ISBN: 978-628-96613-2-3. ISSN: 2414-6390. Digital Object Identifier: https://dx.doi.org/10.18687/LEIRD2025.1.1.491

Design of automatic histological processing equipment for biological samples for teaching use in educational laboratories

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Summary. – This article presents the development of an automatic histological processing machine, which was designed and built for educational use at a low cost. The architecture combined STM32F401 microcontrollers, PID controllers, DS18B20 temperature sensors, bipolar stepper motors, and a Nextion touchscreen to automate the dehydration, impregnation, and inclusion of biological samples. A robust mechanical structure made of stainless steel was designed along with an electronics-based distributed master-slave control system, in accordance with UART communication and monitoring by inductive sensors and limit switches. The performance of the prototype was evaluated using an observation sheet with 10 criteria that were validated in content and appearance by expert judgment. Average values between 3.71 and 4.22 of a maximum possible score (5) were obtained, indicating consistent thermal control, motion repeatability, stability in motion, as well as smoothness, while motor accuracy was automatically calculated. The device is a viable and replicable alternative to commercial systems, providing access to educational technologies in biomedical sciences and bolstering hands-on training for students at universities.

Keywords—Equipment, processor, tissues, biomedical, electronics.

I. Introduction

The education of professionals in biomedical sciences requires teaching environments that combine theoretical knowledge with artistic and technical execution. In other areas, e.g. histology, both the adequate provision of skills training and the need to interact with suitably prepared biological material or specialized materials are crucial [1], [2]. Unfortunately, numerous academic institutions in Latin America have limited resources and cannot afford or easily access commercial biomedical equipment [3].

In an attempt to address this problem, educational research has begun to encourage the development of low-cost, wearable technologies capable of mimicking real biomedical processes. One of the most representative solutions is the Foldscope, a foldable optical microscope that achieves and exceeds magnifications of 140× with low-cost materials to allow its use in schools around the world [4], [5]. Thus, this device has shown that it is feasible to democratize access to scientific knowledge based on principles of frugal science in a pedagogically sound way [6].

In the discipline of histology, tissue processing is crucial for quality diagnoses in light microscopy. The process is comprised of dehydration, clearance, impregnation/embedding steps that are usually performed in high-cost automated devices such as the Tissue-Tek AutoTEC® or AS-410M systems for multi-block treatment (in closed loops) [7], [8]. But many public universities don't have access to those systems, and hands-on learning for students is now severely limited.

Faced with these challenges, some initiatives have emerged, such as OpenWSI, an open-source, low-cost platform that provides detailed digital imaging to scan histological specimens through commercially available components combined with real-time autofocus algorithms [9]. Such solutions are not limited to research laboratories and can be beneficial in teaching as well, as they allow the digitization of slides for pedagogical purposes [10].

In addition, the application of digital technology in the teaching of histology has also reported a beneficial impact on students' self-efficacy and cognitive erosion. For example, Guo et al. created a model of flipped teaching with design thinking using digital histological imaging, remote sessions, and active learning that achieved high acceptance values through student achievement and performance [11]. Regarding publications, we found that the digitization of histological slides (using virtual platforms or NFC and augmented reality) improves participation rates more significantly [12], [13].

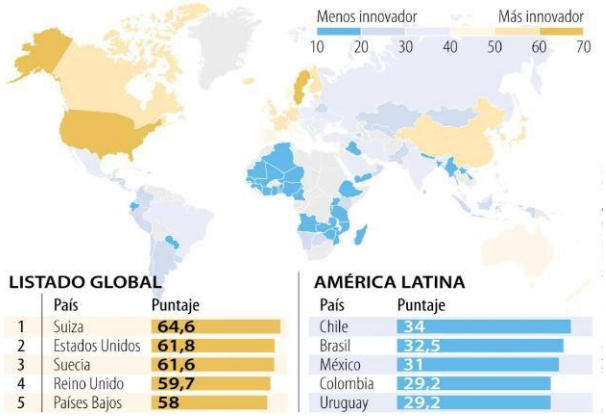


Fig. 1 Top most innovative countries in 2022
Source: "La República" newspaper, Colombia [3]

In the case of Latin America, in 2022 Chile is recognized as the most innovative country according to the Global Innovation Index (GII) published annually by the World

Intellectual Property Organization (WIPO), followed globally in 65th position by Peru; Due to these figures, rigorous political intervention in the promotion of local innovation ecosystems stands out, notably in strategic sectors such as education and health [14].

