Team Results Document

Cornell SensTech

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SensUs

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Parkinson's Disease

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1. Abstract

Cornell SensTech has developed a prototype biosensor for continuous L-DOPA monitoring to support more personalized Parkinson's disease management. Current monitoring relies on intermittent blood draws and symptom diaries, which can miss rapid "on-off" fluctuations caused by changing medication levels. Our sensor measures L-DOPA in interstitial fluid, a skin-accessible fluid that can reflect drug changes without repeated blood sampling. During development, we introduced several technical innovations: a five-layer electrode stack in which gold nanoparticles and PANI accelerate electron transfer, tyrosinase selectively oxidizes L-DOPA, and Nafion and PEG hydrogel membranes reject interferents and biofouling; a 24 µL microfluidic cartridge that exchanges samples across the electrode, enabling continuous measurement on a single sensor with a 3.53 µM limit of detection and excellent linearity (R^2 > 0.98); a 26.3 × 7.2 × 1 mm wireless potentiostat achieving 12-bit voltage control and 16-bit current resolution; and an adaptive algorithm that recalibrates the sensor from its own recent signal history to correct drift. Readings stream to a patient and clinician-facing app offering symptom tracking, accessibility features, food logging, and future prediction of "off" periods. Altogether, the platform connects novel biochemical monitoring with practical Parkinson's care.

2. Biosensor Developed for the Eindhoven Testing Event

2.1. Molecular recognition

Our design utilizes a multilayer dual nanocomposite/enzyme-based system combined with an electrochemical sensing approach to selectively measure L-DOPA concentrations in interstitial fluid (ISF). The gold working electrode is coated in a thin layer of gold nanoparticles (AuNP) that serve as a conductive material and increase the surface area of the electrode, accelerating the transfer of electrons (Zakiyyah et al., 2025). The electrode is then functionalized with the enzyme tyrosinase, which catalyzes the oxidation of L-DOPA into dopaquinone, producing a measurable electrochemical signal that can be used to quantify the concentration of L-DOPA in the ISF (Tesoro et al., 2023; Mollamohammadi et al., 2023).

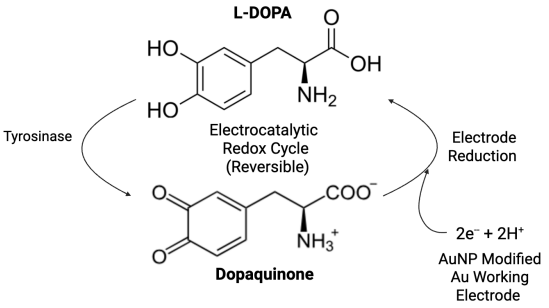


Figure 1: Electrocatalytic Redox Cycle Diagram. Figure made in BioRender.

The active site of tyrosinase contains two copper ions, making it selective toward catechol-containing molecules, such as L-DOPA, ensuring the specificity of our developed biosensor (Fan et al., 2021; Goodarzi et al., 2024). As well, L-DOPA levels in ISF are significantly higher than that of other catechol derivatives such as dopamine, which are seen to remain at baseline before and after L-DOPA administration around the nanomolar scale (Nord et al., 2017; Zhou et al., 2025). Furthermore, our interference panel works to allow us to differentiate the signal measured from L-DOPA from other catechol-containing molecules, ensuring specificity.

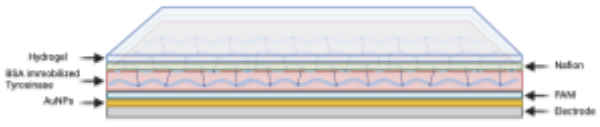


Figure 2. Nanocomposite tyrosinase sensor design layout. Figure made in BioRender.

A thin layer of Polyaniline (PANI) is applied between the gold and enzyme layers, aiding in the immobilization of tyrosinase and electron transfer to the electrode (Dhand et al., 2010). The tyrosinase was crosslinked with Bovine Serum Albumin (BSA) and Glutaraldehyde and coated with a thin layer of Nafion to increase the durability of the enzyme function and to improve the selectivity of our sensing mechanism (Migneault et al., 2004; Chen & Gu, 2007; Alizadeh et al., 2026) (5). Finally, the system was coated with a layer of polyethylene glycol (PEG) hydrogel to act as an anti-fouling and hydration layer. This prevents the binding of dermal proteins in ISF to the sensor matrix, which prevents the sensor from functioning properly (Sarao, 2025).

2.2. Physical transduction

Commercially available gold electrodes were selected as the electrochemical transduction platform because of their high conductivity, biocompatibility, chemical stability, and ease of surface modification (Ling et al., 2020). Gold nanoparticles (AuNPs) were immobilized on the electrodes using a self-assembled monolayer (SAM), increasing the electrochemically active surface area and facilitating electron transfer to improve sensor sensitivity and signal reliability (Li et al., 2020; Shein et al., 2009). During the oxidation of L-DOPA, electron transfer is facilitated through the AuNPs on the electrode, producing a measurable current related to the L-DOPA concentration [3].

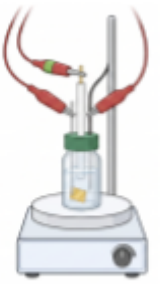


Figure 3: Experimental Testing Setup

Square-wave voltammetry of 12 µM L-DOPA in PBS produced a well-defined oxidation peak at approximately 0.30 V vs. Ag/AgCl (step height 10 mV, pulse amplitude 25 mV, frequency 20 Hz), consistent with reported values for L-DOPA oxidation at gold and modified carbon electrodes. This peak potential was used to guide the selection of the chronoamperometric operating potential, chosen to be 0.4 V (Figure 4).

Chronoamperometry (CA) was then performed at this fixed potential, producing a strong L-DOPA response while limiting interference from compounds such as ascorbic acid and uric acid. The final results report the sensor sensitivity (R^2), and response time; the SWV operating-potential response, CA response, and calibration curve with its linear fit can be seen in Figures [4]–[6].

2.3. Cartridge technology

The cartridge (Appendix D) is designed as a low-volume microfluidic flow cell that positions each ISF sample directly over the active sensing region of the electrode. The continuity of this design is achieved through reversible enzymatic recognition, rapid mass transport through the electrode stack, and controlled fluid exchange through the cartridge. The cartridge contains a 24 µL microfluidic reservoir that forms a well over the working, reference, and counter electrodes. The reservoir measures 8 mm × 6 mm × 0.5 mm and includes rounded edges with a 1.5 mm radius. The rounded geometry was chosen to reduce stagnant regions and dead volume, since residual L-DOPA trapped in corners could contribute to carryover between consecutive samples and affect the current response of the next measurement. The reservoir contains two 0.89 mm ports that connect the cartridge to the pumping system. One port functions as the inlet for incoming ISF, while the second port functions as the outlet to remove the previous sample and direct waste away from the sensing chamber. This geometry allows each sample to pass across the electrode surface in a controlled direction rather than being manually pipetted onto the sensor. Because the chamber volume is smaller than the expected sample volume, the remaining sample can be used to fully exchange the reservoir contents and reduce carryover from the previous measurement. Additionally, the pump mechanism is used as a secondary system to ensure that the contamination from previous samples is minimized.

During each sampling cycle, the fluid is pumped through the inlet until the 24 µL chamber is filled and the sensing region is completely covered. Flow is then slowed to allow for L-DOPA to diffuse to the immobilized tyrosinase layer. The hold time is determined experimentally based on the response time of the full electrode stack, including the PANI, enzyme/BSA/glutaraldehyde, Nafion, and PEG layers. After the current reaches a stable value, the sample is flushed through the outlet and replaced with the next ISF sample. Continuous biosensing is performed by maintaining the biosensor in the microfluidic chamber while a constant potential is applied to the working electrode using CA (Goud et al., 2019). Tyrosinase is used to catalyze the oxidation of L-DOPA to dopaquinone, and the electrode then reduces the generated dopaquinone back to L-DOPA, creating an electrocatalytic redox cycle (Crapnell & Banks, 2023; Tesoro et al., 2023). Because the enzyme is regenerated after each catalytic cycle and the electrochemical/enzymatic reactions are reversible, the measured current tracks the L-DOPA concentration in the fluid currently occupying the chamber. When the incoming L-DOPA concentration increases, the steady-state current increases; when the concentration decreases, the current returns toward its previous baseline after the chamber is exchanged and the electrode re-equilibrates. Continuous operation therefore relies on three linked design features: reversible enzymatic recognition, rapid mass transport through the electrode stack, and controlled fluid exchange through the

cartridge. Rather than replacing the sensor between measurements, the system repeatedly exchanges the fluid inside the reservoir, allowing consecutive ISF samples to be measured over the testing period using the same electrode surface.

2.4. Reader instrument and user interaction

Our device is based on a custom potentiostat featuring a wireless module that runs square wave voltammetry and chronoamperometry (CA) on our electrode system. It spans 26.3 × 7.2 × 1 mm and achieves a 12-bit analog voltage output resolution, 16-bit analog-to-digital current measurement resolution, an $R^2 > 0.98$, and a limit of detection (LOD) of 3.53 uM, while streaming readings wirelessly to a phone for real time display. The clinician-reviewed app provides separate patient and clinician portals through an interface shaped by preferences expressed by Parkinson's patients like display screen settings (customizable text size, audio reader), symptom trends history, community hub, and a privacy considerate AI chatbot along with connection status display, alerts, and medication reminders. Patients' levodopa concentration trends are displayed in the app after denoising the CA signals via Savitzky-Golay filtering and baseline correction. The processed current measurements are then converted into levodopa concentrations by applying the Cottrell equation followed by a linear calibration curve. We hope to implement personalized predictive models that will learn patients' trends to identify "on-off" fluctuations along with app modes controlling sampling frequencies catered to the instability and results of patients' recordings' trends. In the future, users will wear a factory-calibrated microneedle patch that continuously monitors levodopa concentrations without user intervention and automatically syncs with the application.

