

Article

Development of a Low-Cost, Open-Source Quartz Crystal Microbalance with Dissipation Monitoring for Potential Biomedical Applications

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Abstract

Quartz Crystal Microbalance with Dissipation monitoring (QCM-D) systems are widely used for the real-time analysis of mass changes and viscoelastic properties in biological samples, enabling applications such as biomolecular interaction studies, biosensing, and fluid characterization. However, their accessibility has been limited by high acquisition costs. To address this limitation, a low-cost, open-source QCM-D system was developed. Unlike other affordable, open-hardware alternatives, this system is specifically optimized for potential biomedical applications by integrating active thermal control to preserve the physical properties of the samples and dissipation monitoring to characterize their viscoelastic behavior. A 10 MHz quartz crystal with a sensor module and a control and acquisition unit were integrated. The full system was built at a total cost below USD 500. Performance validation showed a temperature stability of ± 0.13 °C, a frequency stability of ± 2 Hz in air, and a limit of detection (LOD) of 0.46% polyethylene glycol (PEG), thereby enabling stable, reproducible measurements and the sensitive detection of small mass and interfacial changes in low-concentration samples. These results demonstrate that key QCM-D sensing capabilities can be achieved at a fraction of the cost, providing an accessible and reliable platform for potential biomedical research.

Keywords: piezoelectric sensor; real-time monitoring; temperature control; viscoelastic properties; biosensing



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1. Introduction

Sensors are regarded as essential tools in modern science and technology, enabling the detection and quantification of physical, chemical, and biological phenomena across a broad range of applications [1]. Among these, piezoelectric sensors are distinguished by their reliance on the piezoelectric effect, through which certain materials are induced to generate an electrical charge in response to mechanical stress or deformation [2]. This effect has been utilized to detect changes in pressure, force, and mass, with the resulting electrical signals being readily measurable and interpretable [3]. In laboratory environments dedicated to biomolecular analysis, diagnostic testing, and disease research, piezoelectric sensors have

been employed to provide real-time, non-destructive, and highly sensitive measurements that contribute to experimental insights and support clinical decision making [4].

The use of a Quartz Crystal Microbalance (QCM) has been widely adopted as a piezoelectric technique for the investigation of surface interactions at the nanoscale [5,6]. In this method, changes in the resonant frequency (f_r) of a quartz crystal sensor are monitored as mass is deposited on or removed from its surface [7]. An advanced variant known as a Quartz Crystal Microbalance with Dissipation monitoring (QCM-D) was designed to simultaneously measure both the frequency shift and the dissipation factor (D), the latter of which represents energy loss due to oscillation damping. This dual-mode sensing capability has enabled the characterization of mass, viscoelastic properties, and the dynamic behavior of interacting materials [8].

QCM-D systems have been increasingly employed in biomedical applications such as biosensing [9,10], drug delivery monitoring [11], and viscosity monitoring of biological fluids [12]. Nevertheless, the adoption of these systems has often been hindered by high acquisition costs, particularly in resource-limited contexts [13]. While commercial platforms from manufacturers such as AWSensors, Biolin Scientific [14], and Gamry Instruments have been designed to offer robust and high-performance solutions [15], their elevated costs have restricted their availability in many research environments. Alternatively, various experimental QCM setups have been developed within academic settings [16], often demonstrating promising performance but lacking the robustness, ease of use, or system integration necessary for broader implementation [17]. Similarly, other piezoelectric sensors, such as Surface Acoustic Wave (SAW) devices, have been investigated through low-cost experimental platforms [18], further highlighting the versatility of acoustic wave-based sensing technologies, although generally not reaching the same level of performance demonstrated by QCM-D systems [19].

Beyond cost considerations, despite the availability of several low-cost QCM designs reported in the literature, most existing open-source platforms present significant limitations that hinder their widespread adoption in biomedical research. These limitations include the absence of active thermal management, which can lead to measurement drift and potential degradation of temperature-sensitive samples, as well as the lack of dissipation monitoring, a key requirement for characterizing the viscoelastic nature of biological interfaces. To overcome these challenges, this work presents an improved QCM-D system based on a previous prototype developed by the authors [20]. Significant changes were implemented to enhance thermal stability and overall measurement performance. The system was designed to be more robust and adaptable to a wider range of laboratory applications. In addition to f_r , it enables D measurements, broadening its applicability to viscoelastic characterization.

The objective of this study is to develop and validate a low-cost, open-source QCM-D system specifically optimized for potential biomedical applications, addressing key limitations of existing affordable platforms.

The main contributions of this work are outlined as follows:

- Cost-effectiveness: Development of a complete QCM-D system with a significantly lower cost than commercial alternatives;
- Active temperature control: Integration of an active thermal management system to preserve the physical properties of temperature-sensitive biological samples;
- Dissipation monitoring: Implementation of a data acquisition routine capable of characterizing the viscoelastic properties of soft biological matter;
- Portability and modularity: A compact, open-source design, allowing for rapid customization and future upgrades;

- Biomedical applicability: A platform suitable for practical analysis of biological fluids, supporting potential applications in biomolecular interaction studies, biosensing, and fluid characterization.

2. Design

The QCM-D system (Figure 1) consisted of a quartz crystal (Figure 1A) placed in a sensor module (Figure 1B), which was connected to a control and acquisition unit via an SMA connector (Amphenol, Wallingford, CT, USA) and gold-plated pogo pins (Preci-Dip, Delémont, Switzerland).

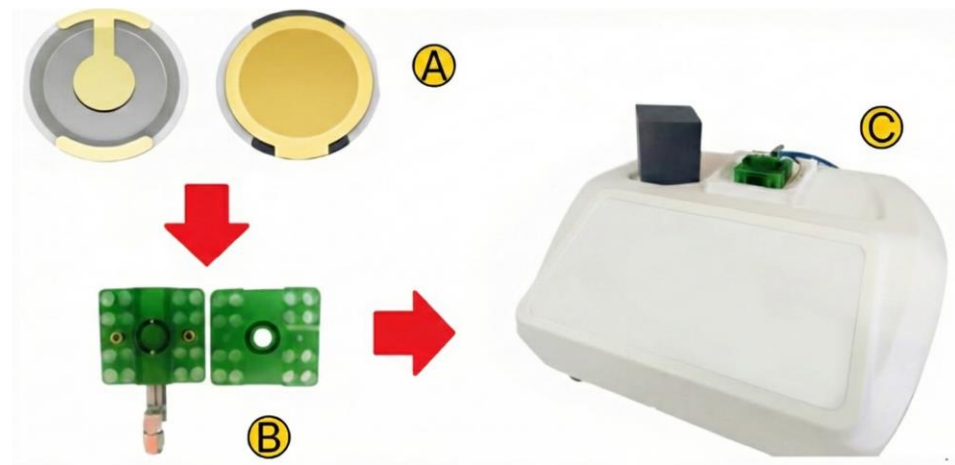


Figure 1. QCM-D system. The quartz crystal (A) is positioned within the sensor module (B), which is placed on the Peltier element located in the housing containing the control and acquisition unit (C). Samples are deposited into the sensor module, after which a protective cover (gray box in (C)) is placed over it. Temperature control is then initiated prior to acquiring the corresponding measurements.

