Team Results Document

BarceL-DOPA



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SensUs

1. Abstract: Summary for the SensUs website

Parkinson's disease is commonly treated with L-DOPA, whose short half-life produces fluctuations in drug concentration that contribute to motor and non-motor symptom variability. Current treatment adjustment relies mainly on intermittent clinical assessment and patient-reported symptoms, as no technology is available for continuous, non-invasive monitoring of L-DOPA levels.

BarceL-DOPA proposes a wearable, reagent-free biosensor based on dielectric impedance spectroscopy for continuous estimation of L-DOPA concentration in interstitial fluid. Unlike conventional affinity-based biosensors, the proposed sensing strategy exploits the intrinsic dielectric properties of L-DOPA, eliminating the need for immobilised receptors, biochemical reagents or irreversible binding reactions. The system combines upstream molecular-weight filtration, low-volume microfluidics, frequency-resolved impedance measurements and multivariable calibration to obtain reproducible concentration-dependent electrical responses.

Benchtop experiments demonstrated distinguishable impedance spectra between PBS and L-DOPA solutions and concentration-dependent electrical behaviour across clinically relevant concentrations, supporting the feasibility of the proposed sensing principle. Stakeholder interviews with neurologists, researchers, a caregiver and a patient confirmed the clinical need for continuous L-DOPA monitoring and highlighted its potential to support treatment optimisation and future closed-loop therapeutic systems. Together, these results support BarceL-DOPA as a promising foundation for future wearable monitoring of Parkinson's disease therapy.

2. AP award: Biosensor developed for the Eindhoven Testing Event

2.1. Molecular recognition

BarceL-DOPA uses a label-free and reagentless sensing strategy based on the dielectric response of L-DOPA. At physiological pH, L-DOPA behaves as a zwitterion with an electric dipole moment, producing concentration-dependent changes in impedance magnitude and phase when exposed to an alternating electric field. Since no molecular receptor is used, the system is not intrinsically selective: the MWCO membrane removes macromolecules but not low-molecular-weight interferents. L-DOPA estimation therefore relies on multivariable impedance analysis, calibration and interference testing. Preliminary experiments showed concentration-dependent differences between PBS and L-DOPA solutions, although selectivity against relevant ISF compounds still requires validation.

2.2. Physical transduction

The physical transduction system measures the frequency-dependent electrical response of the sample using an interdigital electrode and a custom impedance circuit. An initial sweep from 100 Hz to 1 MHz was performed with a 10 mV excitation using the Digilent Analog Discovery 2, an MCP6004-based transimpedance amplifier and a passive high-pass filter to remove the DC component. Custom Python software processed the signals to obtain impedance magnitude, phase, and Bode and Nyquist plots. The region around 75 kHz showed the best differentiation between PBS and L-DOPA under the tested conditions and was selected for subsequent measurements. A brief negative-potential pulse was also applied to potentially reduce L-DOPA adsorption and electrode fouling. The PBS response was used as the baseline, and the resulting electrical features will be incorporated into a calibration model for estimating L-DOPA concentration.

2.3. Cartridge technology

The biosensor features a straightforward design, comprising a disposable screen-printed electrode (SPE), specifically the DropSens C223AT. This electrode integrates a gold working electrode, a gold counter electrode, and a silver reference electrode on a ceramic substrate. A microfluidic channel with an area of 64.8 mm^2 and a height of 0.14 mm, fabricated from polydimethylsiloxane (PDMS), is bonded to the electrode using ARcare® 90106NB adhesive to direct the fluid sample precisely over the electrode surface. The channel volume is approximately 9 µL. It incorporates a single inlet and outlet, both connected via Male Mini Luer tube tuck connectors (Fluidic 1579, microfluidic ChipShop). Flexible tubing, with an internal diameter of 0.8 mm and an external diameter of 1.58 mm,

links the biosensor to the fluid handling system. The inlet is connected to a peristaltic pump responsible for sample injection, while the outlet channels the fluid to a waste reservoir, enabling controlled and continuous sample flow through the microfluidic pathway (Figure 1). Experimental testing suggests that continuous biosensing is achievable due to the displacement flow phenomenon, where the introduction of an interstitial fluid (ISF) sample at the inlet effectively pushes the previous sample out through the outlet.

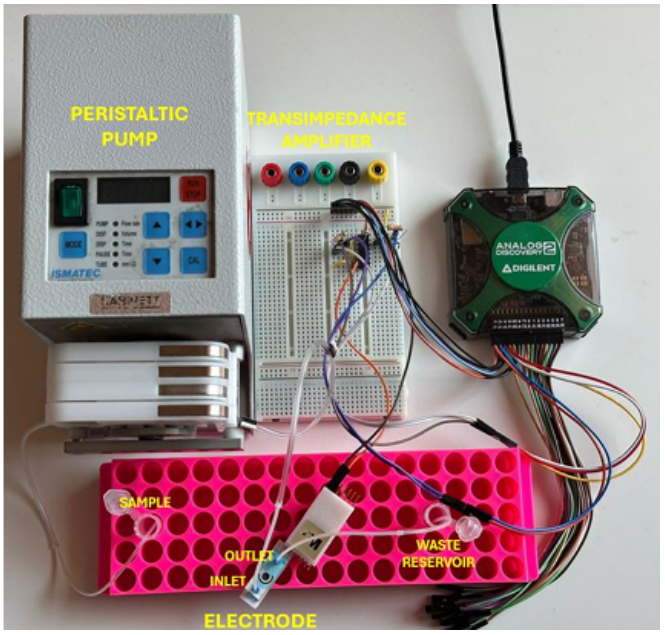


Figure 1. Final BarceL-DOPA microfluidic cartridge illustrating the complete sample pathway from ISF entry to waste collection through MWCO filtration, low-volume PDMS microfluidics and the IDE sensing chamber, supporting continuous sample renewal.

2.4. Reader instrument and user interaction

Custom Python software based on the WaveForms library demodulates the digitised signal to extract amplitude and phase information. A calibration routine generates a reference curve to convert impedance changes into levodopa concentration. The compact benchtop reader uses a microfluidic cartridge that is easily inserted without manual alignment. Measurements can be performed automatically, and results can be transmitted in real time to a user interface showing levodopa concentration and temporal trends. The modular design facilitates scalability and future assay expansion.

3. IN award: Biosensor innovation

3.1. Wearable sensor

The proposed wearable concept is a skin-conformal wearable patch that translates the experimentally validated benchtop sensing principle into label-free L-DOPA continuous monitoring in dermal interstitial fluid (ISF) (Heikenfeld et al., 2019; Kim et al., 2019). The multilayer architecture integrates hollow microneedles, a 10 kDa molecular-weight cut-off (MWCO) filter, a low-volume poly(dimethylsiloxane) (PDMS) microchannel, flexible gold interdigital electrodes (IDEs), and wireless impedance electronics. Passive fluid replacement driven by a downstream capillary absorbent reservoir is designed to enable continuous, bi-directional monitoring without chemical reagent consumption (LeWitt, 2015; Zimmermann et al., 2007). The proposed architecture remains conceptual and will require future engineering optimisation and experimental validation.

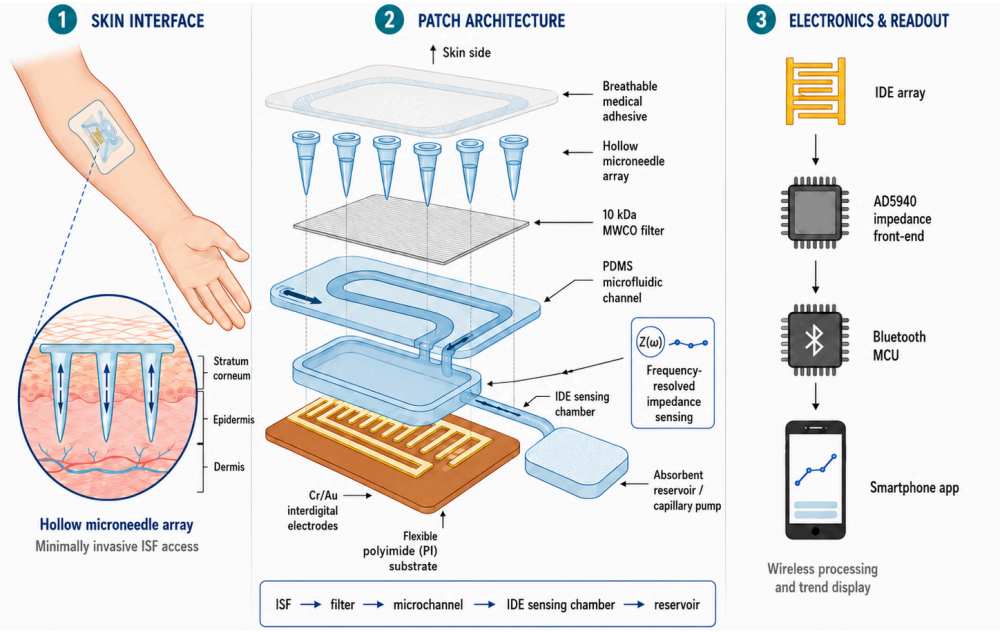


Figure 2. Conceptual architecture of the proposed wearable patch illustrating how minimally invasive ISF extraction, upstream filtration, continuous passive microfluidic renewal, impedance sensing and wireless electronics are integrated into a feasible wearable monitoring platform.

