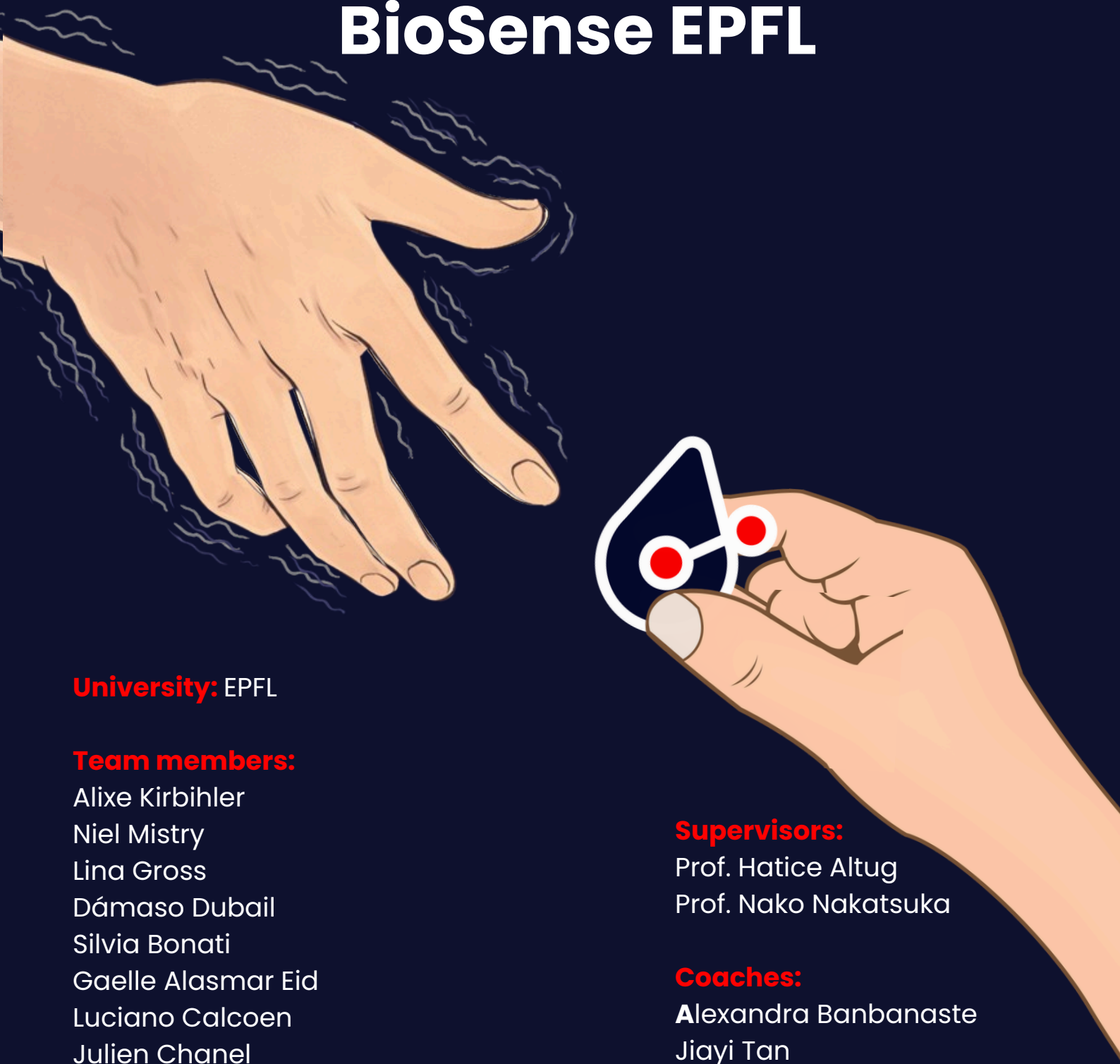
Team Results Document

BioSense EPFL



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SensUs

August 7, 2026

1. Abstract: Summary for the SensUs website

BioSense EPFL investigated the challenge of continuous Levodopa monitoring in interstitial fluid in a detailed and multifaceted way. First, we tried to understand the problem by conducting 45 individual interviews with diverse stakeholders including patients & caregivers, physicians & nurses, and people involved in insurance & regulatory affairs. Through these interviews and extensive research, we gained a comprehensive understanding of the needs and difficulties of the multitude of people affected by Parkinson's Disease, as well as the scientific challenges in this field. We developed a detailed business plan with the guidance of many professors and professionals. On the technological side, we deeply investigated aptamers: single-stranded DNA molecules that can change their shape when they interact with the target molecule. We characterised their properties, chose the best performing one, and attached them to multiple platforms to perform sensing. The team performed countless experiments and continuously iterated to improve the performance of the sensor. We are incredibly grateful to the organisations that supported us financially, the labs that helped us develop the technology, and the countless incredible people we met both in and outside of our team.

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

2.1. Molecular recognition

Aptamers are single-stranded oligonucleotides selected to reversibly bind to specific analytes (Stuber & Nakatsuka, 2024). The biosensor's molecular recognition of *3,4-dihydroxy-L-phenylalanine* (levodopa) is based on a novel aptamer sequence which combines binding parameters compatible with the desired sensing range, excellent selectivity toward the target, and demonstrates ligand-induced conformational change (Nakatsuka, et al., 2018). The structure-switching capability of the aptamer solely in the presence of the target endows the sequence with high selectivity with respect to resembling chemical compounds which do not trigger aptamer conformational rearrangement (Nakatsuka & Andrews, 2017).

2.2. Physical transduction

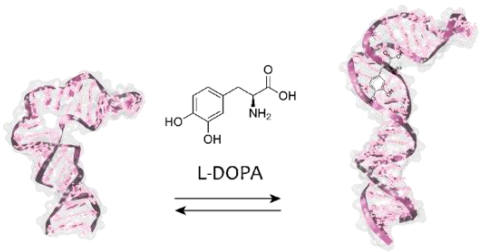


Figure 1: Aptamer conformational change upon levodopa binding (adapted from (Nakatsuka, et al., 2018))

The aptamers are chemically bound to a gold electrode *via* a thiol modification to the *5' end* of the sequence. Upon binding-induced conformational change, a methylene blue tag attached to the *3' end* of the sequence changes position relative to the gold surface, which triggers a target-dependent change in its electron transfer rate (Xiao, Lubin, Heeger, & Plaxco, 2005). By interrogating the electrode with square wave voltammetry, the peak current amplitude detected can be correlated to the concentration of levodopa. To account for baseline drift occurring overtime in ISF and improve signal gain, we utilised the kinetic differential measurement method by interrogating the sensor at two different frequencies (Ferguson, et al., 2013).

2.3. Cartridge technology

The electrode is sandwiched between two SLA-printed components and sealed with an O-ring. The top component contains an inlet and outlet port, which are 1/4-28 UNF threads to interface with a flangeless fitting. This allows PTFE microfluidic tubing to be connected from a microfluidic pump (LSPOne from *Advanced Microfluidics SA*) to the inlet, and from the outlet to a waste container. The exposed pads are then connected to a Palmsens SPE adapter, which allows the Palmsens to excite and measure the electrochemical cell.

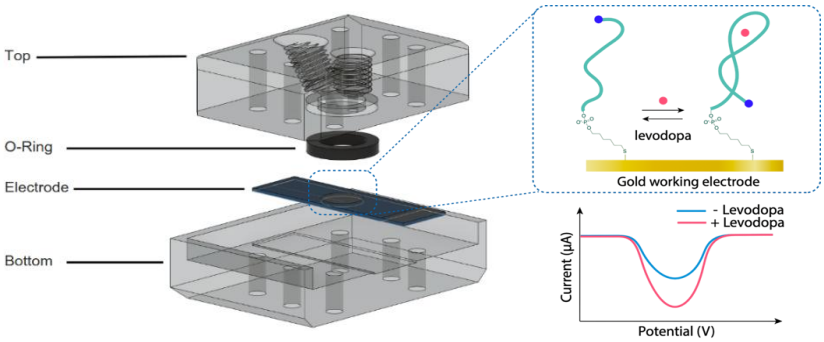


Figure 2: Design of SLA-printed microfluidic channel for E-AB sensing. Two pieces enclose a functionalized electrode with an elastic O-ring to define the inner volume of the chamber. Credits to Alexandra Banbanaste for the schematic on the right.

2.4. Reader instrument and user interaction

Commercial gold screen printed electrodes (DropSens 220-AT) are functionalized in-house by adapting a recently published protocol (Nguyen, Prevot, Fontaine, & Dauphin-Ducharme, 2024). The reader instrument consists of a *Palmsens4* connected to the SPE with an adapter, and a computer that runs custom software to control the microfluidic pump and the Palmsens. To perform measurements, the functionalised electrode is carefully placed in the cartridge, which is bolted tightly to form a seal. The inlet and outlet fittings are screwed in, and a priming and calibration procedure is completed by a button on the Python-based web interface. For each measurement, the user inserts the inlet tube into the next sample and clicks on a button which performs a pre-designed sequence of microfluidic operations and electrochemical measurements. The user interface also shows a live graph of the results obtained, along with a final measured concentration of levodopa in the sample.

We developed a *React-based* dashboard to seamlessly control our microfluidic syringe pump and *PalmSens4* potentiostat. This dashboard allows us to flow samples into our sensor at the appropriate volume and at the adequate timings required for the testing event.