The housing (Figure 1C) containing the control and acquisition unit was dimensioned to balance portability with thermal management requirements. The internal volume was defined to provide sufficient air volume for heat dissipation from the power electronics, minimizing thermal gradients that could interfere with the high-precision sensor environment.

An AT-cut piezoelectric quartz crystal disc with a fundamental frequency of 10 MHz coated with gold electrodes (Novaetech SRL, Pompei, Italy) was used; it had a thickness of 160 μm and a nominal sensitivity of $4.42 \times 10^{-9} \text{ g} \cdot \text{Hz}^{-1} \cdot \text{cm}^{-2}$, with front and back electrode diameters of 11.5 mm and 6.0 mm, respectively.

The sensor module was designed using Fusion 360 (Autodesk Inc., San Francisco, CA, USA) and fabricated via masked stereolithography 3D printing (Crealty, Shenzhen, China) with photosensitive resin (Monoprice, Rancho Cucamonga, CA, USA). The module dimensions were 44 mm $\times$ 40 mm $\times$ 15 mm (W $\times$ L $\times$ H), with a weight of 21.5 g.

The control and acquisition unit integrated a temperature control system based on a TEC1-12706 Peltier cell (MikroElektronika, Belgrade, Serbia) and a frequency measurement instrument, a NanoVNA-H vector network analyzer (from the open-source NanoVNA series, Shenzhen, China). A protective cover (gray box, Figure 1C) was included to minimize external perturbations and to improve thermal control.

The system described in this study was based on the open-source QCM-D system previously reported in [20]. While no improvements to the intrinsic sensitivity (S) or limit of detection (LOD) are claimed, the current configuration incorporates significant practical enhancements in the hardware design and experimental workflow. These modifications were aimed at increasing robustness and ease of use for the specific biomedical applications

addressed in this work. The overall workflow of the proposed system is illustrated in Figure 2.

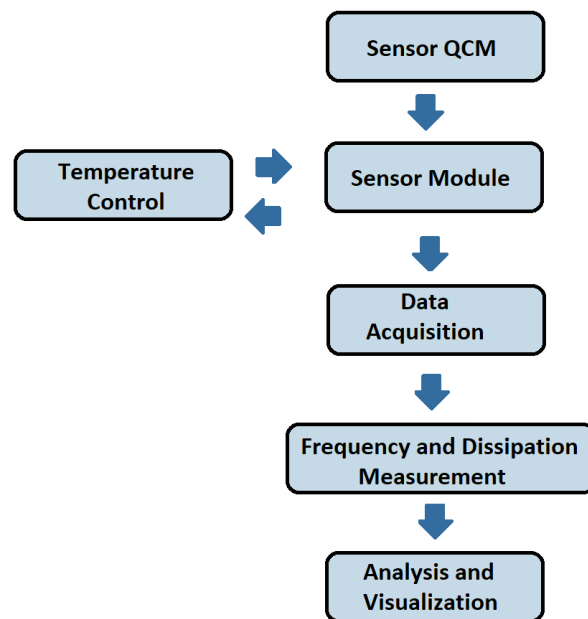


Figure 2. Schematic representation of the overall workflow of the QCM-D system.

2.1. Sensor Module

The design prioritized low maintenance, allowing for quick and easy positioning of the crystal. The top (Figure 3, M1) was secured to the base (Figure 3, M2) using screws that fasten into pre-installed inserts (E-Z Lok, Gardena, CA, USA) (Figure 3, M3), ensuring a firm and durable assembly. A silicone O-ring (Seals R Us, Orlando, FL, USA) (Figure 3, M4) in contact with both faces of the crystal maintained stable pressure and prevented fluid leakage. The sensor module included a custom-designed circuit board (PCB) (Figure 3, M5) developed using KiCad open-source software (version 7.0, KiCad Developers Team), specifically for crystal measurements with the NanoVNA-H. Electrical connection was made using gold-plated pogo pins (Figure 3, M6) and a low-noise SMA connector (Figure 3, M7) to ensure reliable signal transmission. Additionally, a ventilation system was incorporated to improve temperature distribution.

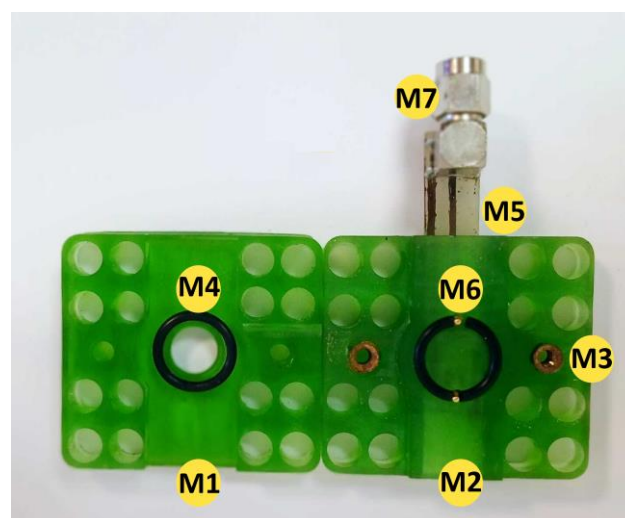


Figure 3. 3D-printed sensor module (M). (M1) Top. (M2) Base. (M3) Inserts. (M4) O-ring. (M5) PCB. (M6) Pogo pins. (M7) SMA connector.

2.2. Control and Acquisition Unit

The Peltier cell (Figure 4, CA1), powered at 12 V and 6 A, was selected as the thermoelectric actuator. An aluminum heat sink, together with thermal grease and a fan (Intel, Santa Clara, CA, USA) (Figure 4, CA2), facilitated the temperature difference between the two Peltier faces. Thermal control had a nominal working range of 18–30 °C and supported bidirectional heating and cooling.