3.1.1. Technological novelty of wearable sensor

Unlike affinity-based biosensors limited by enzyme degradation, receptor saturation, and biofouling (Teymourian et al., 2020; Vaddiraju et al., 2010), BarceL-DOPA utilises reagentless dielectric impedance spectroscopy (Yang & Bashir, 2008). At physiological pH (~7.4), L-DOPA behaves as a zwitterion with a dipole moment. Under an alternating electric field generated by the microfabricated IDEs, dipole orientation alters the localised complex impedance Z(ω) in a frequency-dependent manner (Yang & Bashir, 2008). Combining this physical transduction mechanism with an upstream 10 kDa MWCO filter

excludes high-molecular-weight proteins (e.g., albumin), reducing electrode fouling and supporting reversible continuous ISF sensing (Miller et al., 2016; Wisniewski & Reichert, 2000). Unlike previous approaches relying on biochemical recognition, BarceL-DOPA directly exploits the intrinsic dielectric properties of L-DOPA for concentration estimation. Together, these components define a coherent architecture for future continuous L-DOPA monitoring.

3.1.2. Technical feasibility of wearable sensor

The proposed wearable design relies on established microfabrication, microfluidic, and embedded electronic technologies. The primary transducer consists of chromium/gold (Cr/Au) interdigital electrodes (transitioned from benchtop Au/ceramic SPEs to custom flexible Cr/Au IDEs) photolithographically patterned onto a flexible polyimide substrate to provide high mechanical flexibility while maintaining electrical stability under physiological strain (Kim et al., 2019). A poly(dimethylsiloxane) microfluidic layer (McDonald & Whitesides, 2002) is plasma-bonded to the polyimide substrate to enclose a low-volume sensing chamber. Secure skin attachment and long-term wearability are intended through a breathable, medical-grade acrylic adhesive grid that prevents detachment and reduces sweat accumulation.

Continuous fluid access and sample renewal across the electrode array are driven entirely by passive fluidic mechanisms. Minimally invasive extraction of dermal interstitial fluid (ISF) is achieved through an array of hollow microneedles that penetrate the stratum corneum without stimulating dermal nociceptors (Miller et al., 2016; Ribet et al., 2018). A downstream capillary absorbent pad continuously wicks fluid out of the channel (Zimmermann et al., 2007). This is expected to maintain a stable flow rate ($1 - 5\,\mu L/min$) and rapid sample replacement (response time $\tau < 5\,min$), allowing measured spectra to track concentration changes in alignment with L-DOPA pharmacokinetics (LeWitt, 2015).

Signal acquisition and telemetry are managed by a miniaturised electronics module. A low-power analog front-end (AD5940) executes automated multi-frequency sweeps ($100\,Hz - 1\,MHz$) across the electrodes (Analog Devices, 2023), interfacing with a BLE microcontroller and a thermistor for real-time thermal drift compensation. The modular design couples a low-cost disposable fluidic patch with a reusable electronics pod. The remaining operational challenges, such as baseline drift, motion artifacts, and small-molecule interferents, are systematically addressed using multi-frequency calibration models and baseline differential referencing thereby supporting reliable long-term operation.

3.2. Reliability of sensor output

3.2.1. Technological novelty of reliability concept

The BarceL-DOPA reliability concept introduces a reagentless, multi-layered framework integrating physical sample conditioning, broadband impedance analysis, environmental compensation, and chemometric calibration to improve measurement fidelity towards LC-MS/MS performance. By replacing fragile bioreceptors with dynamic matrix compensation, the platform avoids limitations associated with enzyme degradation and surface passivation.

To maximise readout reliability, the architecture systematically addresses key operational variabilities:

1. **Physical & Fluidic Control:** A 10 kDa MWCO membrane excludes macromolecular biofouling, while an ultra-low-volume (<1 µL) microchannel with capillary extraction prevents sample carry-over.
2. **Spectroscopic Selectivity:** Broadband EIS (0.1 Hz–100 kHz, peak separation at ~75 kHz) paired with PLSR modeling (3–50 µM L-DOPA) extracts |Z| and θ relaxation profiles to improve L-DOPA discrimination from small interferents (dopamine, carbidopa, 3-OMD, ascorbic/uric acid).
3. **Signal & Environmental Correction:** Embedded algorithms are designed to compensate for thermal shifts (Q10 correction), baseline drift, motion artifacts via Signal Quality Index (SQI) filtering, and ISF-to-plasma diffusion delays.

This integrated architecture provides the basis for translating the benchtop sensing principle into a reliable wearable platform.

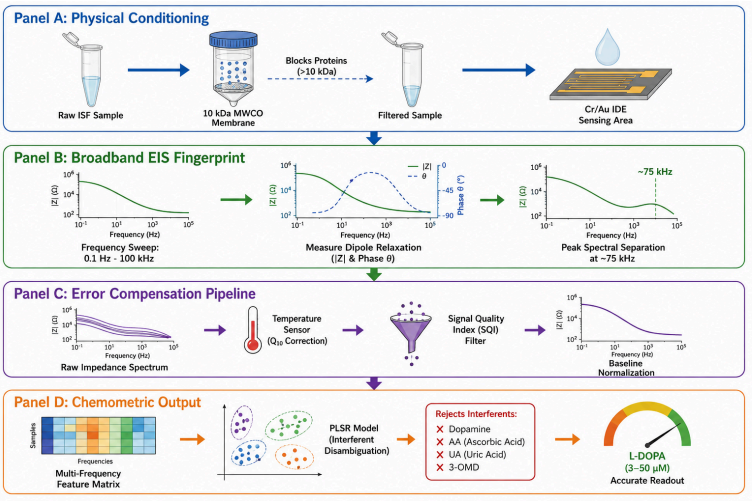


Figure 3. Integrated reliability framework showing how physical sample conditioning, broadband impedance analysis, environmental compensation and multivariable calibration jointly reduce variability and improve measurement robustness.

3.2.2. Technical feasibility of reliability concept

The technical feasibility of the BarceL-DOPA reliability concept was experimentally evaluated through benchtop electrochemical impedance spectroscopy (EIS) using PBS, simulated interstitial fluid (ISF), and L-DOPA solutions across clinically relevant concentrations ($3 - 60\ \mu M$). Electrical acquisition was conducted across $0,1\ Hz$ to $100\ kHz$ using a three-electrode setup to evaluate Nyquist and Bode spectral representations and identify optimal discriminatory features for concentration calibration (Figure 10 Appendix).

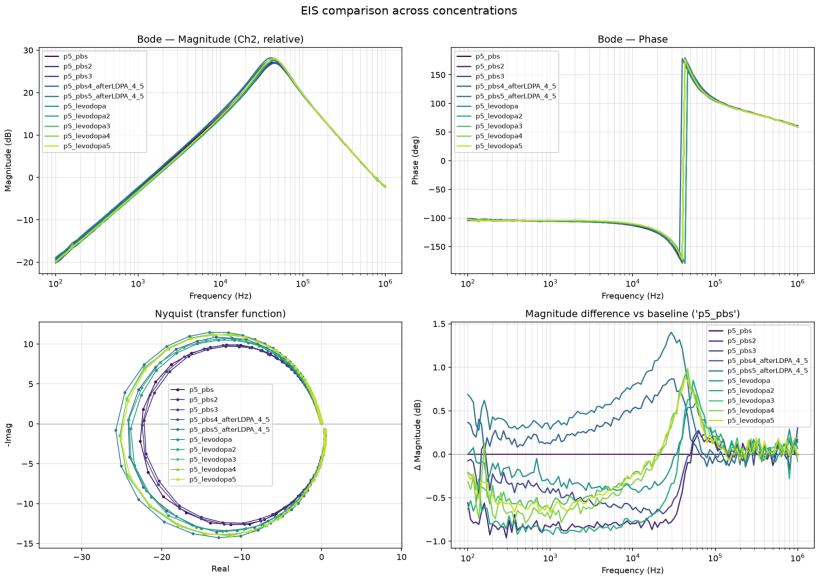


Figure 4. Experimental validation of the proposed sensing principle. Representative Bode magnitude, phase, Nyquist and differential impedance plots demonstrate reproducible concentration-dependent electrical responses and identify frequency regions suitable for reliable L-DOPA discrimination.