3. Biosensor Innovation

3.1. Wearable sensor

Patients with Parkinson's disease require frequent monitoring of their levodopa levels, since motor symptom severity tracks closely with drug concentration in the body. Current clinical practice relies primarily on intermittent blood draws and patient-reported symptom diaries, neither of which captures the rapid pharmacokinetic swings responsible for "on-off" motor fluctuations, where patients cycle between adequately controlled and poorly controlled symptom states as plasma levodopa rises and falls. Because these fluctuations can occur within a narrowing therapeutic window as disease duration and treatment length increase, there is a clear clinical need for continuous, real-time measurement of drug concentration rather than discrete snapshots. Our long-term vision is a wearable biosensor that continuously tracks levodopa concentration in interstitial fluid (ISF), giving patients and clinicians a real-time view of drug levels that can be correlated with dosing schedules and symptom onset.

What makes this concept novel is not a single new material or reaction, but the re-engineering of a chemistry we have already validated on a flat benchtop electrode into a wearable form factor without discarding any of the validated performance. Most reported wearable L-DOPA platforms use either a purely non-enzymatic voltammetric approach (fast, but less selective) or a single-modality enzymatic approach. Our concept keeps the full five-layer benchtop recognition stack intact, a stack that was originally designed for selectivity against a five-compound interferent panel (dopamine, ascorbic acid, uric acid, 3-O-methyldopa, and carbidopa; see Section 3.2) and asks only "how small can this stack become, and how does it stay hydrated and unfouled once it's on a needle instead of a disc." That reframing is what lets us reuse our existing fluidics, PCB, and firmware almost unchanged, rather than redesigning the whole device around a new sensing chemistry.

The microneedle array (Appendix D) is designed to penetrate just past the stratum corneum into the dermis, making continuous contact with ISF rather than requiring a discrete blood draw. This has precedent: a wearable microneedle sensor using square-wave voltammetry and chronoamperometry at unmodified and tyrosinase-modified carbon-paste electrodes has already demonstrated continuous, minimally invasive L-DOPA detection in artificial ISF, validated in a skin-mimicking phantom gel and upon penetration through mouse skin (Goud et al., 2019). We chose ISF over sweat or saliva because it sits physiologically closer to blood and is far more accessible than blood itself, since it is readily available in the dermis and hypodermis where nearly all blood analytes can also be found. This makes a microneedle interface a reasonable middle ground between the invasiveness of a blood draw and the poor blood correlation of sweat- or saliva-based sensing. The broader feasibility of this approach is also supported by work highlighting microneedles as a promising

platform for personalized, minimally invasive sensing and sampling applications (Baker-Sediako et al., 2023). Recent perspectives on continuous protein monitoring in ISF emphasize its potential as an accessible biofluid for tracking physiologically relevant biomarkers over time, further supporting ISF as the sensing medium for continuous monitoring

The main open challenge for wearability is signal drift at the skin interface, a recognized weak point for enzyme-based microneedle sensors over long wear times. One mitigation we can potentially explore is encapsulating the sensing layer inside a hollow microneedle rather than coating the outer shaft, reducing direct fouling of the enzyme layer while still allowing ISF to diffuse in (Baker-Sediako et al., 2023; Saifullah, 2023). Additionally, to address this issue in our design alone, we encapsulate our sensor within a hydrogel matrix. This helps maintain hydration around the enzyme, reduce exposure to fouling species, and stabilize mass transport of L-DOPA to the sensing layer during continuous monitoring (Tehrani et al., 2022).

The wearable concept reuses the same three functional layers as our benchtop system: sample handling, electrical, and software (Chen, 2020). All are reorganized around the microneedle form factor rather than rebuilt from scratch, which is itself part of the innovation: it lets a design validated on the bench carry forward its calibration behavior and interfere rejection into the wearable form, instead of re-deriving sensor performance from zero. For biomaterials, we propose a carbon-paste working electrode modified with immobilized tyrosinase, which catalyzes L-DOPA oxidation, paired with an Ag/AgCl reference electrode and a platinum counter electrode. Because this reaction produces current tied to the instantaneous rate of substrate turnover rather than cumulative buildup, it naturally supports continuous, real-time readout.

For transduction, the three-electrode system connects to a PCB, where a small applied potential drives the enzymatic oxidation of L-DOPA and reads the resulting current as a concentration proxy. We are prototyping this on a Teensy 3.1, running firmware for square-wave voltammetry to find the oxidation potential and chronoamperometry to track concentration over time, using 12-bit voltage control and 16-bit current measurement to balance accuracy with a compact footprint.

For readout, we validate the hardware before trusting a reading by swapping in a resistor for the electrochemical cell and confirming the current matches Ohm's Law across the applied potentials, which catches drift before it looks like a real signal change (Bian et al., 2021). The raw signal is then cleaned with Savitzky-Golay filtering and a best-fit line approximation. Processed readings stream to an app with separate patient and clinician views, where patients see their trends and self-report symptoms while clinicians monitor multiple patients and can reach them directly through emergency messaging.

3.1.1. Technological novelty of wearable sensor

Our wearable levodopa sensor combines unique molecular recognition techniques with a compact device design to target accurate and efficient instrument readings and user accessibility.
The novelty of our design lies in the integration and sequential stacking of multiple layers of the nanocomposite. The electrode surface is first coated with AuNPs to increase surface area and facilitate electron transfer to the electrode. A conductive PANI layer is then placed on top to provide a stable layer for tyrosinase immobilization while maintaining conductivity for electron transport. Tyrosinase is the catalytic element that selectively catalyzes L-DOPA to dopaquinone, which generates the electrons that are transferred. The tyrosinase is stabilized by co-crosslinking the enzyme and BSA with glutaraldehyde. A thin layer of Nafion is then coated on top to selectively repel negatively charged species and minimize interference. Lastly, the PEG hydrogel layer is coated to reduce biofouling and support long term function in ISF. The design is further complemented by utilizing both SWV and CA into the same sensing workflow to characterize the signal produced by the nanocomposite. SWV is first used to accurately establish the optimal oxidation potential of L-DOPA, after which CA is performed at the optimal potential to continuously quantify L-DOPA concentrations in real time.

Utilizing sample handling, electrical, and software components, our biosensor demonstrates our device design novelty. Our 7.2 by 26.3 mm sample handling prototype sits on top of our three-electrode system (working, reference, and counter electrodes) where fluid will flow through and collect over the sensing area.

Our design includes a pump mechanism that is integrated with the sampling prototype to ensure a continuous flow of fluid so new measurements are not impacted by previous samples. For the electrical component, the three-electrode system connects directly to the PCB, which is a design comparable to traditional CGM-style continuous sensors, which are now highly accepted as an effective form of diabetes management (Chen et al., 2017). Through applying a small voltage on the potentiostat, users are able to read current calculated levodopa levels from the sensor. Using the Teensy 3.1 and firmware support standard voltammetric methods with 12-bit voltage control and 16-bit current measurements, our design ensures accurate measurements and sensor wearability with its compact sizing. For the software component, our design includes a novel validation method of comparing our current potentiostat reading to a resistor in place of the electrochemical cell to ensure our reading matches Ohm's Law prediction across applied potentials. Not only does our device secure accurate readings, it also combats external noise through Savitzky-Golay filtering and best fit-line approximations. These individual components work together to guarantee that our device provides the most accurate and efficient readings while also ensuring sensor wearability.

Our device also ensures user accessibility on the software side, through the implementation of user-friendly platforms for both doctors and patients to use with customizable audio and text-size options. On our user interface, patients are able to read their sensor readings as well as self-report symptoms for the doctor to view on their profile. There's also a feature predicting off-periods based on test-users' historical Levodopa concentration level data along with recent instabilities, enabling preventative measures.

3.1.2. Technical feasibility of wearable sensor

Square Wave Voltammetry (SWV) was performed on our modified gold electrode in 12 µM L-DOPA in PBS, scanning 0 to 0.80 V vs. Ag/AgCl with a 10 mV step height, 25 mV pulse amplitude, and 20 Hz frequency. The differential current shows an oxidation peak at approximately 0.30 V vs. Ag/AgCl (Figure 4). This satisfies that L-DOPA produces a measurable electrochemical response on our sensor.

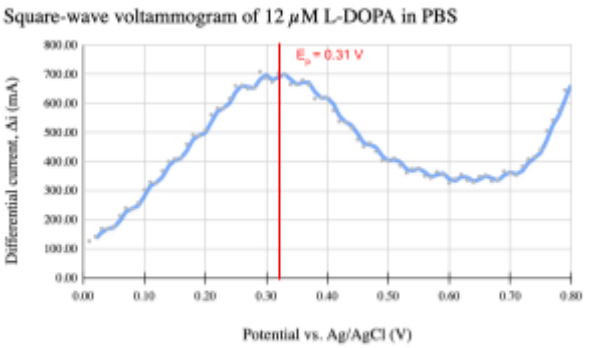


Figure 4: Square-wave voltammogram of 12 µM L-DOPA in PBS at a [AuNP/PANI-modified] gold working electrode. Scan from 0 to 0.80 V vs. Ag/AgCl, step height 10 mV, pulse amplitude 25 mV, frequency 20 Hz.