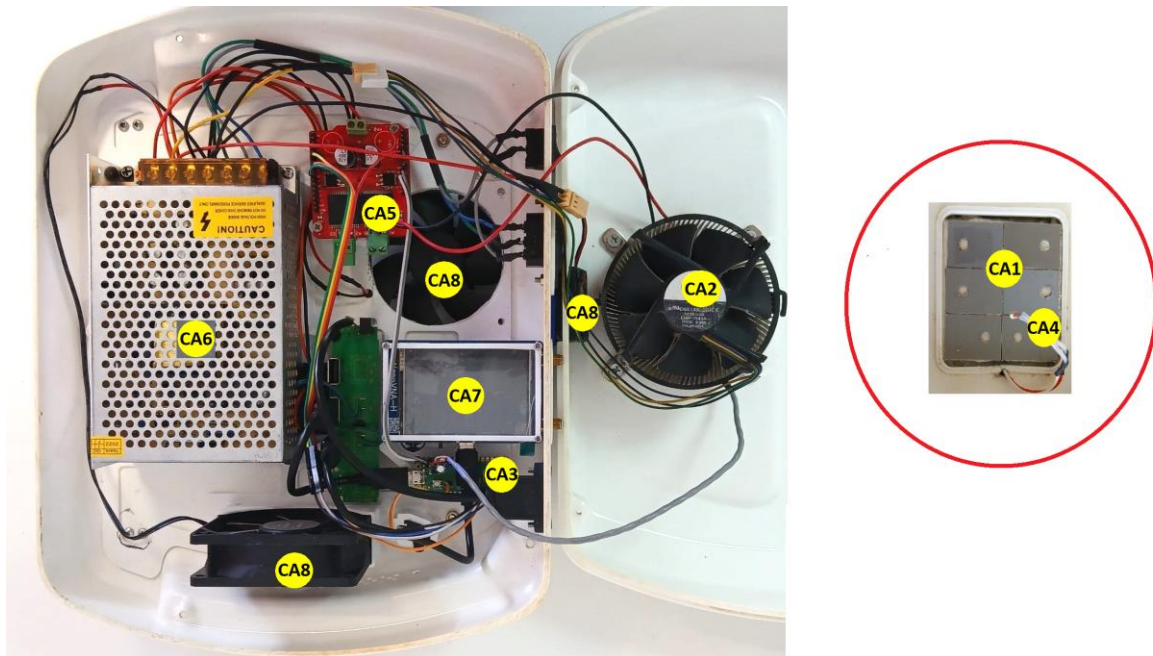


Figure 4. Temperature control and frequency acquisition unit (CA). (CA1) TEC1-12706 Peltier cell. (CA2) CPU fan with aluminum heat sink (12 V, 0.6 A). (CA3) Raspberry Pi Pico microcontroller. (CA4) NTC 3950 thermistor. (CA5) VN12SP30 H-bridge driver. (CA6) Switching power supply. (CA7) NanoVNA-H. (CA8) Fans.

A Raspberry Pi Pico microcontroller (Raspberry Pi Foundation, Cambridge, UK) (Figure 4, CA3) was selected to implement the proportional–integral–derivative (PID) control algorithm. Temperature was monitored using an NTC 3950 thermistor (Eaton, Beachwood, OH, USA) (Figure 4, CA4) embedded in the lateral wall of the sensor module, ensuring close thermal contact with both the Peltier cell and the QCM crystal. The thermistor was integrated into a resistive voltage divider, and the resulting analog signal was acquired through one of the analog-to-digital converter (ADC) channels of the Raspberry Pi Pico.

The firmware used to control the temperature was developed in C specifically to be executed on a Raspberry Pi Pico. The Peltier cell current was regulated via a Pulse-Width Modulation (PWM) signal generated by the microcontroller. A VN12SP30 dual-channel H-bridge driver (Reland Sun, Shenzhen, China) (Figure 4, CA5) rated at 30 A was utilized to drive the thermoelectric actuator. A 12 V/10 A switching power supply (MeanWell, New Taipei City, Taiwan) (Figure 4, CA6) provided power to the driver, cooling fan, Peltier cell, and Raspberry Pi Pico. All measurements were performed after a temperature stabilization period under PID control. Due to the compact geometry of the sensor module and the proximity of the thermistor to the crystal, directional thermal effects were minimized.

The frequency measurement instrument integrated into the QCM housing was a NanoVNA-H (Figure 4, CA7), a compact vector network analyzer capable of measuring S parameters (S11, S21) with a frequency range of 10 kHz to 1.5 GHz. It provided up to 70 dB of dynamic range at low frequencies (50 kHz–300 MHz), with 101 scanning points per

sweep, ensuring suitable resolution for frequency tracking. The device featured a USB-C interface for data transfer and charging and an internal 650 mAh lithium battery.

2.3. NanoVNA Software

The open-source software of the NanoVNA-type H device, originally developed in Python 3.9, was customized to address the specific requirements of biosensing applications. Non-essential tools were removed, the user interface was redesigned, and algorithms were implemented to enable real-time analysis of f_r , D , and temperature. From this curve, f_r was identified as the point where conductance reached its maximum value, while D was calculated based on the bandwidth of the resonance peak [21]. Repeated sweeps were performed over a defined period to monitor the behavior of the sensor over time. Temperature was recorded during each acquisition, allowing for the evaluation of thermal effects on the measurements. The software also included a calibration assistant to streamline the calibration process. Harmonics could be measured up to the ninth harmonic, though not simultaneously, providing additional information about the properties of the sample.

The program could be executed in Python (version 3.9) environments such as PyCharm (version 2023.1) or Visual Studio Code (version 1.107) or compiled into a standalone executable. The output directory for the Touchstone (.s1p) files generated during continuous sweeps was configurable within the SweepWorker module. During multi-segment sweeps, real-time data updates were displayed along with markers highlighting key values. Sweep data could be exported in .xlsx format, focused on the f_r , D , and temperature parameters. Figure 5 presents the customized software in operation, showing the configuration section and the real-time visualization of the recorded data.

