A low-cost, high-throughput solid dosing platform for self-driving laboratories

Rui Zhang[1], Yang Cao[1,2,3], Han Hao[1,2,3], Ishrath Mohamed Irshadeen[1], Nasim Abdollahi[3], Agustinus Kristiadi[4], Stephan Koehler[5], Miriam Mathea[5], Jochen Sieg[5], Philipp Eiden[5], Frank Gu[6, 7], Alán Aspuru-Guzik[1.2,3,6,8,9,10,11,12]

[1]Department of Chemistry, University of Toronto, Toronto, Ontario, Canada. [2]Department of Computer Science, University of Toronto, Toronto, Ontario, Canada. [3]Acceleration Consortium, Toronto, Ontario, Canada. [4]Department of Computer Science, University of Western Ontario, London, Ontario, Canada [5]BASF SE, Ludwigshafen am Rhein 67056, Germany. [6]Department of Chemical Engineering & Applied Chemistry, University of Toronto, Toronto, Ontario, Canada. [7]Institute of Biomedical Engineering, University of Toronto, Toronto, Ontario, Canada. [8]Vector Institute, Toronto, ON, Canada. [9]NVIDIA, Toronto, ON, Canada [10]Department of Chemical Engineering & Applied Chemistry, University of Toronto, ON, Canada [11]Department of Materials Science & Engineering, University of Toronto, ON, Canada [12]Institute of Medical Science, Medical Sciences Building, Toronto, ON, Canada [13]Canadian Institute for Advanced Research (CIFAR), Toronto, ON, Canada

Correspondence to: Alán Aspuru-Guzik alan@aspuru.com

1. Introduction

High-throughput experimentation (HTE) screening is the execution of many small-scale reactions in parallel, most often in a rectangular grid-style wellplate. The standardized nature of HTE apparatus lends the technique a high degree of data standardization and compatible with self-driving lab (SDL) architecture.

When conducting HTE screens, solid reagents are commonly dosed either in solution or suspension, for compatibility with robotic liquid handlers. However, this presents an issue with solids that are heavy and poorly soluble in the reaction solvent. Current solutions to dosing solids in HTE screens are either manual dosing [1], which is time consuming, or using integrated automation platforms, such as those from Chemspeed Technologies [2][3], which are highly precise, but remain slow as each vial must be taken out of its holder, dosed, and then returned to its original position. Furthermore, such robotic platforms are costly for those newly seeking to establish SDLs.

2. System design

To address this gap in HTE automation, we iterated on the design of the dispensing screw commonly utilized in both commercial and academic context as a tunable solid dispensing system [4][5].

The solid dispensing module (Fig. 1) comprises of a dispensing screw driven by a stepper motor, whose rotation angle and speed are controlled via an Arduino board. Apart from the stepper motor and reagent vial, all other components can be economically 3D printed. Due to the modular nature of this design, the solid dosing system can either be implemented as a stationary unit, or be attached to a CNC gantry for wellplate dosing (Fig. 2)

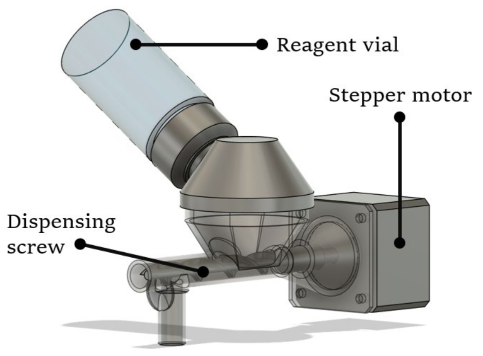

Fig. 1: 3D model of solid dosing module.

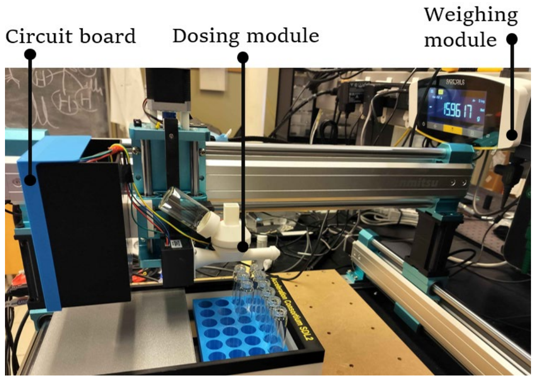

Fig. 2: Solid dosing module attached onto CNC gantry.

To investigate the precision of the solid dosing module, it was programmed to dose into five separate glass vials as in Fig. 2, using one complete revolution of the dispensing screw every time. The mass on the weighing module was logged and the results plotted in Fig. 3.

Two types of solids were tested using this platform. The first was a freely flowing solid, sodium bicarbonate, which was dosed across all five screw diameters with less than 5% coefficient of variation (CV), apart from the 5.0 diameter screw, which reported an 11% CV. Starch was tested as a representative of a poorly flowing solid, and was dosed with 15% CV on the 5.0 mm diameter screw, and less than 10% CV across other diameters.

