Journal of open hardware

(1) Overview

A Smart Centrifuge for Automated Sample Processing with Liquid Handling Robots

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Abstract

The recent development of automation hardware, such as liquid handling robots, offers accelerated and less labor-intensive workflows for material synthesis and assays. Furthermore, increased data redundancy is expected to contribute to higher reliability and reproducibility of communicated results. One current limitation for further deployment, especially in open hardware solutions, is the integration of centrifuges in automated workflows. Conventional centrifuges are unsuitable for modular applications and, crucially, do not offer the required positional control over the samples. This work presents a centrifuge with infrared sensor-derived positional control based on open-source design and cost-effective manufacturing, which is a prototype for integrated operation. Building with modular components, this centrifuge allows further customized adaptations with controlling from the serial port. This work presents the design, construction, validation, functionality testing, and quality control for operation. Besides, the smart centrifuge is compatible with various deck configurations due to an adaptive design, here demonstrated for the pipetting robot OT-2 (Opentrons). This accessible platform offers flexible use in automated synthesis and sample processing in various fields including life sciences, physical sciences, and engineering.

Metadata Overview

Main design files: https://github.com/AdReNa-lab/Centrifuge-with-OT-2

Snapshot of original design files: https://doi.org/10.5281/zenodo.13941029

Target group: Scientists in chemical engineering, materials science, chemistry, biomedical science and related disciplines.

Skills required: Mechanical assembly – easy; Electronics and programming – intermediate; CNC machining – intermediate; Desktop 3D printing – easy.

Replication: No builds known to the authors so far.
See section "Build Details" for more detail.

Keywords

Position control centrifuge; pipetting robot; lab automation; liquid handling.

Introduction

Centrifuges are devices that spin at high speeds and use centrifugal forces to separate components based on their differing densities.[1] With applications ranging from materials synthesis to pathogens analysis in biological fluids, ubiquitous deployment is found in various fields of life sciences, physical sciences and engineering [2-4].

Recently, concepts of automated workflows with programming packages have emerged widely for various applications [5-8]. A typical application is the liquid handling robot, offering accelerated sample handling and greatly reduced user workload [9]. With integrated platforms enabling fully automated procedures [10-12], large-scale explorations of the experimental domain and integration of data science become more feasible when compared to manual approaches. Furthermore, automated processes with shared protocols on widely available platforms also improve data redundancy and results reproducibility [13-15].

However, the deployment of centrifuges in lab automation remains challenging due to stringent requirements on the tube location. Because hardware integration to a pipetting robot requires precise positional control, i.e. an accurate coordinate system needs to be established within the workstation.

In this manuscript, we describe the design, hardware assembly, and operation guide for the centrifuge with positional control that can be deployed in liquid handling robots. A typical integration with the OT-2 for lab automation was demonstrated. Furthermore, the centrifuge can also be used standalone to meet specific purposes. Device fabrication by computer numerical control machining with computer-aided design (CAD) is an ideal way to build the framework. Combined with the open-source program of Arduino, this device demonstrates its potential in achieving customized scientific hardware at a lower cost.