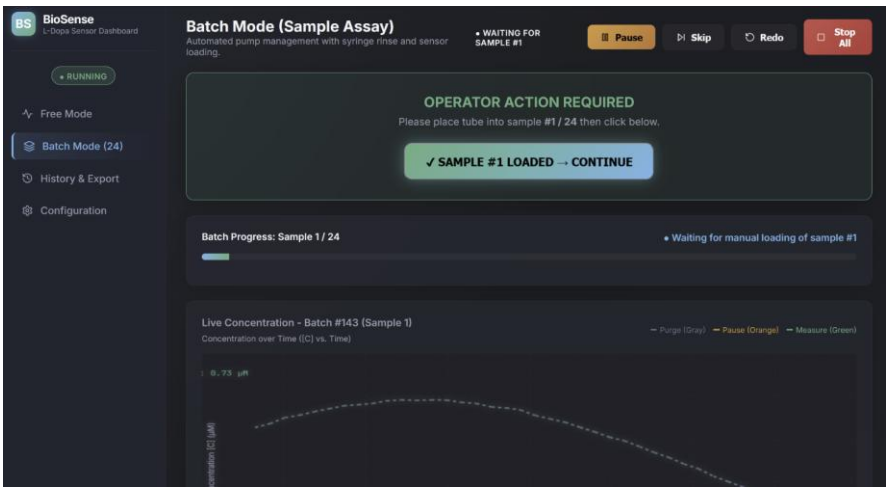


Figure 3: In-house software for sensor and microfluidic control

3. IN award: Biosensor innovation

3.1. Wearable sensor

We envision a wearable sensor that is stuck to the skin using biocompatible adhesive tape. The device would extract interstitial fluid (ISF) via a microneedle that would then be routed over an aptamer-functionalized indium-oxide field-effect transistor (FET) array (Nakatsuka, et al., 2018). Integrated electronics would monitor the change in current induced by target-dependent conformational change of aptamers, functionalised on the indium-oxide channel.

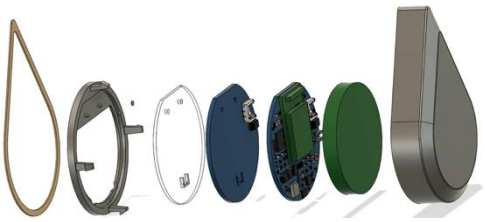


Figure 4: 3D model of a possible wearable design. Design inspired by (Hack, 2026)

3.1.1. Technological novelty of wearable sensor

Wearable devices must demonstrate continuous monitoring and cost-effective manufacturing to be scalable. The proposed biosensor design presents two main novelties: a characterised aptamer specific for Levodopa, and its functionalisation on an indium oxide transistor. An aptamer with favourable binding parameters provides significant advantages over competing methods, enables continuous monitoring, and potentially higher selectivity compared to currently available enzyme-based electrochemical methods (Tesoro, et al., 2023). The advantages of sensing aptamer conformational change with transistors are two-fold: simplified aptamer construction and more straightforward readout electronics. Compared to electrochemical aptamer-based sensors, aptamers functionalised on the transistor surface do not require the addition of a redox reporter, which increases synthesis complexity and cost. Furthermore, since transistors provide inherent signal amplification, they allow for a better integration into small wearables using affordable readout electronics (Stuber A. , et al., 2023).

3.1.2. Technical feasibility of wearable sensor

By characterizing four unpublished levodopa aptamers via isothermal titration calorimetry (ITC) and circular dichroism (CD), we identified a sequence which displayed binding parameters consistent with the desired detection range (Jing & Bowser, 2011), demonstrated strong selectivity toward the target with respect to *L*-tyrosine, and showed target-induced structure switching solely in presence of levodopa. Its sensing capability was then evaluated under continuous sensing conditions by tethering it to a quartz crystal microbalance with dissipation monitoring (QCM-D) chip. Although these measurements

do not directly inform the detection properties of the transistor platform, they nonetheless provide valuable qualitative information regarding the self-regeneration ability of aptamers over multiple cycles, as well as demonstrating the ability of this aptamer to sense changes in Levodopa concentration (Dong, 2024).

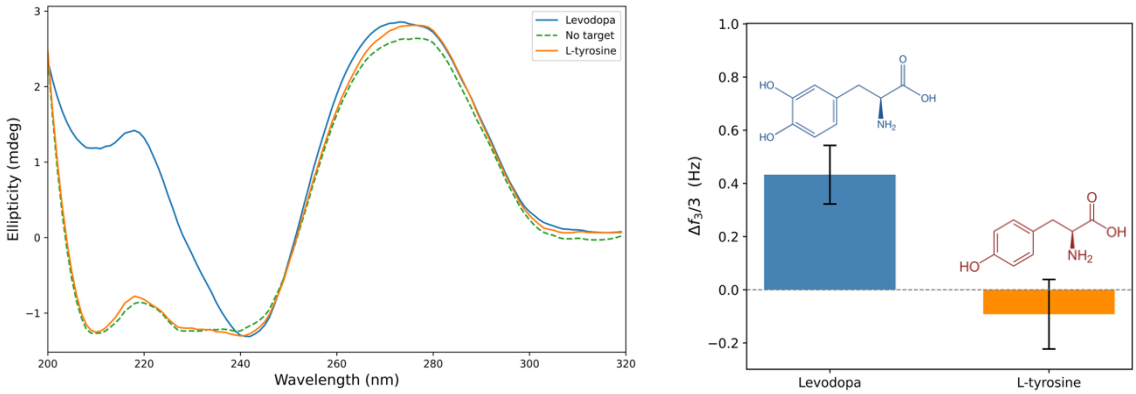


Figure 5: Target binding caused a pronounced ellipticity inversion at 220 nm, indicating conformational rearrangement absent with L-tyrosine. QCM-D confirmed selectivity through a greater normalised frequency shift for levodopa, likely reflecting displacement of the acoustically coupled hydration layer.

Building on the promising linear response obtained with QCM-D, we manufactured indium-oxide transistors following the processing explained in (Nakatsuka, et al., 2018) and tested them. We combined them with the promising aptamer and achieved preliminary results suggesting concentration dependent change.

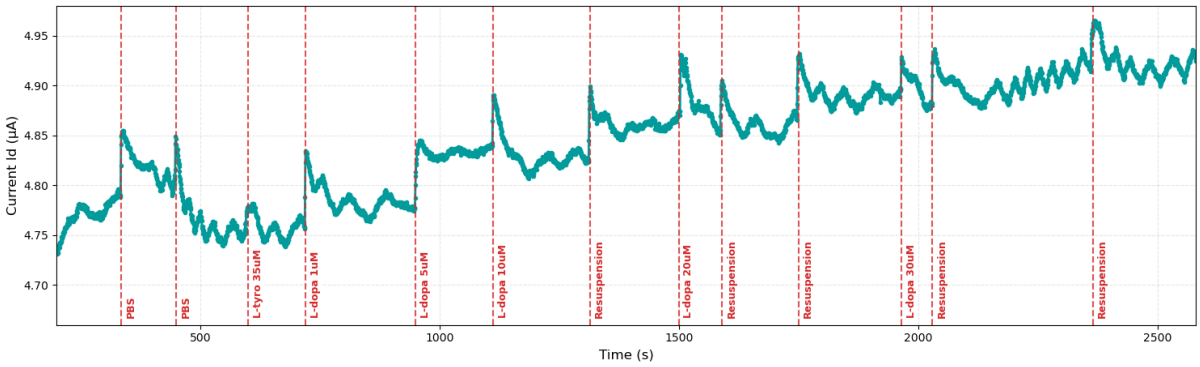


Figure 6: Ids response @ V_{gs} =175 mV of a functionalized transistor with different levodopa concentration. The signal, seems to increase with increasing levodopa concentration. The spikes are due to the residual charges when introducing the solution, however the high frequency variations are still not understood.

We developed an electronic circuit for the transistor-based sensor. We use the AD4195 low-noise high resolution ADC to readout the current and the AD5689 DAC to control our integrated reference electrode. We designed and manufactured the board; we tested basic functionalities of the chips however software

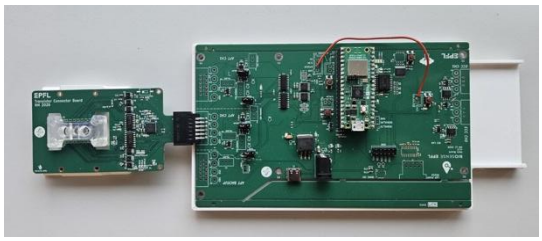


Figure 7: Picture of the transistor-based sensor PCB setup. We developed a microfluidic specifically for the FET, which required the use of a secondary PCB

development for sensing integration still needs to be complete.

3.2. Reliability of sensor output

3.2.1. Technological novelty of reliability concept

Using FETs as a sensing platform is an attractive approach for multiple reasons: first, the transconductance of the transistor provides internal amplification, which allows for low analyte concentration sensing (Stuber A. , et al., 2023). When the aptamers functionalised on the surface of the FETs capture levodopa, they adopt a new conformation, which induces a change in the local charge distribution at the surface of the sensor. Thanks to the aptamers' negatively charged backbone, the transconductance of the device can thus be effectively modulated. Transistors are manufactured in highly controlled microfabrication processes, thus significantly lowering variability between neighboring devices. In addition, parallelization of transistors offers potential increase in sensitivity, thermal drift compensation or target detection. For instance, an array of differently functionalised FETs could be tuned to detect different targets such as several drugs taken by a PD patient. Finally, while FETs can be miniaturized down to 50×50 μm^2, further reduction risks providing insufficient surface area for effective functionalisation.

3.2.2. Technical feasibility of reliability concept

Our transistors have shown to drive more current than bare screen-printed electrode (SPE). Assuming the same sampling rate as in (Booth M. E., 2026), a sensor is expected to measure 288 times in one day, or 2016 times if the device is expected to last the week. As shown in Figure 9, some transistors were shown to work at least a thousand cycles overnight, with signal variation down to ±2%. The current longevity of our transistors is encouraging but the aging of the devices has not yet been continuously tested with the aptamers. The combination of the transistors and the aptamers still need to be further investigated.