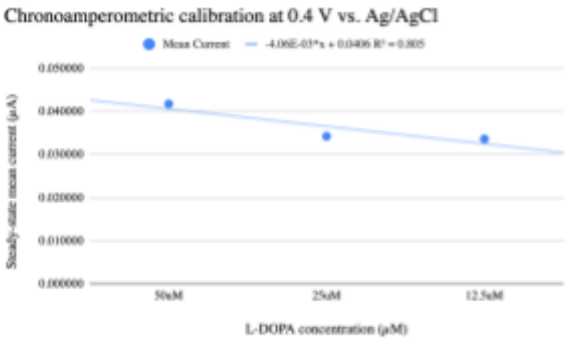


Figure 5: Chronoamperometric calibration of electrode for L-DOPA in PBS at 0.4 V vs. Ag/AgCl

Chronoamperometry was then performed at 0.4 V vs. Ag/AgCl which was selected as the potential because of the SWV peak. Steady-state current was extracted by averaging over a fixed 1.5 second window beginning 6.0 seconds after onset, applied identically to all concentrations. This window was chosen due to a clear plateau being exhibited here suggesting total L-DOPA oxidation. The 25 to 50uM interval was well resolved with a difference of 7.39uA; however, the 12.5 to 25uM interval had a minimal difference. The sensor therefore demonstrated a measurable concentration-dependent response and further testing will confirm this. The current vs concentration was then plotted to yield a calibration curve that can be used to assess unknown concentrations of L-DOPA depending on current when 0.4 V are applied (Figure 5).

3.2. Reliability of sensor output

Interstitial fluid contains several molecules that oxidize at nearly the same potential as L-DOPA, making selective detection challenging. The primary interferents include ascorbic acid and uric acid, as well as molecules directly related to L-DOPA therapy, including dopamine and 3-O-methyldopa (L-DOPA metabolites) and carbidopa, which is commonly co-administered with L-DOPA (Probst et al., 2024; Sajid et al., 2015). Tyrosinase-based sensors further complicate this problem because tyrosinase broadly oxidizes catechols and phenolic compounds (Zaidi et al., 2014). As a result, dopamine and other catechol-containing metabolites undergo the same enzymatic reaction rather than being selectively excluded by the recognition chemistry. We address this interference problem through the multilayer electrode stack described in Section 3.2.1 and through interferent panel testing described in Section 3.2.2.

Beyond this interference-driven inaccuracy, continuous sensors introduce two additional sources of unreliability that are not solved by interferent rejection alone. First, enzymatic drift is a relevant issue where tyrosinase activity gradually declines over the sensor's operating lifetime due to intrinsic enzyme instability, which can cause the current output to fall over time even when the true L-DOPA concentration is unchanged (Bounegru & Apetrei, 2023). To address this, we implement an adaptive baseline correction algorithm that continuously re-estimates the sensor's expected baseline from its own recent signal history, rather than comparing every reading to a single fixed value set at manufacture. Second, electrode fouling may occur when oxidative reaction products or other adsorbed materials accumulate at the electrode surface during repeated measurements, blocking electroactive sites and reducing signal quality (Russo et al., 2021). To mitigate this risk, the pump-driven fluid-exchange system for sample handling described in Section 2.3 will periodically flush the sensing chamber between measurement cycles. Flow-assisted removal of surface residues has been shown to improve the regeneration and long-term stability of microfluidic electrochemical electrodes (Qiang et al, 2010).

3.2.1. Technological novelty of reliability concept

Electrode Surface Stack Integration

The main novelty of our concept lies in shifting L-DOPA quantification from a laboratory-based measurement to continuous, real-time monitoring in interstitial fluid, while maintaining a level of reliability appropriate for clinical decision-making. Current gold-standard methods, such as chromatographic analysis of blood plasma, require invasive blood sampling and involve delays between sample collection and result availability. Our sensor is designed to close this gap by enabling repeated, minimally invasive measurements directly from the body over time. This is achieved through the integrated design of the electrode surface stack, rather than through any single component in isolation. The combination of a gold nanoparticle-modified surface with a conductive PANI interlayer is designed to sustain efficient electron transfer over repeated redox cycles, which is what allows the sensor to track concentration continuously rather than producing a single endpoint signal, as is typical of conventional enzymatic assays. The crosslinked tyrosinase layer, combined with a Nafion selectivity membrane, is intended to preserve enzymatic specificity for L-DOPA over extended use while limiting interference from structurally related electroactive species present in interstitial fluid, a reliability requirement that does not apply to single-use laboratory assays, which do not need to sustain performance over time. Finally, the outer PEG hydrogel layer addresses the challenge of biofouling, which would otherwise progressively degrade a device intended for multi-day use but is not a concern for a single blood draw.

Adaptive Software Algorithm

Although the electrode stack slows sensor degradation, it cannot eliminate it entirely. To account for this, we developed an adaptive baseline correction algorithm that continuously recalibrates the sensor using its own recent measurements instead of relying on a fixed calibration from when the sensor was first manufactured. Over a rolling 18–24 hour window, the algorithm tracks the sensor's typical minimum and maximum current, which represent its current operating range. It then compares this range to the range measured when the sensor was new and rescales future readings accordingly. Because the algorithm only tracks how the sensor's output changes over time, it automatically corrects for both the gradual loss of sensitivity caused by enzyme degradation and baseline shifts caused by surface fouling, without needing to model either process separately. The rolling window only uses past data, allowing the correction to run in real time on the device, and is long enough that normal L-DOPA fluctuations average out while slow sensor degradation remains

visible. The full implementation, simulated dataset, and evaluation are provided as a GitHub link in the Appendix B.

3.2.2. Technical feasibility of reliability concept

The technical feasibility of our reliability concept depends on whether the electrode stack can selectively filter interferents, maintain enzymatic activity over repeated measurements, and sustain reproducible signals across electrodes and trials. The sensor detects L-DOPA concentrations through its layered electrode design, where each layer serves as a critical element when generating a signal. Initially, when the L-DOPA diffuses past the PEG hydrogel and Nafion layers, this step is crucial for filtering out similar molecules or biofouling of the sensor that could hinder the results of the signal. The PEG hydrogel primarily acts as an anti-fouling and hydration later, while Nafion serves as a permselective membrane that helps reject negatively charged interferents such as ascorbic acid and uric acid. To ensure that the signal is the product of just L-DOPA, we will test our biosensor with an interferent panel including ascorbic acid, uric acid, dopamine, 3-O-methyldopa, and carbidopa. These compounds are relevant because they may be present in biological fluid, may oxidize near similar potentials, or are directly related to L-DOPA therapy.

Once L-DOPA reaches the tyrosinase layer, tyrosinase catalyzes its oxidation to dopaquinone. For this reaction to continue occurring accurately over time, we must ensure that the tyrosinase's enzyme activity does not decline. We will evaluate enzyme stability by repeatedly measuring a fixed L-DOPA concentration over time and calculating the percentage of signal retained after repeated measurement cycles and storage. Stored electrodes will be compared against freshly prepared electrodes to quantify retained activity. To evaluate the adaptive baseline algorithm, we will compare corrected vs. uncorrected signal trends over a multi-day repeated-measurement period, assessing whether the correction reduces apparent drift in a fixed L-DOPA standard relative to the raw, uncorrected signal. Then the AuNP-coated electrode reduces the dopaquinone back to L-DOPA, where the electron transfer is measured as a signal. This layer of gold nanoparticles increases the electrode's reactive surface area, improving electron transfer between the redox product and the electrode, and increasing the measurable current response.

Consistency is essential for each electrode because this signal must be reproducible, so variability between electrodes does not shift the calibration curve (Zhou & Liu, 2026). Reproducibility will be evaluated by fabricating multiple electrodes using the same protocol and comparing their calibration slopes, baseline currents, and L-DOPA responses. Low electrode-to-electrode variability would support the feasibility of using a shared calibration curve, while high variability would indicate that each cartridge requires individual calibration.

The key feasibility metrics will include sensitivity, linear range, limit of detection, response time, percent signal change after interferent addition, percent signal retained after repeated measurements, and electrode-to-electrode coefficient of variation. These values will be reported as sensitivity =0.23 μA/μM, R^2 = > 0.805, and LOD = 3.53 μM.

The main technical risks are reduced L-DOPA diffusion through an overly thick PEG/Nafion coating, loss of tyrosinase activity over time, and variability introduced during manual electrode fabrication. These risks will be addressed by optimizing coating thickness, testing repeated-use enzyme stability, and comparing calibration behavior across independently prepared electrodes. This approach allows us to evaluate whether the sensor can produce L-DOPA measurements that are sufficiently selective, stable, and reproducible for reliable output.

3.3. Original contributions

3.3.1 Team Captains

The team developed a biosensor concept centered on tyrosinase-catalyzed oxidation of L-DOPA and a multilayer three-electrode nanocomposite system. During the design process, the team evaluated multiple sensing approaches, including dual DNA aptamer electrode systems and prior nanocomposite-based designs. Although these alternatives provided useful design insight, the aptamer approach was limited by uncertainty around L-DOPA specificity and higher projected manufacturing costs, while previous nanocomposite systems lacked the novelty and disease-specific adaptation required for this year's competition. After multiple design iterations, literature review, technical feedback, and team-led evaluation, SensTech selected a tyrosinase-crosslinked nanocomposite electrode system as the most promising route for continuous L-DOPA monitoring.

