Autonomous titration for chemistry classrooms: preparing students for digitized chemistry laboratories

Florian Häse,[1,2,3,4] Teresa Tamayo-Mendoza,[1,2,3] Carmen Boixo,[5] Jonathan Romero,[1,6] Loïc M. Roch,[1,2,3,4] and Alán Aspuru-Guzik,[2,3,4,7]

[1] Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA 02138, USA

[2] Chemical Physics Theory Group, Department of Chemistry, University of Toronto, Toronto, ON M5S 3H6, Canada

[3] Department of Computer Science, University of Toronto, Toronto, ON M5S 3H6, Canada

[4] Vector Institute for Artificial Intelligence, Toronto, ON M5S 1M1, Canada

[5] Palos Verdes High School, Palos Verdes Estates, California, 90274 USA

[6] Zapata Computing Inc., 501 Massachusetts Avenue, Cambridge, MA, 02139, USA

[7] Canadian Institute for Advanced Research (CIFAR) Lebovic Fellow, Toronto, ON M5S 1M1, Canada

Abstract

The digitalization of the economy is one of the drivers of the fourth industrial revolution. This trend is already heavily permeating biology laboratories and rapidly moving into chemistry as well. Notably, automated laboratories enhance process quality and intensification while freeing researchers from repetitive tasks. With these societal changes in place, students need to be prepared for the advanced digitization of chemistry and science by teaching fundamental chemistry concepts in combination with emerging Industry 4.0 technologies, including programming and automation. We describe an undergraduate classroom exercise at the interface of chemistry, computer science and engineering based on the development of an autonomous titration platform. Following an inquiry learning ansatz, the exercise focuses on standard titration experiments which are first executed manually, then automatically and finally in full autonomy by a student-designed robotic platform. We demonstrate that the exercise introduced in this work enables students to learn fundamental concepts in analytical chemistry, naturally integrates basic aspects of programming and automation, and as a consequence promotes and reinforces the detailed understanding of experimental processes and measurements. The exercise is designed in a collaborative active learning framework to encourage complex critical thinking and creative problem solving and thus prepares students for the next-generation chemistry laboratories.

Keywords

Undergraduate education, inquiry-based learning, multidisciplinary learning, laboratory computing, autonomous experimentation, analytical chemistry

1. Introduction

Higher education in the physical sciences serves several purposes: the dissemination of knowledge, the acquisition of expertise in a field of study, the development and promotion of the inner potential of individuals as well as fostering curiosity, creativity and critical thinking.[1,2] With approximately 69 % of students finding full-time employment in industry within four years after graduation in general,[3] and 60 % of bachelors level chemists working in the private sector in the US in particular,[4] higher education ultimately needs to equip students with the fundamental competencies and skills required for industrial careers. The rise of transformative technologies such as artificial intelligence, digitalization, automation, and robotics catalyzes a transition of the industrial sector to an Industry 4.0.[5,6] For example, technologies based on the Internet of Things (IoT) digitize laboratory environments for remote monitoring and control,[7–9] and autonomous systems are emerging as the next-generation approach to experimentation.[10–20] This transition implies a shift in the set of skills essential for these evolved workplace environments: computer systems and automated platforms might be able to carry out repetitive tasks at economic advantages, but cannot substitute human workforces at tasks that require creative intelligence, improvisation or physical dexterity.[21] Consequently, the challenges of Industry 4.0 pose a demand for more multidisciplinary skill sets,[22] including complex problem solving, critical thinking, and creativity as well as a baseline level of proficiency in algorithmic thinking to operate automated hardware and to complement the necessary domain-specific knowledge.[23] Linking chemistry as the primary subject to aspects of computer science and engineering is therefore of crucial importance to prepare students for these changing work environments.

The implications of the fourth industrial revolution on higher education chemistry have already been acknowledged by the ACS Examinations Institute, which recently adapted the general chemistry anchoring concepts content map (ACCM) for undergraduate curricula in the US.[24] Notably, the revised ACCM emphasizes the importance of careful experiment planning with the intention to reduce interfering measurement noise and to enable a robust execution of the experiment anticipating all possible sources of uncertainties or unexpected behavior. Further, the ACCM encourages the careful analysis of experimental results, including modelization and the importance of mindful interpretations and formulation of general scientific concepts supported by the findings. Among others, these two aspects will become increasingly important in the shifting environment of automated chemistry laboratories.

Classroom activities need to address two major challenges to successfully prepare students for careers that face higher degrees of automation: (i) teaching the fundamentals of chemistry, and (ii) enabling students to familiarize themselves with basic engineering and computer science concepts. Indeed, such multidisciplinary skills and intrinsic curiosity are expected to be key elements for Industry 4.0.[25] In that context, secondary skills can be promoted via interactive education strategies. Inquiry-based practices are emerging as an alternative approach to conventional pedagogical methods to teach laboratory practice.[25–28] As a matter of fact, it has been demonstrated that inquiry-based learning with platforms such as RoboGen offers great opportunities to teach multidisciplinary skills.[29,30] NMRviewers designed with Matlab have been introduced to promote complex data analyses and modeling,[31] and 3D printing has recently been introduced to classrooms to prepare intuitive visualizations of the physical and chemical properties of the elements in the periodic table.[32]