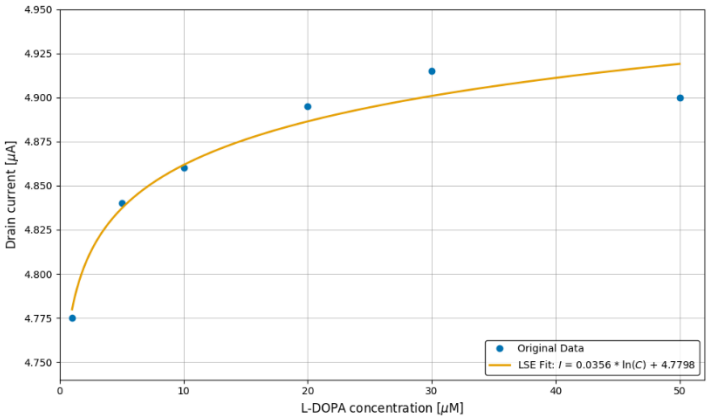


Figure 8: Calibration curve of one transistor functionalized. While working, the transistor used for this example was of low quality, with a smaller current, but is still higher than commercial carbon-SPE which measured to have a maximum oxidation peak current of 1.3uA.

We also designed and manufactured test vehicles containing multiple transistors but due to lack of time we have not yet combined them during sensing and are still using them one at a time. Contact pads have a standardised size and pitch, which standardises the interface the electronics see and prevents changes to the complete back-end circuit.

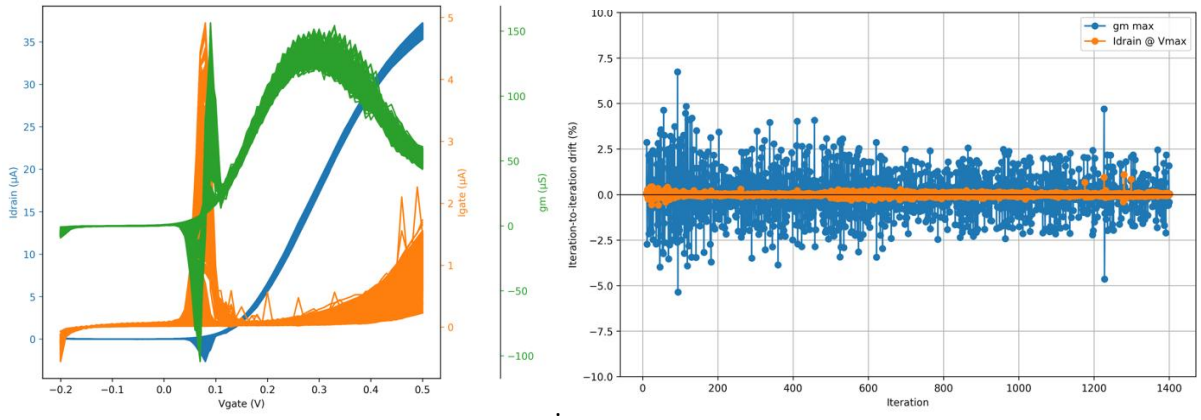


Figure 9: Response curves (with Vds=10 mV) of one transistor over 1400 cycles in PBS. The first ten and last points were removed due to probe not being accurately set up. The current and transconductance drifts relatively little from the initial measurement (after removing the first ten points)

3.3. Original contributions

Supervisor Statement:

The technology builds on the aptamer-functionalized field-effect transistor-based sensing platform first reported by Prof. Nako Nakatsuka (Nakatsuka, et al., 2018). The novel contribution here is extending this platform to a new target (levodopa). The indium-oxide platform that the aptamers were functionalized on is built on one year of prior work by the host lab (CHEMINA, EPFL) led by a PhD student (Sandra Hernández Escobar) replicating and extending the original results to other neurochemical targets. The levodopa-specific aptamer sequences used in this work were suggested by Prof. Nako Nakatsuka who had access to unpublished aptamers through collaboration with Dr. Kyung-Ae Yang at Columbia University who specializes in aptamer selection. With the help of Dr. Minh-Dat Nguyen, a postdoc in the CHEMINA lab, we optimized the sequences for improved signal transduction. The initial functionalization chemistry protocol for attaching aptamers to the transistors was based on the Science 2018 manuscript and knowledge transferred from Sandra who had optimized the protocol the past year.

Under the supervision of the CHEMINA lab (PhD students, Lianxin Xu and Alexandra Banbanaste), the team then carried out the characterization of new levodopa aptamers using QCM-D, CD, and ITC, techniques that confirmed the aptamer underwent a conformational shift and showed satisfactory binding parameters as well as selectivity toward the target, which supported moving forward with that sequence immobilization on the indium oxide transistors.

Adjustment of the functionalization chemistry and the testing setup was conducted jointly between the team and CHEMINA lab, who worked together to optimize the surface chemistry and test different aptamers and conditions. Ideas for microfluidic chamber integration and chip process & layout optimization were proposed by the students. Sandra Hernández Escobar provided ideas and insights from her research into collaborative discussions with the students about channel encapsulation and an in-wafer reference electrode. Both the independent and collaborative ideas were implemented by the students in partnership with CHEMINA.

Testing and setup preparation were carried out jointly by the team and members of the CHEMINA Lab. Device fabrication was performed by Sandra Hernández Escobar in May and

June, and the knowledge was transferred to a team member in July. Then, the team independently fabricated devices alongside Sandra in July and August. One of the students in the team made ten wafers with various modifications and improvements during this period.
Overall, the students were proactive, demonstrated significant initiative, and performed many of the experiments independently.

Prof. Nako Nakatsuka
Tenure Track Assistant Professor
CHEMINA

Team Statement

As team leads, we are incredibly proud of the work that our team has done over the past year. We performed significant literature review, generated ideas both independently and in collaboration with academic references and worked on cutting edge research. Members of our team characterized aptamers, performed a three-step functionalisation protocol on indium oxide FETs and tested these devices alongside PhD students. We also designed and iterated on a microfluidic flow cell to test the FETs, and a member of our team fabricated ten wafers with various process optimizations. Additionally, we designed and partially brought up a custom electronic circuit board to demonstrate sensing with low-cost hardware. We are grateful for external support from Prof. Nako Nakatsuka and Dr. Kyung-Ae Yang for providing the aptamer sequences that we used. Sandra Hernandez Escobar provided protocols and training to functionalise aptamers on FETs and provided ideas and supervision for the wafer fabrication including collaboratively developing ideas for the integrated reference electrode and channel encapsulation. Alexandra Banbanaste and Lianxin Xu trained & supervised a member of our team to characterise the aptamers using various techniques.

Alixe Kirbihler
Co-Team Captain
BioSense EPFL

Niel Mistry
Co-Team Captain
BioSense EPFL

3.4. Bonus Criteria Innovation

The team investigated various regeneration methods to promote faster unbinding kinetics to actively regenerate the device for on-demand sensing. We investigated previous work exploring the subject, including heat (Zhu, et al., 2023), (Dongfang Liu, 2022), (Na-na Sun, 2025); light (Zhang, et al., 2018)., (Trinh, et al., 2022), and pH modulation (Micaela Belleperch, 2018) to promote regeneration. After reviewing the relevant literature, the team participated in ideation for a project to integrate light reactive chemical moieties to

aptamer sequences. This project's experimental setup and feasibility was assessed by the team collaboratively with CHEMINA.

Members of the team also explored alternative architectures for the fabrication of the transistors including different substrates, layouts, and methods to provide better control & repeatability to fabricated devices. In addition, a member of the team generated many ideas to test fabricated devices more frequently during the microfabrication process. Some of these ideas were implemented and provided valuable insights.

Motivated by a lack of repeatability in certain tests, team members ideated and thought of the feasibility of automating the indium oxide transistor fabrication and aptamer functionalisation process cost-effectively. This automation would provide control to critical parameters in the process.

Finally, preliminary literature review was performed on integrating logic circuitry in the same indium oxide transistor topology as the sensor, which could allow for further miniaturization, signal quality improvement, and power efficiency (Kim & Yoo, 2022).

4. TP award: Translation potential

4.1. Customer interviews

4.1.1. Identification of potential stakeholders

We began by contacting scientists and doctors treating Parkinson's Disease (PD) patients, our entry point for identifying relevant stakeholders with expert input. From a literature review and stakeholder interviews, we selected ten stakeholder groups spanning the full care/value journey, including potential collaborating startups. We interviewed, experts across France, Switzerland, Morocco, and the Netherlands.

Table 1 - Stakeholder groups, relevance, and engagement across the PD care

Stakeholder	Relevance	Engagement
Patients with PD	Primary end users; experience ON/OFF fluctuations and dosing unpredictability first-hand	17 individual interviews + 69 questionnaires + 2 group interviews (14 same members twice)
Neurologists	Prescribe/adjust levodopa; would act on continuous-monitoring data	5 interviews + individual MVP follow-up with each
Caregivers/family	Monitor safety and well-being at home	5 interviews + 4 via patient interviews
Nurses	Day-to-day medication support	3 interviews
Diabetes-care doctors + specialists	Lessons from the continuous glucose monitoring (CGM) adoption and pains	2 interviews
Insurance companies	Reimbursement gatekeeper and financial beneficiary	2 interviews
Regulatory professionals	Certification and go-to-market pathway	3 interviews
Pharmacists, hospital administrators, pharma companies, physiotherapists	Distribution, procurement, biomechanical/commercial relevance	Informed by stakeholder analysis and literature (not directly interviewed)
Researchers	Device users, scientific validators, and first paying customer	6 interviews
Future collaborating startups + Startup Experts	Potential technology/commercial partners and advisors	2 interviews
TOTAL	**10 stakeholder groups spanning the full care and value journey**	**45 individual interviews + 2 group interviews + questionnaire**

4.1.2. Interview approach and execution (see Timeline in Appendix A)

Structure & methodology. The interview guide was built from a literature review of PD pathophysiology/pharmacokinetics plus a pilot patient interview, covering five domains: daily life, medication experience, unmet needs, reaction to the sensor concept, and user preferences. Every team member conducted at least one interview. Patients were recruited via Parkinson Move and Défi Parkinson. Fourteen members of a Nyon patient group took part in open feedback first, then structured feedback, capturing input at two key development stages. Neurologists and diabetes-care clinicians followed a parallel guided interview; remaining groups received a short BioSense presentation plus a fixed, group-specific question set (see Appendix B). A structured online questionnaire (regimen, fluctuations, coping/monitoring, device acceptability) still ongoing went to patients via

Parkinson France and our LinkedIn, yielding 69 responses (see Appendix C). All findings were gathered in a summarizing table to extract relevant information.