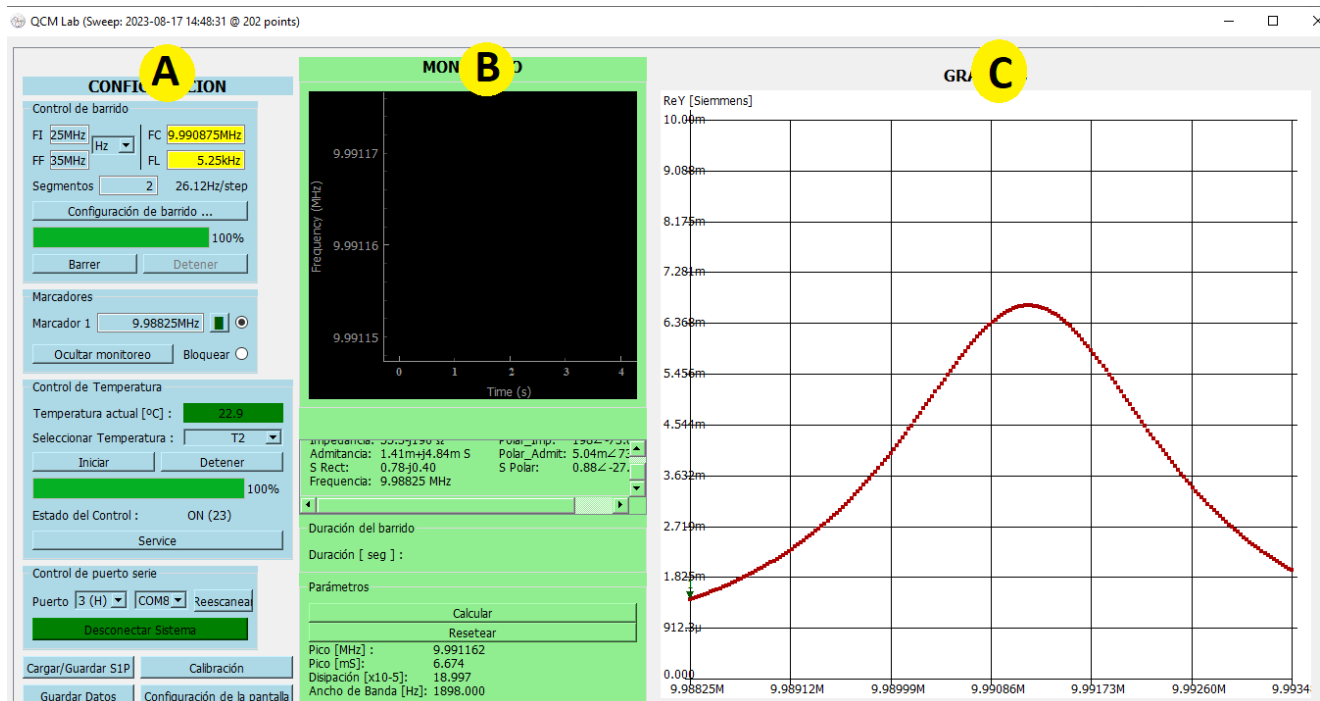


Figure 5. Overview of the customized software and its components. (A) The configuration panel displays real-time data from the active sweep and provides access to tools for setting sweep parameters, adjusting marker positions, connecting the NanoVNA-H device, modifying visualization options, calibrating the instrument, and exporting data. (B) The real-time output section presents a graph of f_r as a function of time, along with marker information. A reset option is included to remove all calculations and clear the temporal plot. (C) The graph shows conductance curves, which are used to evaluate the performance of the sensor, with a focus on f_r and D behavior.

3. Build Instructions

3.1. Materials and Tools

Basic tools such as a soldering iron, leaded solder wire, wire cutters, screwdrivers, tweezers, and multimeters are required for the building of the device. The necessary files for the fabrication, including 3D models and software, are listed in Table 1. Additionally, the complete list of commercial components and parts required is detailed in Table 2.

Table 1. Summary of design files.

Designator	File Name	File Type ¹	Localization of File
D1	Top_sensor_module	3D Printing	Supplementary Materials
D2	Base_sensor_module	3D Printing	Supplementary Materials
D3	Protective_cover	3D Printing	Supplementary Materials
D4	Back_legs_housing	3D Printing	Supplementary Materials
D5	Front_legs_housing	3D Printing	Supplementary Materials
D6	Internal_base_housing	3D Printing	Supplementary Materials
D7	VNA_port_cover	3D Printing	Supplementary Materials
D8	Back_fan_trim	3D Printing	Supplementary Materials
D9	Fan_bracket	3D Printing	Supplementary Materials
D10	Top_holder	3D Printing	Supplementary Materials
D11	Vent_cover	3D Printing	Supplementary Materials
D12	PCB_from_Kicad	PCB Design	Supplementary Materials
D13	Raspberry_Pi_firmware	Software	Supplementary Materials
D14	Device_Software	Software	Supplementary Materials

¹ Open-Source License: Creative Commons Attribution 4.0 International.

Table 2. Bill of materials.

Designator	Component	Number	Cost per Unit—USD	Total Cost—USD	Source of Material
M1	^ Top_sensor_module	1	37.58	37.58	AMAZON
M2	^ Base_sensor_module	1	37.58	37.58	AMAZON
M3	Insert	2	0.09	0.18	AMAZON
M4	O-ring	2	2.72	5.44	Ebay
M5	PCB board	1	7.29	7.29	AMAZON
M6	Pogo-pin	2	1.06	2.12	DIGIKEY
M7	SMA Connector	1	10.66	10.66	MOUSER
E1	Housing	1	50.00	50.00	PRODUCTOS TERMOFORMADOS S.R.L
E2	* Internal base housing	1	24.69	24.69	AMAZON
E3	* Top holder	1	24.69	24.69	AMAZON
E4	* Fan bracket	1	24.69	24.69	AMAZON
E5	* Protective_cover	1	24.69	24.69	AMAZON
E6	* VNA port cover	1	24.69	24.69	AMAZON
E7	* Back fan trim	1	24.69	24.69	AMAZON

Table 2. Cont.