In this work, we describe a set of classroom activities that are designed to address the changing skill requirements bridging chemistry, engineering and computer science. Specifically, the project aims to design a robotic platform for autonomous titration, a common experiment for high school and undergraduate education,[33–36] and can thus be readily integrated into existing curricula. Several classroom experiments focusing on automated titrations have recently been introduced. Early examples report a simple yet precise device to streamline classroom titration experiments at low cost.[37] While the demonstrated apparatus constitutes an automated solution to titration in classroom settings, students were only intended to use the equipment, rather than construct it. Similar devices have been introduced more recently, but still focus on their usage rather than their construction.[38] A more recent example encourages students to build their own automated titrator in a bottom-up approach, where titrations are realized based on a high-level application programming interface (API) provided by the instructor.[39] While this example targets the chemistry and engineering aspects of constructing an automated titration, the software component is still lacking and relies on significant input and preparations of the instructors. A stronger focus on the development of flexible and robust control software in chemical contexts has recently been reported for the visualization of colored reactions on automated experimentation platforms.[40] Similarly, a recent study has demonstrated that this type of educational exercise can lower the obstacles for students of all abilities and classrooms with limited resources to participate in laboratory experiments.[41]

The project proposed in this work is designed with various focus points for different student audiences. We will demonstrate that titration as a process can be automated by student teams, and operated in full autonomy controlled by software written by the students. In this process, students will design and implement a robotic platform to execute titration experiments. Designing a robust control software that determines titrant volumes in real-time encourages students to conceive experimentation strategies that balance device accuracies with targeted measurement resolutions. The project follows a process-oriented guided inquiry learning (POGIL) ansatz,[42–44] which has been used successfully in chemistry classrooms at all levels to promote critical thinking and teamwork. Specifically, the outline of the project intrinsically supports a gradual transition from a structured inquiry framework to an open inquiry framework. Thus, students are enabled to experience the benefits and challenges of transitioning from manual experimentation over automated experimentation to autonomous experimentation.

2. Implementation of autonomous titration in the classroom setting

Titrations are a standard experiment in analytical chemistry and common to most tracks of chemistry education. Notably, the college board requires advanced placement (AP) high school students in chemistry to complete at least two titration experiments to satisfy the course lab requirements,[45] and the general chemistry ACCM for chemistry majors in college explicitly lists titrations as key experiments in analytical chemistry.[24] Titrations are typically conducted to determine the concentration of an unidentified analyte. To this end, a targeted chemical reaction with a standard solution, the titrant, is initiated. Based on the known concentration and volume of the consumed titrant, the concentration of the analyte can be computed.[46] Common titration experiments involve the addition of a base at a known concentration to an acid at an unknown concentration.

Here, we describe a laboratory exercise around titration that was incorporated into a more extensive undergraduate class that focused on scientific computing for students majoring in chemistry. It was organized in a total of four sessions consisting of 90 minutes of a combined lecture and discussion in an open classroom setting,[47,48] followed by a three-hour laboratory session. While this organization of the exercise was well suited for the supervised student groups described further below, adaptations to this structure could be beneficial to adjust for different student backgrounds and education levels. The exercise is set up as an inquiry-based learning problem at different levels: first, students are introduced to the research topic in a structured inquiry framework, but are given more and more freedom at the later stages of the exercise, going to guided and eventually open inquiry, to stimulate their scientific curiosity.[49] As such, the laboratory exercise proposed in this study generally follows the frameworks of POGIL, which has been used successfully in chemistry classrooms at all levels.[42–44] Relevant social skills are implicitly promoted as students are required to work in self-organized teams. The individual sessions were structured as follows:

Session 1: The instructors introduced the students to the theoretical foundations of titrations and motivated them as a historically crucial method in analytical chemistry. Students are instructed to manually perform their own titration experiment. Finally, students are required to formulate explanations for their observations and interpret their findings based on what they learned in the preceding lecture. During this process, students are already exposed to simple coding exercises by programming short scripts to operate a pH probe.

Session 2: This session focuses on the automation of the manual titration experiment from the previous session. Students will design and build an automated dispensing apparatus as well as program the control software. As a first step, the instructors discuss and demonstrate how single peristaltic pumps can be controlled with a Raspberry Pi. Students then integrate the pump and the pH probe into a single device which can (i) dispense a predefined amount of the titrant and (ii) measure the pH probe after a chosen equilibration time without human intervention, thus implementing a single step of the titration procedure.

Session 3: Following the integration of the pumps with the pH meter, students are now tasked to fully automate a titration experiment. This session focuses on the algorithmic aspects of controlling an automated titration workflow, as pH values need to be recorded and stored during the course of the experiment, followed by post-experimentation analyses of the recorded data.

To this end, instructors discuss measurement and resolution accuracies in detail and provide a broader introduction to basic programming patterns in Python. After the automated titrator is implemented, students and instructors jointly discuss the relevant differences to human-operated and automated titrations.

Session 4: In this session, students are tasked to create an autonomous titration platform by combining their automated titrator with a dynamic dispensing strategy for accelerated experimentation without loss of resolution in proximity to the equivalence point. This goal can, for example, be achieved with an adaptive stepping strategy that modulates the dispensed volume based on the current slope of the titration curve. Implementing the adaptive strategy requires a profound understanding of the chemistry of a titration, given that both strong and weak acids and bases could be used in the titration process. In addition, this autonomous approach to experimentation requires the implementation of a robust information feedback loop, as the dispensed amount is conditioned on the history of measured pH values.