The team conceived, refined, and integrated the core sensing approach, including the layered electrode stack, SWV/CA electrochemical workflow, microfluidic sample-handling concept, and Parkinson's-focused mobile interface. Coaches and advisors provided guidance on feasibility, experimental planning, and technical direction, but the team was responsible for selecting the final concept, adapting it to the SensUs Parkinson's disease theme, and developing the prototype-level implementation described in the Innovation section of the TRD. This work demonstrates the team's original contribution in combining enzyme-based L-DOPA recognition, nanocomposite electrochemical transduction, continuous measurement strategies, and patient-centered software into a unified biosensor platform.





Matthew Kiewski (Wet Lab Lead) Alexis Charles (Hardware Lead) Vinesha Shaik (Software Lead)

3.3.2 Team Supervisor

The SensTech team met regularly throughout the year to evaluate sensing strategies for the 2026 SensUs Parkinson's disease challenge. Early discussions considered several possible approaches for L-DOPA detection, including aptamer-based systems and adaptations of previous nanocomposite electrode designs. After reviewing the technical limitations of these approaches, the team selected an enzyme-based electrochemical platform centered on tyrosinase-catalyzed oxidation of L-DOPA.

The final concept developed by the team uses a multilayer nanocomposite electrode stack that combines gold nanoparticles, PANI, immobilized tyrosinase, Nafion, and PEG hydrogel to support L-DOPA detection in interstitial fluid. The team also designed the supporting cartridge, electrochemical workflow, reader concept, and Parkinson's-focused user interface. Coaches and advisors provided feedback on technical feasibility, experimental planning, and design direction, but the core concept selection, design iteration, and prototype development were carried out by the student team.

Over the course of the project, the team showed independence in adapting the sensor to this year's L-DOPA target, identifying relevant reliability challenges, and integrating wet lab, dry lab, and software components into a single biosensor platform. Their work reflects a thoughtful progression from literature review and concept generation to a prototype-level system designed for continuous L-DOPA monitoring and eventual use in Parkinson's disease management.



Warren Zipfel (Team Supervisor)

3.4. Bonus criteria Innovation

Continuous concentration data is only as valuable as what a patient can do with it. We have developed personalized predictive models that learn each patient's levodopa trends from their own historical recordings and use recent signal instability to forecast approaching "off" periods before motor symptoms emerge. Because baseline levels and medication responsiveness vary widely between patients and disease stages the models are patient specific rather than population based: each user's history defines their own normal. We're working on having the prediction layer also drive adaptive sampling modes in the companion app. When a patient's recent trend is stable, the device samples sparsely, conserving power and reducing electrochemical stress on the enzyme layer; when instability is detected, sampling frequency automatically increases to resolve the fluctuation. This transforms the biosensor from a passive monitor into an anticipatory tool enabling preventive action, and reframes sampling frequency itself as a controllable design variable rather than a fixed specification. On another aside, L-DOPA absorption is strongly affected by meals, dietary protein, and constipation, since levodopa competes with dietary amino acids for intestinal transport. This revealed a technical challenge not initially recognized, a physiologically real dip in ISF levodopa after a high-protein meal is indistinguishable, at the sensor level, from enzymatic drift or fouling, and a reliability strategy that "corrects" such a dip would erase clinically meaningful information. The response was to integrate a food log into the companion app so dietary events are time stamped alongside concentration data, giving both our adaptive baseline algorithm and the clinician a way to separate sensor artifacts from true pharmacokinetic variation. This turns a confound into a feature: over time, a patient's logged meals and measured responses map their individual diet–medication interactions, information no current tool captures. Reliable chemistry means little if the electronics drift. During prototyping, a hardware validation protocol was developed in which the electrochemical cell is replaced by a known resistor and the measured current is checked against Ohm's-law predictions across the full range of applied potentials . This cleanly separates electronic faults from electrochemical signal changes.. We propose extending this into an onboard self-test: a reference resistor integrated into the wearable PCB that firmware switches in at startup, allowing the device to verify its own measurement chain before each wear period. Because the concept is independent of analyte and recognition chemistry, it generalizes to any wearable potentiostat, giving it impact beyond L-DOPA sensing.

4. Translation potential

4.1. Customer interviews

Before starting outreach, we mapped the people involved in L-DOPA treatment — patients, caregivers, providers, payers, researchers, and more — and wrote a semi-structured question set for each, calibrated to what that person could speak to firsthand. Going in, the underlying technology was already settled: a wearable biosensor for continuous, real-time Levodopa monitoring. What we hadn't settled on was where in the Parkinson's care journey this device would create the most value, and what a realistic path to adoption and reimbursement would look like. Those two open questions (use case and business model) shaped every guide we wrote, from the pain points we explored with patients to the decision-making processes we asked payers and providers about. The semi-structured format kept interviews comparable across stakeholder types while leaving room to follow up on anything unexpected. Full interview guides are included in appendix A. Notable quotes pulled from our interviews can be found in appendix B.

Determining Use Case

To best understand the problem itself, our interviews began directly with patients and those working closest to them to explore if continuous L-DOPA tracking could be beneficial as a more quantitative means of enabling patients to track and better manage their medications and symptoms. We explored the possibility of simply notifying patients when L-DOPA levels dipped beyond a particular threshold. However, speaking to people, like John Smith (pseudonym) the founder of a specialized Parkinson's exercise and healthcare facility, who works with Parkinson's patients daily and a former physical therapist of 50 years, we quickly began to understand that L-DOPA baseline levels and responsiveness to medication largely vary by person and by the stage of disease progression. Moreover, Smith underscored the paucity of companies seeking to innovate within the Parkinson's space within the U.S., placing further emphasis on the need for innovation and technological improvement, along with the widely open market, within this space. From there, we spoke with a husband, battling Parkinson's, along with his spouse, who acted as his caretaker, to better understand how the disease affects them on a daily basis. The spouse emphasized two key problems, which we went on to place great emphasis on in the development of our biosensor:

1) Current means of determining L-DOPA medication dosages are insufficient. The spouse described how current means require that her husband be "starved" of medication.

2) Caregivers dedicate inordinate amounts of time recording patient symptoms (typically done every 30 minutes) — in what are known as Hauser Diaries — throughout the day due to patient's lack of interoception (i.e. their inability to process internal bodily signals) due to the disease, which the spouse characterized as "almost a full-time job."

It was through this understanding that we began to evolve the purpose of our biosensor and hypothesize that the current market lacks a diagnostic tool to enable proper dosage prescriptions of L-DOPA along with no current technology to efficiently enable the recording of Hauser Diaries.

Seeking to broaden our perspective and gain further evidence for a need within this area, we shifted our interview focus towards physicians and experts. Interviewing academics, like Jack Williams (pseudonym), a psychology Ph.D. candidate who works closely with patients and healthcare professionals in his research. We learned that physicians truly have no effective means of determining L-DOPA medication dosaging, corroborating the existence of the dosing challenge mentioned by the patient. He characterized the current process as largely "trial and error." When interviewing one neurologist, they confirmed the lack of current means of personalizing L-DOPA dosages along with emphasizing the need for technology to simplify Hauser Diaries. The neurologist noted how diaries, while helpful, can be messy and frustrating to quickly and easily analyze. Moreover, diaries can often suffer from practical flaws within the data itself. The neurologist's discussion of symptom tracking compliments what Williams emphasized regarding the heavy burden placed on caregivers to help patients track their symptoms. Williams had mentioned how patients largely fluctuate between "on" (when medication controls symptoms) and "off" (when symptoms control medication) states, making it important — yet difficult— to record symptoms, especially given the patient's lack of interoception.

It was through these interviews that we began to understand the significance of caretakers in patient health. This information turned us towards a new approach of expanding the purpose of our biosenor: not merely as a diagnostic tool but also as a lifestyle tool. As much potential that we saw in the biosensor's role in healthcare, we also questioned the challenges, like that of symptom recording for caretakers, that existed at the intersection of the disease and the daily lives of the patients. Thus, we sought to go back to expand our patient interviews with an emphasis on understanding their daily needs. From interviewing a pool of patients, we learned that Parkinson's patients are often afflicted with depression, become socially isolated, and face a quickly changing family dynamic. These ideas were confirmed by healthcare professionals, like Jane Jones (pseudonym) and Natalie Brown (pseudonym). Jones is a Social Worker and Brown is a Nurse Practitioner at a Parkinson's Disease & Movement Disorders Institute. Jones and Brown not only confirmed these but also went on to provide practical advice on designing our technology. Their discussion was heavily focused on the need for the UI of the technology to be accessible not only to Parkinson's patients with impaired motor symptoms but also to a generally older target audience. Importantly, they also noted how L-DOPA absorption is largely affected by meals, protein intake, and constipation.

Synthesizing our interviews into actionable steps, our team took steps to design an app, which would receive the data from the biosensor and display it with the following integrated into the app.

- Tri-layer User Ecosystem that provides a suitable platform for patients, caretakers/spouses, and physicians to coordinate on patient care
- Features allowing patients and their caretakers/spouses to easily record patient symptoms and observations to alleviate the burden on both parties
- Historical tracking to determine baseline levels of L-DOPA and prescribe personalized dosages
- Food log to provide physicians with better context into responsiveness to L-DOPA medication
- Accessibility features, like voice readers, larger buttons, and an easy-to-use interface were prioritized with common Parkinson's symptoms (e.g. dyskinesia) and the target demographic of older populations in mind.
- Community based features to enable patients to find resources for Parkinson's in their local region to combat the social isolation and changing lives often faced by patients

4.2. Design of validation study (max. 2 pages)

Selection of the Problem

Stakeholder interviews identified a central limitation in current Parkinson's care: clinicians lack an objective and continuous method for connecting a patient's L-DOPA exposure with changes in symptoms over time. Medication adjustments are therefore informed largely by brief clinical assessments, patient recollection, and handwritten symptom diaries. Patients may struggle to recognize symptoms such as dyskinesia accurately, while caregivers often spend considerable time documenting behavioral and motor changes. Clinicians also reported that food intake, constipation, medication timing, and disease progression can influence treatment response, making incomplete symptom records difficult to interpret.