Overall Implementation and design

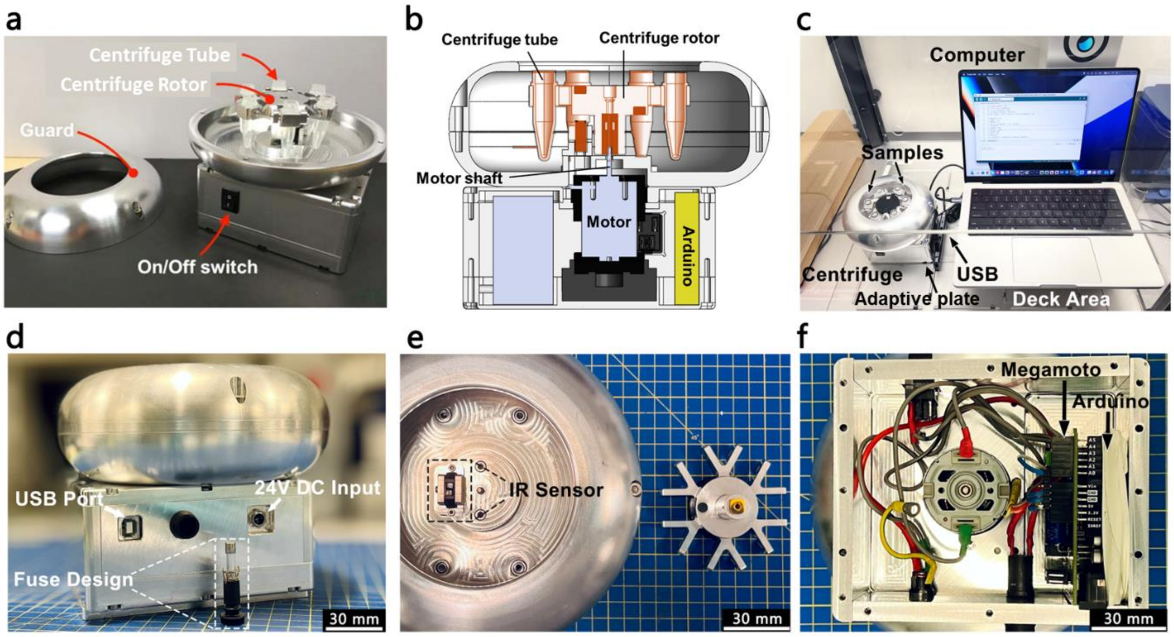

Figure 1 Illustration of the smart centrifuge. a) General structure of the device. b) Cross-sectional view of device design and assembly. c) Photo of the typical integration with the OT-2. d) Extra fuse design to enhance safety. e) IR sensor used for capturing the threshold value when finding home position. f) Compatible and compact design with the dual controller.

The overall design of the smart centrifuge is exhibited in ***Figure 1a.*** The hardware mainly contains two parts: the housing assembly and the electronic accessories. The housing assembly consists of rectangular plates and round guards, which are made via CNC milling (HAAS VMC CNC Mill). The top and bottom motor plate is designed with notches to accommodate the DC motor. The centrifuge rotor with swinging bucket to hold the sample tubes was connected via the DC motor shaft to the bottom motor, this design and assembly was shown in a cross-sectional image on ***Figure 1b***. For integration with the OT-2, an adaptive bottom plate was required to fit the standard footprint of its deck area (***Figure 1c***). To realize this, a cast aluminium tool plate served as physical interface. The reserved screw holes are used to secure the structure with common fasteners. All the plates have a fillet design to minimize the potential harm. Therefore, the assembly and disassembly can be completed easily without adhesives.

The electronic part is based on an Arduino microcontroller, which can be used to interface with PC, and to drive the motor with a commercial MegaMoto board. This motor was the key to realize the positional-control function, as the stepping technique is based on a phenomenon referred to as cogging torque by nudging the commutator into positions governed by the arrangement of the permanent magnets in the motor. Detailed setup for the torque characterization and its properties patterns can be found in the Supplementary Information, along with parameters for the DC motor summarized in a datasheet. The current motor has a torque constant around 0.0235 Nm/A, enabling its cogging torque property and application in fixed position. For the use case presented here, it enables positional control without complicated design.

All functions were realized by the command line sent from the computer through the Arduino serial monitor, therefore the USB connection is necessary during the operation as it ensures the serial communication (9600 bps) between the computer and the centrifuge (***Figure 1c*)**. The power input of this device was based on 24 V DC, a general AC-DC switching power supply could be used to meet the purpose, with detailed model listed in the BOM (***Figure 1d***). To realize the function of finding the home position, an IR sensor is embedded under the centrifuge rotor (***Figure 1e***) with an inserted plastic to capture the threshold value in fixed coordinates. The extended MegaMoto motor control shield is compatible with Arduino Uno, allowing for a compact design within the inner structure (***Figure 1f***). As a result, the electronic connection can be assembled conveniently using commercially available parts. The current device has a USB port so that it can be driven by a computer using the provided program written in C/C++.

The implementation of the device is user-friendly and cost-effective, allowing for further customized modification. All the designed drawings, Arduino program, and auxiliary details are provided in Supplementary Sections and can be found in the project’s repository.

