Low-Cost, High-Precision Liquid Handling: A CNC-Based Approach to Reagent Dispensing

Monique Ngan[a], Nipun Kumar Gupta[a], Harrison Anderson Mills[a], Owen Alfred Melville[a]

[a] *Acceleration Consortium, University of Toronto, Toronto ON, Canada* nipun.gupta@utoronto.ca

1. Introduction

Accelerated materials research uses high-throughput (HT) experimentation and artificial intelligence to quickly discover new catalysts, binders, electrodes, membranes, and organic lasers to combat climate change, enhance human health, reduce pollution, and lessen dependence on fossil fuels. HT experimentation demands extensive reagent mixtures, which can be error-prone and labour-intensive if prepared manually. Liquid dispensers can significantly automate and accelerate reagent preparation. However, most currently existing liquid dispensers are quite dear,[1–5] or designed only for aqueous reagents and are incompatible with common organic solvents[6–11]. Integrating many of these liquid dispensers into fume cupboards is not feasible due to a large footprint.

Herein, we discuss our progress in developing a liquid dispenser based on a CNC (Computer Numerical Control) machine chassis with a compact footprint (35.0 × 40.0 × 30.0 cm), syringe pumps, tube fittings, and 3D-printed components. The total cost of the build is approximately CAD 2500, significantly lower than the other liquid handlers in the market. The price could be lowered by strategically sourcing the components. Our system has capabilities comparable to many commercial dispensers, and we plan to upgrade it to include the ability to aspirate and dispense solutions with a pipette tip.

Our liquid dispenser achieves high accuracy and precision (up to>90% in some instances) in dispensing organic solvents and aqueous solutions of strong acids. It can dispense liquids with viscosities of up to 10000 cps with decent accuracies and precision (~90%) at high dispense volumes. However, the accuracy of the volume dispensed for lower volumes (<0.25 mL) is lower (~70%). We believe this problem is highly suited for machine learning (ML)-assisted optimisation, and we intend to use ML to maximise the dispensed volume accuracy.

The CNC machine utilised here has a working area of 28.4 x 18.0 x 4.0 cm and can accommodate two well plates (or vial racks of similar dimensions); more can be added if a CNC machine with a larger working area is used. Thus, the tool we demonstrate herein can help democratise science and accelerate discovery by acting as the basis of a platform for HT organic synthesis.

2. Results and Discussion

We validated with a broad range of organic solvents and corrosives. We chose organic solvents notorious for solubilising most plastics: tetrahydrofuran (THF), toluene, ethyl acetate, dichloromethane (DCM), and acetone. For corrosives, we will dispense sulphuric acid, as it dissolves some of the most rigid plastics, such as polyether ether ketone (PEEK), commonly used for high-performance liquid chromatography (HPLC) fittings. We also dispensed viscosity standards to determine the viscosity range in which this system can operate without hindrance.

Figure 1A shows the liquid dispenser, and panel B shows the home-built 3D-printed dispenser head. The system is controlled via a Python script, and all the packages necessary to control it are freely available. We are preparing a Python package to help novice users control the liquid dispenser without requiring a strong programming background.

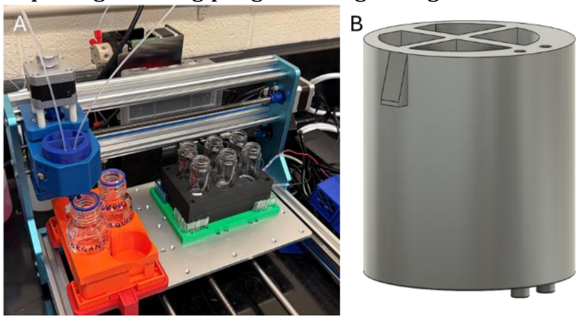

Figure 1: (A) An image of the liquid dispenser consists of a CNC machine deck, tubing, 3D printed dispenser head, a syringe pump with a 2.5 mL syringe. The CNC-machine deck with a 20mL vial rack and a 50mL bottle rack with vials, (B) A model of the 3D-printed dispenser head