Ethics. Written informed consent, voluntary participation, and optional anonymisation applied throughout; no clinical claims were made, and data handling followed the General Data Protection Regulation (GDPR) (EU 2016/679) and the Swiss nLPD/nFADP (RS 235.1) (Swiss data protection law). Raw data will be deleted within 2 years of study close.

Documentation. Individual interviews were audio-recorded with consent and transcribed manually; group sessions were documented via written minutes. All recordings, transcripts, minutes, and consent forms are stored on an access-restricted, EPFL-managed Google Drive folder. The French questionnaire responses were collected via EU Survey and archived alongside the interviews.

4.1.3. Interview results and conclusions (see Survey, Summary and Quotes in Appendix B)

Clinicians. All 7 neurologists wanted confident, real-time dosage adjustment: a symptom-vs-dosage report, not raw data. Trusting it over self-report requires a validated Interstitial Fluid (ISF)–symptom correlation, interpretation training, and flagging protein-intake timing as a confound (Rusch, Flanagan, Suh, & Subramanian, 2023).Diabetes-care clinicians agreed, stressing that trust needs an accepted comparator, and that not all patients can use apps.

Patients and caregivers. The dominant need was certainty that dosage is adequate; priorities were ease of use, low cost, clarity, and reliability, and several compared it unprompted to a glucose monitor. Most requested features: meal/protein logging, ON/OFF tracking, and adherence logging. The questionnaire (n=69, Appendix B) corroborates this at scale: 92% report dose-linked symptom fluctuations and 83% self-adjust their doses, yet 44% track nothing and only 9% use an app, and 83% feel their neurologist, seen only 1–2×/year, lacks information between visits. 92% would accept wearing a continuous levodopa sensor. Women also raised hormonal-cycle effects on medication response.

Insurers and regulators. Both prioritised reduced falls, ER visits, and hospitalisations from ON/OFF episodes for reimbursement, consistent with the average per-patient societal costs in Europe €20,911-€100,000 (most severe cases) (Wijers, Ravi, Evers, Tissingh, & van Mastrigt, 2024).

Researchers. The main obstacle is the lack of a validated motor symptoms-ISF–CSF relationship. Patients in Hoehn & Yahr stage 3/4 were the priority population.

All stakeholders validated the need for a sensor. Across the interviews, four themes (objective dosing data, a validated ISF–symptom relationship, adherence tracking, and measurable safety) define the scope in Section 4.2.1.

4.2. Design of validation study

4.2.1. Selection of the problem

Insurers/regulators want measurable falls/complication reductions, not device features. Section 4.1.3 surfaced four connected problems defining this study's scope: no objective, continuous measure of levodopa exposure, with dosing relying on subjective reports (cited by 95% of patients as their top concern); an unestablished ISF–symptom relationship and clinician distrust of self-report as the sole reference; adherence uncertainty ("did I take my dose?") driving patient/caregiver anxiety; and insurers/regulators seeking measurable falls/complication reductions rather than device features.

Our study establishes the ISF–symptom correlation against an objective reference (wearable tremor tracking + 9-item Wearing-off Questionnaire (WOQ-9) as a supplementary comparator only). (Stacy, et al., 2005) and (Stacy, et al., 2008) validated wearable motor-symptom monitoring replaces patient diaries; and adherence hardware is already commercially proven, requiring integration rather than invention (§4.2.2).

4.2.2. Conceptual design and use case (see Appendix D for Reader Design)

Since needs vary widely by symptom severity, tremor, digital comfort, and disease stage (§4.1.3), BioSense lets each patient use the option that suits them while the clinician always gets one standardised dataset. At Minimum Viable Product (MVP) stage we tested this variability, not a finished product: a 3D-printed sensor-patch mock-up (two sizes/placements, arm, abdomen); two app tiers (simplified logging-only vs. complete mode with live curve, schedule, alerts, history), tested within-subject; and a separate clinician dashboard (§4.2.3). For patients unable/unwilling to use a smartphone, a standalone reader, modelled on CGM handheld readers (Didyuk, Econom, Guardia, Livingston, & Klueh, 2021), reminds patients to dose and logs ISF data silently for the clinician. Longer term, adherence logging would be automated via commercially proven dispensers (e.g., Wisepill's RT3000), validated across chronic-disease populations (Haberer, et al., 2010) (Liu, et al., 2015), removing "did I take my dose?" as a source of anxiety using market-proven hardware. Since self-report alone can't establish how ISF levodopa relates to motor symptoms, we therefore engaged with Sense4Care, whose CE-marked STAT-ON™ wearable objectively classifies PD motor state from movement (Rodríguez-Martín, et al., 2022), and plan to use it as an independent reference during a calibration period.

4.2.3. Validation study design (see Appendix D and E for App Design and Full Survey/Results)

As no functional sensor exists yet, this stage validated the conceptual design, both apps, form factor, and clinician app, against needs via usability, not measurement accuracy.



Patient dashboard (11 patients, within-subject): trust scored 4.64/5, daily-use comfort 4.36/5; 8/11 (73%) preferred the complete mode, though simplified mode rated nearly as easy for daily use: the split motivating three tiers (§4.2.2); 10/11 (91%) wanted mode selection to be a shared patient–clinician decision; symptom logging was unanimous (11/11), nutrition and activity pages each wanted by 10/11 (optional add-ons). Sensor mock-up (two sizes/placements): comfort scored 3.67–4.73/5; size S and arm placement equally preferred (75%, 75%), no skin irritation reported.



Clinician dashboard was tested separately against clinicians' needs. Together, results confirm usability and showed a need for education on L-DOPA concentration in ISF.

Scope. The table below outlines the planned Phase 2 studies that establish this relationship and generate the falls/motor-fluctuation data decisive for reimbursement. BioSense remains a monitoring/alerting tool only.

Table 2 - Combined design synopsis (See detailed Synopsis in Appendix G)

Parameter	Study 1: Analytical Accuracy & ISF–motor-state correlation	Study 2: Clinical Applicability; falls, Quality of Life (QoL), dosing utility
Design	Prospective, single-arm, multi-center: (a) analytical validation vs. chemical reference (microdialysis, HPLC/LC-MS); (b) correlation vs. STAT-ON + WOQ-9. V3/V3+ framework (Goldsack, et al., 2020) (Bakker, et al., 2025); (a) STARD 2015, (b) observational.	Prospective, multi-center effectiveness study, initiated once Study 1 confirms adequate accuracy/correlation. STROBE-guided.
Population	Idiopathic PD, H&Y 1–4, stable levodopa, age 40–85, Switzerland.	Idiopathic PD, H&Y 3–4, motor fluctuations + fall risk, stable levodopa, age 40–85, multi-site.
Key exclusion	Dermatological conditions precluding patch wear; cognitive impairment; concurrent interventional trials.	Same as Study 1.
Sample size	n ≈ 50-60 (pragmatic; TBC by power calc).	TBC by power calc (fall-rate effect size, Study 1 variance).
Duration	14-day concurrent wear; visits d0/7/14; ~12-mo recruitment.	3–6-mo wear; baseline + monthly visits; ~12–18-mo recruitment/follow-up.
Primary endpoints	(a) Bland–Altman agreement vs. chemical reference; (b) correlation, ISF-levodopa vs. STAT-ON motor state.	Falls/near-falls incidence; QoL change (PDQ-39).
Secondary endpoints	Sensitivity/specificity of ISF-derived OFF detection; adherence-logging accuracy; effect of data-visibility on engagement.	Dose-adjustment frequency (ISF-trend vs. Standard of Care (SoC); neurologist workflow impact; patient dosing anxiety/confidence.
Statistical analysis	Bland–Altman; correlation/regression; ROC sensitivity/specificity.	Time-to-event (falls); pre–post QoL; comparative dose-adjustment analysis.

4.3. Bonus criteria Translation Potential (See Appendix H,I,J,K, for manufacturing costs, cost-benefit projection, development timeline, and market selection.)

BioSense' Solution is a skin-worn sensor that continuously measures levodopa in ISF, making visible the drug-level fluctuations neurologists cannot see between appointments. The problem, patient and payer are specific: moderate-stage (Hoehn & Yahr 3) patients (falls-driving fluctuations), and a primary claim of measurable reduction in falls and fall-related injuries. Clinicians named confident, real-time dosage adjustment as their central need: BioSense is being validated toward that decision-support role.

Table 3 - The BioSense Solution

1 - SKIN PATCH	2 - ISF READING	3 - THREE-TIER ACCESS	4 - CLINICIAN VIEW
Microneedle-scale sensor worn on the arm. Minimally invasive, waterproof (top user request).	Reads levodopa in ISF in real time, the drug fluctuations clinicians cannot see today.	Simplified app, complete app, or standalone reader. Patient picks the mode that suits them.	All tiers feed ONE standardised symptom vs dose report. Aiding clinicians in dosing.

Our defensible contribution (bench-validated):

Selective recognition: a novel engineered aptamer differentiates levodopa from interferents (dopamine, *L*-tyrosine).
Therapeutic-range readout: monotonic detection across 3 to 50 µM, the clinically relevant patient window.
Reagent-free continuous sensing: a self-regenerating aptamer senses for hours with no added reagent or user care.

Switzerland is BioSense's institutional, legal and IP home (team, infrastructure access, regulatory contacts, and spin-off). The Netherlands, and through it the EU, is the first commercial market: CE marking under EU MDR/IVDR; the Dutch NZa 'small-scale experiments' policy funds up to three years of pilot reimbursement, and ZonMw's Passende Zorg framework funds value-driven care and clinical effectiveness studies.