(2) Quality control

Safety

The centrifuge can be controlled via the Arduino program, which ensures its practicality. Considering its spinning feature, a risk assessment is imperative. Firstly, the power source for the electronics is recommended to be unplugged during the assembly or when not in use. Secondly, electronic cables should be kept away from the device to avoid accidental wire winding.

To maximize the safety, additional design features have been considered. There is a robust round safeguard outside the centrifuge rotor to protect users from the unexpected touch. Such guard could also be used to avoid the leakage of chemical reagents during the improper operation. In addition, separate power supply circuits from the Arduino ports enables the relocation function to be realized without the main power supply. General Maximum Credible Accident (MCA) tests were found to be compliant with the BS EN 61010-2-020:2017 standard for safety recommendation. Furthermore, brief operation suggestions were also listed for safety guideline after referring to the standard. Considering the structural strength of accessories, the suitable working temperature for the device would be within 0 - 40°C. The actual loading should also be controlled within 1 mL for each tube to avoid the overloading of voltage. It is recommended that a specific enclosure area with physical shields can greatly improve safety while operating.

Compared with commercial centrifuges, which require high voltage, this portable and mini-sized device runs on 24 V DC supply.

Calibration

There is no need to frequently calibrate the device since the motor speed at the rated voltage should be similar in general cases. However, some application scenarios may require specific motor speeds with different working loads. This function was also integrated within the Arduino program. Users can simply input the command line <calibration> to realize the purpose. Overall, a calibration test is recommended for each device to better know its spinning features. The calibration of the motor voltage and RPM could be done via checking the related curves with the help of a tachometer (***Figure 2a***). When the calibration program is activated, the device will follow the speed-stepping sequence (***Figure 2b***). For example, to complete the calibration with 6 tubes, 1 ml of water was added to each tube as 1 loading unit.

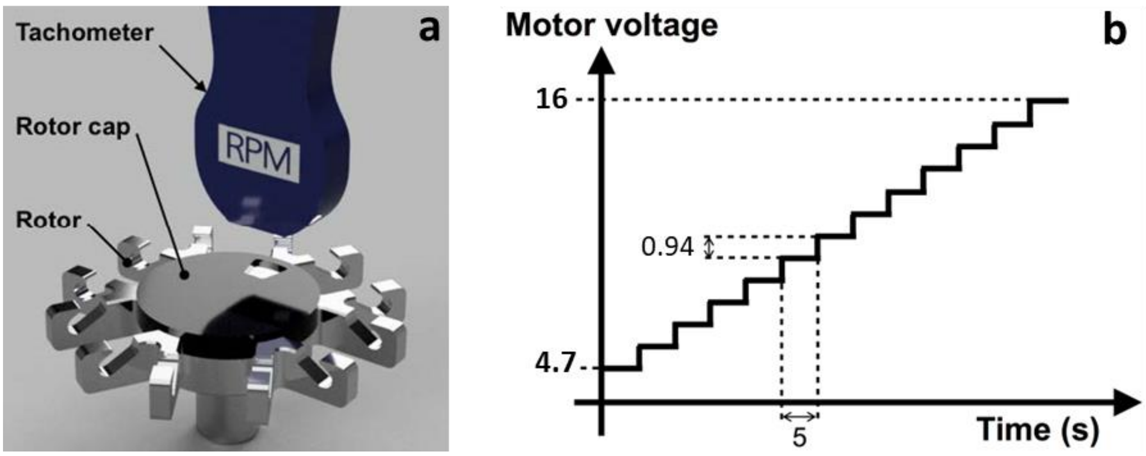

Figure 2 Illustration of the calibration: a) Method: the tachometer is placed vertically above the centrifuge rotor cap. b) The stepped sequence of the motor voltage.

With the recorded data, the calibrated curve can be established using the supplied template. After entering the respective readings, the equation will calculate g-force values and plot the graph with terms for polynomial fit. As summarized in ***Figure 3a-b***, calibration for loading conditions of 2,4 and 6 tubes were completed for reference of typical centrifugation process. Measurement was repeated three times for each loading condition to ensure the accuracy. The motor showed similar features under different loadings with only a slight difference in the curves (which can simply treat as the same), indicating the generalization in most cases. By entering the updated terms into the code (***Figure 3c***), the total calibration is finished.