Designator	Component	Number	Cost per Unit—USD	Total Cost—USD	Source of Material
E8	* Vent cover	2	24.69	24.69	AMAZON
E9	* Legs	4	24.69	24.69	AMAZON
CA1	TEC1-12706 Peltier cell	1	10.80	10.80	DIGIKEY
CA2	Fan and Heatsink 12 V 0.6 A	1	20.00	20.00	eBAY
CA3	Raspberry Pi Pico	1	18.65	18.65	AMAZON
CA4	NTC 3950 analog sensor	1	0.55	0.55	DIGIKEY
CA5	VNH2SP30 30 A 2-channel driver	1	42.00	42.00	AMAZON
CA6	Power supply 12 V/10 A	1	20.57	20.57	AMAZON
CA7	Nano Vector Network Analyzer	1	40.85	40.85	eBAY
CA8	12 V, 80 mm fan	2	5.05	10.10	DIGIKEY
CA9	Resistor 100 Kohm	1	0.03	0.03	DIGIKEY
CA10	Electrolytic Capacitor	1	0.03	0.03	AMAZON
PC1	Power Cable	1	3.0	3.0	DIGIKEY
PC2	Power connector	1	2.0	2.0	DIGIKEY
PC3	2-Channel Relay Module for Arduino 12 V	1	4.0	4.0	eBAY
PC4	Switch	1	1.0	1.0	DIGIKEY
PC5	Hub	1	6.88	6.88	AMAZON
PC6	15 cm USB-A to Micro USB Cable	2	3.03	6.06	eBAY
PC7	15 cm USB-A to USB-C Cable	2	2.00	4.00	eBAY
PC8	USB Type-A Male to Type-B Male Cable	1	1.00	2.00	eBAY
PC9	Crystal openQCM 10 MHz	10	28.40	284.00	open QCM

* 3D-printed parts with polylactic acid (PLA); a single 1.75 mm 1 kg PLA filament was used, with a cost of USD 24.69. ^ 3D-printed parts with resin.

3.2. Sensor Module Construction

1. Fabricate the custom PCB (M5).
2. Solder the SMA connector (M7) and pogo pins (M6) onto the PCB.
3. Print the pieces (M1 and M2) with a 3D printer.
4. Attach the soldered PCB (step 2) to the sensor module base (M2) using glue.
5. Insert O-rings (M4) into the base and the upper part of the sensor module.
6. Insert two pogo pins (M6) where the lower O-ring sits.
7. Place two inserts (M3) in M2.
8. Perform a leak test. Before actual use, assemble the module with two strips of indicator paper between the parts. Add distilled water, wait for one hour, and verify that the paper remains dry.

3.3. Housing and Accessories

1. Print the 3D accessories (Figure 6).
2. Mark and drill holes in the housing (E1) for the air outlet, the Peltier module, and the power and signal connectors.
3. Mount the 3D-printed accessories inside the E1 housing.
4. Attach the components to the pre-cut holes.
5. Secure all elements with screws or adhesive as needed.
6. Ensure proper airflow and cable routing inside the housing.



Figure 6. Housing and accessories (E). (E1) Housing. (E2) Internal base housing. (E3) Top holder. (E4) Fan bracket. (E5) Protective cover. (E6) VNA port cover. (E7) Back fan trim. (E8) Vent cover. (E9) Legs.

3.4. Power Supply and Communication

1. Connect the 12 V/10 A power supply (CA6) to the mains via the power cable (PC1) and connector (PC2).
2. Install a switch (PC4) in series with the live line to allow for manual control of power delivery.
3. Power the cooling fans (CA2, CA8) and the VNH2SP30 30 A dual-channel driver (CA5) directly from the power supply.
4. Utilize a commercial USB hub (PC5) to centralize communication between the NanoVNA-H (CA7), the Raspberry Pi Pico (CA3), and the host PC via a USB cable (PC8).
5. Integrate two relays (PC3) that act as switches, allowing the Raspberry Pi Pico and NanoVNA-H to power on only when the power supply is active.

3.5. Temperature Control

1. Load the firmware onto the Raspberry Pi Pico and connect the microcontroller to the USB port while holding down the BOOTSEL button. It mounts as a storage device named RPI-RP2. Download the firmware from Supplementary Materials, then drag and drop the .uf2 file onto the RPI-RP2 drive.
2. Connect an electrolytic capacitor (CA10) between pins 36 and 35 of the Raspberry Pi Pico to filter noise.

3. Build a resistive voltage divider with an NTC 3950 (CA4). Connect the NTC 3950 between 3.3 V (pin 36) and the middle node (pin 34). Connect a fixed 100 k Ω resistor from the middle node to GND (pin 33).
4. Connect the VNH2SP30 driver (CA5) to the Raspberry Pi Pico (CA3) by making the following connections:
 - a. VNH2SP30 GND to Raspberry Pi Pico GND (pin 39);
 - b. VNH2SP30 +5 V to Raspberry Pi Pico 5 V (pin 40);
 - c. VNH2SP30 EN1 to Raspberry Pi Pico (pin 17);
 - d. VNH2SP30 B1 to Raspberry Pi Pico (pin 14);
 - e. VNH2SP30 A1 to Raspberry Pi Pico (pin 15);
 - f. VNH2SP30 PWM to Raspberry Pi Pico (pin 16).
5. Connect the VNH2SP30 driver (CA5) to the power supply (CA6); then, connect the Peltier cell (CA1) to the output terminals (A1 and B1) of the driver.

4. Operating Instructions

4.1. Sensor Module Assembly and Usage

The sensor module is composed of two main parts: the top and the base. The base contains pogo pins, which establish the electrical connection with the QCM crystal. The assembly and usage procedure is performed as follows:

1. The screws are loosened using an Allen wrench.
2. The base is separated from the top, and the top is placed with the inner side facing upward.
3. The quartz crystal is positioned onto the O-ring inside the top.
4. The base is repositioned onto the top.
5. It is verified that the electrodes on the back of the crystal are in proper contact with the pogo pins on the base.
6. The screws are tightened with the Allen wrench to securely close the sensor module.

Once assembled, the liquid sample is deposited directly onto the crystal surface using a micropipette. For demonstration purposes, distilled water was used (Figure 7). For actual measurements, the type and conditioning of the liquid sample should be selected according to the specific application. Finally, the protective cover is placed over the sensor module to ensure stable conditions and optimal contact.



Figure 7. Batch-mode operation using distilled water. The sample is deposited directly onto the crystal using a micropipette, without circulation. Once the active area of the crystal is fully covered, the measured f_r and D are independent of the total deposited sample volume [22,23].

4.2. Crystal Cleaning

The cleaning protocol can be adjusted based on the specific characteristics of the sample (see Figure 8). The following steps describe the standard procedure:

1. Immersion: Submerge the crystal in a 2% Sodium Dodecyl Sulfate (SDS) solution for 5 min to remove protein residues and contaminants (Figure 8A).
2. Rinsing: Rinse the crystal thoroughly with distilled water to remove all traces of detergent (Figure 8B).
3. Drying: Dry the crystal surfaces using a gentle stream of high-purity nitrogen gas or filtered compressed air to prevent water spots (Figure 8C).