Table 4 - Phased Business Model

Phase & timeline	Primary customer & claim	Regulatory status	Revenue model
Phase 1 Research use 2026–2028	Research labs, core facilities, pharma / CROs. Claim: research tool, no medical claim.	Research Use Only (RUO). Fastest, lowest risk route to revenue.	RUO device + patches; platform licences; reader + data-software.
Phase 2 Observational ~2028–2030	First patient cohorts. Study 1: analytical accuracy vs HPLC/LC-MS + ISF–motor correlation vs STAT-ON / WOQ-9.	Becomes a medical device; first human study.	Clinical partnerships, grants.
Phase 3 Decision support ~2030–2034	Study 2: clinical applicability: falls/near-falls, QoL (PDQ-39), dosing utility. Show falls decline.	CE mark (EU MDR, Class IIb).	Patient subscription + clinic licensing.
Phase 4 Dosing support 2035+	Partly automated dose guidance, the role clinicians asked for.	Highest evidence burden.	Reimbursed device + data licensing.

Table 5 - Key risks & mitigation

Obstacle	Why it matters	Addressed by
No functional sensor yet	Delays the clinical evidence the claim depends on.	Phase-1 RUO revenue from research labs funds and de-risks the build before any medical claim is made.
ISF-symptom,link unproven	Clinicians will not trust it over self-report.	Two-study plan: Study 1 validates analytical accuracy and ISF-motor correlation; Study 2 proves clinical applicability.
No FDA predicate for an ISF wearable	US De Novo / PMA route is slow and costly.	Launch EU-first (MDR Class IIb); NZa and Passende Zorg fund pilot reimbursement in evidence generation.
Single-analyte market looks narrow	Limits addressable market and investor appeal.	Recognition chemistry re-tuned for other analytes (TDM, metabolic markers): a platform, not one product.

5. Team and support

5.1. Contributions of the team members



Alixe Kirbihler: Characterised unpublished aptamer sequences for their affinity and selectivity using techniques such as ITC and CD spectroscopy, as well as spearheading the testing of the electrochemical based sensors. As one of the co-captains of the team, she also organised the overall efforts of the team, ensured cohesiveness, and handled administrative tasks.

Niel Mistry: Characterised different types of transistors for their stability and evaluated them with sensing experiments. Designed PCBs for the readout electronics, and the microfluidic chamber for the transistor designs. As the other co-captain, he also organised overall efforts and handled administrative tasks.

Dámaso Dubail: Designed, manufactured and tested microfluidic design. Gave support in firmware development. Helped in the manufacturing of the TFT in cleanrooms.

Luciano Calcoen: Designed, improved and manufactured TFT in cleanrooms. Helped design the electronic circuitry and microfluidics.

Lina Gross: Led the business team, coordinating and participating in stakeholder interviews, grant applications, and entrepreneurship initiatives, while also conducting the relevant literature review to inform our strategy. Additionally, contributed to the microfluidics team: performed literature review and worked on the cable flow setup.

Gaelle Alasmar Eid: Was the person responsible for communication and outreach. Conducted experiments to test and improve aptamer-based sensing.

Charlotte Mercier: Conducted experiments to test and improve aptamer-based sensing.

Lara Mansour: Conducted experiments to test and improve aptamer-based sensing.

Silvia Bonati: Conducted experiments to test and improve aptamer-based sensing and supervised electrochemistry experiments. Conducted interviews and realised the user software.

Nabil Bellamy: Provided guidance on the microfluidics team division as well as developed full interface for sensing control and measurements taking.

Theo Maechler: Aided the Business Team in designing prototypes and oversaw the production of the sensor's outer casing.

Julien Pierre Chanel: Developed Section 4.3 on translation potential, mapping the business model, regulatory strategy, and Dutch pilot reimbursement pathways. Assisted in the two-stage clinical validation study and contributed to stakeholder interviews.

5.2. People who have given support

Dr. Anne-Laure Mahul-Mellier: Supported us throughout the project by helping us connect with numerous patient groups and facilitating meaningful exchanges with the community. Through her extensive network and dedication, she helped us bring our project to a wider audience and increase its visibility beyond the laboratory. She provided continuous encouragement, valuable advice, and unwavering support throughout our journey. Her enthusiasm and belief in our project motivated us to pursue our goals and maximize the impact of our work.

Catherine Edelmann Esseiva: Provided enthusiastic support for our team, as well as being a passionate patient advocate. She connected us with her expansive network, supported us generously with her time and testimony, and provided fast feedback to us whenever we requested it.

CHEMINA

Professor Nako Nakatsuka: Welcomed Alixe and Niel into her laboratory, allowed them to do custom credited projects and shared her expertise in aptamer research, providing valuable guidance and support throughout the project.

Dr. Emily Schafer: Supervised Niel's semester project on organic electrochemical-based transistors and provided her feedback & expertise throughout this process.

Dr. Dat Nguyen: Optimized the aptamer sequence for the E-AB sensor and provided extremely valuable guidance and support throughout the E-AB experiments and experimental procedures.

Alexandra Banbanaste: One of our coaches, Alexandra supervised Alixe's project and supported us throughout the development of our work. She guided us in the characterization of the aptamer sequence, shared her expertise, and provided valuable

advice to help us improve our experiments and overcome challenges. Her continuous support and encouragement were invaluable at every stage of the project. In addition, she contributed to our team identity by designing our team T-shirt.

Sandra Hernández Escobar: Fabricated many wafers of indium oxide transistors, trained and coached Niel to functionalise the transistors on them, and supervised & supported Luciano for the wafer fabrication. Her enthusiastic support and encouragement were extremely motivating for us.

Lianxin Xu: Supervised Alixe's semester project and trained Alixe on the ITC & CD techniques.

Ali Elmorsy: Provided advice on the microfluidic design in discussions with Niel.

Leo Salgado Chane Pane: Inspired the microfluidic design with a design from his lab.

Jessica Empain: Managed Niel, Alixe and Luciano's stay at CHEMINA administratively.

<u>BIOS</u>

Professor Hatice Altug: Provided logistical support and feedback throughout the year.

Jiayi Tan: Provided access to equipment, logistical support, and feedback throughout the year.

Marie Rodriguez: Secretary of the lab that managed approvals for all our expenses and handled many administrative tasks with speed and efficiency.

<u>BCI</u>

Professor Sandro Carrara: Coordinated 3 student projects and provided his valuable insights in the electrochemical approach.

Francesca Rodino: Supervised Silvia's semester project, invaluable guidance and advice on the electrochemical approach

Roberta Grasso: Co-supervised Dámaso's and Nabil's semester project.

Junyan Qian: Co-supervised Dámaso's and Nabil's semester project.

Philippe Abdel Sayed: Provided us training, access, and maintained a wet-lab space for us to develop & test our prototypes.

Cyril Badertscher: Founder of Parkinson Move, one of our sponsors. Also, a patient who provided his testimony and insights.

Luc Levan: President of the Defi Parkinson association: generously agreed to support us financially.

Clémence Bardier-Lefèbvre: The secretary general of *Fondation pour la rechereche en bioologie et medicine*. She managed our relationships with philanthropic foundations and

coordinated administratively with EPFL Philanthropy to ensure we receive the money responsibly.

Louise Ruffini: A member of Parkinson Switzerland, disseminated a questionnaire and supported us.

The Nyon-La Côte Patient Group: Generously invited us into their patient group to discuss our ideas, provide feedback and participate in the study we held. Special thanks to Mr. Privat for coordinating the meetings alongside Dr. Mahul-Mellier.

Mr. André Catana: Provided support and insights on the business plan, especially on IP protection.

Ms. Dejean, Ms. Zatorska, Mr. Bavato, Ms. Timmermans, Ms. Fuzzati, Ms. McIntyre, Aishwarya Gujare: Professionals we interviewed, who provided valuable insights on their various fields.

Dr. André Zacharia, Dr. Julien Bally, Dr. Eric Morel, Dr. Cecile Alexandra Hubsch: Neurologists we interviewed and provided us with valuable insights.

5.3. Sponsors and partners

Défi Parkinson: Generously supported us financially and had very kind words about our project.

Parkinson Move: Generously supported us financially and invited us to a fundraising run that they hosted. Very supportive of our project.

Fondation pour la recherche en biologie et medicine: Generously supported us financially and provided administrative support for philanthropic donations.

EPFL MAKE: Generously supported us financially, and provided the space and resources for prototyping our designs including electrical assembly and test equipment

EPFL CMi: provided logistical support and valuable resources into the TFT microfabrication in their cleanrooms.

RTS: Featured us in an episode of their podcast, provided us with significant publicity.

An Anonymous Donor: Generously supported us financially after hearing our appeal on national radio.

Palmsens: Provided insights during the Meet the Partners event, and provided us with a discount for their products.

Parkinson's Insights: provided insights on user interface and the patient experience.

6. Final remarks

Continued development. Several team members intend to continue this work through an EPFL spin-off beyond SensUs 2026, with the aim of integrating it into an existing laboratory.

