TEAM RESULTS DOCUMENT

TruSense

UNIVERSITY

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1. Abstract: Summary for the SensUs website

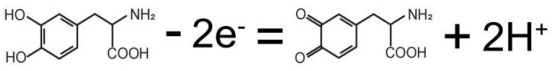
TruSense introduces a coin-sized wearable patch that painlessly samples interstitial fluid with hollow microneedles. An engeneering enzyme CoDH catalyzes the oxidation of levodopa (L-Dopa) to dopaquinone, exhibiting superior selectivity and an enhanced current signal. The patch encloses a centimeter-scale micro-electrochemical workstation designed with ultra-low-power MCU and high-precision ADC, enabling accurate potential output and nA-level current-to-voltage conversion, while integrated Bluetooth and RTC to ensure low-power, reliable data transmission.

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

2.1. Molecular recognition

To specifically recognize levodopa, we employ a protein-engineered copper dehydrogenase (CoDH) derived from the thermostable multicopper oxidase McoP of Pyrobaculum aerophilum, which natively oxidizes levodopa with high specificity and exhibits exceptional thermostability . To eliminate the oxygen dependence of the native enzyme, we disrupted the T2/T3 trinuclear copper center by introducing the double mutation H396A/H459A, forcing the T1 copper center to transfer electrons directly to the electrode via a direct electron transfer (DET) mechanism. An additional F290I mutation, identified through directed evolution, was incorporated to boost catalytic activity, yielding the triple mutant F290I/H396A/H459A whose residual oxidase activity falls below 1.5% of the single-mutant level. This DET-type CoDH stoichiometrically links the levodopa concentration to the Faradaic current at the electrode, enabling its quantitative detection without any oxygen- or mediator-dependent step.



2.2. Physical transduction

The dopaquinone produced by the enzyme reaction is detected eletrochemically. We employ Cyclic Voltammetry (CV), a technique where a triangular potential waveform is applie to the electrode, to measure the faradaic current resulting from the electron transfer during the oxidation or reduction of dopaquinone. To achieve high sensitivity, selectivity and stability, we make a engineering enzyme CoDH from McoP and constructed a multi-layered electrode. A foundational layer of DTSSP acts as a cleavable crosslinker that covalently links enzyme via primary amine groups. Upon this is our engineering enzyme. On the top of the layer is 20% Nafion, which serves to exclude macromolecules such as proteins, and negatively charged molecules. These designs ensures both highly sensitive and selective detection and robost operational stability.

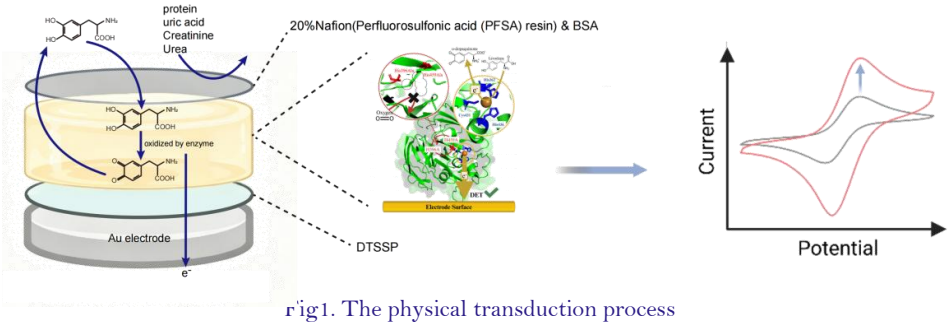


Fig1. The physical transduction process

2.3. Cartridge technology

In the actual completed boxed test model, the chip technology section primarily consists of the packaging of a microfluidic chip and a biological detection chip.

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The microfluidic chip uses PDMS as the baseboard material. Along the direction of fluid flow, the internal channels sequentially consist of a sample injection zone, a diversion channel, a serpentine flow resistor, a reaction detection zone, and a terminal capillary pump waste liquid zone. To ensure sufficient reaction time between the sample and the electrodes, the serpentine flow resistor in the middle section is designed with 3 sets of bends, reaching a total length of 38.8mm. In the reaction zone, the fluid will make full contact with the biological detection chip (sensing electrode) at the bottom. This electrode employs a three-electrode system compositely modified with ZIF-GO and tyrosinase, which can specifically catalyze the redox reaction of levodopa, thereby precisely converting the concentration changes of the drug molecules into subsequent readable, weak electrochemical signals.