3. Experimental section

The titration experiment can be set up for different laboratory settings and different levels of difficulty. For example, titration curves obtained from titrations with strong acids and bases simplify the implementation of the algorithmic controls as only one equivalence point needs to be considered, but require special safety measures during the experimentation process. Experiments with weak acids and bases can be realized with common household items such as lime juice and baking soda, but increase the challenge of implementing robust control software due to the more complexly recorded titration curves. In this work, we present two titrations: (i) common household items, comprising vinegar, baking soda and red cabbage juice, (ii) common laboratory chemicals comprising NaOH, H_3PO_4 and pH indicator. Details on the experimental setup and the robotic platform are summarized in the Supporting Information (see Sec. S.1). Hazards and safety measures are detailed in the Supporting Information (see Sec. S.3).

3.1 Manual pH measurements

In the first session, students prepare, perform, and analyze two manual titrations: (i) a simple titration to find the equivalence point, and (ii) another titration to record an entire titration curve. For the first titration, the students will determine the volume of titrant necessary to identify the equivalence point of a given analyte with the change of color of a pH indicator. Then, they will confirm their results with a pH probe and the theoretically calculated volume. In the second titration, the students will record the titration curve for a more quantitative assessment with the aid of a pH probe. Instructors will closely guide the students at every detailed step of the procedure. In these first titration experiments, the students write a simple Python script to digitally record the pH measurements at the operator request. Instructors will provide detailed guidance to explain the necessary steps to control the pH meter. The manual pH measurements are completed after fully resolving a titration curve.

3. 2 Automated pH measurements

In this session, the students design, implement and test an automated dispensing apparatus controlled with an algorithmic protocol. The dispensing system is assembled from a Raspberry Pi. Specific volumes are poured by two peristaltic pumps, one for the analyte and one for the titrant. Details on the setup are provided in the Supporting Information (see Sec. S.1). The control algorithm progressively iterates between: (i) adding a specific and suitable amount of titrant, (ii) measuring a pH value at a given time and (iii) recording the obtained measurements. The instructors guide the students through the steps of developing an algorithm to automatically add a given amount of titrant to the analyte. This step involves a calibration of the peristaltic pumps (see Supporting Information, Sec. S.2). With this task, students leverage the knowledge they gained from the manual experiments. They determine a suitable amount of titrant to be added, balancing the time requirements of the procedure and the desired accuracy to confidently resolve the equivalence point.

In the next step, the automated titrant dispensing will be combined with automated pH measurements to realize a fully automated titration procedure. The automated pH measurements can be implemented in two approaches: (i) using the pH probe for direct quantitative measurements and (ii) using a webcam for indirect measurements *via* color changes of an added indicator solution. While the pH meter enables more accurate measurements, the use of a webcam provides the opportunity to introduce students to computer vision for chemistry laboratories.[40,50–52] The goal of the automation of the titration process such that titration curves can be fully resolved with a single command of the operator. Details on pH measurements with both approaches are outlined below.