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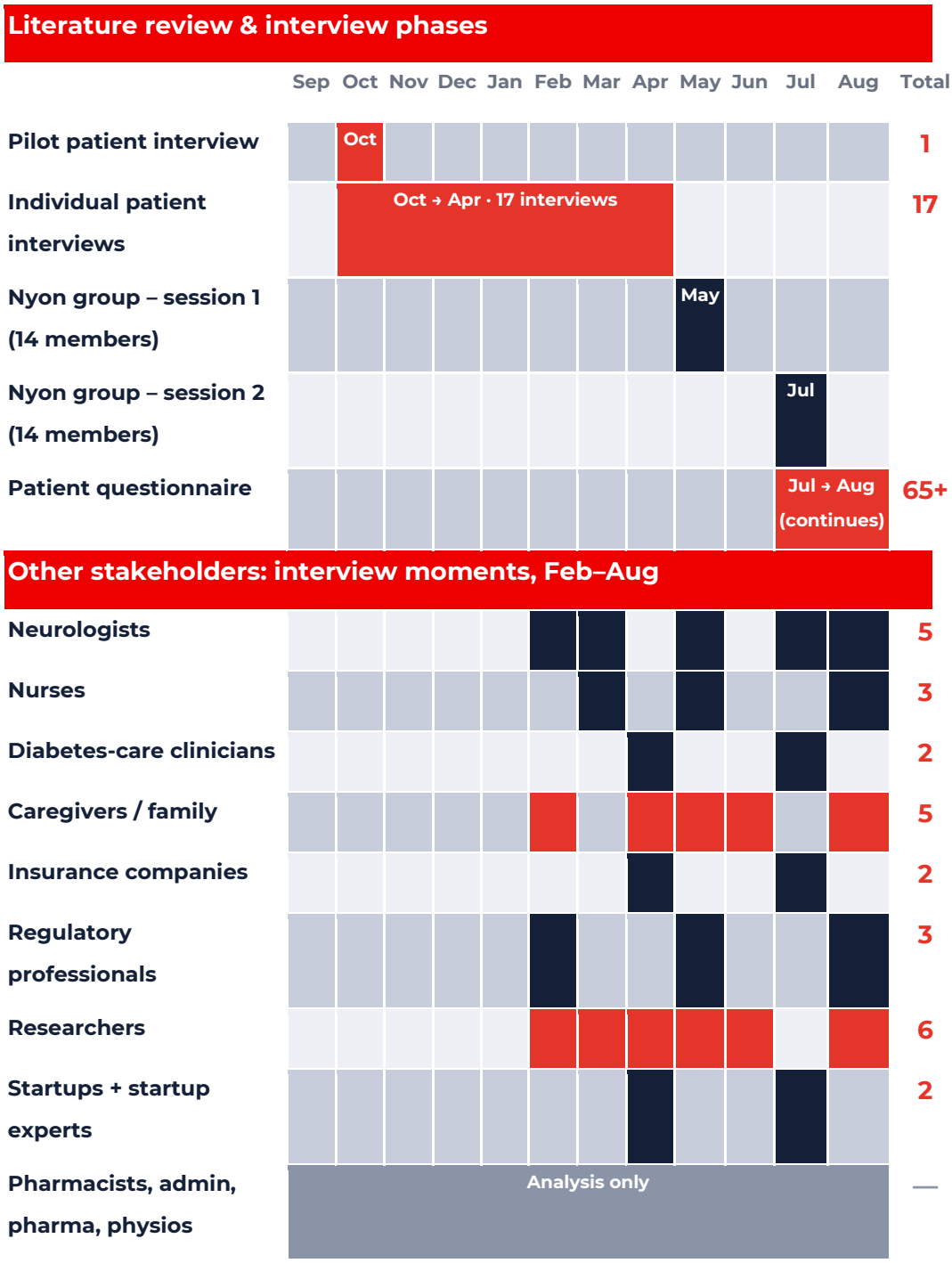
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Appendix

A. Literature Review and Interview Timeline



B. Interview Forms, Conclusions and Quotes

- Link to the Patient Interview Template
- Link to The Patient Consent Form (in French)
- Link to the Doctor Interview Template (First Meeting)
- Link to The Doctor Consent Form (in French)
- Group Specific Question Sets

Stakeholder groups, relevance, and engagement across the PD care	
Stakeholder	**Relevance**
Patients with PD	Want certainty their medication is working; several spontaneously compared the device to a glucose monitor.
Neurologists	All 7 want a symptom-vs-dose report, not raw data; trust needs a validated ISF–symptom correlation.
Caregivers / family	Monitor safety at home; want adherence clarity ('did I take my dose?').
Nurses	Day-to-day medication support; front line for practical usability.
Diabetes-care clinicians	CGM-adoption lessons: trust needs an accepted comparator; not all patients can use apps.
Insurers	Reimburse only on demonstrated falls / ER / hospitalisation reduction, not projected.
Regulators	CE-first pathway; demonstrated effectiveness is decisive for approval.
Pharmacists, admin, pharma, physios	Distribution, procurement & biomechanical relevance; informed by analysis, not interviewed.
Researchers (first paying customer)	Blocked by the missing validated ISF–symptom relationship; named H&Y 3–4 the priority study population.

Interview direct quotes

Neurologists

- "I only see my Parkinson's patients twice a year. I'm making dosing decisions based on what they remember to tell me." *(17.02.26 - CHUV)*
- "I would need to learn to use the data but if it works the concentration level would be of great help" *(08.07.26 - HUG)*

Nurses

- "Patients call in confused about whether a bad afternoon was the disease or the dose. We have no information to help them figure that out." *(24.03.26 - Canada)*

Diabetes-care clinicians

- "The patients need and want very different things, some cannot use a phone and don’t want a continuous sensor, others swear by them" *(02.07.26 - HUG)*
- "During a medical session, we spend a lot of time downloading the data from the reader. There is no centralized app for each sensor brand." *(09.07.26 - HUG)*

Caregivers / family

- "I'm the one who notices when he's freezing up, not him. I wish there was something more objective than 'today looks bad.'" *(08.02.26 - Lausanne)*

Insurance companies

- "We would probably reimburse a continuous monitor if it reduced falls and hospitalizations, show us that data and then we can talk further." *(23.04.26 - Italy)*

Researchers

- "Every trial of a Parkinson's therapy is built on self-reported diaries. That's the biggest confound in the field right now." *(19.05.26 - Lausanne)*
- "If your sensor correlates well with STAT-ON, you've already cleared a bar most wearables never reach." *(03.08.26 - Radboud University)*

Startups / startup experts

- "Your first paying customer probably isn't the patient: it's whoever controls the reimbursement pathway." *(29.04.26 - Spain)*

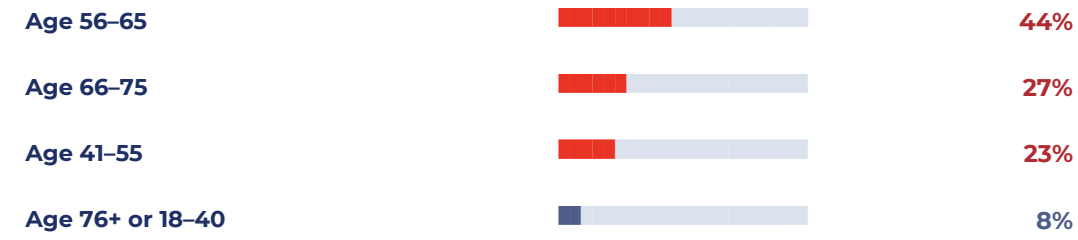
C. Questionnaire Respondent Summary - Patient Needs

BIOSENSE EPFL

Independent survey of people living with Parkinson's on levodopa, mapping who they are, how they take their treatment, and where today's care falls short.

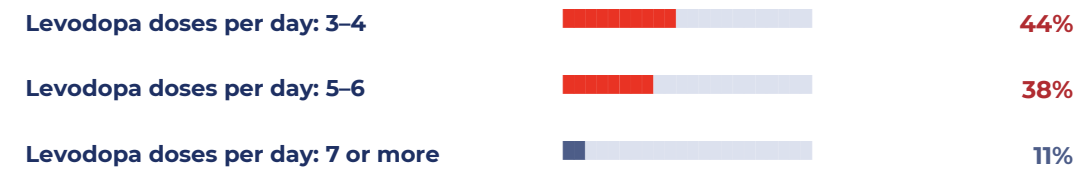
n = 69 patients | EU-wide online survey, 2026 | Self-reported

A Who responded



Also: 64% male · 44% diagnosed >10 yrs, 36% 5–10 yrs · 59% moderate stage, 17% advanced · 81% no deep-brain-stimulation or pump.

B Treatment reality



83%

adjust their own doses at least sometimes

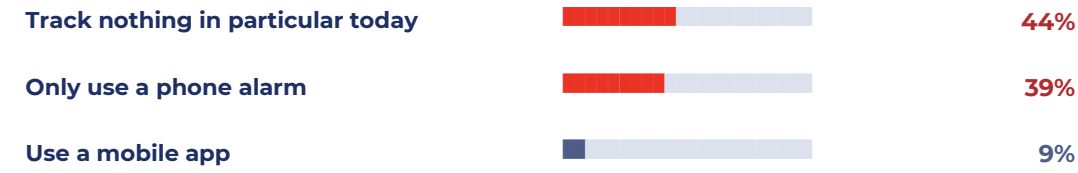
92%

experience symptom fluctuations tied to their doses

89%

are aware of the ~20-min onset delay after a dose

C Monitoring & follow-up gap



83%

72%

52%

feel their neurologist lacks information between visits

see a neurologist only 1–2 times per year

avoid activities (driving, sport, outings) due to fluctuations

KEY INSIGHT · PATIENT DEMAND

92% of patients would wear a continuous levodopa monitor.

The 69-patient survey shows strong, unmet demand for exactly the device BioSense is building.

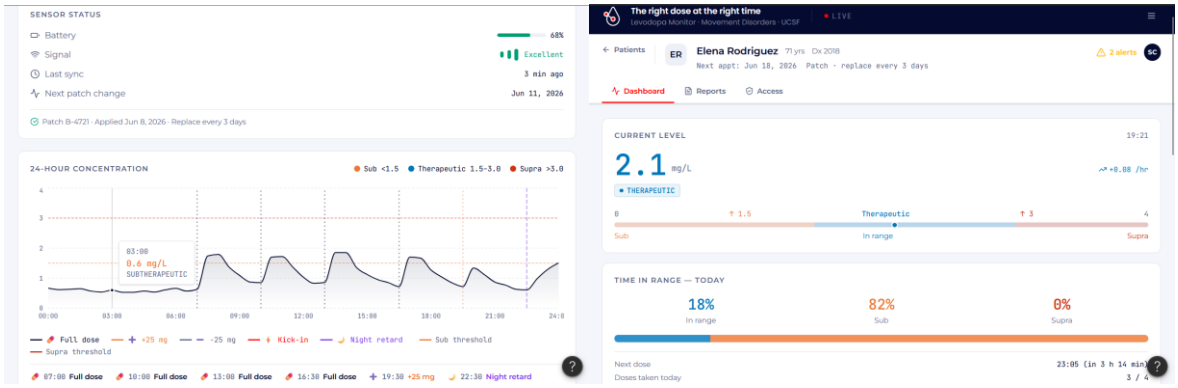
D. LevoDose App

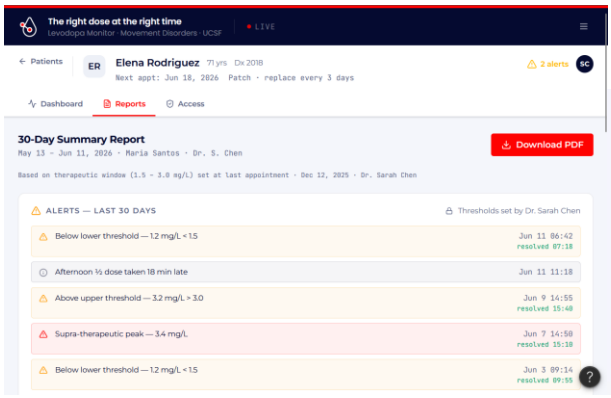
- [LevoDose App for Doctors and Patients](#) *(clickable link)*

To access the Patient App go to one of the patients then click: “Access”, choose between “Basic, Simplified or Complete”, and at the bottom go to “Open Patient Interface”.