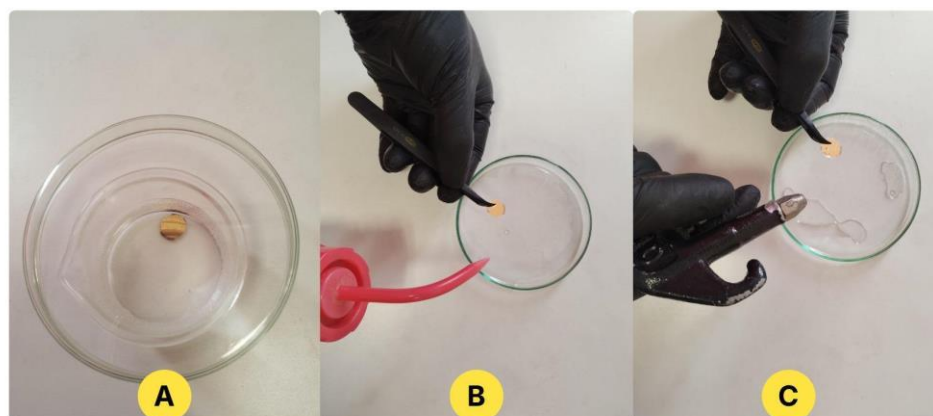


Figure 8. Crystal cleaning procedure. The crystal is immersed in 2% SDS (A), then thoroughly rinsed with distilled water (B) and dried with pure nitrogen gas (C).

4.3. Custom Software

Once the system setup is complete and the NanoVNA-H is connected to the PC, the device is turned on, and the software is launched. The program automatically detects the instrument and its communication port. A continuous sweep is initiated by clicking the “Connect” button, which performs a basic sweep. During these initial sweeps, the sweep parameters are adjusted to achieve the desired resolution and timing. In the sweep configuration panel, the “Find Resonance” option is selected to determine the working frequency and conduct a refined sweep. Subsequently, the “Continuous Sweep” function is activated, and the number of sweeps to be performed is specified according to the required acquisition time. The resulting Touchstone files are saved in the previously selected directory. After the acquisition is complete, the data is exported in .xlsx format by selecting “Save Data.”

5. Validation

Potential noise in the reported data was reflected in the standard deviations (SDs) of temperature, f_r , and D signals under steady-state conditions, which were quantified throughout Section 5 and used for the estimation of S and LOD.

5.1. Temperature Performance

The system was evaluated across a temperature range of 18 °C to 30 °C, with 4 °C increments. Three independent experiments were performed on three different days. At each step, the system was held at the target temperature for 30 min to determine the time required to reach and maintain thermal stability. Figure 9 shows the temperature–time profile for one representative day during the entire thermal cycling protocol.

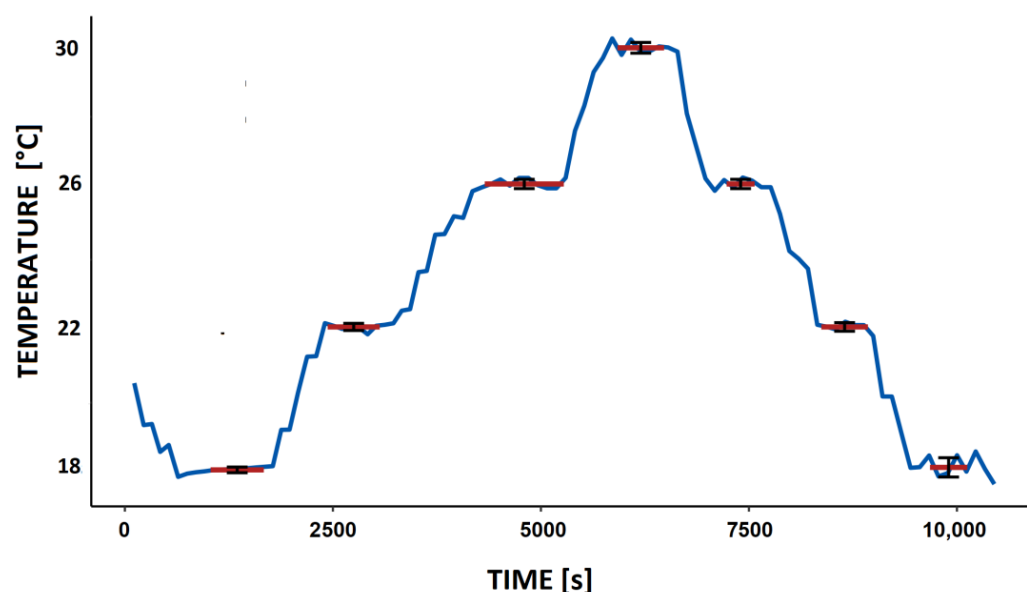


Figure 9. Temperature–time profile for one representative day. The system exhibits a rapid response to setpoint changes and maintains temperature with minimal fluctuations during steady-state intervals. Error bars represent the SD of the temperature measurements under steady-state conditions.

The mean and SD of the temperature at each setpoint were calculated from the three independent experiments, as shown in Table 3. The average SD across all stable intervals was 0.13 °C.

Table 3. Temperature stabilization times and steady-state values during the thermal cycling steps.

Temperature Step [°C]	Stability Time [s]	Stable Temp. (Mean $\pm$ SD) [°C]
18	639	18.12 $\pm$ 0.08
18 to 22	626	22.12 $\pm$ 0.10
22 to 26	950	26.12 $\pm$ 0.13
26 to 30	560	29.93 $\pm$ 0.15
30 to 26	336	26.12 $\pm$ 0.13
26 to 22	560	22.12 $\pm$ 0.12
22 to 18	448	18.19 $\pm$ 0.27

The temperature for extracting characterization features was determined by evaluating the stability of f_r and D at the third harmonic, which provides higher sensitivity to variations in mass and viscoelastic properties than the fundamental frequency [24]. Measurements were taken after one hour of thermal equilibration. The condition with the lowest variability in both parameters—quantified through SD—was considered the most stable. A temperature of 26 °C was selected, as it exhibited the lowest SD in both f_r and D .

At 26 °C, measurements were conducted across three independent experiments on different days, with two replicates per experiment. In air, the system showed frequency stability with an SD of 2 Hz and dissipation stability within 0.0001×10^{-6} over one hour. In measurements with distilled water, the SD was 19 Hz for f_r and 0.0021×10^{-6} for D . Analysis of the initial data indicated that a minimum stabilization time of approximately 15 min is sufficient to reach acceptable measurement of f_r and D .