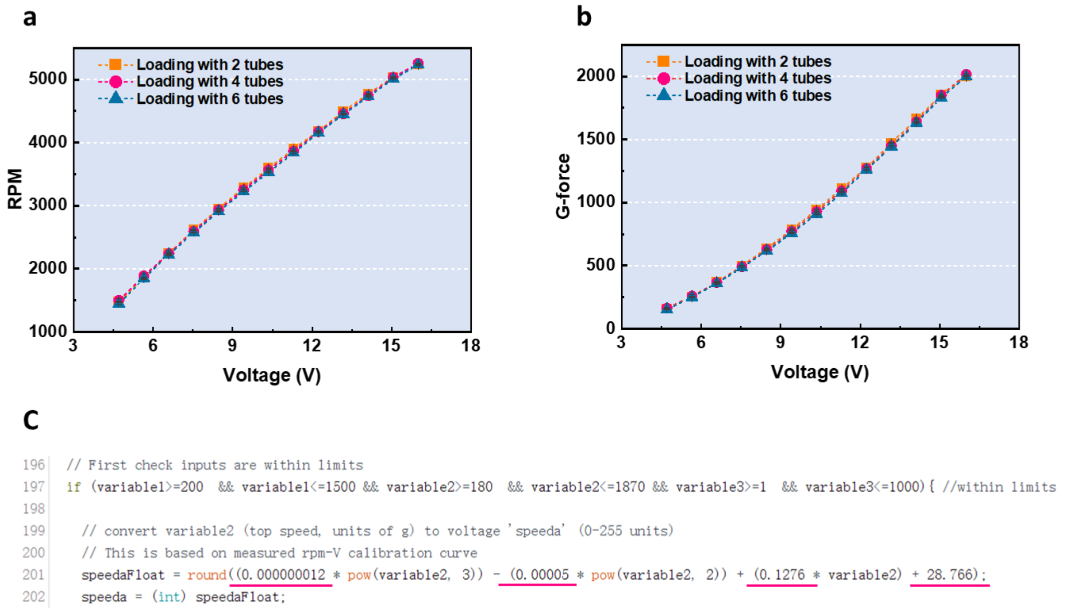

Figure 3 Demonstration of the calibration: a-b) Results of the calibrated curve, 1 ml of DIW was added in each tube as 1 loading unit. c) Update of the Arduino code based on calibration data.

General testing

A laptop is required to complete the testing protocols of the centrifuge. Once the device is connected, tests can be carried out by sending input strings through the serial port. The typical setup is exhibited in ***Figure 4a***. Generally, the centrifuge has three main functionalities: finding the home position, customized centrifugation, and calibration test. All the functionalities follow a general string format, detailed explanation with the setup can be found in the supplementary materials.

The function of finding the home position is used to reset the centrifuge rotor to fixed coordinates. Herein, tubes with deionized water (DIW) were used in testing samples at 50 % duty circle (***Figure 4b***).