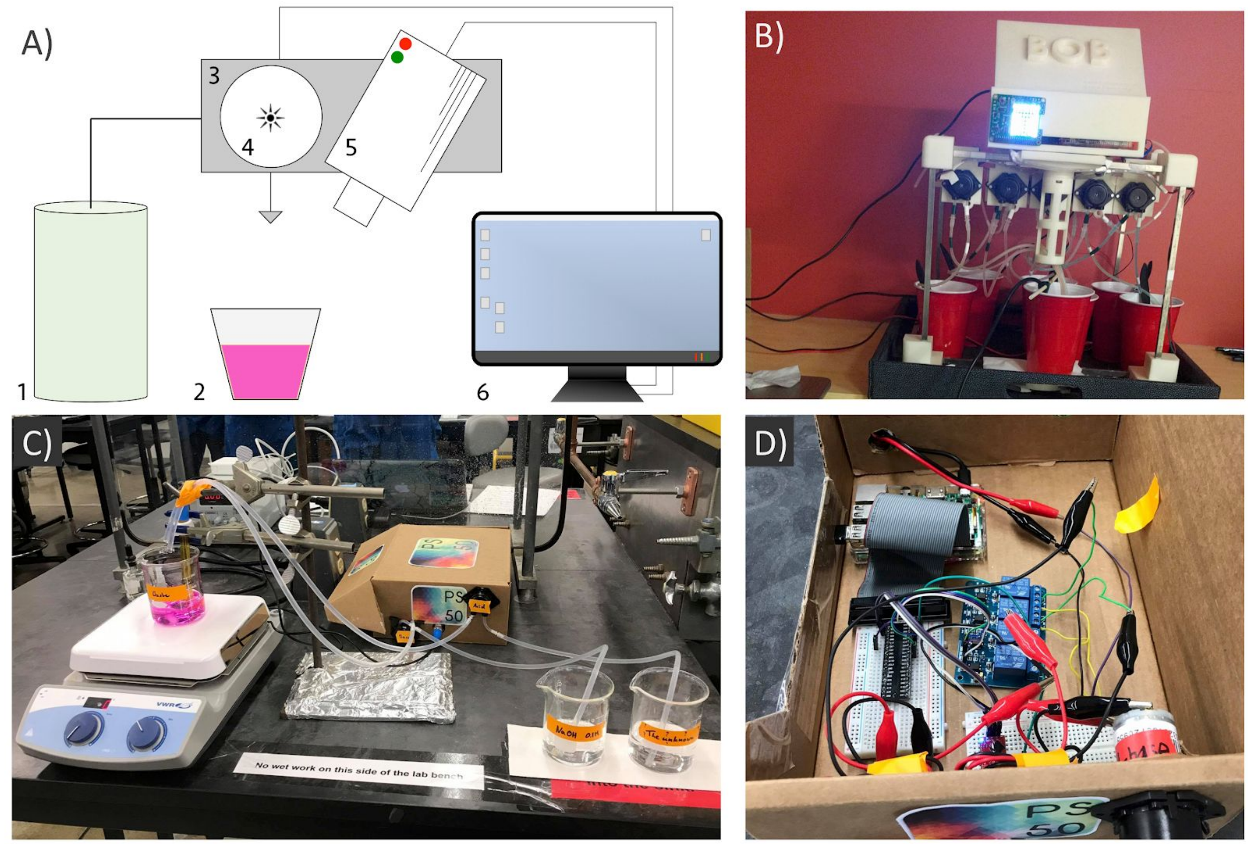

Figure 1: *Illustration of the experimental setups. (A) Sketch of the webcam-based titration experiment. (B) Setup for webcam-based titration (C) Setup for pH meter controlled titration (D) Pump control unit based on a Raspberry Pi.*

3.2.1 Automated titrations with the pH meter

The pH probe is used to directly measure the pH of the analyte-titrant solution. As the analyte-titrant solution needs to equilibrate after the titrant has been added, an appropriately chosen wait time needs to be added to the algorithmic procedure. Suitable choices for this wait time can be inferred from prior experiences with the manual titration experiments. Extensions to a *blind,* constant wait time consist of repetitive measurements to actively probe changes in the measured pH over time. Only when the measured pH does not exhibit significant changes beyond expected measurement uncertainties a measurement is taken. Fig. 1c illustrates the setup with a pH meter.

3.2.2 Automated titration with a webcam and an indicator

Webcam images can be used to study titrations *via* the color change of an added indicator in a computer vision approach.[40,53,54] With the webcam, an image of the analyte-titrant solution is obtained, from which the color can be extracted by analyzing the RGB color code of the solution. The image analysis can be conveniently realized with the third-party python library *OpenCV*.[55] The library supports various methods for shape detection to automatically detect the location of the beaker as well as image processing methods to account for different lighting conditions. If a quantitative analysis of the titration process is desired with the webcam, the webcam needs to be calibrated first. This can be done with selected single-point measurements during which both the color (RGB) of the indicator and the corresponding pH value (either measured with the pH meter, or *via* a known solution) are recorded. Similar to the direct measurements with the pH meter (see Sec. 3.2.1) the algorithmic automation of the titration procedure consists in an iteration between titrant dispensing and color detection.

3.3 Autonomous pH measurements

Finally, the automated titration platform is transformed into an autonomous platform. The key idea is to supply the control software with an algorithmic approach to determine the amount of titrant to be added to the solution dynamically, such that the overall time of the titration is reduced while retaining a sufficient resolution of the titration curve around the equivalence point. To this end, on-the-fly decision-making strategies are developed and implemented into the control software. Students can explore various strategies such as adaptive stepping approaches that condition the amount of titrant to be added on the history of recorded pH measurements and the expected shape of the titration curve. Students need to leverage their experience with titration experiments to formulate reasonable expectations and assumptions about the procedure. Adaptive stepping can be implemented at various degrees of sophistication ranging from discrete, hard-coded step choosing based on current pH values over more flexible approaches that estimate the location of the equivalence point based on probabilistic models or by direct comparisons to titration curves recorded during previous experiments.

4. Realizing autonomous titration in the classroom setting

Following the classroom exercises proposed in Sec. 3, we proceed with reporting the results that two different student groups obtained in the class. One group (three students) implemented automated titration with a pH probe together with an algorithmic approach for the online analysis of the recorded titration curve to determine equivalence points and pKa values (see Sec. 4.1). The other group (two students) created an autonomous titration robot that adaptively determines the amount of titrant to be added using a webcam (see Sec. 4.2).

4.1 Automated titration using a pH probe

Automated titrations with the pH probe were implemented following the steps outlined in Sec. 2 and 3. When implementing the titrant dispensing mechanism, the students observed substantial relative dispensing errors for small dispensing volumes as the pumps dispensed the titrant by the drop. Repeating the calibration experiments revealed that the dispensing inaccuracies are dominated by systematic errors, which allowed for an algorithmic correction by a simple linear regression. Careful analysis of the dispensing behavior of the peristaltic pumps as well as their experience from the manual experiments motivated the student group to fix the amount of titrant to be added to 1 ml per iteration, thus balancing the dispensing accuracy with the desired resolution of the equivalence point and the runtime of the experiment. Fig. 2a reports a titration curve that was recorded with the automated titration platform implemented by the student group of a fixed amount of H_3PO_4 0.1 M as an analyte solution and NaOH 0.1 M as a titrant.