Complete results for all temperature levels are provided in the Supplementary Materials.

5.2. Analytical Validation: Repeatability, Sensitivity, and Limit of Detection

To assess repeatability, S , and LOD, measurements of water and different concentrations of PEG (2%, 5%, and 10%) were taken on three consecutive days under controlled

temperature conditions (26 °C) (see Figure 10). PEG was specifically selected because it allows for the controlled simulation of viscoelastic loading effects, similar to those produced by protein layers, which is relevant to D monitoring.

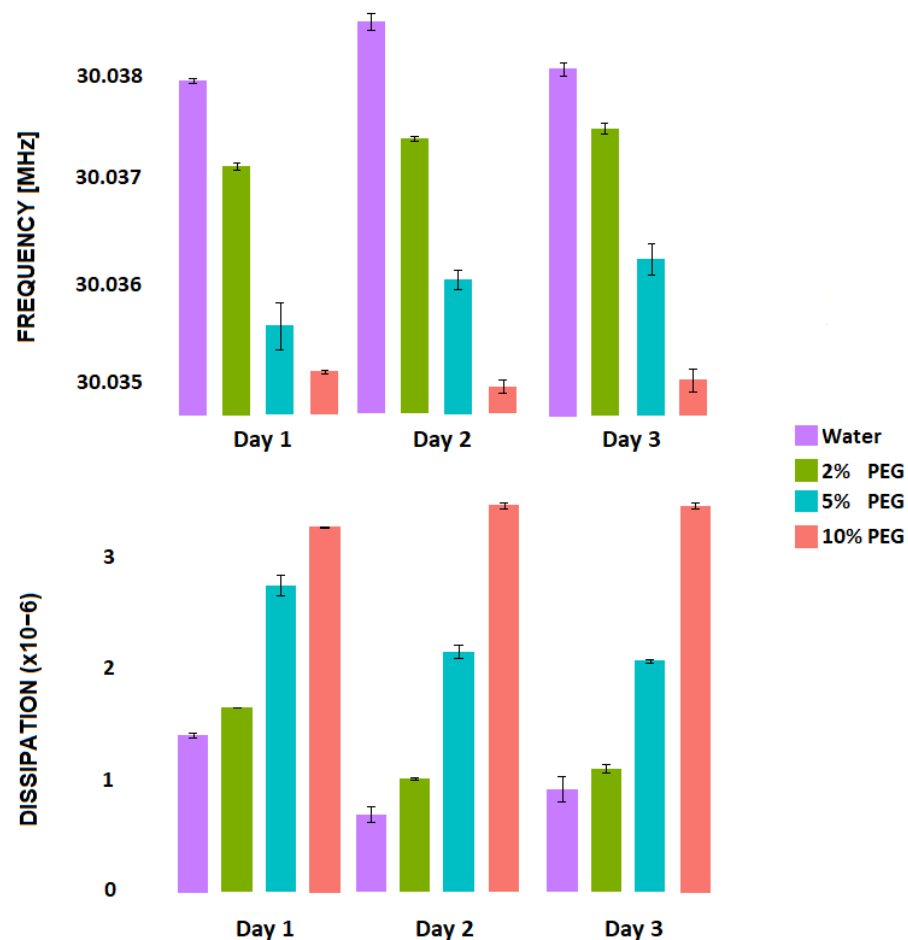


Figure 10. Frequency and dissipation shifts for distilled water and PEG solutions (2%, 5%, and 10%) measured over three consecutive days at 26 °C. Bars indicate mean $\pm$ SD (20 replicates per day).

As shown in Figure 10, measurements performed over three consecutive days exhibited consistent responses across all PEG concentrations. SDs were consistently below 365 Hz for frequency and 0.67×10^{-6} for dissipation, confirming good inter-day repeatability.

Sensitivity was calculated as the slope of the linear regression of the steady-state frequency and dissipation shifts relative to distilled water across increasing PEG concentrations (see Figure 11). This approach quantifies the sensor response to increasing viscoelastic loading. The calculated frequency sensitivity was -284.82 Hz/% PEG, while the dissipation sensitivity was 0.294×10^{-6} /% PEG.

With an S of -284.82 Hz/% PEG and a baseline SD of 40 Hz, the LOD was estimated using the formula expressed as $\text{LOD} = 3.3 \times \text{SD}/S$ [25], resulting in approximately 0.46% PEG. This indicated that the sensor could detect PEG concentrations starting from this threshold, demonstrating its dilute solution analysis capability. This estimation follows IUPAC guidelines, which calculate the LOD based on the signal-to-noise ratio of the baseline and the sensitivity of the sensor [26].