Experimental testing demonstrated concentration-dependent impedance spectra, identifying 75 kHz as the optimal operating frequency. The feasibility of the proposed concept was supported by MWCO filtration and low-volume microfluidics to reduce fouling and carry-over, targeted 75 kHz measurements with negative potential pulses to mitigate electrode passivation, and proof-of-concept experiments demonstrating the potential of dielectric spectroscopy for continuous L-DOPA monitoring. Further validation against clinically relevant interferents and LC-MS/MS remains necessary.

3.3. Original contributions

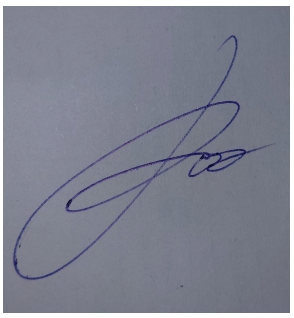
3.3.1 From the Team

The innovative concepts presented in Sections 3.1 and 3.2 were conceived, developed and experimentally evaluated by the team throughout the SensUs project. After critically evaluating conventional affinity-based biosensors, we proposed a reagent-free dielectric sensing strategy based on broadband impedance spectroscopy for continuous L-DOPA monitoring, leading to the design of the sensing principle, wearable architecture and reliability framework. We also carried out the complete experimental work, including sensor fabrication, impedance measurements, frequency analysis and proof-of-concept validation, using the results to iteratively optimize the sensing concept.

3.3.2. From the Supervisor

The BarceL-DOPA project reflects the team's ability to identify a relevant clinical challenge and translate it into an innovative engineering solution. By combining broadband dielectric impedance spectroscopy with microfluidic sample handling and multivariable data analysis, the students developed a coherent and well-reasoned concept for continuous L-DOPA monitoring. Throughout the project, they demonstrated critical thinking, scientific curiosity and the capacity to iteratively improve their design based on experimental evidence. My contribution focused on providing scientific guidance, technical feedback and support during the evaluation of the proposed concepts, while the project's conception, implementation and experimental work remained the responsibility of the team.

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Giovanni Vescio (Team Supervisor)	Joana Ros Alonso (Team Captain)	Ester López Oliva (Team Captain)

3.4. Bonus criteria Innovation

An unexpected finding emerged during benchtop characterization: continuous frequency sweeps across the full 0.1 Hz–100 kHz range progressively degraded the electrode response over repeated cycles, indicating adsorption-driven passivation of the Cr/Au sensing surface by L-DOPA and its oxidation products — a fouling mechanism rarely discussed for reagent-free dielectric platforms outside enzymatic and affinity-based systems (Wisniewski & Reichert, 2000).

Rather than treating this as a limitation, the team turned it into a design opportunity: restricting acquisition to targeted tracking at the ~75 kHz discriminating frequency and interleaving brief negative-potential pulses between measurements substantially reduced electrode fouling without any additional reagents, coatings, or replaceable components. This suggests that measurement-protocol design, rather than surface chemistry alone, can be an effective, low-cost lever for extending the operational lifetime of reagent-free dielectric biosensors — a strategy with relevance beyond L-DOPA monitoring to other continuous wearable platforms.

A second original contribution was the adoption of a frequency-domain sensing philosophy. Instead of selecting a single operating frequency, the team proposed extracting information from the complete impedance spectrum—including magnitude, phase and Nyquist features—to generate a dielectric fingerprint of the sample. This strategy increases the amount of analytical information available and provides greater flexibility for future multivariable calibration methods capable of compensating environmental variability and interferents.

Although further validation is required, this design process illustrates an innovation-driven development process in which unexpected technical challenges were identified and turned into design improvements, maximising the future potential of the biosensor.

4. TP award: Translation potential

4.1. Customer interviews

4.1.1. Identification of potential stakeholders

To build a holistic understanding of the clinical, operational, and daily care challenges of Parkinson's Disease, we identified a diverse spectrum of target stakeholders:

Clinical & Technical Panel: Dr. Antoni Callen (Neurologist with extensive experience in Levodopa titration), Gemma Colomé (Biotechnologist), Dr. Christian Stephan-Otto and Dr. Christian Núñez (Neuroimaging specialists). This multidisciplinary panel was interviewed jointly to compare expert viewpoints on physiological monitoring.

Specialized Clinical Practice: Dr. Berta Pascual, a neurologist specializing in Parkinson and movement disorders, was interviewed to evaluate longitudinal patient follow-up, dosing limitations, and clinical workflow requirements.

Front-Line Nursing Care: Maria Angeles López Martín, an auxiliary nurse with direct daily experience in Parkinson's care, was interviewed to capture non-motor symptoms, administration challenges, and practical bedside observations.

Family & Home Care Perspective: Núria Pascual Torrecillas, a family caregiver of a Parkinson's patient, provided non-clinical insights regarding daily medication routines, wearing-off observations, and home usability requirements.

Patient Perspective: Ramiro Pérez Blasco was interviewed individually to capture first-hand experience of ON/OFF motor fluctuations, treatment timing challenges, and the daily quality-of-life impact of Levodopa therapy.

Quantitative Stakeholder Survey (N = 141): To validate qualitative findings across broader populations, we conducted a structured survey targeting 6 key groups: Healthcare Professionals (n=10), Pharmaceutical Experts (n=11), MedTech Developers (n=7), Caregivers (n=11), Parkinson's Patients (n=2), and the broader Biomedical/Engineering Community (n=100) (see Annex A for complete survey methodology and statistical analysis).

4.1.2. Interview approach and execution

Qualitative interviews were prepared by reviewing each professional's clinical or technical background. Meetings followed a standardized protocol: an overview of the BarceL-Dopa team and SensUs competition goals, informed consent acquisition for recording and document inclusion, and structured questioning across five thematic blocks:

1. Clinical context and Levodopa pharmacokinetics.
2. Current therapeutic alternatives and open-loop limitations.
3. Feedback on our label-free interstitial fluid (ISF) biosensor concept.

4. Future clinical integration and continuous use cases.
5. Regulatory compliance, business model, and translation hurdles.

To complement qualitative insights, the quantitative survey was deployed online using 5-point Likert scales (1 = Strongly Disagree, 5 = Strongly Agree) alongside open-ended feedback fields, segmenting questions by stakeholder role.

4.1.3. Interview results and conclusions

Qualitative Clinical and Nursing findings

- **Clinical Context & Kinetic Fluctuations:** Dr. Callen and Dr. Berta Pascual emphasized that Levodopa remains the primary therapeutic baseline for PD. However, its short elimination half-life ($\sim 60 - 90\,min$) leads to systemic concentration peaks and troughs, causing severe motor fluctuations (dyskinesia vs. akinesia). Dr. Pascual noted that stress, sleep disruption, and dietary protein competition introduce unpredictable absorption lags.
- **Front-Line Nursing & Non-Motor Insights:** Maria Angeles López Martín highlighted critical, lesser-known daily realities from nursing practice:
    - Non-Motor Wearing-Off: Anxiety spikes, sudden diaphoresis (sweating), and severe fatigue frequently precede motor tremors, signaling sub-therapeutic levels long before motor logs record them.
    - Gastric Motility Delays: Gastroparesis causes medication to remain in the stomach for hours, leading to delayed onset ("delayed ON") and prompting unnecessary extra dosing.
    - Nighttime Akinesia & Pill Burden: Patients prescribed up to 21 pills per day face extreme cognitive burden, while nocturnal immobility severely degrades sleep quality and increases caregiver strain.
- **Caregiver Perspective:** Núria confirmed that medication duration progressively shortened over time for her grandfather, forcing frequent neurologist visits based solely on subjective symptom logs.
- **Limitations of Existing Alternatives**: Duodenal gel infusions (Duodopa) and subcutaneous pumps (foslevodopa) provide continuous administration but operate open-loop without real-time concentration feedback.
- **Feedback on Biosensor Concept:** Interstitial fluid (ISF) was unanimously recognized as a practical, minimally invasive matrix. Neurologists noted that while ISF-to-plasma diffusion delay and cross-reactivity from interferents must be calibrated, continuous dielectric tracking offers unprecedented objective visibility.