The automated titration platform was controlled via a command-line interface implemented by the students. Recorded titration curves were analyzed in real-time in a two-step approach by: (i) constructing a continuous approximation of the titration curve based on the measured pH values, and (ii) using the continuous approximation, identify the equivalence point and the pKa values. The continuous approximation is constructed from a linear combination of sigmoidal functions and implemented in Python using the numerical libraries theano[56] and numpy.[57] As sigmoidal functions resemble the general shape of a titration curve, particularly for titrations with strong acids and strong bases, the student group identified this approach as being a numerically robust method to efficiently regularize experimental noise.

4.2 Automated titration using a webcam

After calibration following the steps outlined in Sec. 3 with observations similar to those reported in Sec. 4.2, the webcam was set up to take several images of the solution to reduce the influence of stochastic variations in the illumination of the beaker. From the ensemble of images, the students computed an average image and applied blurring and median filters (21x21 pixels) to account for variations in the lighting conditions, etc. The image was processed by creating a gray-scale copy of the average image, on which a shape recognition algorithm based on the Hough transform[58] was applied to detect the location of the beaker containing the solution. Students determined appropriate parameter values in a trial-and-error approach, testing several parameter values following the one-factor-at-a-time (OFAT) approach,[59] and manually confirming that the beaker had been detected correctly. Once the beaker had been detected, the color of the solution was determined from the processed image. Note that measured RGB codes were normalized to ensure robustness against varying lighting conditions.

Fig. 2B reports the normalized RGB difference between a solution and a target color in a titration procedure using a webcam. The students used lime juice as the analyte (weak acid), baking soda as the titrant (weak base), and red cabbage juice as the indicator. The initial solution was pink (acidic) and as the titrant was added it first turned purple and eventually turned blue (neutral to basic). Details on the chemicals are provided in the Supporting Information (see Sec. S.1 and S.3.2).

Due to the absence of a sudden color change, the student group correctly concluded that the titration must involve a weak acid and a weak base. This choice of chemicals, however, increased the difficulty of precisely measuring the equivalence point compared to the experiments reported in Sec. 4.1. To overcome this obstacle, the students implemented a procedure to measure the distance to a target color, rather than a change in color. With this procedure, the color of the indicator solution at pH 7 can be measured as a reference, such that the equivalence point is determined based on the color distance to this reference color. A minimum color difference indicates the equivalence point such that titrations of a weak base (e.g. baking soda) with a weak acid (e.g. lime juice) are possible even without a sudden and drastic color change. With the color-distance measure, the webcam pH detection was executed in two different modes: (i) aiming for three inflection points at 4.7, 9.7, 12.1 (see Fig. 2B.1) and (ii) running the titration to completion while recording the RGB distance of the color of the solution to the color of the solution at pH 7 (see Fig. 2B.2).

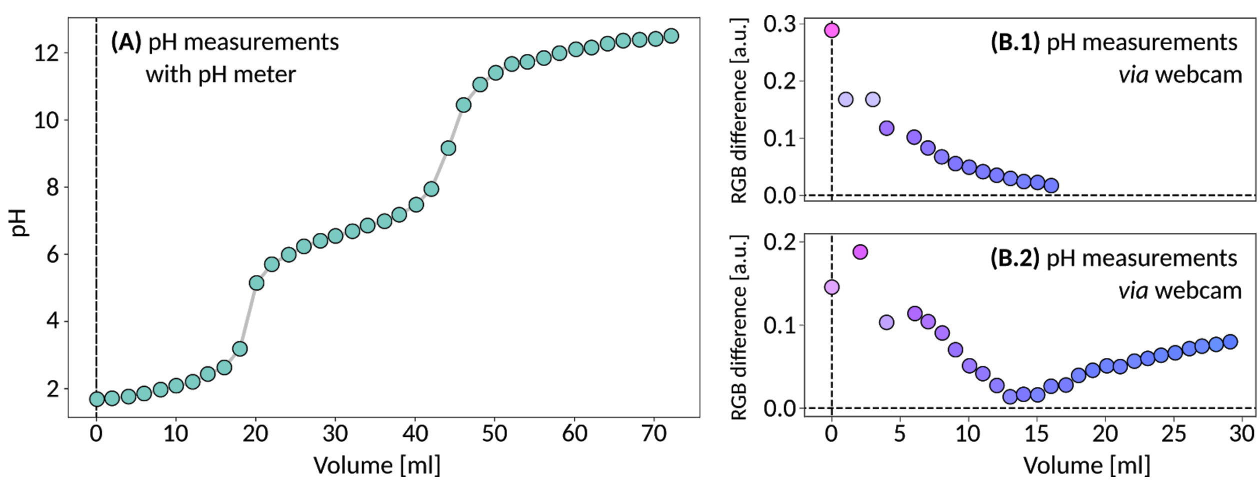

Figure 2: *Summary of the results. (A) Titration curve obtained with an automated titration platform constructed by students based on pH meter for a titration of* H_3PO_4 *and NaOH. (B) Indicator color change recorded with a webcam-based autonomous platform of the titration of baking soda and lime juice. In both cases, basic titrants are added to acidic analytes.*

4.3 Enabling autonomous experimentation via adaptive titrant additions

Instead of adding the same amount of titrant for each step until the target color was reached, the titration was made adaptive in the webcam experiment. An adaptive stepping method to determine the amount of titrant to add enables the addition of relatively large volumes as long as the solution is far from the equivalence point and can gradually decrease the volume to increase the resolution of the recorded titration curve around the equivalence point. Such an approach can reduce the overall experimentation time without compromising the accuracy in the targeted measurements.