Based on these findings, we defined the selected problem as the absence of a practical home-monitoring system that combines continuous L-DOPA measurements with structured patient and caregiver observations. This information gap limits clinicians' ability to identify wearing-off periods, distinguish insufficient treatment from adverse effects, and personalize medication schedules. The interviews further showed that any proposed system must account for the motor, visual, and technological challenges experienced by an older Parkinson's population. These findings directly informed the development of the SensTech use case.

Conceptual Design and Use Case

SensTech consists of a continuously wearable microneedle patch that measures L-DOPA concentrations and transfers the data to a connected digital platform. The platform includes separate interfaces for patients, caregivers, and clinicians. Patients can review simplified medication trends and complete short symptom check-ins. Authorized caregivers can record observable symptoms, receive missed check-in notifications, and support medication adherence. Clinicians can review longitudinal L-DOPA measurements alongside medication timing, meals, and patient- and caregiver-reported symptoms.

The system is intended to support, rather than independently determine, clinical treatment decisions. By presenting objective biochemical measurements together with contextual symptom data, our sensor could help clinicians recognize patterns that are not visible during isolated appointments. The patient interface uses large touch targets, text-and-icon status indicators, stacked response buttons, read-aloud functions, and adjustable text sizes. These features were selected specifically to reduce difficulties associated with tremor, bradykinesia, impaired contrast sensitivity, and limited familiarity with smartphone technology.

Validation Study Design

Because the functional biosensor was not yet available for extended patient testing, we isolated two critical assumptions for validation:

1) Patients and caregivers can use the app interface to document symptoms more efficiently than a conventional diary
2) Combining simulated continuous L-DOPA measurements with symptom reports improves clinicians' interpretation of treatment response.

The first study involved 10 people with Parkinson's disease and their primary caregivers. Participants completed standardized symptom-recording tasks using both a conventional Hauser diary-style form and the SensTech prototype. The order of the two systems was randomized. Participants recorded medication intake, meal timing, and symptoms including tremor, rigidity, dyskinesia, fatigue, digestive health, and medication "off" periods. We measured task-completion time, completion rate, input errors, number of symptoms recorded, perceived burden on a five-point scale, and System Usability Scale scores. Short semi-structured interviews were conducted after all our testing to explain participants' ratings.

The prototype produced a 60% higher task-completion rate and fewer recording errors than the diary format. Participants completed the structured check-in more quickly and rated it as less burdensome. Patients particularly valued the large buttons, simplified wording, and read-aloud function. Caregivers reported that a separate observation portal would eliminate the need to maintain extensive handwritten notes. Participants also emphasized that patient and caregiver entries should remain visibly distinguishable and that the patient should control who can access their information. Configurable reminders were preferred over mandatory notifications.

The second study involved six healthcare professionals with experience in Parkinson's care, including neurologists, nurse practitioners, and allied healthcare professionals. Each participant evaluated standardized patient scenarios under two conditions. The first condition displayed medication timing and conventional symptom-diary entries. The second displayed the same information together with simulated continuous L-DOPA trends and separately labelled patient and caregiver observations. We measured interpretation time, confidence in identifying wearing-off or dyskinesia on a five-point scale, agreement between clinicians, and whether the participant would recommend a treatment review.

Clinicians interpreted the combined-data scenarios more consistently and reported greater confidence in identifying clinically relevant treatment-response patterns. The continuous trend display was considered most useful when aligned with medication intake, meals, and symptom timing. Participants stated that the system could support earlier and more informed treatment reviews, particularly when patients were unable to describe symptom fluctuations reliably. However, clinicians strongly preferred filtered summaries over unrestricted streams of raw data and configurable alerts to reduce alert fatigue. They also emphasized that

SensTech should flag patterns for review to discuss with a clinician rather than generate autonomous dosage recommendations as that could be dangerous to the patient and exacerbate side effects of L-DOPA usage.

Conclusions and Design Changes

The validation study supported the usability and perceived clinical value of the proposed system. Results indicated that short, button-based symptom check-ins could reduce documentation burden, while caregiver observations could improve the completeness of records. The clinician study suggested that combining symptom reports with continuous L-DOPA measurements could improve the interpretation of treatment-response patterns compared with symptom diaries alone.

Several design changes were made in response. Patient and caregiver observations are now displayed as separate data sources, reminder frequency can be customized, and the clinician portal prioritizes summarized trends and clinically relevant deviations. Access permissions remain controlled by the patient, and the platform does not recommend medication changes automatically. Future validation will use a functional biosensor to assess measurement accuracy, long-term adherence, patch comfort, agreement with reference L-DOPA measurements, and whether the system improves real clinical decisions over an extended monitoring period.

4.3. Bonus criteria Translation Potential

Determining the Business Model

We began by interviewing patients and clinicians — the stakeholders who would use and pay for the technology directly. A patient managing his "off" periods with an abundance of phone alarms pushed back on an assumption we'd carried in: he expected the companion software bundled with the device itself, saying he abandons health tools that "nickel and dime" him — a view two-thirds of the patients we later spoke with shared. Additionally, a neurologist raised another concern: under fee-for-service billing, fewer in-person visits could mean less revenue for his practice, making continuous monitoring a harder sell to physicians even if it improved patient outcomes.

On the payer side, a reimbursement specialist at a regional health plan explained that FDA clearance alone isn't enough — securing Remote Patient Monitoring (RPM) coverage would require evidence the device reduces total costs, most convincingly through fewer fall-related ED visits, and that hardware and software should bill under a single combined code to avoid claim denials. This offered a partial answer to the revenue concern raised earlier: RPM-specific billing codes compensate providers for time spent reviewing monitoring data between visits, giving practices a path to recoup revenue that fee-for-service wouldn't capture.

Moreover, it ought to be noted that some patients expressed hesitation about constantly needing to wear a biosensor, noting concerns about skin irritation, inconvenience, and apprehension regarding changes in lifestyle. Thus, in response to these concerns, our team designed a patient usage and purchasing model that minimizes the need for continuous wear while still providing healthcare providers with the data necessary to optimize L-DOPA dosing. The patient usage and purchasing model involves the use of the biosensor for about 3 weeks at a time (which would require a replacement of the biosensor approximately once) or however long it takes for their healthcare provider to determine optimal dosages of L-DOPA medication for the patient. Given that a proper dosage is determined and that no issues arise regarding the determined dosaging, patients could follow up in 3-4 months and rewear the device for another period of time to determine if any changes in dosage are necessary and understand disease progression. If the patient is unhappy with the dosage or feels that the dosage is too strong or too weak, they can quickly follow up with their provider and determine a plan of action, which might involve rewearing the patch to determine a new dosage. This business model on the scale of the individual patient is intended to balance clinical utility with patient convenience and comfort in order to maximize patient acceptance and optimize patient purchase/use frequency.

Go-To-Market Strategy

We also sought to understand how revenue could be generated and sustained over time. A clinical trial coordinator described pharmaceutical sponsors as eager to replace costly periodic blood draws used in L-Dopa clinical trials with continuous pharmacokinetic data, pointing to a B2B trials channel that could fund development ahead of a slower consumer and payer rollout. Beyond who would pay, we needed a realistic path to a first sale. A hospital procurement director explained that large health systems utilize a Value Analysis Committee to approve new devices, a process that can take 9–12 months, and recommended starting with independent neurology practices instead, where purchasing decisions move faster. Sustaining longer-term consumer revenue, however, would depend on distribution: a pharmacy director noted that recurring patch refills should be automated and routed through a pharmacy, rather than the clinic, since patients tend to abandon wearables if reordering is a hassle.

Together, these conversations pointed us toward our model: device and software sold as one bundle, reimbursed through RPM codes tied to reduced ED visits, launched first through independent neurology practices to sidestep hospital procurement delays, and funded early through pharmaceutical trial partnerships.

Nevertheless we determined that entry into large health systems would still be favorable later on. Our justification for this would be the fact that no other entity is able to put the device in the hands of hundreds to thousands of eligible patients at the scale that a health system is able to do. Moreover, as a product spreads throughout respected large health systems, it not only becomes a part of standard care but also gains credibility amongst other physicians and, more notably, insurers. While, again, integration of the device into large health systems is a costly and time-intensive endeavor, it stands as a favorable step following the aforementioned launch in order to gain a pathway to broader payer adoption.

5. Team and Support

5.1. Contributions of the team members

Business & Outreach:
Ian Chang: B&O team lead; Helped construct IP section.
Sofia Mykytenko: Contributed to stakeholder outreach through cold outreach and interviews, gathering insights for our validation planning; helped construct IP section

Wet Lab:
Matthew Kiewski: Wet Lab Lead; Led weekly meetings throughout the year, helped to finalize sensor design, and contributed to producing deliverables. He is next year's President.
Lauren Willson: Helped to complete deliverables and finalize sensor design. She is next year's Vice President
Andrew Lebowitz: Helped to complete deliverables and finalize sensor design. He is next year's Wet Lab Lead.
Jerry Jin: Helped to complete deliverables and finalize sensor design

Dry Lab:
Vinesha Shaik: Helped to design a full-stack app, predictive algorithm and signal processing pipeline. She is next year's Dry Lab Software Lead.
Alexis Charles: Helped to develop dry lab components, create CAD models and finalize sensor design. She is next year's Dry Lab Hardware Lead.