2.2 Figures and tables

In this section, we report the preliminary data that we have gathered to understand the system's limits to assist in designing an ML optimisation problem. We utilised 2.5 mL and 0.5 mL syringes. We dispensed the full syringe volume (2.5 mL and 0.5 mL, respectively), half the syringe volume (1.25 mL and 0.25 mL, respectively), and ten percent of the syringe volume (0.25 mL and 0.05 mL, respectively) at a fixed flow rate of 0.1 mL/sec. A 2 sec delay (the time delay herein) was added between the draw and dispense steps for the initial exploration. An ethylene tetrafluoroethylene (ETFE) tubing with 1/16" outer diameter connects the reservoirs to the pumps, and the pumps to the dispenser head. The reported values for accuracy are averages of six independent dispenses.

We calculated the volumes based on the weights of the dispensed solvents. We weighed the glass vials before and after dispensing solvents. We capped them immediately afterward to minimise solvent evaporation, which can be significant for low-boiling-point solvents such as dichloromethane and acetone.

The preliminary data are presented in Fig. 2A and B for 2.5 mL and 0.5 mL syringes, respectively. We observe at least 90% accuracy for all solvents when dispensing 2.5 mL and 1.25 mL volumes and significant variation in accuracy for 0.5 mL volumes using a 2.5 mL syringe. The accuracy for the 0.5 mL syringe shows a similar trend, where higher accuracy is noted for higher volumes. We intend to modulate the flow rates and the time delay in the next set of experiments for the initial experiments and will move to an ML-assisted approach. We observe precision

Low-Cost, High-Precision Liquid Handling: A CNC-Based Approach to Reagent Dispensing

Monique Ngan[a], Nipun Kumar Gupta[a], Harrison Anderson Mills[a], Owen Alfred Melville[a]

[a] *Acceleration Consortium, University of Toronto, Toronto ON, Canada* nipun.gupta@utoronto.ca

~90% for most dispensed volumes, which suggests that the system's dispensed volumes are highly reproducible, and the system can become reliable after careful calibration studies.

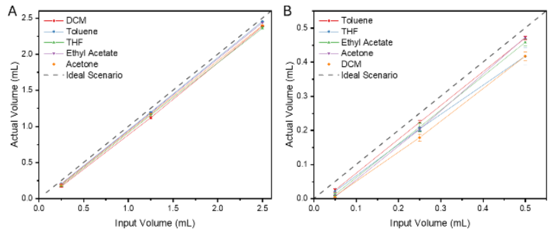

Figure 2: Input volume vs the actual volume dispensed for toluene (red), THF (blue), ethyl acetate (green), acetone (violet) and DCM (orange) for 2.5 ml (A) and 0.5 mL (B) syringes. The error bars are calculated on data obtained from six independent experiments.

We also tested our platform with 10, 200, 1000, and 10000 cps viscosity standards, as shown in Fig. 3. For these studies, we used a 50 µL syringe and ETFE tubing with 1/8' outer diameter. We observed that the time delay has a much more substantial effect on the accuracy than the flow rate. We also observe here that notably, the precision was correlated to the accuracy for the chosen dispense value, as higher precision was observed for higher dispense volumes.

The one-parameter-at-a-time Edisonian optimisation method could achieve accuracy of approximately 90% in some instances, but it is highly inefficient and time-consuming. An ML-assisted approach should help us find better and consistent solutions. Constructing a multi-objective optimisation problem that maximises accuracy and precision while not significantly increasing the delay time might be possible.