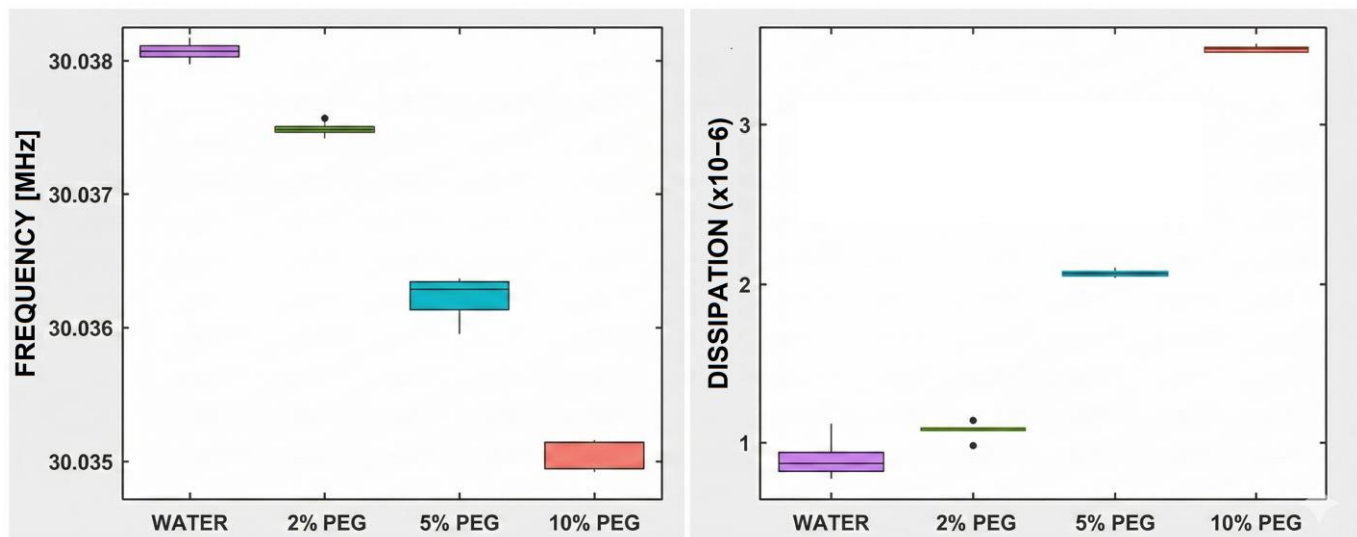


Figure 11. A clear monotonic trend was observed, demonstrating that the sensor reliably detects variations across the tested range. Sensitivity analysis was conducted using data from one representative experimental day selected based on consistent sensor performance and thermal stability across all tested PEG concentrations.

6. Conclusions

This study presented the design, construction, and experimental validation of a low-cost, open-source QCM-D system tailored for biomedical applications. The system was developed using off-the-shelf components, including a NanoVNA-H for frequency acquisition device and a Raspberry Pi Pico for temperature control, all integrated into a housing with active thermal regulation. Custom software was implemented for real-time monitoring of f_r , D , and temperature.

The system demonstrated reliable performance across key metrics: a temperature stability of ± 0.13 °C, a frequency stability of ± 2 Hz in air, and a dissipation stability of $\pm 0.0001 \times 10^{-6}$ under steady-state conditions. Repeatability tests with PEG solutions (2%, 5%, and 10%) over three consecutive days showed an SD below 365 Hz in batch mode, confirming robust inter-day consistency. Sensitivity analyses yielded -284.82 Hz/% PEG and 0.294×10^{-6} /% PEG. Based on baseline variability, the LOD was estimated at 0.46% PEG. The LOD reported in this work corresponds to a specific experimental configuration and should therefore be interpreted as an application-dependent performance metric rather than an intrinsic detection limit of the system.

Compared to commercial systems, the developed prototype was distinguished by its accessibility. While instruments such as the QSense Omni (Biolin Scientific, Gothenburg, Sweden) [14] and X4 Advanced Multichannel QCM-D system (AWSensors, Valencia, Spain) [27] provide superior measurement performance and advanced automation at significantly higher cost, the presented system offered sufficient measurement quality for the targeted experiments at a total cost below USD 500.

Specifically, the proposed platform prioritizes low cost, modularity, portability, active temperature control, and dissipation monitoring within an open-source framework, making it particularly suitable for early-stage research, methodological development, and laboratories with limited access to high-end instrumentation. Accordingly, the system should be regarded as a complementary tool rather than a replacement for commercial QCM-D platforms, providing sufficient measurement quality and stability for targeted validation experiments and potential biomedical research applications.

Recent efforts to democratize QCM technology have led to the development of portable systems, particularly for educational purposes. For instance, a low-cost QCM system was

proposed for visualizing reaction kinetics in secondary chemistry education [28]. While such systems are effective for qualitative demonstrations and basic kinetic studies in controlled environments, the proposed system enhances these capabilities by integrating dissipation monitoring and active thermal management. These features are essential for the quantitative analysis required in complex biomedical applications.

Several limitations of the current prototype in comparison with commercial QCM-D systems should be acknowledged. First, the use of a single harmonic entailed a loss of spectral information, which is often used to characterize complex viscoelastic films. Second, while the temperature regulation was effective, its precision does not yet match that of high-end commercial modules. An alternative solution, i.e., liquid cooling, was considered but not implemented due to increased system complexity and maintenance requirements. Finally, the current sensor module, optimized for batch operation, lacks functionality in flow mode and would benefit from the use of more durable, chemically resistant materials for long-term applications.

Future developments will be directed toward refining thermal control, including the exploration of advanced thermal modeling approaches such as fractional-order descriptions, which have been shown to better capture thermal dynamics in systems exhibiting memory effects and complex heat diffusion behavior [29]. Additionally, subsequent research will focus on enabling the simultaneous measurement of harmonics, enhancing time resolution, and integrating fluidic automation. Thus, the system is positioned as a viable tool for early-stage research and the democratization of QCM-D technology in biomedical contexts.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/hardware4010004/s1>. 3D Models and Hardware: this folder contains the STL files for system fabrication and the PCB design file from KiCad; Figures and Results: this folder contains the manuscript figures in PNG format and the complete validation results; Software and Firmware: this folder contains a RAR file named Software, which includes the customized device software developed in Python and the RAR file named Raspberry Pi firmware for temperature control.

Name	Type	Description
3D Models and Hardware	Zip	STL files for system fabrication and PCB design file
Figures and Results	Zip	Article figures and complete validation results
Software and Firmware	Zip	Device software (developed in Python) and Raspberry Pi firmware for temperature control

Author Contributions: Conceptualization, G.G.M., A.P., J.I.C., and M.A.Z.; methodology, G.G.M., M.J.M., and M.A.Z.; software, G.G.M. and M.J.M.; validation, G.G.M. and M.A.Z.; formal analysis, G.G.M.; investigation, G.G.M. and M.A.Z.; resources, J.M.R., J.I.C., A.P., and M.A.Z.; data curation, G.G.M.; writing—original draft preparation, G.G.M. and M.A.Z.; writing—review and editing, G.G.M., A.P., J.I.C., M.J.M., and M.A.Z.; visualization, G.G.M., M.J.M., and M.A.Z.; supervision, M.A.Z.; project administration, J.M.R. and M.A.Z.; funding acquisition, J.M.R. and M.A.Z. All authors have read and agreed to the published version of the manuscript.

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Abbreviations

The following abbreviations are used in this manuscript:

ADC	Analog-to-Digital Converter
CA	Control and Acquisition Unit
D	Dissipation
f_r	Resonance Frequency
LOD	Limit of Detection
M	Sensor Module
NTC	Negative Temperature Coefficient
PCB	Printed Circuit Board
PEG	Polyethylene Glycol
PID	Proportional–Integral–Derivative
PLA	Polylactic Acid
QCM	Quartz Crystal Microbalance
S	Sensitivity
SAW	Surface Acoustic Wave
SD	Standard Deviation
SDS	Sodium Dodecyl Sulfate
SMA	SubMiniature version A
VNA	Vector Network Analyzer

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