5.2. People who have given support

Nayan Banerjee: Provided guidance on biosensor development and help to educate members on usage of machinery and novel lab techniques. Provided use of lab space and equipment.
Kelphart Lab: Provided guidance and supervision for biosensor synthesis. Provided use of lab space and equipment.

5.3. Sponsors and partners

Cornell University's College of Engineering Student Project Teams Organization has aided in providing the team with lab space, funding support, and team member recruitment processes. The team is currently in the process of acquiring sponsors, and does not currently have any other outside support.

6. Final Remarks

Over the past year, Cornell SensTech carried a levodopa biosensor from concept to a working benchtop system, a tyrosinase based multilayer electrode with a demonstrated concentration dependent response, a microfluidic cartridge for continuous sampling, custom wireless potentiostat hardware, and companion software designed around the people who will actually use it. The competition is only a milestone, not the finish line. Our next steps are innovative: translating our validated electrode stack to the microneedle wearable format, completing interferent, stability, and reproducibility testing, and executing our validation study, as well as translational:: bundled device and software pricing, remote patient monitoring reimbursement, and first deployment through independent neurology practices.What shaped us most, however, were not electrodes but conversations. Sitting with patients, caregivers, and clinicians taught us that a biosensor succeeds only if it eases real daily burdens like the trial and- error of dosing, the near full time job of symptom diaries, the isolation that accompanies this disease. That perspective turned our device from a measurement tool into a care tool, and it is a lesson we will carry beyond this project.

We are deeply grateful to our advisor, Professor Zipfel, and our coaches Nayan Banerjee and Professor Ibrahim for their guidance. To the Cornell departments and sponsors whose support made this work possible; and above all to the Parkinson's community of Tompkins County, whose openness and honesty shaped every design decision we made. We look forward to Eindhoven, and to learning from teams around the world working toward the same goal: better lives for our patients.

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8. Appendix

Appendix A: Full Interview Guides

This appendix presents comprehensive, semi-structured question guides for each stakeholder group relevant to ParkinSense, our continuous biosensor for monitoring L-DOPA levels in Parkinson's disease patients. Not all questions need to be asked in every interview — these guides serve as master templates to ensure thematic depth and consistency across interviews.

A note on approach: *these guides are built for open-ended customer research, not full concept validation. Questions focus on current behaviors, workflows, decision-making processes, and unmet needs. Deliberately avoid asking stakeholders directly whether they would pay, reimburse, or purchase at a specific price — those signals should be inferred from what stakeholders share about current costs, alternatives, and decision criteria, not asked for outright.*

1. Parkinson's Disease Patients on Levodopa Therapy

A. Diagnostic Journey

- When and how did you first notice symptoms that led you to a Parkinson's diagnosis?
- What symptoms or changes prompted you to see a doctor?
- Can you walk us through the steps of your diagnostic journey? Which specialists were involved?
- How long did it take before you received a definitive diagnosis?
- Were there misunderstandings or delays during that process?

B. Starting and Adjusting Levodopa

- When did you start levodopa therapy, and how was your initial dose determined?
- How often has your dosing schedule changed since you started?
- Who typically initiates those changes — you, a family member, or your doctor?
- How often do you and your neurologist review or adjust your regimen?
- What has the process of finding "the right dose" felt like for you?

C. Living with Motor Fluctuations

- Can you describe what an "off" period feels like for you?
- How predictable are your on/off fluctuations throughout the day?
- How do you currently know a dose is wearing off, before symptoms become noticeable?
- Have you experienced dyskinesia (involuntary movements)? How do you tell it apart from other symptoms?
- What do you currently do, if anything, to track or anticipate these fluctuations (apps, journals, alarms, routines)?

D. Daily Life and Routine

- Walk us through a typical day, from your first dose to your last.
- How does medication timing affect your ability to work, socialize, drive, or run errands?
- What activities have you had to modify or give up because of unpredictable symptoms?
- How do meals, exercise, sleep, or stress affect how well your medication works?

E. Care Experience and Support

- What emotional or social support (family, support groups, social workers) have you received?
- How would you describe communication between your neurologist and other providers you see, like physical therapists or nurses?
- In your view, what are the biggest pain points in current Parkinson's care?

F. Wearable Levodopa Monitoring

- How important would continuous insight into your levodopa levels be for your peace of mind or daily decisions?
- What concerns or reservations would you have about wearing a device like this?
- What would it need to show or alert you to in order to actually change how you manage your day?
- Who else — family, caregiver, doctor — would you want to see this data, and how?

2. Caregivers of Parkinson's Patients

A. The Caregiving Role

- How did you come into a caregiving role, and how has it evolved over time?
- What does a typical day look like for you as a caregiver?
- How much of your time goes toward managing medication timing versus other caregiving tasks?

B. Observing Symptom Fluctuations

- How do you notice when your patient's medication is wearing off?
- What signs do you look for, and how reliable do they feel?
- Has a fluctuation ever caught you off guard? What happened?

C. Medication Management

- How involved are you in administering or reminding about levodopa doses?
- What tools or systems do you currently use to track dosing and timing (pill organizers, alarms, apps)?
- What happens, practically, when a dose is missed or delayed?

D. Emotional and Practical Burden

- What has been the hardest part of supporting someone through unpredictable symptoms?
- How has caregiving affected your own work, health, or social life?
- What kind of support — respite care, support groups, social workers — have you sought or used?

E. Communication with the Care Team

- How do you communicate what you observe at home to the neurologist or care team?
- Do you feel your observations are captured and used in treatment decisions?
- What would make it easier for you to share this information?

F. Wearable Levodopa Monitoring

- Would having objective data on medication levels change how you support your loved one day to day?
- What would you want a device like this to alert you to?
- What concerns would you have about a device like this — for your loved one, or for yourself as a caregiver?

3. Neurologists

A. Diagnosis and Treatment Planning

- What tests or criteria do you use to diagnose Parkinson's disease?
- How do you decide when to initiate levodopa therapy versus other treatment options?
- What does a standard treatment plan and titration schedule typically look like?

B. Levodopa Titration and Dosing Strategy

- How do you determine and adjust a patient's levodopa dose and schedule?
  - What signals do you rely on to know a regimen isn't working — patient-reported, observed, or other?
  - How much do you weigh what a patient tells you versus what you observe in the exam room?
- How often do you see patients during titration, and how does that cadence change once they're stable?
- Why isn't levodopa response measured more objectively or frequently today, and what barriers exist?

C. Monitoring Motor Fluctuations

- How do you currently assess "on/off" fluctuations and dyskinesia between visits?
- How reliable do you find patient diaries or self-reports of these fluctuations?
- Which additional signs or tools do you rely on to guide treatment adjustments?

- If a patient reports a fluctuation but isn't due back for weeks, how do you respond?

D. Advanced Therapies and Escalation

- At what point do you consider advanced therapies, like deep brain stimulation or infusion pumps?
- What role does understanding a patient's fluctuation pattern play in that decision?

E. Wearable Levodopa Monitoring

- Do you see advantages to continuous, objective levodopa level data in your clinical decision-making?
- What would this data need to show, and at what frequency, to be clinically useful rather than noise?
- What evidence or validation would you want to see before recommending this to patients?
- Could you connect us with other neurologists or movement disorder specialists for follow-up interviews?

4. Movement Disorder Physical Therapists

A. Practice and Patient Population

- What proportion of your caseload is Parkinson's patients, and at what stages of disease?
- How does a typical treatment plan differ for someone early versus later in their levodopa treatment?

B. Assessing Motor Fluctuations Functionally

- How do you assess whether a patient's mobility issues stem from medication timing versus disease progression?
- What do you observe physically when a patient is "off" versus "on"?

C. Coordination with Medication Timing and Care Team

- How do you communicate your functional observations back to the neurologist?
- What's the biggest disconnect you see between what happens in the clinic or gym and what the neurologist sees during a visit?

D. Wearable Levodopa Monitoring

- Would objective levodopa level data change how you plan or time sessions?
- What features or data would be most useful to you as a physical therapist?
- What concerns would you have about a wearable device for patients with mobility or dexterity challenges?

5. Parkinson's / Movement Disorder Specialty Nurses

A. Clinic Workflow

- Walk us through a typical patient visit: what's assessed, how long it takes, and who's involved.
- How many times per year do patients typically come in, and how much time do you spend per patient?
- What do you do when a patient calls between visits reporting new or worsening symptoms?

B. Patient Education on Medication Timing

- How do you educate patients and families on levodopa timing and factors like food or protein intake?
- What are the most common points of confusion or non-adherence you see?
- How do patients typically track their doses and symptoms at home today?

C. Monitoring and Follow-Up

- What do you currently rely on to assess whether a patient's regimen is working between visits?
- Are you involved in any home-monitoring programs? How much time does reviewing that data take?

D. Wearable Levodopa Monitoring

- How would continuous levodopa data change how you triage patient calls?

- Which patient groups do you think would engage with an associated app, and which wouldn't?
- What interface or alert information would be most useful to you day to day?

6. Social Workers Supporting Movement Disorder Patients

A. Patient and Family Support

- What kinds of support do you typically provide to Parkinson's patients and their families?
- What are the most common practical or emotional challenges you help navigate?