To go back to the Doctor’s view go to: “Back” in the top right corner.

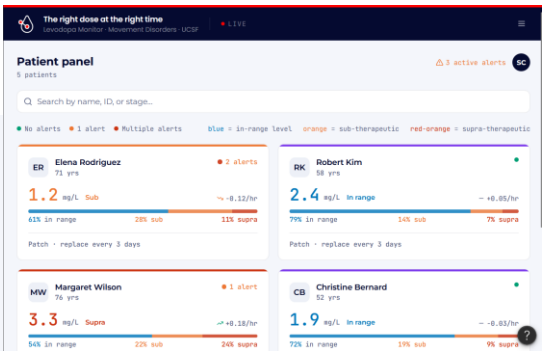
Doctor’s View:



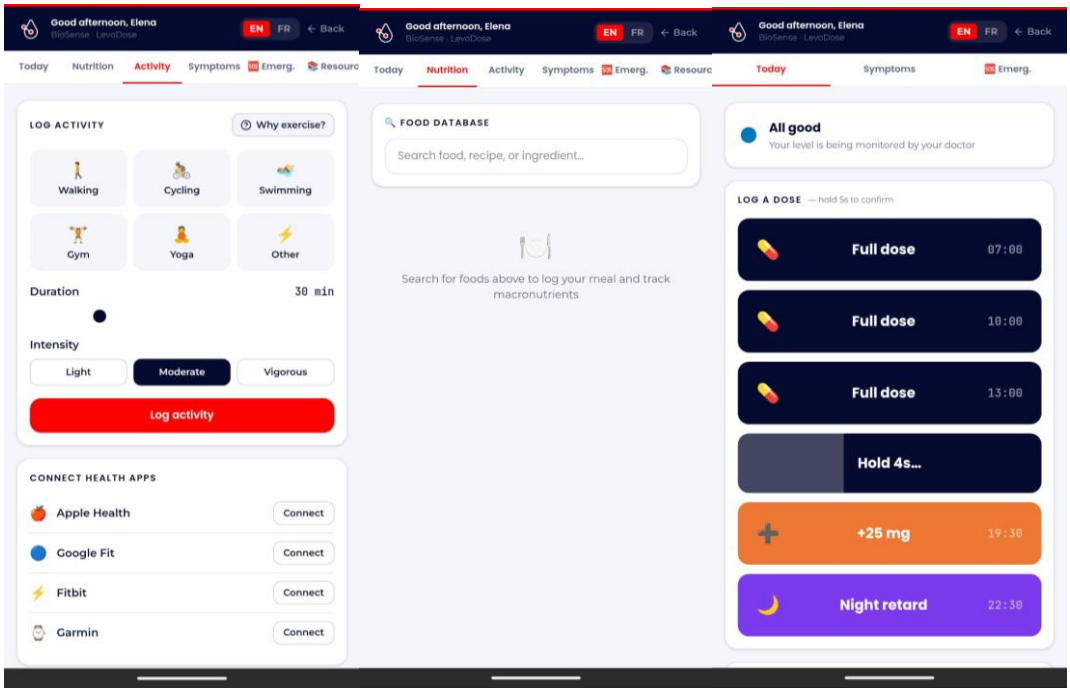


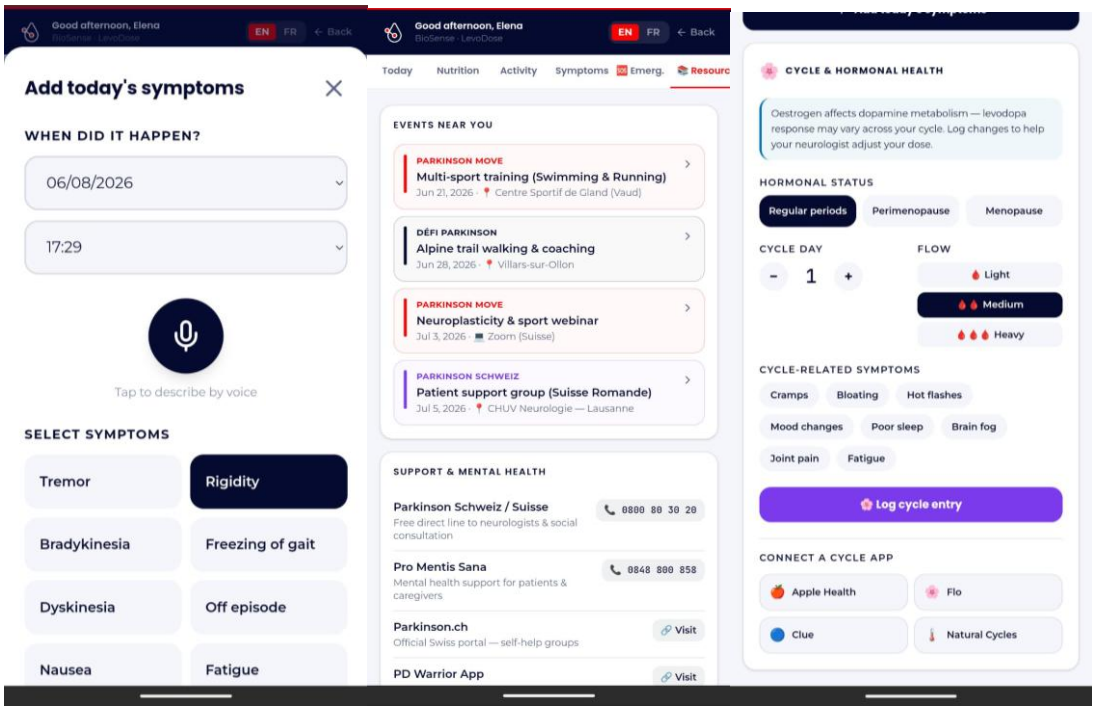






Patient's View:





E. LevoDose App Feedback - MVP Survey Forms and Response Summary

- MVP Sensor Form (in French)
- MVP App Form (in French)



8/11

prefer the Complete mode overall

89%

would act on the app's dose recommendation (8 of 9)

10/11

want the mode chosen jointly with their doctor

Most-wanted feature pages: Symptoms 11 · Nutrition 10 · Activity 10 · Emergency 10 · Resources 6

F. Sensor Wear-Test - MVP Survey Response Summary

BIOSENSE **EPFL**

Patient wear-test of the BioSense capteur - comfort by body placement and everyday movement, size and discretion, and preferences for form, colour and alerts. Bars show mean scores on a 5-point scale.

n = 12 patients | **5-point scale · 1 → 5** | **1 incomplete response excluded**

A Comfort by placement



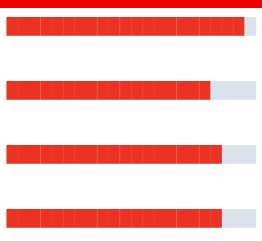
Forearm — during walking (Q3)	4.36
Belly — during walking (Q4)	3.67
Self-applying on the forearm (Q5)	4.00
Self-applying on the belly (Q6)	3.90

B Everyday movements



Sit-to-stand transitions (Q7)	4.46
Raising both arms overhead (Q8)	4.23

C Size, shape & discretion



Overall comfort — Size S (Q9)	4.73
Overall comfort — Size M (Q10)	4.09
Discreet enough to wear in public (Q11)	4.42
Shape didn't hinder movement (Q12)	4.41

D Final preferences

0/11

reports of skin irritation — 100% clear

9/12

prefer Size S

9/12

prefer forearm placement

Preferred colour: skin-tone 9/12. **Most-wanted features:** waterproof 10, LED 9, small display 8.