4.2. Design of validation study

4.2.1. Selection of the problem

The problem defined directly from our stakeholder panel and nursing consultation is the **complete absence of objective, real-time, non-invasive feedback on systemic Levodopa levels**. BarceL-DOPA solves this by providing a continuous, quantitative dielectric readout of L-DOPA dynamics in interstitial skin fluid.

4.2.2. Conceptual design and use case

This is precisely the gap our sensor aims to fill, offering a **non-invasive,** wearable biosensor capable of continuously measuring Levodopa concentration in interstitial skin fluid, using impedance and permittivity sensing via interdigital electrodes.

The device is intended for chronic, at-home monitoring of Parkinson's disease patients undergoing Levodopa therapy. In the future, this could make a real difference for families, who often struggle to judge whether medication is working or needs adjusting, and for clinicians, who could remotely gather objective data on a patient's Levodopa levels without requiring an in-person visit. This would also allow doctors to schedule follow-ups based on actual physiological need rather than relying solely on reported symptoms, and to anticipate disease progression rather than reacting to it. By providing more objective information on the dose a patient actually needs over time, the sensor could also support a more accurate assessment of the disease stage and its rate of progression. Looking further ahead, this monitoring capability could be integrated into a mobile app that reminds patients when to administer their dose, stores historical data, and tracks trends over time.

4.2.3. Validation study design

To evaluate analytical performance and clinical translation feasibility, a two-tiered prospective validation protocol has been engineered: **Tier 1 (Benchtop Analytical Validation)** and **Tier 2 (Prospective Pilot Clinical Validation).**

Tier 1: Benchtop Analytical & Bio-Matrix Validation Protocol

- **Matrix Preparation:** Experiments utilize simulated ISF (bovine serum diluted 1:3 in PBS, filtered through $10\,kDa$ MWCO membranes) spiked with calibrated L-DOPA concentrations ($3 - 50\,\mu M$).
- **Electrical Acquisition Parameters:** Three-electrode interdigitated setup, AC sinusoidal amplitude $10\,mV$, zero DC bias ($V_{DC} = E_{OCP}$), performing broadband logarithmic frequency sweeps from $0,1\,Hz\ to\ 100\,kHz$.

- **Analytical Sensitivity & Calibration:** Minimum N = 6 concentration levels measured in triplicate (n = 18). Calibration curves validate the relationship $\Delta Z = f(C_{L-DOPA})$at the optimal $\sim 75\,kHz$ frequency feature. Target performance metrics: linear regression coefficient $R^2 > 0,95$, Limit of Detection ($LoD = Blank + 3\sigma$), Limit of Quantification ($LoQ = Blank + 10\sigma$), and concentration estimation error $< 15\%$ on independent test samples.
- **Selectivity Matrix:** Interference testing evaluates percentage signal deviation (%Δ) when L-DOPA ($20\ \mu M$) is mixed with key physiological interferents at maximum clinical concentrations: L-tyrosine ($100\ \mu M$), L-phenylalanine ($100\ \mu M$), dopamine ($5\ \mu M$), ascorbic acid ($50\ \mu M$), uric acid ($200\ \mu M$), carbidopa ($10\ \mu M$), 3-OMD ($20\ \mu M$), and entacapone ($10\ \mu M$). Maximum acceptable interference threshold is set at $\leq 15\%$.
- **Stability & Reversibility:** Intra-assay and inter-chip precision are benchmarked for coefficient of variation ($CV\% < 10 - 15\%$). Reversibility is tested via dynamic fluidic cycling between blank ISF and $30\ \mu M$ L-DOPA solutions over 2 hours (24 discrete measurement cycles) to confirm absence of electrode fouling or memory effect hysteresis.

Tier 2: Prospective Pilot Clinical Validation Protocol

Following lab validation, a pilot clinical study will be conducted with a cohort of Parkinson's patients (n = 25) receiving oral Levodopa/Carbidopa therapy:

1. **Kinetic Correlation:** Sensor-derived ISF concentration curves will be continuously logged and compared against serial venous blood plasma samples quantified via reference High-Performance Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS).
2. **Clinical Symptom Alignment:** Temporal ISF L-DOPA curves will be correlated against clinician-assessed Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III motor scores and patient dyskinesia/off-time logs.
3. **Acceptability Criteria:** Clinical validation will be considered successful if a Pearson correlation coefficient $r \geq 0,85$ between ISF sensor trends and plasma LC-MS/MS profiles, with an ISF-to-plasma diffusion lag consistently quantified within 15-25 minutes.

4.3. Bonus criteria Translation Potential

Inter-team consultations

Instead of working in isolation, we initiated informal collaborative meetings with fellow engineering and biosensing teams in the competition—specifically **Biosense EPFL** and **G-Pulse**. These sessions allowed us to exchange technical knowledge, test ideas, and avoid costly design mistakes. Beyond accelerating technical progress, this initiative fostered a healthy, supportive competitive environment. By learning from each other's challenges and successes, we were able to iterate and refine our design much faster, saving considerable development time.

Stand Booths at University Fairs

With the booths we aimed to share our project and participation in the community with the general interested public. We organized it at an engineering university fair to try and be strategic about the audience, because in that location there was a higher probability of people interested in our technology so we were more likely to connect with them about what we were doing.

Another benefit we encountered was overcoming the challenge of presenting our goal product to the general audience. We learnt how to adapt our explanations and translate complex scientific concepts into simpler language, making it understandable and attention catching to the different levels of technological knowledge from our visitors. This exercise was highly valuable for our business plan as it helped us to start to understand how to merge marketing in technology.

Regulatory and Quality Strategy

To anticipate future clinical translation, the team conducted a preliminary regulatory landscaping exercise. Under the EU Medical Device Regulation (Regulation (EU) 2017/745), a wearable L-DOPA biosensor intended for continuous, non-invasive monitoring would likely fall under Class IIa, pending formal risk-based classification. ISO 13485:2016 (quality management systems) and ISO 14971:2019 (risk management) were identified as the core standards to integrate into a future quality management system, alongside ISO 10993-1:2018 for biocompatibility testing of the microneedle array and skin-contact materials. Mapping this pathway early is intended to reduce time-to-market risk for a potential BarceL-DOPA spin-off.

5. Team and support

5.1. Contributions of the team members

- **Joana Ros**: Co-captain: co-managed project planning, contributed to research and early lab experiments.
- **Ester López**: Co-captain: co-managed project planning, contributed to research and early lab experiments.
- **Cèlia Sans**: Contributed to electronics, data processing, and project and lab organisation.
- **Steven Castellanos**: Contributed to electronics design, data analysis, and experimental testing.
- **Hugo Berthet**: Contributed to microfluidics research and prototype assembly.
- **Intisar El Khabbati**: Contributed to biochemical research.
- **Sara El Khateb**: Contributed to literature research and report writing.
- **Adrián Gamito**: Contributed to electronics, signal testing, and data acquisition.
- **Helena Garcia**: Contributed to literature research and report writing.
- **Marc Guevara**: Contributed to literature research.
- **Alba Navarro**: Contributed to electronics design and experimental testing.
- **Eric Pajares**: Contributed to electronics design and experimental testing.
- **Laia Santos**: Contributed to research, early-stage laboratory experiments and general project development.
- **Carlos Solanas**: Contributed to electronics design, and data analysis.
- **Júlia Soler**: Contributed to electronics design, data analysis, and experimental testing.

5.2. People who have given support

- **Giovanni Vescio** (Supervisor): Provided general guidance and hosted experimental testing in his laboratory.
- **Jordi Colomer** (Supervisor): Researcher and professor who offered technical advice and supervision on electronics development.
- **Raul Sanchez** (Team Coach): Researcher and professor who provided guidance on molecular recognition principles.
- **Ana Arana and Bruna Català** (Student R&D Advisor): Provided technical guidance, leveraging their research and development experience to optimize lab testing.
- **Elvira López** (Marketing and Media): Managed social media platforms, created promotional posts, and designed competition content, drawing on her studies in Law and Pharmaceutical Marketing.
- **Laia Colomé** (Student Advisor & SensUs Alumna): Provided key technical advice based on her previous SensUs experience and research background.