The adaptive stepping algorithm implemented by the student group conditioned the amount of added titrant *t* on the norm of the difference between the normalized target color *vt* = (*rt*, *gt*, *bt*) and the normalized color of the solution *vs* = (*rs*, *gs*, *bs*). Specifically, *t* was set to be proportional to the norm of the color differences (see Eq. 1). Normalizing the recorded color RGB codes improved the robustness of the method with respect to ambient light fluctuations.

$$t = 2 \| v_t / (r_t + g_t + b_t) - v_s / (r_s + g_s + b_s) \|. \quad (1)$$

When the solution color was far from the target color, the pump time (amount of titrant added) was significantly larger than when the solution color was close to the target color. A maximum and minimum value for the pump times had to be met, however, balancing pump dispensing accuracies and expectations on the shape of the titration curve based on the manual experiments. For the experiments shown in Fig. 2B, the minimum was set to 1 ml and the maximum to 2 ml. If the calculated pump time was too high or too low, it was modified to be the maximum or minimum, as appropriate. The titration was stopped when the norm of the difference to the normalized target color was below 0.02 or when the value of red was less than half the value of blue in the normalized RGB code of the solution (see Fig 2B). These values were determined by the student group based on the manual titration experiments.

5. Conclusion

In this work, we described a classroom exercise for the development and deployment of an autonomous titration platform from the ground up to promote and foster the development of the skills that chemistry undergraduates need for successful careers facing the emerging digitization of chemistry laboratories. The proposed exercise is organized in a three-step active learning framework during which students are gradually given more freedom to encourage their independence as future researchers. First, students acquire the chemical background of titrations as an important technique of analytical chemistry and grow intuition by running titration experiments manually. Then, students implement an automated titration platform that requires a thorough understanding of all experimental aspects of the titration process while exposing the students to basic engineering and programming concepts. Finally, students learn to carefully analyze their experiments and balance experimental uncertainties with desired accuracies by adding adaptive algorithmic methods to control the amount of titrant added during the course of the experiment.

The classroom exercise can be realized with inexpensive and readily available materials which can be varied and adjusted to the interests and backgrounds of the students as well as the intended scope of the exercise. We presented the results of two different student groups who executed this classroom exercise with a pH probe and a webcam to monitor the progress of the titrations of different chemicals. Both student groups successfully implemented the automated and then autonomous titration platforms. While the manual titration experiments equipped them with a basic understanding of the titration process, it was due to the automation tasks that students realized important details including dispensing accuracies and measurement uncertainties. By automating the titration process, our students were actively encouraged and successfully managed to implement robust experimentation protocols which enabled titrations without human intervention. This classroom exercise therefore not only teaches the basic principles of titrations but periodically reinforces the conveyed concepts and draws attention on the details of the procedure.

The active learning framework in which this classroom exercise was organized presented an effective strategy to overall spark excitement with the students and to promote their curiosity, creativity and independence. We found that the gradual shift from structured inquiry for the manual titration experiments to open inquiry for the implementation of the autonomous titration platform constitutes an adequate compromise to balance the potentially different backgrounds of the students while enabling them to develop and express their own research interests. In addition, by working in small teams our students improved their secondary skills including communication, self-organization and planning ahead while working on this exercise, as has been reported for other team-based learning environments.[60,61] Although such active-learning pedagogies are typically more demanding on the teaching staff, efficient methods to scale active-learning to large classrooms have recently been reported.[62]

Overall, we believe that this classroom exercise is well suited to equip undergraduate level students with the skills required for successful professional careers and prepares them for the emerging transition to an Industry 4.0.

Acknowledgments

The authors gratefully acknowledge the students who participated in this project and would like to thank Dr. Nicholas Colella and Dr. Rae Moore for preparing some of the materials and chemicals used in the classroom exercises as well as Sukin Sim and Tim Menke for helpful feedback and discussions. F.H. gratefully acknowledges support from the Herchel Smith Graduate Fellowship and the Jacques-Emile Dubois Student Dissertation Fellowship. T.T-M. thanks CONACyT for scholarship No. 433469. L.M.R and A.A.G were supported by the Tata Sons Limited - Alliance Agreement (A32391). A.A.-G. Is thankful to the Canada 150 Research Chairs Program for their generous support. The authors thank Dr. Anders Frøseth for their generous support. This work relates to the Department of Navy award (N00014-19-1-2134) issued by the Office of Naval Research. The United States Government has a royalty-free license throughout the world in all copyrightable material contained herein. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the Office of Naval Research.

