice users. This group included researchers experienced with pipettes as well as undergraduates with little to no experience pipetting at all. After a quick overview of the operation of the pipette measurements were taken after the volunteers adjusted the pipette to 200, 50, 20 and 10 μL .

For the printed pipette the 1000 μL tips were used for the 200 μL measurement. 100 μL tips were used for the 50, 20 and 10 μL measurements.

compare the force required to press the button.

compare the weight of the pipettes

Figure 4. Novice User efficacy. Novice users were asked to pipette volumes of 200, 50, 20 and 10 μL without the use of a scale.

Results and Discussion

Our printed pipette had a comparable accuracy to a commercial pipette (Table 1). The commercial pipette has a digital readout that allows the user to adjust precisely to set values where the printed pipette is adjusted by eye according to graduations. Due to being unable to re-set the printed pipette back to the exact mechanical location it may be hard to compare directly with the commercial pipettes. This is certainly the cause of the lower accuracy and wider deviation although it's performance is impressive. Despite this additional variability the printed pipette's accuracy and precision approaches the ISO 8655 standard.

The Novice user data demonstrates that even someone inexperienced with pipetting and unfamiliar with our design is able to use out pipette accurately with out the use of a scale. The systematic error trended towards over estimating the displacement. This is likely due the function of adjusting the volume where it is easier to start at a lower displacement and increase it by unscrewing, or releasing compression of the spring. This explains the negative systematic error as the user avoids 'going over'.

This pipette improves on existing open design pipettes in several ways. It requires only two printed parts, a syringe, and some hardware. It is able to reach into a 15 mL conical tube which is a routine requirement for cell culture. No permanent connections using tape or glue are required for assembly allowing worn out or broken part to be replaced easily. Assembly does not require a membrane that may wear or stretch and require tedious replacement. No validation or calibration is required. The pipette can be assembled and used to accurately pipette micro volumes without first validating with a scale.

The only major limitation of this design compared to the briopipette is the option for a pipette tip ejector, although incorporation of a similar design in our pipette would

not leave room for it to reach into a 15 mL conical tube. Our pipette requires a syringe and some additional hardware where briopipette's additional parts can be obtained virtually anywhere. The briopipette also allows step-wise shifts in displacement allowing the user to quickly change to a relative volume

Table 1. ISO 8655 for 100-1000 uL comparing a commercial pipette with our printed pipette used with existing 3 mL syringe scale and an adjusted scale

		Mean	Systematic Error	% Sys. err.	Random Error	% Rand. err.
1000 uL	ISO 8655, 100-1000 uL	1000	8.00	0.80	3.00	0.30
	Commercial Pipette	1002.98	2.98	0.30	1.72	0.17
	Printed Pipette	949.29	-50.71	-5.07	0.60	0.06
	Printed Pipette Scale	1003.57	3.57	0.36	0.89	0.09
500 uL	ISO 8655, 100-1000 uL	500	8.00	1.60	3.00	0.60
	Commercial Pipette	503.67	3.67	0.73	0.49	0.10
	Printed Pipette	475.99	-24.01	-4.80	4.75	1.00
	Printed Pipette Scale	503.62	3.62	0.72	1.64	0.33
200 uL	ISO 8655, 100-1000 uL	200	8.00	4.00	3.00	1.50
	Commercial Pipette	204.61	4.61	2.30	0.15	0.07
	Printed Pipette	186.55	-13.45	-6.72	1.31	0.70
	Printed Pipette Scale	201.87	1.87	0.94	1.47	0.73
100 uL	ISO 8655, 100-1000 uL	100	8.00	8.00	3.00	3.00
	Commercial Pipette	104.29	4.29	4.29	1.65	1.58
	Printed Pipette	94.02	-5.98	-5.98	4.81	5.12
	Printed Pipette Scale	101.00	1.00	1.00	1.05	1.04

For more information, see ??.

Supporting Information

References

1. Baden T, Chagas AM, Gage G, Marzullo T, Prieto-Godino LL, Euler T. Open Labware: 3-D Printing Your Own Lab Equipment. PLOS Biology. 2015;13(3):e1002086. Available from: <http://dx.plos.org/10.1371/journal.pbio.1002086>.
2. Pearce JM. Open-source Lab; 2014.
3. Fullerton JN, Frodsham GCM, Day RM. 3D printing for the many, not the few. Nature Biotechnology. 2014;32(11):1086–1087. Available from: <http://www.nature.com/doi/10.1038/nbt.3056>.
4. Pearce JM. Building Research Equipment with Free, Open-Source Hardware. Science. 2012 sep;337(6100):1303–1304. Available from: <http://dx.doi.org/10.1126/science.1226328>
<http://www.ncbi.nlm.nih.gov/pubmed/22984060>
<http://www.sciencemag.org/cgi/doi/10.1126/science.1228183>.