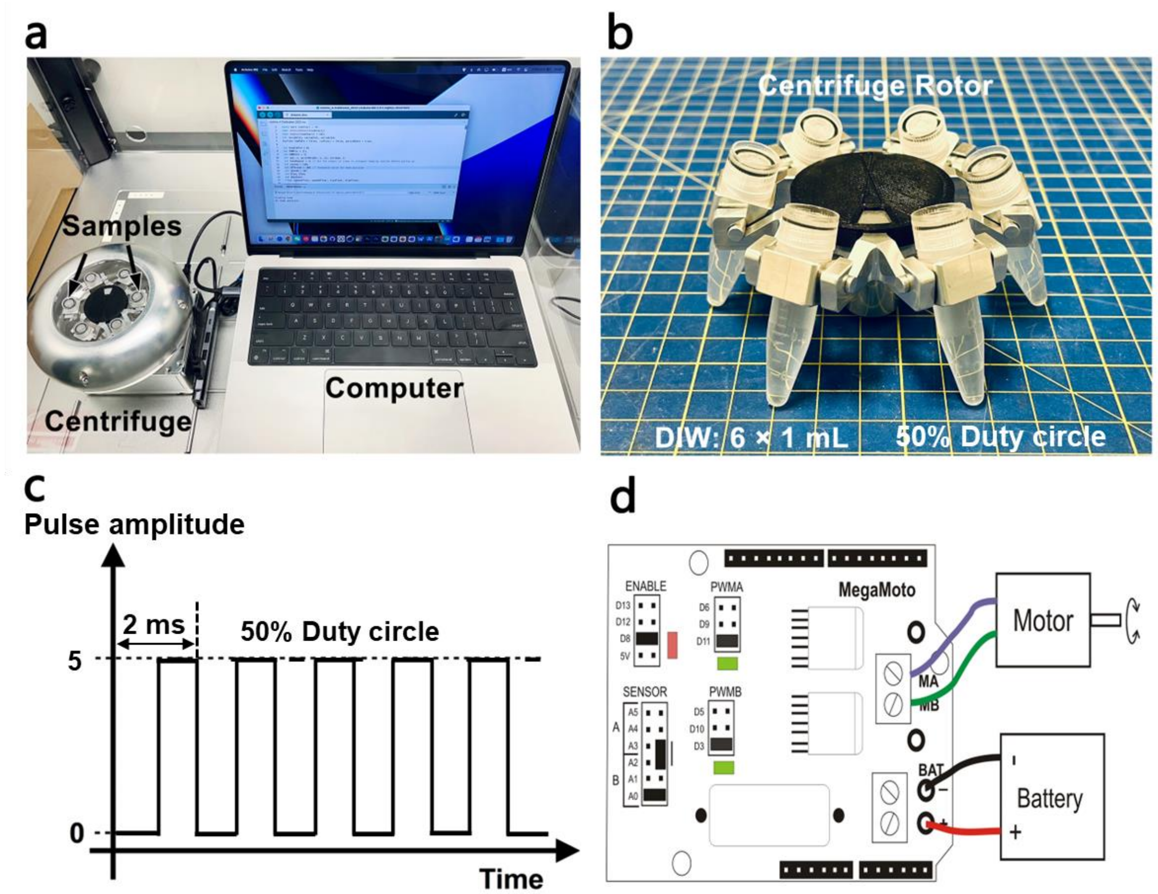

Figure 4 Illustration of the general testing. a) Typical setup for the testing, which includes the smart centrifuge, a computer, and a USB cable. b) Deionized water served as test samples. c) Plot of the amplitude signal with time in finding the home position. d) H-bridge mode connections for the Megamoto board.

The pulse amplitude signal (50% duty circle) is sent to the motor, which corresponds to the motor voltage at 12V, resulting its stepping motion (*Figure 4c*). A key point behind the stepping technique is the phenomenon called cogging torque, by nudging the commutator into positions governed by the arrangement of the permanent magnets in the motor. The centrifuge rotor (with swinging buckets to hold the tubes) is therefore nudged into different rest positions during the step motion until the one corresponding to the home position is found. The precise control of the fixed positions was realized by the coordination drive of the motor control shield via H-bridge mode (*Figure 4d*). Since the loading accessory was central symmetry, therefore once the stepping motion ends with a fixed position, finding the home position was realized. For the use case presented herein, it enables positional control without complicated design. The reliability of this function was explained under the application section with OT-2.

The function of customized centrifugation has highly flexible features. As shown in **Figure 5**, this functionality accelerates the centrifuge up to a set speed and is held constant for a set amount of time. The acceleration and deceleration can also be set for designated purposes. The max speed refers to the g-force (units of g) acting on each liquid sample while the acceleration is defined as increase in g-force per second (units of g/s). The relationship between motor voltage and g-force with calibration was explained in the previous section.