References

1. Fortino, A. The purpose of higher education: to create prepared minds. (2014).
2. Chan, R. Y. Understanding the purpose of higher education: An analysis of the economic and social benefits for completing a college degree. *Journal of Education Policy, Planning and Administration* **6**, 1–40 (2016).
3. Cataldi, E. F., Siegel, P., Shepherd, B. & Cooney, J. *Baccalaureate and Beyond: A First Look at the Employment Experiences and Lives of College Graduates, 4 Years On (B&B:08/12). NCES 2014-141*. (2014).
4. Careers in Industry - American Chemical Society. *American Chemical Society* https://www.acs.org/content/acs/en/careers/college-to-career/chemistry-careers/careers-in-industry.html.
5. Lazo, M. A. A. Schwab, Klaus. The Fourth Industrial Revolution. Ginebra: World Economic Forum, 2016, 172 pp. *Economía* vol. 41 194–197 (2018).
6. Tabor, D. P. *et al.* Accelerating the discovery of materials for clean energy in the era of smart automation. *Nature Reviews Materials* vol. 3 5–20 (2018).
7. Perkel, J. M. The Internet of Things comes to the lab. *Nature* **542**, 125–126 (2017).
8. Prabhu, G. R. D., Witek, H. A. & Urban, P. L. Telechemistry: monitoring chemical reactions via the cloud using the Particle Photon Wi-Fi module. *Reaction Chemistry & Engineering* **4**, 1616–1622 (2019).
9. Radmannia, S. & Naderzad, M. IoT-based electrosynthesis ecosystem. *Internet of Things* **3-4**, 46–51 (2018).
10. Häse, F., Roch, L. M. & Aspuru-Guzik, A. Next-Generation Experimentation with Self-Driving Laboratories. *Trends in Chemistry* vol. 1 282–291 (2019).
11. Bédard, A.-C. *et al.* Reconfigurable system for automated optimization of diverse chemical reactions. *Science* **361**, 1220–1225 (2018).
12. Steiner, S. *et al.* Organic synthesis in a modular robotic system driven by a chemical programming language. *Science* **363**, (2019).
13. Granda, J. M., Donina, L., Dragone, V., Long, D.-L. & Cronin, L. Controlling an organic synthesis robot with machine learning to search for new reactivity. *Nature* **559**, 377–381 (2018).
14. Nikolaev, P. *et al.* Autonomy in materials research: a case study in carbon nanotube growth. *npj Computational Materials* vol. 2 (2016).
15. Fitzpatrick, D. E., Battilocchio, C. & Ley, S. V. A Novel Internet-Based Reaction Monitoring, Control and Autonomous Self-Optimization Platform for Chemical Synthesis. *Org. Process Res. Dev.* **20**, 386–394 (2016).
16. Moosavi, S. M. *et al.* Capturing chemical intuition in synthesis of metal-organic frameworks. *Nat. Commun.* **10**, 539 (2019).
17. Sun, S. *et al.* Accelerated Development of Perovskite-Inspired Materials via High-Throughput Synthesis and Machine-Learning Diagnosis. *Joule* **3**, 1437–1451 (2019).
18. Umehara, M. *et al.* Analyzing machine learning models to accelerate generation of fundamental materials insights. *npj Computational Materials* vol. 5 (2019).
19. Langner, S., Häse, F., Perea, J. D. & Stubhan, T. Beyond Ternary OPV: High-Throughput

Experimentation and Self-Driving Laboratories Optimize Multi-Component Systems. *arXiv preprint arXiv* (2019).
20. MacLeod, B. P. *et al.* Self-driving laboratory for accelerated discovery of thin-film materials. *arXiv [physics.app-ph]* (2019).
21. Vermeulen, B., Kesselhut, J., Pyka, A. & Saviotti, P. P. The Impact of Automation on Employment: Just the Usual Structural Change? *Sustain. Sci. Pract. Policy* **10**, 1661 (2018).
22. Innovation, M.--M. Mission Innovation--Accelerating the Clean Energy Revolution, 2017.
23. Gray, A. The 10 skills you need to thrive in the Fourth Industrial Revolution. in *World Economic Forum* vol. 19 (2016).
24. Holme, T., Luxford, C. & Murphy, K. Updating the General Chemistry Anchoring Concepts Content Map. *Journal of Chemical Education* vol. 92 1115–1116 (2015).
25. Kirchner, M. D. Teaching the Industrial Internet of Things. (2017).
26. Cuartero, M. & Crespo, G. A. Using Potentiometric Electrodes Based on Nonselective Polymeric Membranes as Potential Universal Detectors for Ion Chromatography: Investigating an Original Research Problem from an Inquiry-Based-Learning Perspective. *J. Chem. Educ.* **95**, 2172–2181 (2018).
27. Bowen, R. S., Picard, D. R., Verberne-Sutton, S. & Brame, C. J. Incorporating Student Design in an HPLC Lab Activity Promotes Student Metacognition and Argumentation. *J. Chem. Educ.* **95**, 108–115 (2018).
28. Wheeler, L. B., Clark, C. P. & Grisham, C. M. Transforming a Traditional Laboratory to an Inquiry-Based Course: Importance of Training TAs when Redesigning a Curriculum. *J. Chem. Educ.* **94**, 1019–1026 (2017).
29. Auerbach, J. E., Concordel, A., Kornatowski, P. M. & Floreano, D. Inquiry-Based Learning with RoboGen: An Open-Source Software and Hardware Platform for Robotics and Artificial Intelligence. *IEEE Transactions on Learning Technologies* 1–1 (2018) doi:10.1109/tlt.2018.2833111.
30. Kokosy, A., Micea, M. V. & Saey, P. A professional project based learning method in mobile robotics. *2014 IEEE Frontiers in Education Conference (FIE) Proceedings* (2014) doi:10.1109/fie.2014.7044409.
31. Arrabal-Campos, F. M., Cortés-Villena, A. & Fernández, I. Building ‘My First NMRviewer’: A Project Incorporating Coding and Programming Tasks in the Undergraduate Chemistry Curricula. *J. Chem. Educ.* **94**, 1372–1376 (2017).
32. LeSuer, R. J. Incorporating Tactile Learning into Periodic Trend Analysis Using Three-Dimensional Printing. *Journal of Chemical Education* vol. 96 285–290 (2019).
33. Dominguez, V. C. *et al.* The Characterization of a Custom-Built Coulometric Karl Fischer Titration Apparatus. *J. Chem. Educ.* **87**, 987–991 (2010).
34. Sheppard, K. High school students’ understanding of titrations and related acid-base phenomena. *Chemistry Education Research and Practice* **7**, 32–45 (2006).
35. Po, H. N. & Senozan, N. M. The Henderson-Hasselbalch Equation: Its History and Limitations. *J. Chem. Educ.* **78**, 1499 (2001).
36. Murphy, J. Determination of phosphoric acid in cola beverages: a colorimetric and pH titration experiment for general chemistry. *J. Chem. Educ.* **60**, 420 (1983).