5.3. Sponsors and partners

- **Polytechnic University of Catalonia (UPC)**: Funded the official SensUs registration fee, provided a research space and full access to Prof. Giovanni Vescio's electronics laboratory, procured hardware materials, and offered institutional promotion.
- **University of Barcelona (UB)**: Funded core operational expenses, provided full access to wet-lab infrastructure and advanced chemical characterization equipment, and supplied specialized reagents and raw materials.

6. Final remarks

Participating in SensUs allowed our team to experience the full development cycle of an innovative biosensing technology, from identifying an unmet clinical need to designing, experimentally validating and communicating a potential healthcare solution. Beyond the technical achievements, the project strengthened our ability to work in multidisciplinary teams, critically evaluate scientific literature, engage with clinical stakeholders, and translate engineering concepts into solutions with potential clinical and societal impact.

We would like to sincerely thank our supervisors and coaches, Giovanni Vescio, Jordi Colomer and Raul Sanchez, for their continuous guidance, technical support and encouragement throughout this project. We are equally grateful to the researchers and clinicians who generously shared their expertise during the stakeholder interviews, helping us better understand the clinical challenges of Parkinson's disease and the potential value of continuous L-DOPA monitoring. Finally, we thank the University of Barcelona, the Polytechnic University of Catalonia (UPC), and the SensUs organisation for providing the opportunity and environment that made this project possible.

Following the competition, we aim to further develop the proposed dielectric sensing strategy by expanding its experimental validation, evaluating clinically relevant interferents, and investigating the relationship between interstitial-fluid and plasma L-DOPA concentrations. Although additional validation will be required before clinical translation, our results suggest that the concepts developed throughout this project provide a promising foundation for future wearable technologies enabling more personalized Parkinson's disease management and, ultimately, improving patients' quality of life.

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8. Appendix

8.1 Customer Interviews Template

Clinical context and unmet need

- Can you describe what your day-to-day routine with Levodopa medication looks like? / How do you decide the dosing schedule of Levodopa for each patient?
- Do you notice clear differences between right after taking a dose and right before the next one?
- Have you noticed that the medication's effect changes over time, or is affected by things like meals, stress, or sleep?

Current alternatives and their limitations

- What limitations do you see in current dosing systems (oral, duodenal pump, subcutaneous foslevodopa)?
- How do you currently monitor a patient's response to treatment between visits?
- Have you had cases where a patient's condition worsened because fluctuations weren't detected in time?

Feedback on our biosensor concept

- Would you feel comfortable wearing/recommending a non-invasive device that continuously monitors Levodopa levels?
- Do you think knowing medication levels in real time would help manage the disease more precisely?
- What technical or clinical challenges do you think would be most important to address for such a sensor to be trustworthy?

Clinical vision and future use case

- How would you value the integration of a Levodopa sensor with infusion systems like foslevodopa, similar to a closed-loop artificial pancreas?
- Do you see more value in a hospital-based device or an outpatient/home-use wearable?
- Which patients would benefit most from continuous, non-invasive Levodopa monitoring?
- Would a mobile app that reminds patients of doses and stores data over time be useful?

Regulatory and translational considerations

- What regulatory or clinical validation requirements do you think should be prioritized?
- What evidence would be needed to demonstrate real clinical benefit and support adoption in the healthcare system?

Note: the questions on Current alternatives and their limitations, Clinical vision and future use case, and Regulatory and translational considerations were only asked to clinical experts.

8.2 Customer Interviews Main Takeaways

8.2.1 Joint interview with Dr. Antoni Callen (neurologist), Gemma Colomé (biotechnologist), Christian Stephan-Otto and Christian Núñez (neuroimaging)

Dr. Callen explained that Levodopa's short half-life causes pulsatility, driving the motor and non-motor fluctuations patients experience over time, and that current alternatives to oral administration still lack real-time, non-invasive feedback on actual levels. The panel responded positively to our biosensor concept, validating interstitial fluid as a proxy for plasma levels and flagging selectivity against interferents as the main technical challenge. He also highlighted closed-loop integration with subcutaneous delivery as the most compelling future application, and the group outlined a realistic regulatory and commercialisation pathway via a university spin-off.

8.2.2 Individual interview with Dr. Berta Pascual (neurologist)

Dr. Pascual reinforced that Levodopa's narrowing therapeutic window is a central challenge as the disease progresses, adding that factors like diet, stress and sleep also destabilize fixed dosing schedules. She noted that current monitoring relies mainly on intermittent, partly subjective clinical interviews and caregiver observations. She considered our biosensor concept clinically relevant but stressed the need to validate its correlation with plasma levels, and was more cautious than Dr. Callen about closed-loop automation, suggesting decision support as a more realistic first step.

8.2.3 Individual interview with Núria Pascual Torrecillas (family member of a Parkinson's patient)

Núria described how her grandfather's medication effect wore off faster over time, requiring repeated dose adjustments based on visibly observed symptoms rather than objective data. She highlighted the physical and emotional burden on her mother as primary caregiver, particularly during OFF periods. She confirmed that real-time information on medication levels would have brought peace of mind and helped doctors adjust treatment more precisely, and suggested integration with a mobile app for dose reminders and data tracking.

8.2.4 Individual interview with Maria Àngeles López Martín

María Ángeles López Martín highlighted the practical challenges of caring for Parkinson's patients from a nursing perspective. She explained that patients often experienced clear ON–OFF fluctuations, with increasing restlessness, rigidity and loss of motor control as

Levodopa wore off, while many cognitively preserved patients were fully aware of these changes. She also emphasized that symptom severity was influenced by stress, sleep quality, seasonal changes and the frequent presence of comorbid neurodegenerative disorders, making individualized care essential. Based on her experience, she considered that continuous, objective monitoring of Levodopa levels could help healthcare professionals identify OFF periods earlier, support clinical decision-making, and reduce uncertainty for both caregivers and patients, provided the system is reliable, easy to use and clinically validated.

8.2.5 Individual interview with Ramiro Pérez Blasco (Parkinson's patient)

Ramiro Pérez Blasco described a typical day living with Parkinson's disease, explaining which daily activities become easier or more difficult depending on symptom severity. They identified the times of day when symptoms and mood tend to worsen, particularly during medication OFF periods. They outlined their current medication regimen, including the type of medication taken, the number of daily doses, and the time required to notice its effects after each dose. The patient also reflected on the benefits and limitations of the treatment, highlighting how symptom control fluctuates throughout the day and emphasizing the importance of timely medication adjustments.

8.3 Photographic Evidence of Interviews



Figure 5. Online interview session at Parc Sanitari Sant Joan de Déu with Dr. Antoni Callen, Gemma Colomé, Christian Núñez and Christian Stephan-Otto. Conducted by members of the BarceL-Dopa team.

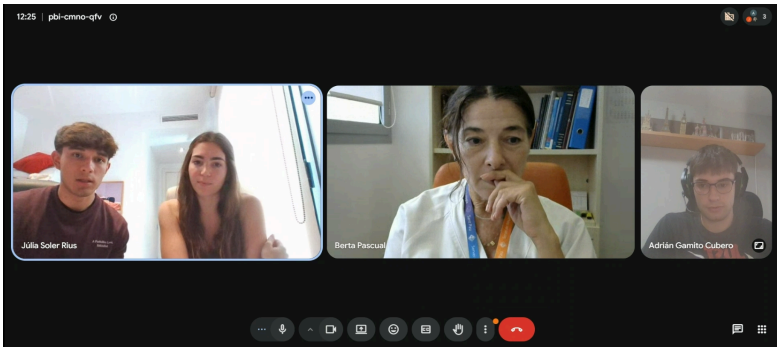


Figure 6. Online interview session with Dr. Berta Pascual. Conducted by members of the BarceL-Dopa team.

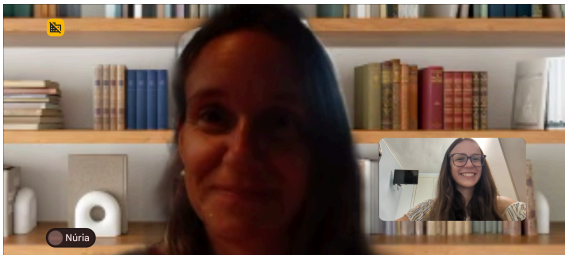


Figure 7. Online interview session with Núria Pascual Torrecillas (family member of a Parkinson's patient). Conducted by a member of the BarceL-Dopa team.