G. LevoDose Standalone Reader Design



H. Complete Study Synopsis

Analytical Accuracy & ISF-Motor-State Correlation Study	
Parameter	**Description**
Title	Analytical accuracy of continuous ISF-levodopa monitoring against a chemical reference, and correlation with objective motor state and patient-reported wearing-off across the PD severity spectrum
Design	Prospective, single-arm, multi-center observational study with two distinct components: (a) analytical validation, ISF-levodopa readings benchmarked against a chemical reference standard (e.g., microdialysis sampling with plasma/ISF levodopa quantified via HPLC or LC-MS), confirming the sensor measures levodopa concentration correctly; and (b) clinical/downstream correlation, ISF-levodopa trace compared against STAT-ON motor-state classification and patient-reported wearing-off, testing whether ISF levels track symptoms. Conducted per the V3/V3+ framework for biometric monitoring technologies (Goldsack, et al., 2020) (Bakker, et al., 2025);; component (a) reported per STARD 2015 diagnostic-accuracy guidelines, component (b) reported as an observational correlation study (STARD does not apply, since there is no diagnostic ground truth for symptom state)
Population	Idiopathic PD, Hoehn & Yahr stage 1–4, on a stable levodopa regimen, age 40–85, able to give informed consent; recruited across diverse ethnic groups in Switzerland.
Key Exclusion	Dermatological conditions precluding patch wear; cognitive impairment precluding questionnaire completion; concurrent interventional trial participation
Sample Size	n ≈ 30–40 (pragmatic size for an agreement/calibration study; to be confirmed by formal power calculation)
Duration	14-day concurrent wear of BioSense and STAT-ON per patient, with clinic visits at day 0, 7, and 14 for chemical-reference sampling; ~12-month recruitment window across multiple sites
Primary Endpoints	(a) Agreement between sensor-reported and chemically-referenced (HPLC/LC-MS) levodopa concentration, via Bland–Altman limits of agreement (Bland & Altman, 1986, 2007); (b) correlation between continuous ISF-levodopa concentration and STAT-ON motor-state classification)
Secondary Endpoints	Sensitivity/specificity of ISF-derived OFF-episode detection vs. WOQ-9 and STAT-ON; accuracy of adherence-logging vs. observed dosing; patient-facing data visibility (whether real-time access to their own ISF trace affects engagement/retention)
Statistical Analysis	Bland-Altman agreement statistics; correlation/regression of ISF vs. motor-state data; ROC-based sensitivity/specificity
Safety	Minimal-risk; component (a) involves a brief in-clinic reference sample (e.g., microdialysis or blood draw), component (b) is non-invasive monitoring only; no change to standard-of-care treatment or dosing

Regulatory Role	Analytical- and clinical-validation components of the V3 framework, feeding the technical file for CE marking under EU MDR/IVDR (§4.3)

Clinical Applicability (Falls, QoL, and Dosing-Utility) Study	
Parameter	**Description**
Title	Clinical applicability of continuous ISF-levodopa monitoring: falls, quality of life, and dosing-adjustment utility in moderate-to-advanced PD
Design	Prospective, multi-center observational effectiveness study, initiated only once Study 1 confirms adequate sensor accuracy and ISF–motor-state correlation; reported per applicable real-world-evidence and STROBE guidance
Population	Idiopathic PD, Hoehn & Yahr stage 3–4 with documented motor fluctuations and fall history/risk, on a stable levodopa regimen, age 40–85, able to give informed consent; recruited across multiple sites in [country/region] with attention to demographic/ethnic representativeness
Key Exclusion	Dermatological conditions precluding patch wear; cognitive impairment precluding questionnaire completion; concurrent interventional trial participation
Sample Size	To be confirmed by power calculation based on expected fall-rate reduction effect size and Study 1 variance estimates
Duration	Extended wear period of [3–6 months, TBD] per patient, a 14-day window is unlikely to be sufficient to detect meaningful change in falls or QoL; clinic visits at baseline and regular intervals (e.g., monthly) across a ~12–18-month recruitment/follow-up window across multiple sites
Primary Endpoints	Falls/near-falls incidence over the study period; change in quality-of-life score (e.g., PDQ-39) from baseline
Secondary Endpoints	Clinical usefulness: frequency and magnitude of levodopa dose adjustments made using ISF-trend data vs. standard of care; neurologist time-per-patient/workflow impact, given the growing PD patient population relative to slower growth in neurologist supply; patient-reported anxiety/confidence around dosing
Statistical Analysis	Time-to-event/incidence-rate analysis for falls; pre–post comparison of QoL scores; descriptive/comparative analysis of dose-adjustment frequency and clinical decision impact
Safety	Minimal-risk, non-invasive monitoring only; no change to standard-of-care treatment or dosing
Regulatory Role	Real-world clinical-utility evidence supporting the post-market/clinical evidence file for CE marking under EU MDR/IVDR (§4.3), complementing Study 1's analytical and correlation validation

I. Manufacturing cost structure

Manufacturing Cost Structure: Phase 1, research-tier / researcher-as-first-client version of BioSense		
Cost Component	**Description**	**Cost driver / benchmark**
Microneedle array (sensing patch substrate)	Micromolded biocompatible polymer array	Low-cost, high-speed, mass-producible (Hu, Ko, Song, & Xu, 2026)
Electrochemical/aptamer sensing layer	Levodopa-selective functionalisation of microneedle electrodes	Demonstrated at lab scale (Fang, et al., 2022) (Asci, et al., 2022); scale-up cost not yet quoted
Sensor–electronics integration	Alignment and bonding of the sensing layer to the microelectronics/readout circuit	Dominant cost driver of the whole device (Hu, Ko, Song, & Xu, 2026)
Reusable reader electronics	Flexible printed circuitry (PET/TPU substrate), BLE module, battery	Suited to high-volume, low-cost fabrication (Hu, Ko, Song, & Xu, 2026)
Packaging & biocompatible encapsulation	Skin-contact housing, adhesive	Comparable to existing wearable CGM patches

External benchmark. Abbott's FreeStyle Libre 3 Plus, a commercial single-use continuous glucose monitoring (CGM) sensor with a simplified electronics design, retails at roughly $85–120 (≈£65–90) per 15-day sensor without insurance (SingleCare, 2026) (GoodRx, 2026), equivalent to an annualized retail price of roughly $2,070–2,920/year (≈£1,570–2,220/year). Hu et al. (2026) cite a manufacturing cost of approximately $100 per 15-day unit for this sensor family, meaning retail price sits close to, and only modestly above, estimated manufacturing cost, consistent with the industry's known thin per-unit margins on disposable CGM sensors, which are typically offset by reader/subscription revenue rather than patch sales alone.

Because BioSense's disposable patch uses the same broad microneedle-array manufacturing approach, the ~$100/15-day figure is a realistic cost target ceiling to design toward once BioSense's own bill of materials is finalised, not a comfortable cost floor with wide margin built in. No BioSense-specific manufacturing quote exists yet, since a functional sensor has not been built (§4.2); the figures above are literature-derived benchmarks, not proprietary quotes, and should be treated as an order-of-magnitude target rather than a final costing.

J. Cost–benefit evaluation: researchers as first paying customer

Comparable, already-commercialised PD motor/symptom research-tier wearables give a verified price anchor for what academic and clinical research groups currently pay for continuous PD monitoring in general (NICE, 2024, as reported in Rodríguez-Martín & Pérez-López, 2024):

Cost-Benefit evaluation: researchers as first paying customer			
Device	**Sensors**	**Price (research-tier)**	**Data provided**
PDMonitor™	5 body-worn	~£350/month (~£4,200/yr,≈$5,500/yr)	ON/OFF, bradykinesia, dyskinesia, tremor, FoG, gait, inactivity
STAT-ON™	1 waist	~£1,600/year (≈$2,100/yr)	ON/OFF, bradykinesia, dyskinesia, FoG, gait, falls, inactivity
BioSense (Phase 1 RUO, proposed)	**1 patch + reader**	**Target: £1,600–£4,200/yr (≈$2,100–5,500/yr), (anchored to above)**	**Continuous ISF–levodopa concentration + adherence trace (not measured by any device above)**

Neither PDMonitor™ nor STAT-ON™ measures levodopa exposure directly; both are motor-symptom monitors. They therefore define the price ceiling a research group is already willing to pay for continuous PD monitoring in general, not a directly competing product, a favourable comparison for BioSense's own RUO pricing.

Cost to researcher: anchored to the range above, BioSense RUO pricing at or below £1,600–4,200/year (≈$2,100–5,500/year) per device would remain attractive to grant-funded academic budgets. Cross-referencing against Appendix A, this annual price range sits at or above the ~$2,070–2,920/year (≈£1,570–2,220/year) annualized manufacturing-cost target: pricing toward the lower end of the range would leave thin margins similar to those seen in commercial CGM disposables, while pricing toward the upper half (closer to the PDMonitor™ anchor) leaves a more comfortable margin. As with any early-stage device, margins are expected to be thin at low sales volume and to improve as manufacturing scales. Final margin will depend on BioSense's own bill of materials once confirmed against Section A.

Benefit to researcher: BioSense would be the first device to provide continuous ISF-levodopa data directly, rather than only motor-symptom proxies, letting researchers

reduce reliance on costly, labour-intensive Hauser-diary and repeat clinic-visit data collection, which existing literature shows correlates poorly with objective measures (as cited in Rodríguez-Martín & Pérez-López, 2024).

Net case: even priced near the top of the comparator range, a research group avoids the recurring labour cost of diary transcription and repeat clinic visits, while gaining data (a direct ISF–symptom correlation) unavailable from any existing device on the market, the evidence this Phase 1 stage is specifically designed to generate.

K. Development Timeline

	Phase 1 RUO		Phase 2 Observational		Phase 3 Decision support				Phase 4 Dosing		
Workstream/year	**2026**	**2027**	**2028**	**2029**	**2030**	**2031**	**2032**	**2033**	**2034**	**2035**	**2036**
Functional sensor prototype											
MVP: patch + app + dashboard											
First users: research labs - RUO revenue											
Study 1 · analytical accuracy & ISF–motor correlation											
Study 2 · clinical applicability (falls, QoL, dosing)											
CE mark - EU MDR, Class IIb											
Decision-support & dosing rollout											

L. Market Selection

Validate in Switzerland, launch where ties exist, and scale on one dossier.

Market Selection: Reasoning				
Market	**Role**	**Pros**	**Cons**	**Decision**
Switzerland	Foundation & validation	Zero-cost validation via EPFL / CHUV / CSEM; legal, IP & spin-off home ('health valley')	Small market (~15k patients); dual (non-EU) regulatory track	HQ & validation. Not first sales
Netherlands	First market. Pilot (pre-CE)	Warmest ties; single EU-MDR track; NZa + 'Veelbelovende Zorg' pilot funding	Clinical investigation first (MDR Art. 62)	First commercial launch
Germany & France	EU scale-up	Largest EU base (DE); Paris Brain Institute (FR); same MDR dossier reused	DE reimbursement slow; FR a cold start	Scale after CE. No new submission
United Kingdom	Free ride-along	Covered automatically once the EU-MDR CE mark exists	—	No separate decision needed
US, Japan & beyond	TBD	Large, prevalent markets	Costly; local-entity rules; no relationships; US FDA ~$3–5M, 2.5–5.5 yr	Out-license after CE + NL/EU data