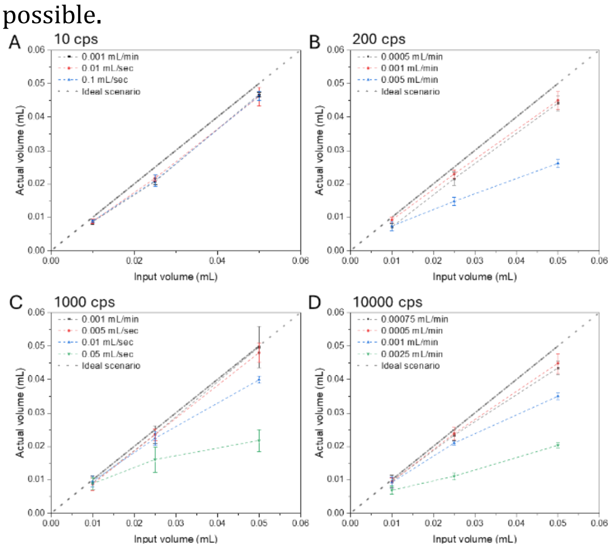

Figure 3: Input volume vs the actual volume dispensed for (A) 10 cps, (B) 200 cps, (C) 1000 cps and (D) 10000 cps viscosity standards. The delay time is 1 sec for 10 and 200 cps, 2 sec for 1000 cps and 5 sec for 10000 cps. The error bars are calculated on data obtained from five independent experiments.

Our preliminary data suggests that the liquid dispenser system can achieve high accuracy and precision in dispensing various common organic solvents and viscous liquids, and we intend to improve upon the metrics by integrating ML into our system.

3. Acknowledgements:

This research was undertaken partly thanks to funding provided to the University of Toronto's Acceleration Consortium from the Canada First Research Excellence Fund Grant number CFREF-2022-00042.
Dr Han Hao, Acceleration Consortium, University of Toronto wrote the Python package to assist in interfacing with the syringe pump.

4. References:

(1) *Tecan Liquid Handling & Automation*. https://lifesciences.tecan.com/products/liquid_handling_and_automation (accessed 2025-03-10).

(2) *Flex | The next generation of lab automation is here*. https://opentrons.com/robots/flex (accessed 2025-03-10).

(3) *Leading edge Solutions for Lab Automation & Digitalization*. https://www.chemspeed.com/ (accessed 2025-03-10).

(4) *Liquid Handling*. https://www.zinsserna.com/tools_liquidhandling.htm (accessed 2025-03-10).

(5) *Robots*. https://www.northrobotics.com/robots (accessed 2025-03-14).

(6) Carvalho, M. C.; Murray, R. H. Osmar, the Open-Source Microsyringe Autosampler. *HardwareX* **2018**, *3* (January), 10–38. https://doi.org/10.1016/j.ohx.2018.01.001.

(7) Keesey, R.; LeSuer, R.; Schrier, J. Sidekick: A Low-Cost Open-Source 3D-Printed Liquid Dispensing Robot. *HardwareX* **2022**, *12*, e00319. https://doi.org/10.1016/j.ohx.2022.e00319.

(8) Faiña, A.; Nejati, B.; Stoy, K. EvoBot: An Open-Source, Modular, Liquid Handling Robot for Scientific Experiments. *Appl. Sci.* **2020**, *10* (3), 814. https://doi.org/10.3390/app10030814.

(9) Florian, D. C.; Odziomek, M.; Ock, C. L.; Chen, H.; Guelcher, S. A. Principles of Computer-Controlled Linear Motion Applied to an Open-Source Affordable Liquid Handler for Automated Micropipetting. *Sci. Rep.* **2020**, *10* (1), 1–10. https://doi.org/10.1038/s41598-020-70465-5.

(10) Yoshikawa, N.; Darvish, K.; Vakili, M. G.; Garg, A.; Aspuru-Guzik, A. Digital Pipette: Open Hardware for Liquid Transfer in Self-Driving Laboratories. *Digit. Discov.* **2023**, *2* (6), 1745–1751. https://doi.org/10.1039/d3dd00115f.

(11) ? *Science Jubilee* ⚡ ⚙️ — *Science Jubilee 0.3.2.post1.dev140+gbc38447 documentation*. https://science-jubilee.readthedocs.io/en/latest/ (accessed 2025-03-10).