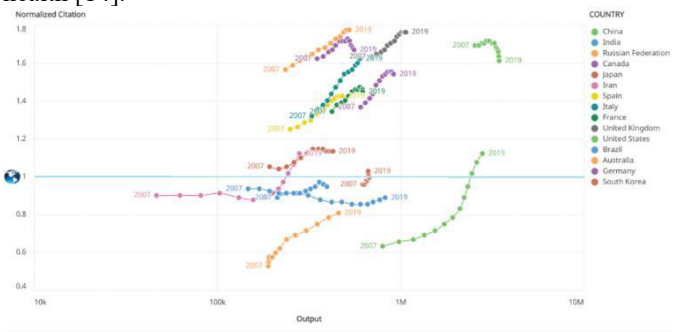


Fig. 1 Top most innovative countries in 2017-2019

The present research addresses this challenge by suggesting the development, simulation and real integration of an automatic histological processing apparatus to be used in university practical laboratories. The objective of this processor is to operate in a similar way to commercially available equipment but making use of low-cost electronic components and modified methods for automation, all oriented towards practical application (reducing dependence on the import of external technology) with contributions towards the training of competent professionals in the field.

II. METHODS

Tissue processing device development

In this section the results obtained for the elaboration of the research project are shown, for the first stage of the development of the tissue processing device the conceptual, mechanical and electronic design stages are considered, all these stages are appreciated in the operating scheme.

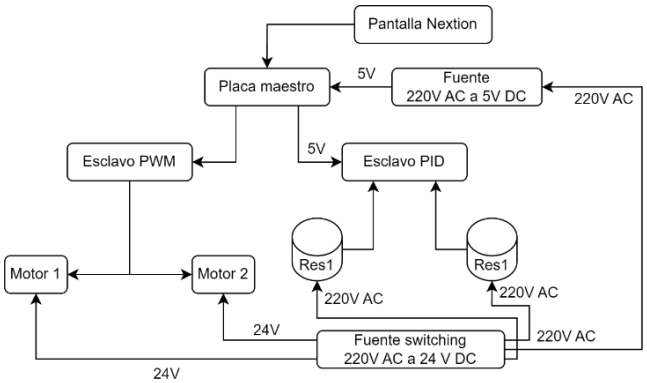


Fig. 2 Diagram of the system's operation
Source: Own elaboration

A. Conceptual design: The goal of the conceptual design of an automatic tissue processing equipment is to create a robust, efficient, and user-friendly system. The following are the technical features and improvements of the proposed design oriented to electronic engineering:

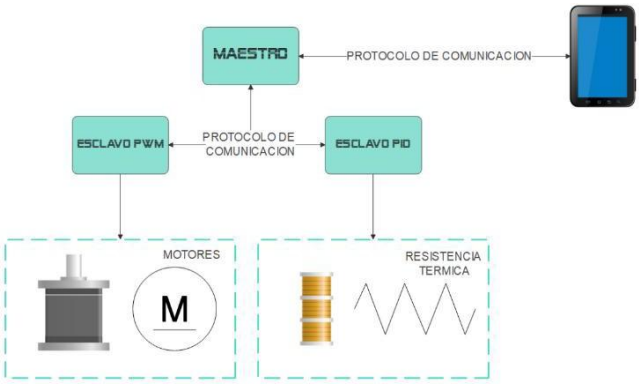


Fig. 3 Design of the operating scheme
Source: Own elaboration

System Architecture: A design based on the ARM® Cortex® STM32F401 microcontroller architecture will be used, which will be chosen based on its energy efficiency, processing capacity and performance. The master card and slave card will work together to perform essential system and user interface operations.