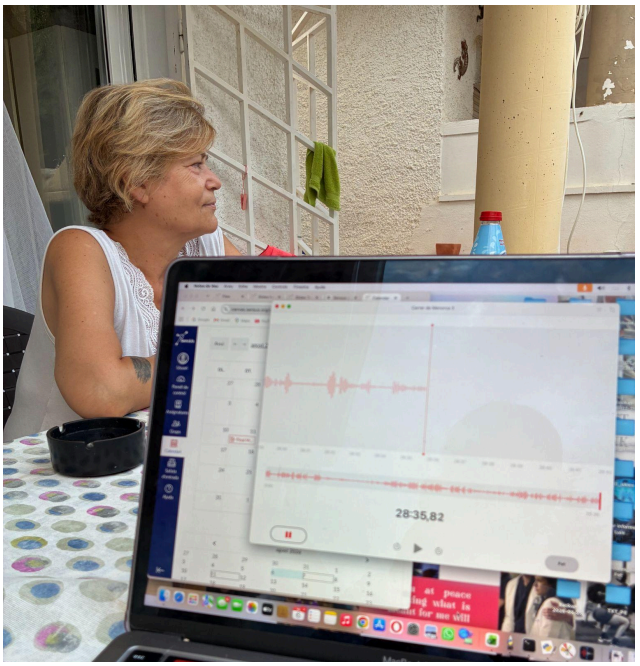


Figure 8. Presential interview with Maria Ángeles López Martín.



Figure 9. Presential interview with Ramiro Pérez Blasco (Parkinson's patient). Conducted by a member of the BarceL-Dopa team.



Figure 10. Online interview with G-Pulse team.

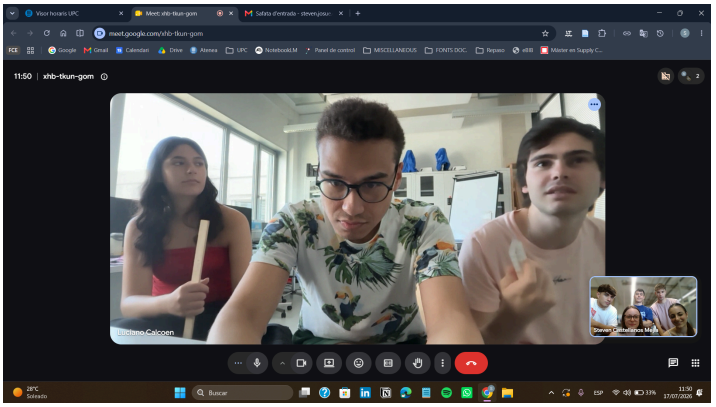


Figure 11. Online interview with Biosense EPFL team.

8.4 Quantitative Stakeholder Survey Validation

To complement qualitative expert interviews and establish empirical validation for the BarceL-DOPA platform, a comprehensive online quantitative survey was conducted. A total of 141 validated responses were collected across six distinct stakeholder groups.

A. Stakeholder Demographics Breakdown

Stakeholder Category	Sample Size (n)	Percentage of Total	Primary Analytical Focus
Caregivers & Family Members	11	7.8%	Care burden, daily practicality, wearing-off observations
Healthcare Professionals	10	7.1%	Clinical utility, treatment optimization, workflow integration
Pharmaceutical Industry Experts	11	7.8%	Pharmacokinetic tracking, drug development, market synergy
MedTech & Biomedical Professionals	7	5.0%	Technical feasibility, sensing innovation, digital health fit
Parkinson's Patients	2	1.4%	Quality of life, device comfort, therapy understanding
General Public & Engineering Community	100	70.9%	Broad technological impact, support for non-invasive MedTech
Total Validated Sample	141	100.0%	Multi-Perspective Validation

B. Detailed Quantitative Results by Cohort (5-Point Likert Scale)

Healthcare professionals (n=10)

Neurologists, clinical researchers, nurses, and physiotherapists.

Survey Statement	Mean (1–5)	Std Dev (SD)	Median
Continuous L-DOPA monitoring provides clinically valuable information	4.30	0.67	4.00
Objective L-DOPA measurements could improve treatment optimization	4.50	0.53	4.50
Non-invasive monitoring system is beneficial for patients	4.60	0.52	5.00
Continuous monitoring reduces trial-and-error dose adjustments	4.30	0.82	4.50
Longitudinal patient data supports better clinical decision-making	4.60	0.52	5.00
Technology could be integrated into routine clinical practice	4.70	0.48	5.00
Overall clinical potential of BarceL-DOPA technology	4.20	0.79	4.00

Pharmaceutical Industry Experts (n=11)

Drug development, clinical research, and regulatory affairs professionals.

Survey Statement	Mean (1–5)	Std Dev (SD)	Median

Significant unmet need for objective levodopa monitoring	4.27	0.79	4.00
Technology could improve Parkinson's disease management	5.00	0.00	5.00
Strong commercial potential of the innovation	4.82	0.40	5.00
Technology complements existing Parkinson's drug therapies	4.73	0.47	5.00
Pharmaceutical companies would benefit from continuous data	4.36	0.81	5.00
Technology appears scalable and feasible for commercialization	4.00	1.00	4.00
Overall industry potential for BarceL-DOPA	4.55	0.69	5.00

Medtech and Biomedical Engineers (n=7)

Medical device developers, sensor engineers, and digital health specialists.

Survey Statement	**Mean (1–5)**	**Std Dev (SD)**	**Median**
The physical sensing principle is innovative	4.57	0.53	5.00
Dielectric sensing offers advantages over enzymatic sensing	4.43	0.79	5.00
Technology can be integrated into wearable medical devices	4.71	0.49	5.00
Innovation fits well within current digital health ecosystem	4.71	0.49	5.00

Interest in collaborating or supporting technical development	4.71	0.49	5.00
Overall significant impact on the MedTech sector	4.71	0.49	5.00

Caregivers and family Members (n=11)

Survey Statement	**Mean (1–5)**	**Std Dev (SD)**	**Median**
Difficulty knowing when patient medication is working properly	3.55	1.57	4.00
Continuous monitoring would make daily caregiving easier	4.27	1.10	5.00
Objective measurements reduce daily care uncertainty	4.09	1.30	5.00
Earlier detection of medication fluctuations improves management	4.36	1.03	5.00
Wearable monitoring device is practical for everyday use	4.45	0.93	5.00
Would recommend this technology if proven effective	4.55	1.04	5.00

General Public and Engineering Community (n=100)

Survey Statement	**Mean (1–5)**	**Std Dev (SD)**	**Median**
Non-invasive devices significantly improve quality of life	4.68	0.60	5.00

Biosensor research for Parkinson's disease is an important area	4.65	0.61	5.00
Would support adoption of non-invasive health technologies	4.64	0.70	5.00
Overall confidence in BarceL-DOPA potential	4.58	0.78	5.00

C. Summary of Qualitative Survey Feedback

Open-ended survey responses highlighted three critical adoption factors:

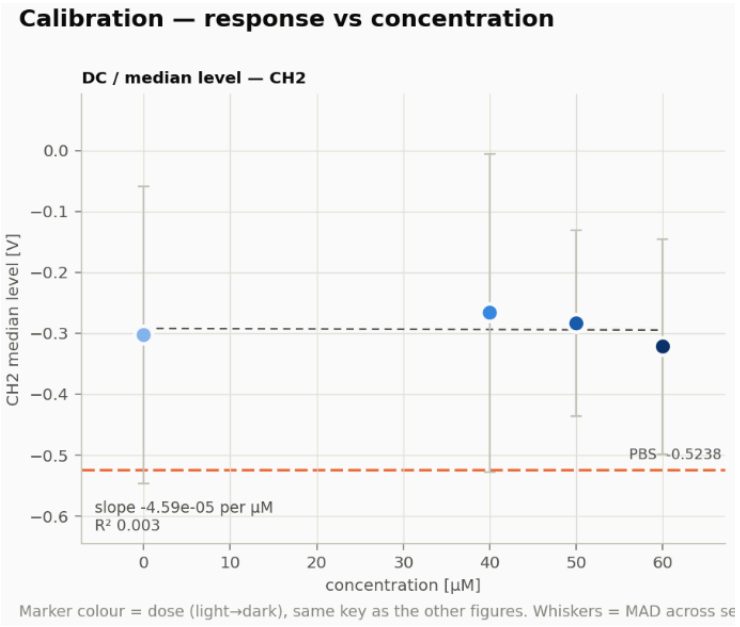
1. **Demand for Patient Autonomy:** Caregivers emphasized that the primary value of BarceL-DOPA lies in empowering patients to carry out daily tasks independently without constant fear of sudden "OFF" periods.
2. **Clinical Protocol Training:** Clinicians highlighted the need for straightforward training modules to help healthcare teams interpret dielectric trend curves efficiently.
3. **Urgency of Non-Invasive Diagnostics:** Multiple respondents stressed the urgent need for tools that eliminate trial-and-error dosing in advanced neurodegenerative care.