Table 2. ISO 8655 for 30-300 uL comparing a commercial pipette with our printed pipette used with existing 3 mL syringe scale and an adjusted scale

		Mean	Systematic Error	% Sys. err.	Random Error	% Rand. err.
300 uL	ISO 8655, 30-300 uL	300	4.00	1.33	1.50	0.50
	Commercial Pipette	301.19	1.19	0.40	0.53	0.18
	Printed Pipette	286.91	-13.09	-4.36	0.42	0.15
	Printed Pipette Scale	299.11	-0.89	-0.30	0.48	0.16
200 uL	ISO 8655, 30-300 uL	200	4	2	1.5	0.75
	Commercial Pipette	200.06	0.06	0.03	0.46	0.23
	Printed Pipette	193.40	-6.60	-3.30	2.86	1.48
	Printed Pipette Scale	200.57	0.57	0.28	0.86	0.43
50 uL	ISO 8655, 30-300 uL	50	4	8	1.5	3
	Commercial Pipette	49.02	-0.98	-1.96	0.10	0.20
	Printed Pipette	49.62	-0.38	-0.76	1.26	2.53
	Printed Pipette Scale	48.73	-1.27	-2.54	1.11	2.27
30 uL	ISO 8655, 30-300 uL	30	4	13.3	1.5	5
	Commercial Pipette	29.08	-0.92	-3.06	0.09	0.31
	Printed Pipette	29.22	-0.78	-2.59	0.31	1.07
	Printed Pipette Scale	27.78	-2.22	-7.41	1.37	4.93
20 uL*	ISO 8655, 30-300 uL	20	4	20	1.5	7.5
	Commercial Pipette	NA	NA	NA	NA	NA
	Printed Pipette	18.70	-1.30	-6.48	0.38	2.01
	Printed Pipette Scale	17.94	-2.06	-10.29	1.87	10.42
10 uL*	ISO 8655, 30-300 uL	10	4	40	1.5	15
	Commercial Pipette	NA	NA	NA	NA	NA
	Printed Pipette	11.95	1.95	19.52	0.73	6.08
	Printed Pipette Scale	7.64	-2.36	-23.64	0.38	4.92

* The 20 uL and 10 uL volumes are out of the range in this case but we wanted to demonstrate that the pipette is capable of even smaller volumes.

5. Chai Biotechnologies Inc. Open PCR; 2016. Available from: <http://openpcr.org/>.
6. Rosenegger DG, Tran CHT, LeDue J, Zhou N, Gordon GR. A High Performance, Cost-Effective, Open-Source Microscope for Scanning Two-Photon Microscopy that Is Modular and Readily Adaptable. PLoS ONE. 2014;9(10):e110475. Available from: <http://dx.plos.org/10.1371/journal.pone.0110475>.
7. Makerbot Industries. Thingiverse; 2016. Available from: <https://www.thingiverse.com/>.
8. National Institutes of Health. NIH 3D Print Exchange. 2016; Available from: <http://3dprint.nih.gov/>.
9. GitHub Inc . GitHub. 2016; Available from: <https://github.com/>.
10. Garvey C. DremelFuge; 2009. Available from: <https://www.thingiverse.com/thing:1483>.

11. Zhang C, Anzalone NC, Faria RP, Pearce JM. Open-Source 3D-Printable Optics Equipment. PLoS ONE. 2013;8(3).
12. Baden T. Raspberry Pi Scope. 2014; Available from: <http://3dprint.nih.gov/discover/3dpx-000609>.
13. Walus K. A Fully Printable Microscope; 2014. Available from: <http://3dprint.nih.gov/discover/3dpx-000304>.
14. Wijnen B, Hunt EJ, Anzalone GC, Pearce JM. Open-Source Syringe Pump Library. PLoS ONE. 2014;9(9):e107216. Available from: <http://dx.plos.org/10.1371/journal.pone.0107216>.
15. Symes MD, Kitson PJ, Yan J, Richmond C, Cooper GJT, Bowman RW, et al. Integrated 3D-printed reactionware for chemical synthesis and analysis. Nature Chemistry. 2012;4(5):349–354. Available from: <http://eprints.gla.ac.uk/68744/>.
16. Baden T. Biropette: customisable, high precision pipette.; 2014. Available from: <http://www.thingiverse.com/thing:255519>.