Communication: Cards will communicate with each other via UART using a variety of sounds to maximize data flow and reliability. To ensure the integrity of the transmitted data, robust communication protocols will be implemented.

Important Process Control

- High-precision DS18B20 temperature sensors will be used to monitor paraffins and provide reliable temperature control measurements.
- Compared to mechanical relays, solid-state relays offer fast response and long service life.
- Each heating element will have optimized PID control loops, ensuring accurate and stable temperature control.

User Interface: The Nextion touchscreen provides an enhanced graphical interface and user experience to users. The display will make it easy to schedule processing cycles and display the system status in real time.

Motor Control: The master board will control the bipolar stepper motors to perform precise vertical and circular movements, which are essential for automated sample handling.

Additional sensors: To increase safety and avoid collisions or overloads in the system, inductive and limit switch sensors will be integrated to monitor the position of mechanical components.

Processing Automation

The system will fully automate the dewatering, pre-impregnation and infiltration processes, reduce variability and improving the reproducibility of results.

B. Mechanical Design: To ensure the functionality, durability, and safety of an automatic biological tissue processing system, it is important to meticulously consider the mechanical aspects when designing and building the system. The essential

mechanical components and their technical considerations are described below.

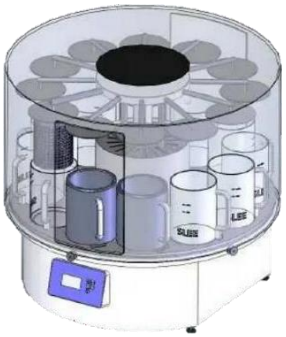


Fig. 4 Structural design of the equipment
Source: Own elaboration

i) **Structure and reach**: The structure must be strong and stable to support the weight of all operating components, from electronic boards to motors and process stations. Stainless steel is recommended for its corrosion resistance and ease of cleaning, which are essential in laboratory conditions.

ii) **Motion systems**: vertical and circular in nature require bipolar stepper motors due to their precision and reliability. Couplings and related mechanisms must allow for precise and smooth movement of samples through the different stages of processing.

iii) **Trays and containers**: The handling and transport of biological samples depend on these components. Their design should ensure the stability of the samples and facilitate their insertion and extraction.

iv) **Stations involved in the process**: Each station must be created to facilitate a specific process, such as infiltration or dehydration, and must be compatible with the temperature control and fluid handling system.

C. Electronic design: The technical aspects of the automatic processing system of biological tissues focus on the use of electronic components of high precision and reliability. Below is a breakdown of the components and their function within the system:

Temperature Sensor: The DS18B20 temperature sensors were chosen for their accuracy and digital communication capability, which reduces noise in the signal and improves the reliability of temperature measurements for paraffin control.

Heating resistors: Connected through solid-state relays, which allow for quick switching without physical wear, they have the ability to maintain the necessary temperatures during paraffinization.

Nextion Touchscreen: Provides a rich, customizable user interface that makes it easy for the operator to interact with the system, provides visual feedback, and allows for intuitive, real-time adjustments.

Limit switches for inductive sensors: To ensure operational safety and integrity of samples and equipment, they provide accurate position detection and control the limits of mechanical motion.

Microcontroller STM32F401: These microcontrollers are the core of the system, running control and data management algorithms efficiently. They have sufficient processing power and resources to handle complex tasks.

Electronic circuit stages

Power Stage: HLK-10M05 step-down transformer is used in the power supply to convert the power grid voltage from 220VAC to a lower output voltage. A diode jumper is then used to rectify this AC output voltage to continuous voltage. It is finally filtered with the C7 and C14 electrolytic capacitors to obtain a controlled output voltage of 5VDC.

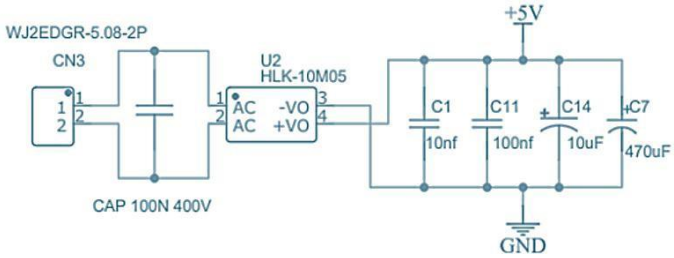


Fig. 5 Power source from 220v AC to 5v DC
Source: Own elaboration

Clock Module: The DS3231 clock module has a CR1220 battery backup that works without external power to keep time records. I2C communication via SDA and SCL allows for the reading and writing of date and time stamps.