B. Care Coordination

- How do you coordinate with neurologists, nurses, and other providers on a patient's care plan?
- Where do you see the biggest gaps in communication or continuity of care?

C. Resource Navigation, Access, and Equity

- What barriers do patients face in accessing specialist care, therapies, or new technologies?
- How does cost or insurance coverage factor into the recommendations you're able to make?
- What concerns would you have about equitable access to a new monitoring device like this?

D. Wearable Levodopa Monitoring

- Where do you see this kind of technology helping, or potentially adding burden, for the patients you work with?
- What would need to be in place — support, education, financial assistance — for patients and families to realistically use a device like this?

7. Parkinson's Disease Researchers

A. Research Focus and Current Studies

- What is your current research focus within Parkinson's or movement disorders?
- What role does levodopa response or motor fluctuation data play in your work?

B. Use of Biomarkers and Measurement in Research

- How do you currently measure or estimate levodopa levels or motor fluctuations in your studies?
- What are the limitations of current measurement approaches — patient diaries, UPDRS scoring, wearable accelerometers?
- Have you seen studies limited or complicated by poor measurement quality?

C. Data Collection Challenges

- What challenges arise when integrating wearable or sensor technologies into a study protocol?
- How do you manage data variability across sites, patients, or visits?
- What validation or regulatory hurdles have you encountered with novel devices?

D. Wearable Levodopa Monitoring

- What research applications do you see for continuous, objective levodopa monitoring?
- What would this technology need to demonstrate to be adopted in a research setting?
- Could you connect us with other researchers or ongoing studies for follow-up interviews?

8. Insurers / Payers / Reimbursement Specialists

A. Coverage Decision Process

- Walk us through how a new remote monitoring or wearable device typically moves through your coverage decision process.

- Who is involved in that decision, and what evidence do they weigh most heavily?
- What comparable devices or precedents — continuous glucose monitors, cardiac monitors — have informed past coverage decisions?

B. Evidence and Outcomes

- What clinical or economic evidence would you need to see to consider covering a device like this?
- How do you currently think about the cost of unmanaged motor fluctuations — falls, ER visits, hospitalizations — in your Parkinson's population?
- What outcomes would need to improve, and by roughly how much, for this to be considered valuable?

C. Reimbursement Pathways

- What reimbursement pathways exist today for continuous monitoring devices in chronic or neurological disease?
- Where have similar devices succeeded or struggled to gain coverage, and why?

D. Wearable Levodopa Monitoring

- What questions would your team ask before considering a device like this for coverage?
- What partners, pilot programs, or data would make you more comfortable engaging with a company like ours early on?

9. Clinical Trial Coordinator

A. Current Workflow

- How are L-DOPA levels current measured during clinical trails
- How frequently are blood samples typically collected

B. Value of Continuous Monitoring

- What data from continuously monitoring L-DOPA levels allow you to collect that you can't do today
- Do you believe a pharmaceutical company would be willing to adopt this technology for clinical trials? If so, why?

C. Pharma as a Customer

- Who would typically make the decision to purchase a technology like this for a clinical trial?
- What budget would something like this come out of?

10. Hospital Procurement Director

A. Adoption Process

- Can you walk me through how a hospital evaluates a new medical device and decides whether to adopt it?
- How long does this process typically take? What does the rough timeline look like?

B. Barriers to Adoption

- What's the most common reason a new medical technology gets rejected
- Have you seen promising technologies fail to be adopted and why?

C. Alternatives

- Would you recommend large health systems as a customer for early-stage medical technology
- Where else would you recommend looking to market early-stage medical technology besides large health systems

11. Pharmacy Director

A. Refill Process and Adherence

• What does the refill process look like from the patient's perspective?

• Do patients commonly forget to reorder recurring medical supplies?

B. Business Model

• From your perspective, what is the best way to structure recurring medical-supply fulfillment?

• What would make this product operationally attractive—or unattractive—to a pharmacy?

Appendix B: Important Quotes from Interviews

Physical Therapists

"Every patient responds to L-DOPA differently. There isn't a universal baseline, which is why treatment has to be personalized."

"Parkinson's is an area that lacks innovation. There are very few companies developing technologies that truly address patients' everyday needs."

Parkinson's Patients

"Some days my medication works well... and other days it doesn't. It's difficult to know why."

Patient's Spouse/Caregivers

"To adjust his medication, doctors sometimes have to take him off of it completely. They starve him of medication. It’s almost like torture."

"Recording symptoms feels like a full-time job. I'm constantly recording symptoms...

Academics

"Medication dosing is still largely a trial-and-error process because clinicians don't have objective data to guide adjustments."

"Patients cycle between 'on' and 'off' states throughout the day, making symptom tracking essential but incredibly challenging."

"Caregivers often shoulder much of the responsibility for monitoring symptoms because patients may have reduced awareness of their own condition."

Neurologists

"We currently don't have a reliable way to personalize L-DOPA dosing for individual patients."

"Patients recording symptoms are clinically valuable, but they're often inconsistent, time-consuming to review, and difficult to analyze."

"An objective system that combines medication levels with symptom tracking could significantly improve clinical decision-making."

Social Workers

"Technology should support both patients and caregivers, not just address the medical side of the disease."

"Accessibility is critical. Any app should be designed with older adults and Parkinson's symptoms in mind."

Nurse Practitioners

"Medication response depends on more than dosage. Meals, protein intake, and constipation can all influence how well L-DOPA is absorbed."

"Simple, accessible interfaces are essential because many patients experience motor impairments that make complex apps difficult to use."

"Providing physicians with medication data alongside symptom and lifestyle information would create a much more complete picture of patient health."

Insurerer

"You can't just show us that it works, show us that it'll actually benefit the the patient and cut visit costs"

Clinical Trial Coordinator

"The ability to continuously measure drug levels could make clinical trials both richer and potentially less burdensome for patients."

"I could see pharma being an early customer because they already have a budget for this type of data."

Hospital Procurement Director

"Large health systems don't just decide to buy a new device. You have to get through a Value Analysis Committee, and that process can be pretty extensive"

Pharmacy Director

"The biggest risk isn't necessarily whether patients like the device—it's whether they remember to reorder their patches."

"If patients are going to call the clinic every-single time they need a refill, you're going to lose people."

Appendix C: Complete Software Overview

Live build: https://parkin-sense-gamma.vercel.app/

Patient portal: add ?role=patient

Clinician portal: add ?role=doctor

Demo logins: robert, margaret, frank, helen

Demo password: parkinsense

All data in the deployed build is synthetic. No reading originates from hardware, and no entry describes a real person. The application demonstrates the software architecture that would sit on top of the biosensor. It is not a medical device.

1. System Architecture

1.1 Application Block Diagram

The application is partitioned into two portals: the measurement concern and the interpretation concern are separate, and are designed for different users. The patient portal is optimised for a single user with a movement disorder – enlarged type, large touch targets, read-aloud on every card. The clinician portal is optimised for scanning several patients quickly, at normal density with no enlargement and no audio. Both read the same stores through the same modules, so the two views cannot disagree about a number. Role is selected by URL parameter, allowing both portals to be open in two browser tabs during evaluation.

1.2 Software Architecture

The application uses a layered architecture analogous to the firmware stack in section 8.3, and for the same reason: to separate the parts likely to change from the parts that must not. Layer 1 reads the role parameter and mounts the correct navigator. Layer 2 holds cross-cutting context — who is holding the device, and how the interface should render. Layer 3 holds persistence, signal generation and derived analysis, and contains no interface code. Layer 4 is presentation and charting, reaching storage only through layer 3. Layer 5 composes

screens and user flow.

Layer 3 subdivides three ways, the most consequential structural decision in the codebase. Signal generators are pure functions producing the sensor trace and roster; this is the single seam at which real hardware would be substituted, and replacing them with a Bluetooth transport reading the LMP91000 front-end would require no change to any chart, screen or analysis module. Persistent stores — symptoms, meals, doses, exercise, notepad, messages, notes, profile — each expose the same load, save and remove triad, are namespaced by store and patient identifier, and fail closed to an empty list rather than throwing. Derived analysis stores nothing, so a summary can never drift out of step with the entries it describes.

2. Detailed Implementation

2.1 Technology Selection Rationale

Expo SDK 54, React Native 0.81 and React 19 let one source tree target web, iOS and Android. The web export is what is deployed; the same code runs natively on a phone paired to the sensor over Bluetooth without a rewrite.

Persistence uses AsyncStorage, which resolves to localStorage on web. There is no backend by design: health data never leaves the device, so the demonstrator carries no server, no account system and no transport security surface. Speech synthesis is likewise on-device, so no protected health information is ever in transit — a cloud service would have made every spoken reading a disclosure. Mapping uses Leaflet with keyless OpenStreetMap endpoints, avoiding a billing dependency and the transmission of a patient's location to a commercial provider.

Charting is hand-drawn with react-native-svg rather than a library, because the required marks — a shaded therapeutic band, dual axes at different scales, protein bars on the baseline, dose markers on the top rail, solid versus dashed reporter encoding — are not expressible in a general-purpose library without fighting it.

2.2 Data Model and Persistence

Every storage key carries the patient identifier, so a read for one patient cannot return another's data even under a programming error. Every check-in, dose and message records whether it was entered by the patient or the care partner: care partners perform a substantial share of real-world symptom logging, and a clinician must be able to distinguish a self-report from an observation rather than having the two silently merged. The distinction carries into presentation, where colour encodes the symptom and line style encodes the reporter. Records are reshaped as they are loaded, never rewritten in place, so a failed migration cannot corrupt stored data. Fourteen days of synthetic history — roughly 41 check-ins, 42 meals, 45 dose events and 8 activity sessions per patient — seed only into a store that is empty or holds nothing but previously seeded rows. All time-series placement is by absolute timestamp rather than clock hour, since a multi-day axis contains each hour more than once.