3. Results and application

3.1. Dosing precision

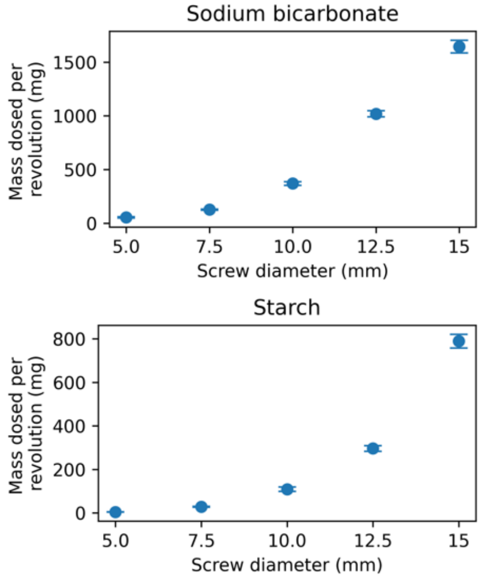

Fig. 3: Plots of mass of sodium carbonate and starch dosed across five screw diameters.

3.2. Incorporation within automated solubility measurement pipeline

To demonstrate the incorporation of this platform within a larger SDL ecosystem, we conducted a series of solubility studies of organic analytes across three binary solvent systems. Preliminary studies were conducted to establish the amount of desired excess analyte, after which this baseline mass was dosed into 15 vials over 2 wellplates, including threefold repetition for each solute-solvent combination.

After solid dosing is complete, the vial rack was transferred onto the deck of an Opentrons OT-2 liquid handler, and solvents were dosed into each vial following a binary mixture recipe. The mixtures were subsequently sealed, agitated with an orbital mixer, and their concentrations analysed with UPLC.

Plots of computed analyte concentrations across the binary solvent systems for one example analyte are shown in Fig. 5. The CV of all measurements were generally low across the board, with a maximum of 8% and average of 3% over 15 different mixtures, demonstrating robustness of the automated workflow.

In summary, a low-cost, open-source solid dispensing module was designed and tested with both well- and poorly-flowing solids. The module can be implemented both as a standalone unit, or incorporated into broader SDL workflows as a mobile unit for dosing into wellplates with higher efficiency than current manual or automated methods.

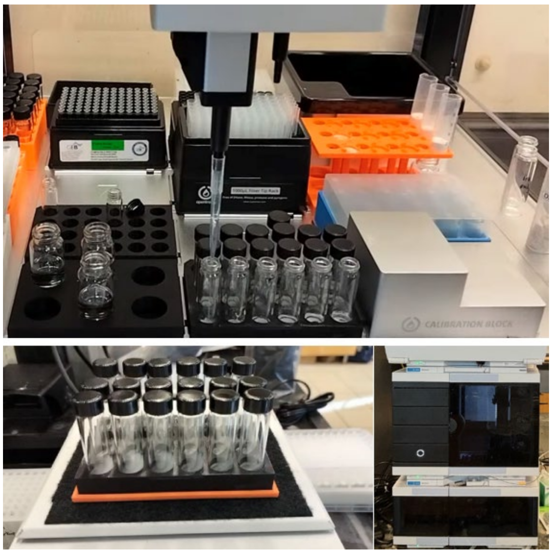

Fig. 4: Additional components of automated solubility measurement workflow – binary solvent system setup with Opentrons OT-2, orbital mixing for agitation, and UPLC for concentration measurement.

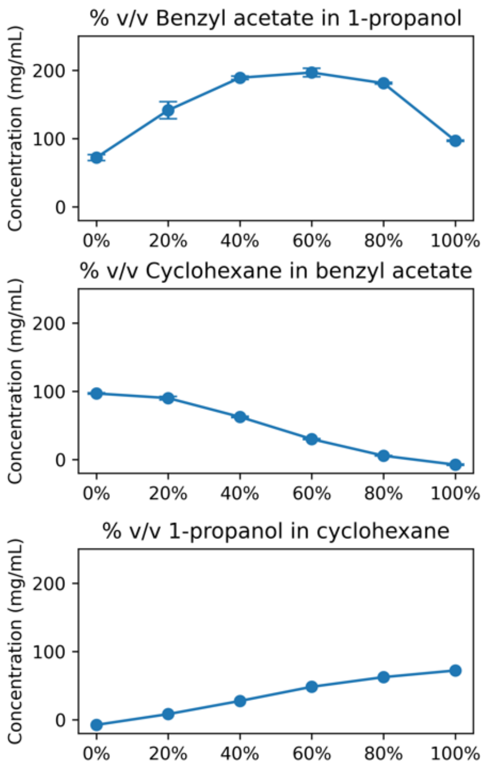

Fig. 5: Plots of measured concentration of an organic analyte across three binary solvent systems.

Acknowledgments

We thank the University of Toronto, Acceleration Consortium and BASF for financial support.

References

[1] Cook, A., Clément, R. & Newman, S. G. Reaction screening in multiwell plates: high-throughput optimization of a Buchwald–Hartwig amination. Nat Protoc 16, 1152–1169 (2021).
[2] Strieth-Kalthoff, F. et al. Delocalized, asynchronous, closed-loop discovery of organic laser emitters. Science 384, (2024).
[3] Vriza, A., Chan, H. & Xu, J. Self-Driving Laboratory for Polymer Electronics. Chem. Mater. 35, 3046–3056 (2023).
[4] Kruppa, F., Weiß, U., Oberdorfer, B. & Wilke, B. Increasing the dosing accuracy of a screw dosing device by inline measurement of the product density. Packag Technol Sci 36, 185–194 (2022).
[5] Zhang, T., Lin, H., Chen, Y. & Viswanathan, V. SALSA: A low-cost self-driving lab for salt solubility assessment for battery electrolytes. (2025) doi:10.26434/chemrxiv-2025-17lfp.