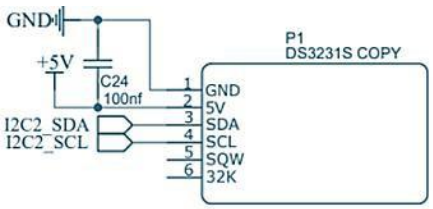


Fig. 6 DS3231 clock module connection
Source: Own elaboration

Microcontroller Connection Pins: The STM32F401CDU6 microcontroller has an internal LDO regulator that provides you with a supply voltage of 3.3V. To produce the precise clock signal, it uses an external 32KHz quartz oscillator. The microcontroller uses the C programming language to process digital input and output signals.

LED Diode Connection: Light-emitting diodes (LEDs) have a series resistor that limits the current they can emit based on the supply voltage. To energize the LED and turn it on, the STM32 activates the corresponding GPIO.



Fig. 7 DS3231 clock module connection
Source: Own elaboration

Connecting Inductive Sensors

The LC oscillator, which produces a magnetic field, is located in the upper and lower inductive sensors. When detecting a metallic object, its amplitude changes, which activates the output transistor.

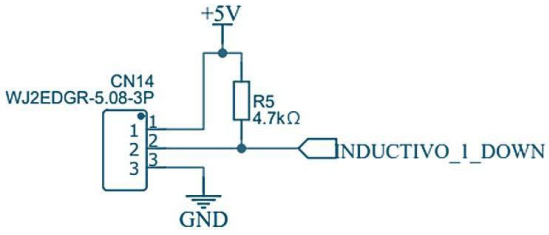


Figure 8. Connection of indicator LEDs
Source: Own elaboration

Communication via slave cards

On the TX and RX pins, UART communication between the STM32 and the slave card converts serial data into modulated signals. The protocol used is used to send motor control commands (PWM, direction, enable). On the slave card, MOSFETs act as switches by connecting the power voltage to the motor terminals. The speed is regulated by quickly switching with the PWM signal. The rotation of the motor is reversed by changing the polarity. Current sensing circuits in the drivers protect MOSFETs and motors from overloads.

In addition, they have the ability to send status signals to the STM32. The 40-pin slave card connection which can convert the voltage of the 5VDC source to the levels needed for MOSFETs and logic. Filtering capacitors reduce the amount of noise in the system.

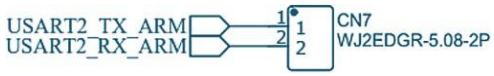


Figure 9. UART Communication
Source: Own elaboration

Buzzer connection

The buzzer is a type of transducer that can transform an electrical signal into sound. The NPN transistor acts as a switch from an STM32 GPIO.

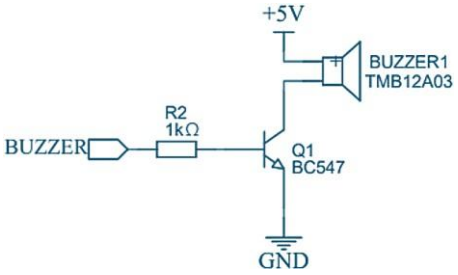


Figure 10. Buzzer Communication
Source: Own elaboration

Display Nextion

The TX and RX pins on the STM32's UART connect the Nextion display. UART communication converts bytes of serial data into modulated signals on the pins. Nextion's own serial protocol is used by the STM32 to receive and send touch events.