3. Software Implementation Details

3.1 Off-Period Forecasting Algorithm

Levodopa clears approximately exponentially after a dose peak, so ln(C) declines approximately linearly against time [1, 2]. An ordinary least squares regression of ln(C) against time t, of the form $\ln C(t) = \ln C0 - kt$, gives the elimination rate k as the negative of the fitted slope. Time remaining is $t_{remaining} = \ln(C_{latest} / C_{floor}) / k$.

Four constants govern the behaviour. The regression window is 90 minutes rather than the last two readings: with a sensor sampling every minute or two, consecutive readings differ mostly by noise, and dividing a noisy difference by a small interval would make the estimate swing violently between samples. A minimum of four points constrains the fit. An r-squared of 0.6 gates the output. The horizon is 240 minutes, beyond which the next scheduled dose has landed. It is being improved to accommodate 2 weeks worth of data from the patients as calibration to predict the ideal path of change over the course of the upcoming weeks/months to check if the patient is on track with predicted trends.

The model declines to answer under four conditions, each returning a distinct state rather than a number: the level is already below the floor, a present fact rather than a forecast; the trend is rising or flat; the fit is below threshold; or the solved time exceeds the horizon. Output is always an interval, widening as fit quality falls, since a point estimate would imply a precision the regression does not support. The forecast card carries a mandatory panel stating how the estimate was derived, what perturbs it, and emphasizes that medication must never be altered on the basis of the prediction.

3.2 Therapeutic Window Individualisation

The therapeutic window is stored per patient rather than as a global constant. The default is 500 to 1500 ng/mL, bounded by the concentration range associated with optimum therapeutic response, reported as 0.3 to 1.6 mg/L — that is, 300 to 1600 ng/mL — during controlled levodopa infusion [1]. A per-patient window is used because the minimum therapeutically effective concentration itself varies several-fold between individuals, reported from 3 to 12 nmol/mL in fluctuating patients, and because the duration rather than the magnitude of the motor response tracks plasma concentration [2]. The window also narrows with disease duration and with the emergence of dyskinesia, as the concentration that relieves symptoms and the concentration that induces involuntary movement converge [4, 5]. Across the roster the windows run from 450 to 1600 ng/mL; Helen's is narrowest at 500 to 1250, which is why her readings flag high most readily. Individualisation propagates to time in range, level tone, the shaded band on all three charts, and the forecast floor.

3.3 Dyskinesia Risk Model

Dyskinesia is not modelled as a high-concentration phenomenon alone. Peak-dose dyskinesia occurs at the time of highest brain concentration of levodopa; diphasic dyskinesia occurs at the beginning and end of dosing, as the concentration rises into and falls out of the therapeutic range — that is, at comparatively low readings — and is reported as more troublesome than the peak-dose form [4]. The risk function therefore evaluates both concentration and direction of travel. Flagging only the upper bound would have told a patient reporting involuntary movement at a low reading that their experience was not possible, when in fact it is well described. The synthetic data reflects this: the dyskinesia item is seeded against a post-dose peak curve, inverse to the wearing-off curve driving stiffness, tremor and slowness.

3.4 Nutrient-Interaction Model

Levodopa is a large neutral amino acid and competes with dietary amino acids both for absorption in the gut and for transport across the blood-brain barrier by the LAT1 carrier. In fluctuating patients, meals reduced peak plasma levodopa concentration by 29 percent and delayed absorption by 34 minutes; bypassing

absorption entirely by constant infusion produced a stable clinical state for up to 36 hours [3]. High-protein intake therefore reduces levodopa absorption; it does not enhance it. Common clinical guidance is to take a dose 30 to 60 minutes before a protein-containing meal, although reviews note there is no consensus on a standard protein-restriction or protein-redistribution protocol, and recommend individualised management [6]. This is why the time of a meal is as clinically relevant as its composition.

The meal log records a protein tier — little or none, some, a lot, or not sure — with a description and a time, flagging a meal only when it is high protein and within 60 minutes of a dose, because an application that comments on every meal is one that patients stop reading. The not-sure tier ensures uncertainty never blocks logging, and can be completed later from History.

3.5 Symptom Instrument

Ten items, each scored 0 to 4 in a consistent direction where higher is always worse, grouped as Movement (stiffness, tremor, physical slowness, extra movements), How you felt (tiredness, pain, thinking felt slow, speech was hard) and Digestion (constipation, fullness or bloating). The verbal anchors follow the MDS-UPDRS convention, where 0 is normal, 1 slight, 2 mild, 3 moderate and 4 severe, so that scores recorded here remain legible to a clinician already familiar with that scale [7]. Sleep is captured separately as a quality using three states with facial icons, since it does not share the 0 to 4 semantics, and a free-text field captures anything the instrument does not.

Slowness and tiredness are separate items because bradykinesia and fatigue are distinct constructs with distinct management; constipation and bloating are separate because they vary independently. Every item carries a written definition, displayed by default, since a score of 3 for extra movements is meaningless unless every rater understands the same thing by it — dyskinesia in particular is routinely confused with tremor, so its definition explicitly contrasts the two. Input is five discrete buttons per item rather than a slider, because a slider requires a sustained, precisely terminated drag, the exact motor action a tremor degrades. Each button shows both its numeral and its verbal anchor, from 0 None to 4 Severe.

3.6 Dose-Event Model

Three event types are recorded — taken, missed and extra (rescue) — because a missed dose and a normal pre-dose trough are indistinguishable on the concentration trace alone and demand opposite clinical responses. Rescue doses are counted separately: adherence is taken divided by the sum of taken and missed, since an unscheduled dose is not evidence of adherence and pooling the two conceals both facts. A rising rescue count is itself the signal that off periods are breaking through the regimen. Dose events appear as markers on the upper rail of the clinician chart, filled for taken and hollow for missed. The reminder is stated as a schedule, never an instruction.

3.7 Activity Model

Activity is recorded with type, intensity, duration and time. Regular exercise has the most consistent evidence base of any non-pharmacological intervention in Parkinson's disease for motor symptom improvement. The summary leads with active days out of seven rather than total minutes, because consistency is what the evidence supports. The application does not claim a single session raises a levodopa reading; the defensible claim is that activity correlates with how the day goes.

3.8 Clinician Data Freshness

Patient-entered records propagate to the clinician portal by the browser storage event, which fires in other tabs whenever a tab writes to local storage, so a check-in saved in the patient tab appears in the clinician tab in the same instant with no polling latency. A four-second poll acts as fallback. A status line reports when records were last refreshed, so a clinician can always distinguish current data from a view that has stopped updating; precision in this labelling is treated as a safety property of the interface.

3.9 Accessibility Implementation

Read-aloud is on by default, with a speaker control on each patient card that becomes a stop control during playback, and units expanded for natural pronunciation — 1120 ng/mL is spoken as eleven twenty nanograms per millilitre. Text scaling offers three steps up to 1.3 times, persisted between sessions and applied as a multiplier at every type declaration rather than a page zoom, so layout reflows rather than overflowing. No state is signalled by colour alone: every badge carries an icon and a word. Primary controls are 64 pixels in the minor axis, and no interactive target falls below 44 pixels, meeting WCAG 2.1 Success Criterion 2.5.5, whose stated intent is to help users who have trouble activating a small target because of hand tremors or limited dexterity [9]. The clinician portal is deliberately excluded from all of this, because a clinician triaging a roster needs density.

4. Validation of the Forecasting Model

4.1 Methodology

A walk-forward backtest evaluates one narrow question: when the model stated that n minutes remained until the level would fall below the floor, how long did it actually take? At each hourly step the model sees only the readings up to that step, so no information leaks backward. The actual crossing is interpolated log-linearly between the bracketing samples, matching the decay the model assumes. Steps at which the model declined are counted by reason but not scored, since a backtest must not grade numbers the model never uttered.

4.2 Results

The backtest ran against the fourteen-day synthetic dataset across four patients, using per-patient floors, with 48 hourly samples each. Across all forecasts the model issued 21 predictions with a median absolute error of 79 minutes, 24 percent within 30 minutes of the actual crossing. Excluding the 6 forecasts a scheduled dose interrupted, it issued 15 predictions with a median absolute error of 51 minutes, 33 percent within 30 minutes. Per patient, as forecasts issued, median error overall, then median with dose-interrupted forecasts excluded:

Robert: 4 forecasts, 264 minutes, falling to 5 minutes.

Margaret: 5 forecasts, 64 minutes, unchanged at 64 minutes.

Frank: 7 forecasts, 98 minutes, falling to 89 minutes.

Helen: 5 forecasts, 51 minutes, falling to 41 minutes.

The model declined to predict at 149 of 170 steps, which is the designed behaviour: it commits to a number only when the trend supports one. The declines were 59 rising trends, 59 already below floor, 24 with insufficient fit and 7 beyond horizon, with a further 6 steps having no off-period ahead to score against. Where

the decay curve runs uninterrupted the fit is precise — Robert's median error is 5 minutes across forecasts a scheduled dose did not intercept, the excluded cases being those in which the level was lifted by medication the model was not given. Supplying recorded and scheduled dose times is therefore expected to bring the general case close to the uninterrupted case, and the dose log of section 3.6 already captures that input.

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Appendix D: Cartridge and Microneedle Patch images