37. Hernlem, B. A Versatile and Economical Automated Titration Apparatus. *Journal of Chemical Education* vol. 73 878 (1996).
38. Verner, I. M. & Revzin, L. B. Towards Automation of Manual Operations in a High School Chemistry Laboratory. *Volume 3: Design; Tribology; Education* (2008) doi:10.1115/esda2008-59037.
39. Famularo, N., Kholod, Y. & Kosenkov, D. Integrating Chemistry Laboratory Instrumentation into the Industrial Internet: Building, Programming, and Experimenting with an Automatic Titrator. *Journal of Chemical Education* vol. 93 175–181 (2016).
40. Vargas, S. *et al.* Team-Based Learning for Scientific Computing and Automated Experimentation: Visualization of Colored Reactions. *J. Chem. Educ.* **97**, 689–694 (2020).
41. Soong, R. *et al.* Rethinking a Timeless Titration Experimental Setup through Automation and Open-Source Robotic Technology: Making Titration Accessible for Students of All Abilities. *Journal of Chemical Education* (2019) doi:10.1021/acs.jchemed.9b00025.
42. Farrell, J. J., Moog, R. S. & Spencer, J. N. A Guided-Inquiry General Chemistry Course. *J. Chem. Educ.* **76**, 570 (1999).
43. Moog, R. S. & Spencer, J. N. POGIL: An overview. *Process oriented guided inquiry learning (POGIL)* **994**, 1–13 (2008).
44. Simonson, S. R. *POGIL: An Introduction to Process Oriented Guided Inquiry Learning for Those Who Wish to Empower Learners*. (Stylus Publishing, LLC, 2019).
45. Price, P. D. & Kugel, R. W. The New AP Chemistry Exam: Its Rationale, Content, and Scoring. *J. Chem. Educ.* **91**, 1340–1346 (2014).
46. Whitney, W. D. & Smith, B. E. *The Century Dictionary and Cyclopedia: The Century cyclopedia of names... ed. by Benjamin E. Smith*. vol. 11 (Century Company, 1911).
47. Kohl, H. *The Open Classroom: A Guide to a New Way of Teaching*. (1970).
48. Barth, R. S. So you want to change to an open classroom. *Phi Delta Kappan* **53**, 97–99 (1971).
49. Banchi, H. & Bell, R. The many levels of inquiry. *Science and children* **46**, 26 (2008).
50. Eppel, S. Setting an attention region for convolutional neural networks using region selective features, for recognition of materials within glass vessels. *arXiv [cs.CV]* (2017).
51. Eppel, S. & Kachman, T. Computer vision-based recognition of liquid surfaces and phase boundaries in transparent vessels, with emphasis on chemistry applications. *arXiv [cs.CV]* (2014).
52. Eppel, S., Xu, H., Bismuth, M. & Aspuru-Guzik, A. Computer vision for recognition of materials and vessels in chemistry lab settings and the Vector-LabPics dataset. (2020).
53. Ballard, D. H. & Brown, C. M. Computer vision. englewood cliffs. *J: Prentice Hall* (1982).
54. Sonka, M., Hlavac, V. & Boyle, R. *Image processing, analysis, and machine vision*. (Cengage Learning, 2014).
55. Bradski, G. & Kaehler, A. *Learning OpenCV: Computer Vision with the OpenCV Library*. ('O'Reilly Media, Inc.', 2008).
56. Al-Rfou, R. *et al.* Theano: A Python framework for fast computation of mathematical expressions. *arXiv preprint arXiv:1605. 02688* (2016).
57. Oliphant, T. E. *A guide to NumPy*. vol. 1 (Trelgol Publishing USA, 2006).
58. Hough, P. V. C. Machine analysis of bubble chamber pictures. in *Conf. Proc.* vol. 590914

554–558 (inspirehep.net, 1959).
59. Friedman, M. & Savage, L. J. Planning experiments seeking maxima. *Techniques of Statistical Analysis* 365–372 (1947).
60. Kirkpatrick, M. S. Student Perspectives of Team-Based Learning in a CS Course: Summary of Qualitative Findings. in *Proceedings of the 2017 ACM SIGCSE Technical Symposium on Computer Science Education* 327–332 (ACM, 2017).
61. Smith, M. K. *et al.* Why peer discussion improves student performance on in-class concept questions. *Science* **323**, 122–124 (2009).
62. Ruder, S. M. & Stanford, C. Strategies for Training Undergraduate Teaching Assistants To Facilitate Large Active-Learning Classrooms. *J. Chem. Educ.* **95**, 2126–2133 (2018).