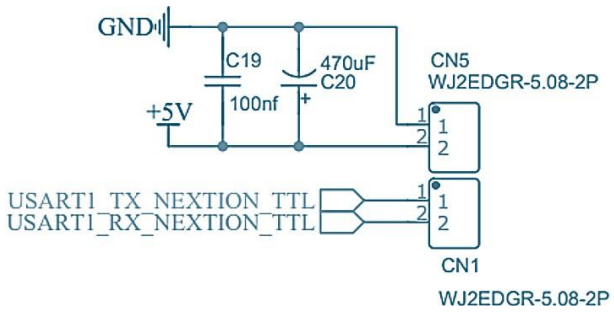


Figure 11. Nextion Display Connection
Source: Own elaboration

Signals for circular and vertical motor drivers

The slave card drivers control the vertical and circular motors. The power circuitry of this card uses MOSFETs to control the current and direction of rotation of the motors according to PWM signals

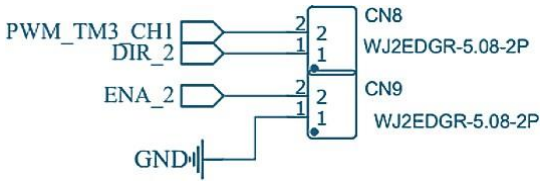


Figure 12. Motor Controller Signal
Source: Own elaboration

Late-stage upper and lower stroke sensors

Actuated limit switches connect the STM32's input pin to the internal direct ground switch. When they are not actuated, a thrust resistance maintains a high level. In short, the STM32's digital electronics help the system integrate sensors, actuators, human interface, and processing.

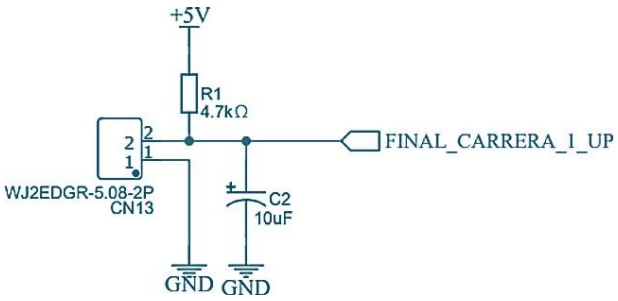


Figure 13. Motor Controller Signal
Source: Own elaboration

III. Results

A. Preparation of the instrument

The instrument used to measure the degree of functionality of the device was by means of an observation sheet based on 10 criteria used to verify compliance with

Mechanical Functional Assessment ()

Repeatability and Accuracy Testing (c1): The accuracy of the displacements and the ability to reproduce these movements under different conditions were examined.

Strength and Durability Analysis (c2): The components were subjected to endurance tests to assess their strength and their resistance to continuous use.

Optimized calibration (c3): Components have been adjusted and calibrated to ensure ideal timing and alignment.

Circuit Control

Control Circuit Verification (c4): Tests were performed to verify the accuracy and efficiency of the circuits that control the movement and operations of the equipment.

Measurement Circuit Analysis (c5): Ensuring that measurement circuits produce accurate and reliable readings is an important part of process monitoring.

Power Circuit Evaluation (c6): The power circuits were evaluated to ensure they handled the required loads without overheating or failing.

Monitoring the operation of motors and sensors

These particular tests focused on evaluating the performance and reliability of the sensors and stepper motors. These were the key points:

Sensor Accuracy (c7) – Sensor response and accuracy were evaluated under a variety of operating conditions.

The operation of the PAP (c8) motor: An evaluation of the performance of the motors was carried out in terms of movement accuracy, response to commands and energy efficiency.

Temperature Regulation Tests

In tissue processing, maintaining an accurate temperature is critical. The tests included:

Evaluation of PID control (c9): The PID control was found to work well to maintain the desired temperatures.

Performance of heating elements (c10): examined how heating elements and temperature sensors maintained ideal conditions in paraffin baths.

To collect data from the results obtained, an instrument was applied (see Table 1), which was subjected to a validation method by expert judgment based on the following parameters: clarity (p1), objectivity (p2), timeliness (p3), organization (p4), sufficiency (p5), intentionality (p6), consistency (p7), coherence (p8), methodology (p9) and relevance (p10).