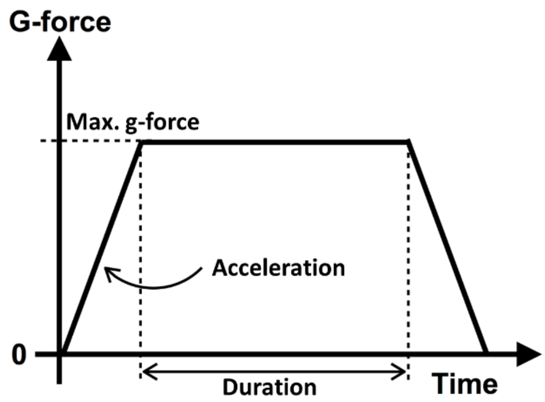

Figure 5 Rotation parameters during a typical centrifugation procedure.

(3) Application

Use case(s)

Modular Combination with Pipetting Robots

The customized centrifugation with the automated process is ideal for high throughput synthesis in materials science or processing of biological samples. For instance, we have integrated the centrifuge within the pipetting robot to demonstrate the automated procedure of gold nanoparticles (AuNPs) surface modification. Generally, the ligand exchange protocols, herein thiol-for-oleylamine (OAm), require repetitive centrifugation for sample work-up [16-18]. Mixed solvent of ethanol and OAm-AuNPs precursors were aspirated by the OT-2 robot and then dispensed into the centrifuge tubes (4:1 v/v) for further centrifugation at 4500 rpm and 25 °C. Considering the high efficiency of the pipetting robot, modular integration can greatly accelerate the workflow of materials synthesis, especially in high throughput systems with machine learning approaches [5, 6, 19]. The typical application setup was shown in ***Figure 6a***. The position of tubes can be defined via the fixed coordinate system once the diameter data is obtained, therefore the OT-2 can accurately complete the protocol for OAm-AuNPs, as illustrated in ***Figure 6b***. The repeatability test for finding home position was investigated via the OT-2 testing protocol which was also provided in the Supplementary Information. Generally, finding home was conducted after spinning for 1 minute. Then, 1mL of DIW was aspirated by the OT-2 and then filled into each tube for testing the reliability, since it was a programmable validation, the operation was repeated for 50 rounds with the mentioned protocol file. Overall, this function was quite reliable as only 1 time of small deviation was observed. During that case, though the tip touched the inner edge of one tube, OT-2 still completed the test as usual. Therefore, positional repeatability is reliable since the coordinates were fixed in the protocol.

Normally, the pipetting process for one batch of OAm-AuNPs centrifugation can take at least 9-10 minutes (batch time). Besides, the gap time for closing lids, setting the manual procedure, and operating devices should also be considered. Therefore, the total preparation time may be defined as the sum of the individual steps mentioned above. In this case, we compared the time consumption between the herein presented integrated and a conventional manual workflow using a ThermoFisher X1R centrifuge.