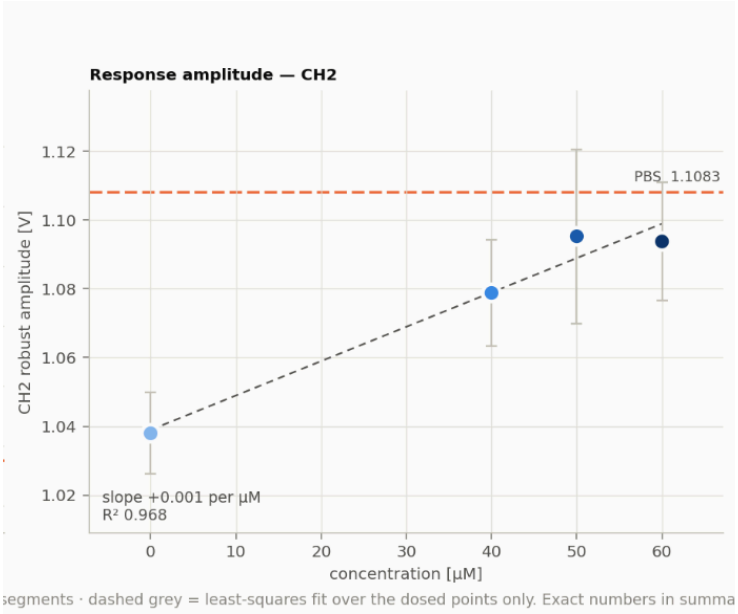
8.5 Empirical calibration and signal normalization:

Empirical calibration and signal normalization across L-DOPA concentration levels ($0 - 60\ \mu M$).

- **(Left - DC / median level):** CH2 DC offset shows minimal correlation with L-DOPA concentration ($R^2 = 0.003$), confirming negligible DC bias interference.
- **(Center - Response amplitude):** CH2 robust amplitude exhibits a positive linear response ($R^2 = 0,968$, slope $+ 0,001\ V/\mu M$) relative to the PBS baseline ($1,1083\ V$).
- **(Right - Drive-normalised response):** CH2/CH1 amplitude ratio removes common-mode excitation variations, achieving superior linearity ($R^2 = 0,987$, slope $+ 0,0308\ V/\mu M$) across the physiological sensing range ($0 - 60\ \mu M$).

Error bars represent Median Absolute Deviation (MAD) across measurement segments. Dashed grey lines denote least-squares linear fits over dosed concentration points.





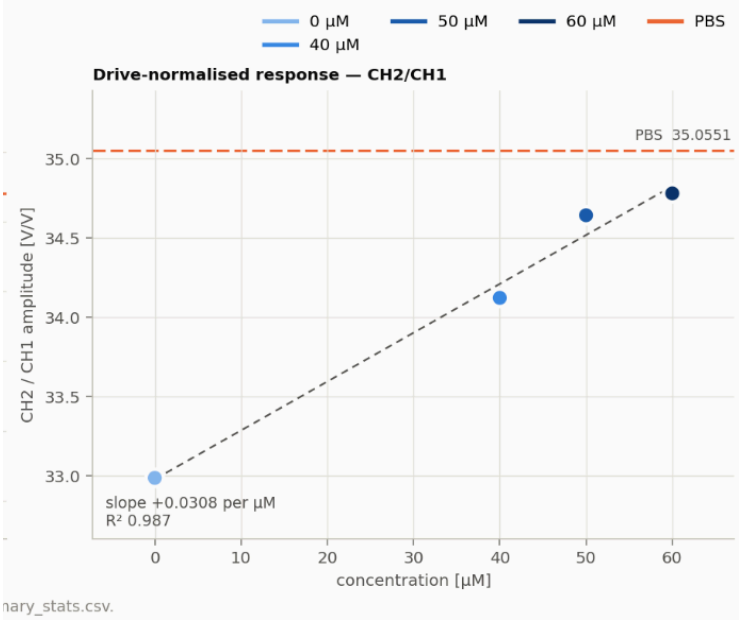


Figure 12. Empirical calibration of impedance response as a function of L-DOPA concentration.

Figure 13. Signal normalisation relative to the PBS baseline across the EIS frequency spectrum.

Figure 14. Calibration model and linear regression of the normalised impedance response.

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8.6 Empirical calibration and signal normalization:

Analog front-end circuit topology and equivalent electrochemical cell model used for EIS simulations ($0,1\ Hz\ to\ 100\ kHz$).

- **Control Loop & Potentiostat (U1, U2):** Implemented using ultra-low input bias current operational amplifiers (AD549). U1 generates the excitation signal, while U2 operates as a voltage follower (buffer) to drive the Counter Electrode (CE). This control loop applies a 10 mV AC sinusoidal perturbation superimposed on a 0.4 V DC bias between the Working Electrode (WE) and the Reference Electrode (RE), while driving the Counter Electrode (CE) and minimizing current flow through the RE.
- **Electrochemical Cell Model:** The sensor-fluid interface is modeled via an equivalent Randles circuit featuring solution bulk resistance ($R_{bulk} = 5\ k\Omega$), series resistance ($R_S = 100\ \Omega$), interfacial double-layer capacitance ($C_{dl} = 1\ \mu F$), and charge-transfer resistance ($R_{ct} = 10\ k\Omega$).
- **Current-to-Voltage Readout (U3 - TIA):** A transimpedance amplifier maintains the Working Electrode (WE) at virtual ground while converting the resulting electrochemical current into an output voltage (V_{OUT}) through a $10\ k\Omega$ feedback resistor (R_3).

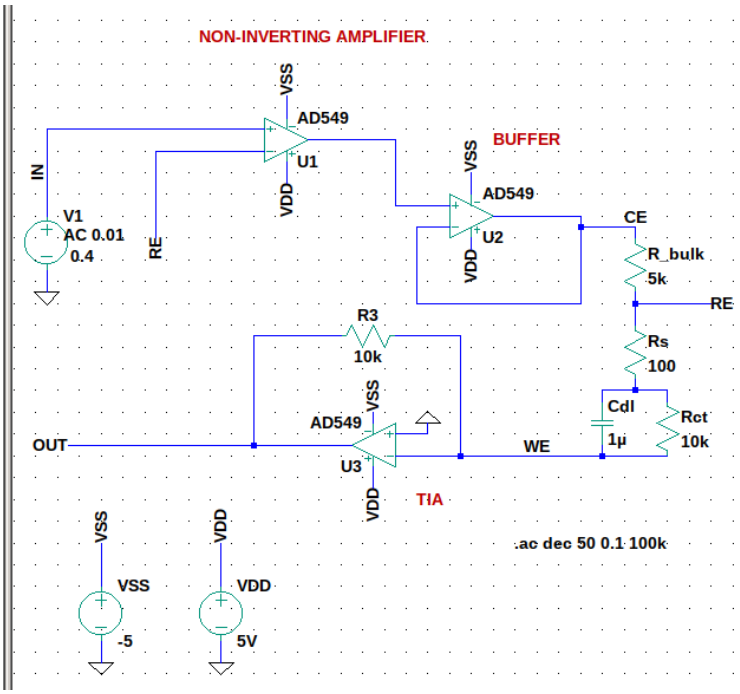


Figure 15. Analog front-end circuit topology and equivalent electrochemical cell model used for electrochemical impedance spectroscopy (EIS) simulations over the frequency range of 0.1 Hz–100 kHz.

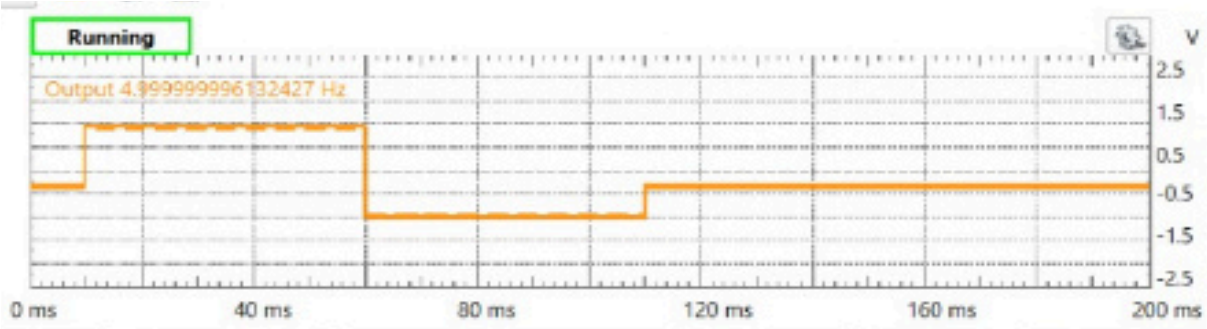


Figure 15. Input wave. +1Vand immediately after -1V.