TABLE I
Expert Judgment Validation Results of Data Collection Instruments

Criterion	Judge 1	Judge 2	Judge 3	Judge 4	Judge 5	Judge 6	p value
c1	1	1	1	1	1	0	0.0546875
c2	1	1	1	1	1	1	0.0078125
c3	1	1	1	0	1	1	0.0078125
c4	1	1	1	1	1	1	0.0078125
c5	1	1	1	1	1	1	0.0078125
c6	1	1	1	1	0	1	0.0546875
c7	1	1	0	1	1	1	0.0546875
c8	1	1	1	1	1	1	0.0078125
c9	0	1	1	1	1	1	0.0546875
c10	1	1	1	1	0	1	0.0546875

TABLE II
Results of the Observation Sheet

Observation sheet										
	Mechanical functionality			Electronic functionality						
Observers	P1	P2	P3	P7	P8	P9	P10	P11	P12	P13
1	4,80	3,90	3,90	4,60	3,40	4,20	4,50	4,80	4,30	4,50
2	3,90	4,80	4,80	4,60	3,10	3,60	3,70	4,80	4,60	4,10
3	3,10	4,20	4,00	3,30	3,30	3,40	4,90	4,20	3,10	4,40
4	3,30	4,20	3,90	4,10	4,70	3,30	4,40	3,10	3,80	3,40
5	4,60	4,60	4,20	4,70	3,50	3,20	3,40	3,60	4,50	3,50
6	3,70	3,90	3,70	3,80	3,60	3,60	3,60	4,90	4,10	3,70
7	4,10	3,70	3,60	4,30	5,00	3,30	3,80	3,30	4,10	4,40
8	4,00	4,90	3,20	3,70	5,00	4,60	3,70	4,80	3,50	4,20
9	3,80	4,70	4,80	3,20	3,70	4,40	4,40	3,90	4,40	3,30
10	3,80	3,30	4,00	3,90	3,60	3,50	3,30	3,20	4,40	3,20

IV. Discussion of Results

The WCIO score by expert opinion indicated important evidence of relevance and validity of the criteria to be used in an evaluation form to present the performance of an automatic histological processing device.

Table I shows that most of the criteria have significant values below 0.05, demonstrating a good agreement among the

judges on the validity of each item. Especially the criteria c2 (Strength and Durability Analysis), c3 (Optimized Calibration), c4 (Control Circuit Verification), c5 (Measurement Circuits) and c8 (PAP Motor Operation) showed relevant P values, reaching a strong statistical significance (p=0.00786), consolidating their suitability as evaluation indicators.

But c1 (Repeatability and Accuracy), surpassed by the parameters of c6 (Power Circuits), c7 (Sensor Accuracy), c9 (PID Control); and pt=c10 (Heating Elements). They obtained p-values of 0.0546, just slightly higher than the regular significant lines for other criteria described of all the values in Table-4a. This implies the need for further examination or conceptual refinement of these items to improve clarity/relevance as interpreted by experts.

Regarding the results using an observation sheet applied to ten observers (see Section III. A Comparative Study of Mechanical and Electronic Functionality in Table 1), an analysis was carried out between both mechanical and electronic functionalities. On average, rates were at high levels (3.1 to 5 on a 5-point scale), which is indicative of high perceived functioning for evaluators.

Of the most significant scores obtained from the criteria, P1 (Repeatability), P11 (Temperature Control) and P12 (Thermal Resistance) achieved average values close to or greater than 4.5, demonstrating through the analysis the high precision in the mechanisms of movement, temperature control in unnecessary conditions for histological processing. This confirms the response of the PID system and the performance of the heating element in paraffin baths.

On the other hand, factors such as P5 (Clarity of the Control Panel) and P6 (Structural Strength of Moving Parts) presented a remarkable level of dispersion with observers, as well as moderate scores (some below 3.5 points), which implies less than optimal values in terms of ergonomics or design of machinery features for this line of equipment.

As for the analysis of the stepped motor and sensor function, its stable performance was demonstrated. The values of P8 (Motor Response to Commands) and P9 (Motor Power Consumption) indicate a reasonable degree of electronic integration, allowing for the necessary synchronization in automated sample handling.