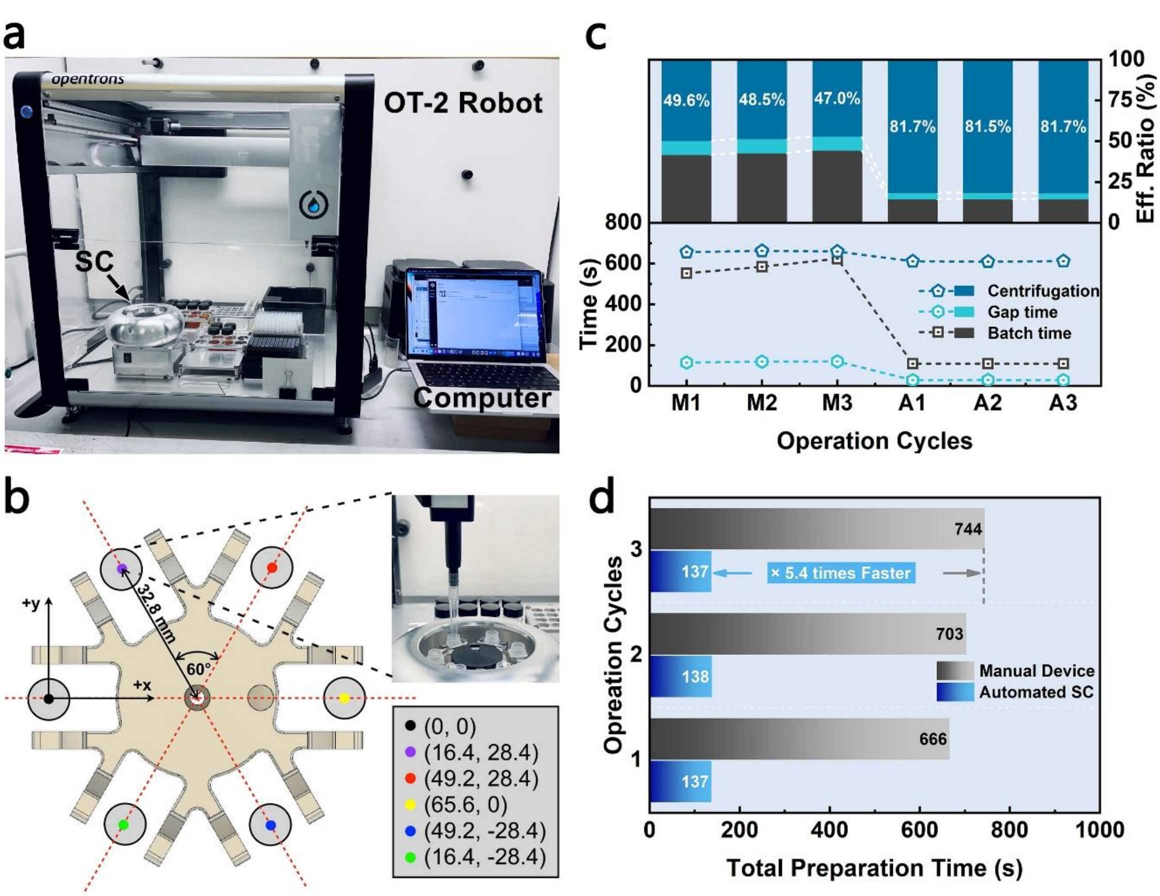

Figure 6 Modular application. a) Integration of the smart centrifuge within the Opentrons robot. b) Visualization of the coordinate system with corresponding optical image in insert. c) Comparison of the fractional time requirements for three consecutive cycles with manual (M1-M3) and automated operations (A1-A3). d) Comparison of the total preparation time between the manual and the automated procedure.

Figure 6c shows the time consumption during three operation cycles, respectively. By deploying an automated protocol with the OT-2 robot and the herein presented smart centrifuge, similar workflows can be completed within 2 minutes (109 s), while the manual method took around 10 minutes (from 552 s to 624 s). In comparison, the actual centrifugation accounted for only 47.0% of the total time in the manual approach, while for the automated procedure, centrifugation accounted for 81.7% of the total processing time. This demonstrates that automated procedure not only greatly reduce requirements on manual labor and improve reproducibility, it also enables overall faster processes. While the speed for manual operation typically decreases with continuous repetitive work, the automated operation maintains high efficiency, exhibiting a nearly 5.4 times faster speed compared with manual operation in the third cycle investigated herein (**Figure 6d**).

Reuse potential and adaptability

Due to the modular design and open-source features, the smart centrifuge can be extended to various research fields. Apart from the combined application within the automated synthesis, scientists can take advantage of its portable and miniaturized features to carry out work under space and resource-limited environment. Besides, by extending the functionality of the multi-steps centrifugation, researchers can accurately control the experimental variable in the field of digital chemistry. Compared with conventional approaches, the smart portable centrifuge can greatly improve the efficiency and allow researchers to focus on key sections in the workflow.

(4) Build Details

Availability of materials and methods

The hardware construction and assembly require a 3D printer for coupling components and a CNC mill to manufacture tool plates. Fasteners and cast tool plates can be easily found in most hardware workshops. Cast tool plates with a size of 180mm x 100mm x 6mm and M4 cap-heads x 25mm are recommended. The SLA resin and 3D printers were sourced from Formlabs and they are readily available in individual quantities from their website. A detailed format bill of related materials can be found in the Supplementary section for reference.

The motor was obtained from SciQuip, which provided the type of a DC brushed motor, see detailed information listed in the BOM. The motor selection is important as the positional control function was realized through the cogging torque property. Other electric components such as the Arduino, IR sensors and other necessary cables can be found from various suppliers (herein Amazon). Users can download Arduino IDE freely from its official website to control the device and edit its protocol. Lastly, all design documents are available for further modification with customized demand.