8.7 Microfluid channel design

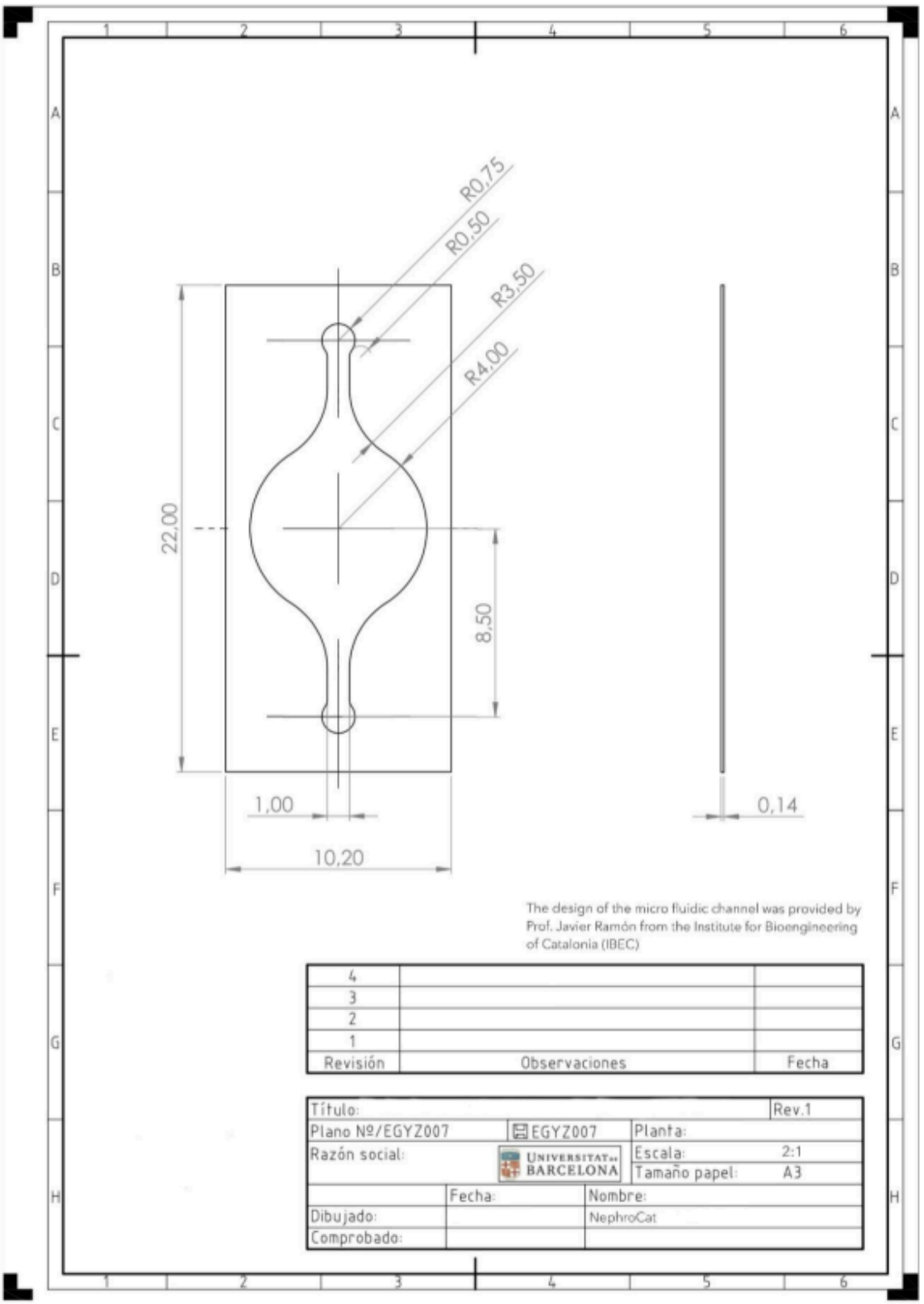


Figure 17. Microfluid channel design provided by PhD candidate Martín Ruíz from Professor Javier Ramón's group at the Institute for Bioengineering of Catalonia (IBEC).

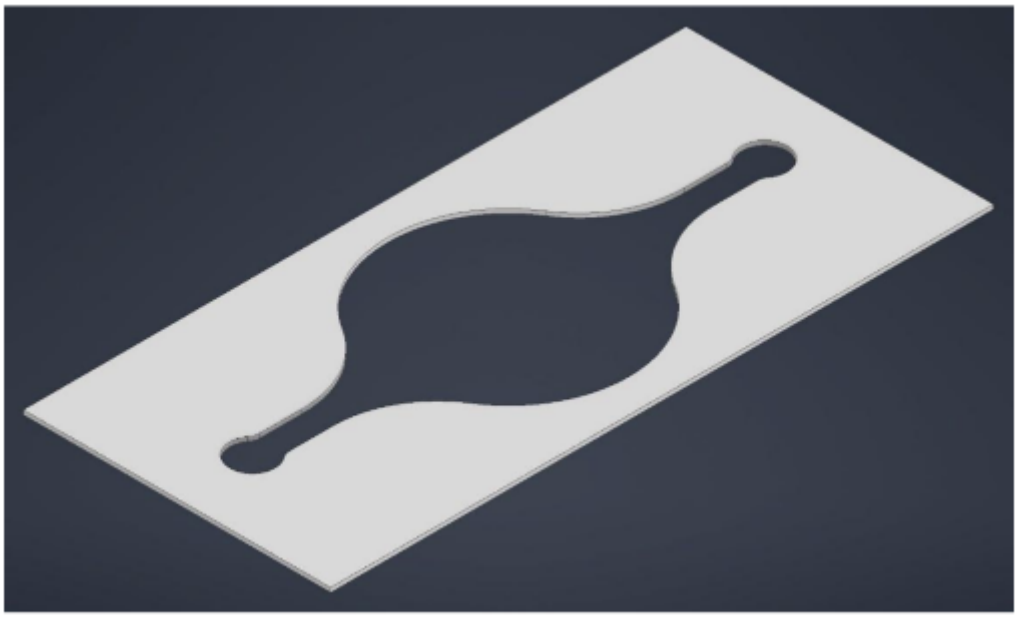


Figure 18. Three-dimensional (3D) model of the microfluid channel.

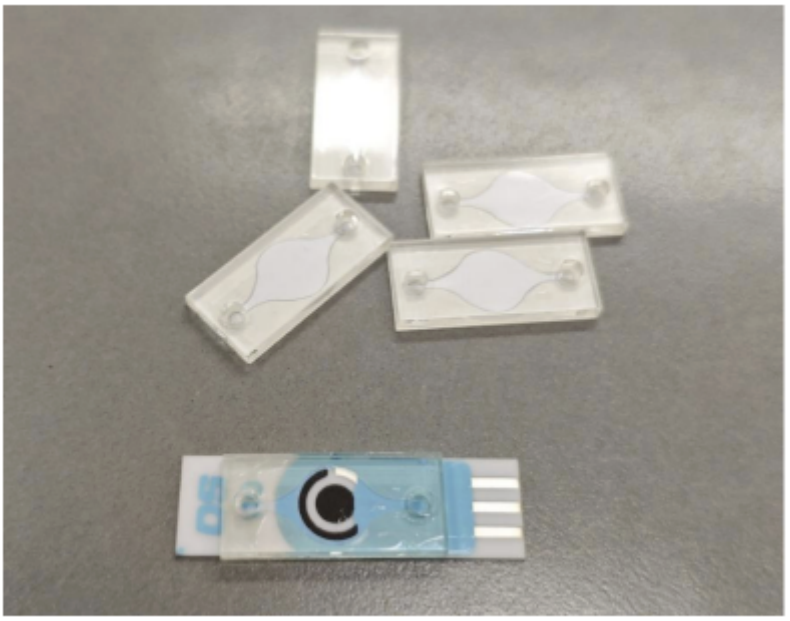


Figure 19. Microfluidic channel attached to an electrode surface.