Finally, criterion P10 (Synchronization between Sensor and Actuator) obtained a mean of 4.3, indicating that the components to find objects are well synchronized with those that act on them. That timing is crucial to avoid errors in equipment operation, particularly in automated processes, where everything can be time.

In general, the results obtained support both the evaluation tool and the design of the functional prototype. Although deficiencies in the details were revealed, the overall performance of the equipment confirms that it is technically feasible to provide educational support in the histology laboratory.

V. Conclusions

Validity of the Assessment Instrument

The instrument applied was evaluated by expert judgment and demonstrated strong consistency in most of the evaluation criteria. Six of the ten items examined had $p \leq 0.0078$, showing a statistically significant agreement on their relevance and clarity. This lends credibility to the methodological soundness of this instrument for future use in similar settings.

Excellent Performance of the Whole Appliance

The data collected in the observation sheet represent a reasonable mechanical and electronic operation of the devices, respectively. The mean score of all items was 3.71-4.22 points (out of 5), indicating that, in general, the prototype satisfies a standard to high level of accuracy, control and operation.

Outstanding Thermal and Motor Accuracy

Criteria related to operation (P11, P12) and stepper motor response also received high scores with low variability in score, ensuring that the PID control system together with the power electronics designs are providing adequate control to the crucial parameters of the histological process.

Variability in Perception and Design Criteria

A specific investigation of, for example, P8 (clarity of the control panel) or P9 (structural strength), showed a coefficient of variation greater than 13%, suggesting dispersion in terms of observers' opinions. This indicates that there is room for improvement for new devices in terms of ergonomics and design from a Human-Machine Interface point of view.

Viability in an Educational Environment

After a full evaluation of the data, it can be stated that the device works well and could work reliably as didactic support equipment in an educational histology laboratory. The automation, as well as the user-friendly interface, really improve the teaching and learning process by demonstrating the processing of biological material.

VI. Recommendations

Optimize control panel ergonomics

The control panel is easy to use, for ease of use and operator safety. In view of the high variability among observers in terms of criterion P8 (clarity with respect to the control panel) with a coefficient of variation value reaching approximately 18.56%, it is advisable to redesign the user interface in terms of readability, button layout, function signaling and visual feedback. This will minimize operational errors and improve the user's educational experience.

Strengthening the physical structure of the mobile system

Strengthening of the mechanical configuration system. A review of the moving mechanical elements (criterion P9) is recommended, namely in terms of strength structure and tolerance to cyclic loads to achieve durability under operating conditions commonly found in university laboratories.

Expand validation testing with more experts and end users

To consolidate the robustness of the instrument and generalize these findings, we suggest that the validation be replicated with more expert judges and end users (both professors and laboratory technicians), considering their contributions both for the optimization of the design and for the calibration of the evaluation criteria.

Implement improvements to sensor-actuator synchronization

Although the timing scores (P10 and P11) were positive, testing at higher loads or temperatures would be needed to be confident in the robustness of the sensor's response, as well as the stability of the PID control over an extended period.

Develop a technical operation and maintenance manual

Prepare an O&M manual. Since schools will be using the proposed resource, a comprehensive manual should be designed with specific instructions for operating the device, as well as information on its calibration and maintenance. Teachers and students will find this document a useful aid, it will save a lot of time when using the device while ensuring its longevity.

Include a digital parameter logging module

Add a digital parameter logging device. In future editions, it is recommended to add an automatic logging system (via a microSD or USB interface) with critical parameters such as temperature and processing times, as well as the number of cycles in the engine. This would allow the traceability of the process and inclusion in proposals for continuous improvement.

Consider benchmarking with commercial teams

Discuss comparative testing with commercial products. Finally, a comparison with commercial systems can be made both in accuracy and costs (including processing time) to verify accuracy and ease of use. This would position the instrument as an affordable and practical solution for histological instruction.

VI. Acknowledgements

We thank the National University of Callao for being the managing entity of the scientific dissemination of the results of the research work. In turn, we thank the Office of the Vice-Rector for Research, for motivating students and teachers to grow in the research experience through training to participate in prestigious international events such as LEIRD 2025.

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