Ease of build / Design decision

The parts of the smart centrifuge can be assembled easily by users with some intermediate skills for the general structure assembly, it only requires some fasteners without any permanent adhesives. The options for the motor need to calculate the g-force and its diameter. Besides, the torque constant of 0.0235 Nm/A is identified in the current setup, this could be a reference in building or exploring replacement. The most advanced part of the build would be the CNC mill operation for the aluminum well plates as specific cast materials and consumables are needed for its structure assembly (intermediate knowledge with the help of specific operators). The modular design of components can minimize the required effort; we assess that the building process could be completed easily if the required materials are sourced in advance.

Operating software and peripherals

The smart centrifuge is based on the Arduino Uno, the program is compiled under Arduino IDE (V2.0.2), which is compatible on Windows 10, Linux, and Mac OS. The program package for the device was written in C/C++ and depends on many common built-in libraries. In this work, the test runs on a Mac OS 12.6 Monterey system.

Dependencies

The position control of the DC motor requires a driver board, in this device the Robot Power MegaMoto (with power chips: 2 ea. BTN7960B) “H-bridge” control shield is used. In addition, MegaMoto is easy to connect general-purpose power amplifier designed to work with the Arduino hardware compatible CPU units.

Hardware documentation / build instructions / files location:

Hardware repository: Zenodo
Name: Centrifuge-with-OT-2
Persistent identifier: DOI: 10.5281/zenodo.13941029
License: CERN-OHL-S license
Publisher: Adaptive and Responsive Nanomaterials (AdReNa) lab / Yueyang Gao
Date published: 2024-10-16

Software code repository: GitHub
Name: routine_4.ino
License: MIT License
Publisher: Adaptive and Responsive Nanomaterials (AdReNa) lab / Yueyang Gao
Identifier: https://github.com/AdReNa-lab/Centrifuge-with-OT-2
Date published: 2024-10-15

(5) Discussion

Conclusions

In this study, we present a smart centrifuge with highly customized features for modular scientific applications. By using the open-source Arduino, the device could be controlled via general operating systems. Furthermore, the documentation is open-source and will allow further modification. The deployed materials are generally accessible and can be mass-produced, the total cost is inexpensive. With the several protection properties, safety is also enhanced during general operations.

Successful deployment in a pipetting robot with ligand exchange protocols was demonstrated herein. Researchers can take advantage of its modular application like automated synthesis or high throughput analysis. For studies that require portable and parametric centrifugation, this proposed design may meet those demands with affordable methods. Considering the highly customized integration with the robot platform, this device not only demonstrates great compatibility but also shows huge potential in simplifying working procedures in automated workflow.

Future Work

The current design has met the intended expectation of portable and modular application, but some features are envisioned for further improvement. The motor used was disassembled from a small low budget centrifuge with related information listed in the Supplementary section. Future models may integrate an upgraded motor, which could achieve higher rpm while maintaining the same power supply. Implications on g-force and motor diameter may need to be considered. While the functionality of the current design is practical, an upgraded version of the position control system is worth exploring. Finding a motor that achieve high rotational speeds >2000 g while offering positional control via an encoder is non-trivial. The addition of an optical encoder to the motor shaft would aid positional control and could also be used for a speed control loop.

Paper author contributions (CRediT)

Gao Yueyang: Manuscript writing, program modification (updated version), functionalities test, OT-2 robot application, file preparation
Redfearn Andrew: Prototype design and assembly, program development (earlier version), file preparation, data analysis
Dawes Simon: Hardware manufacturing, drawings design, file preparation
Shi Jialei: Motor characterization, Supplementary file preparation
Taylor Alaric: Project supervision, hardware manufacturing, validation assistance
Wurdemann Helge: Project supervision, characterization suggestions
Guldin Stefan: Project supervision, literature review, manuscript suggestions, documentation, validation assistance

All authors have reviewed the manuscript before submission.

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Competing interests

The authors declare that they have no competing interests.

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Software: Any of the Open-Source Initiative approved license