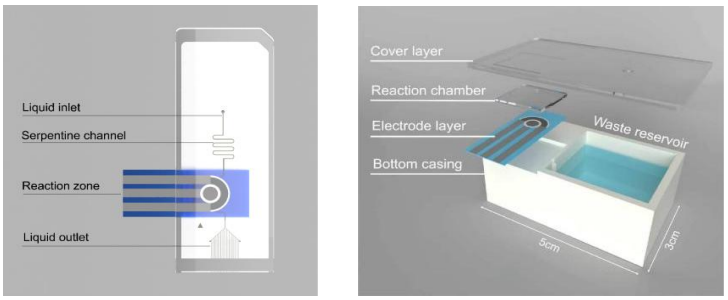


Fig2. The design and simulation of microfluidic cartridge

2.4. Reader instrument and user interaction

In terms of signal reading, a centimeter-scale, highly integrated miniature electrochemical In terms of signal reading, a centimeter-scale, highly integrated miniature electrochemical workstation was designed. This hardware platform takes the Texas Instruments ultra-low-power microcontroller MSP430FR2433 as its core, equipped with a discrete potentiostat composed of a high-precision digital-to-analog converter (DAC8563) and a low-noise precision dual operational amplifier (AD8606). In actual operation, the DAC8563 is responsible for outputting high-resolution constant excitation potential and bias voltage, while the AD8606, configured as a transimpedance amplifier, utilizes its extremely low input bias current characteristics to precisely and linearly convert the microampere to nanoampere-level weak Faraday current generated by the levodopa redox reaction on the detection chip into a voltage signal. Subsequently, this signal is digitally acquired via the MCU's built-in ADC, and ultimately packaged and transmitted in real-time through a low-power Bluetooth module (KS6368) to a smartphone APP. The APP features two core modules: Calibration--users input standard concentrations, and the system automatically fits a custom baseline for each electrode; and Measurement--real-time currents are converted to levodopa concentrations and displayed as dynamic concentration--time curves.

To address levodopa' s narrow therapeutic window, the APP provides concentration warnings (pop-ups/vibration) when levels approach upper/lower limits. A “one-click medication check-in” adds time anchors to the curve for tracking drug onset and metabolism. Historical data and medication records can be exported as tables or images for sharing with clinicians, aiding precise dose adjustment.

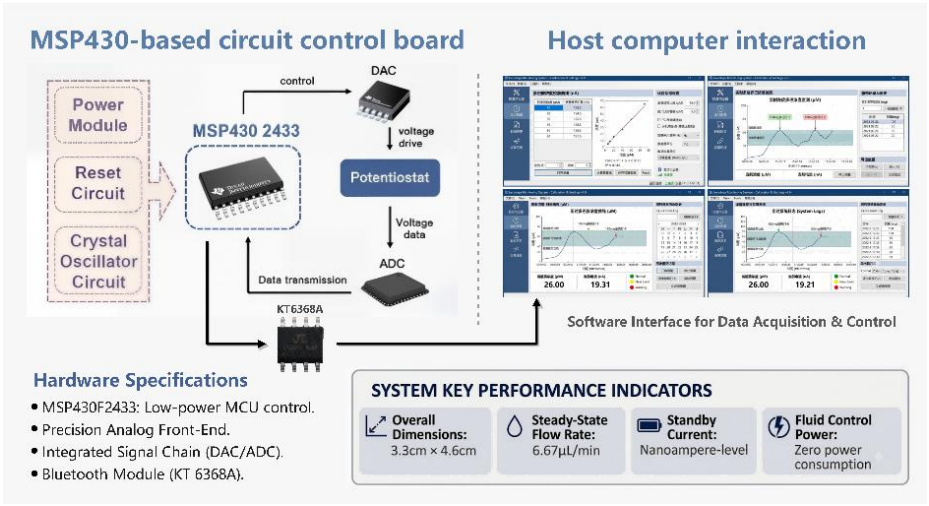


Fig 3. The schematic diagrams of reader instrument and user interaction

3. IN award: Biosensor innovation

3.1. Wearable sensor

3.1.1. Technological novelty of wearable sensor

This project has achieved a high degree of wearability and humanization in system integration and morphological design. Through high-density circuit routing and layered modular packaging, the overall physical dimensions are extremely compressed to 3.3cm*4.6cm, entirely adapting to a lightweight smartwatch. In the front-end sampling stage, the 3D-molded microneedle model adopted by the system can gently extract subcutaneous interstitial fluid in a minimally invasive/non-invasive manner, eliminating the pain of traditional needle pricks; at the same time, paired with a flexible skin-friendly base that conforms to the natural curvature of the human wrist, it greatly enhances the comfort for patients wearing it at home for a long time.

In terms of endurance and energy efficiency management, this project has achieved deep low-power innovation. The system ingeniously integrates two core energy-saving strategies: "passive microfluidics" and "low-power hardware selection". At the fluid physics level, the system abandons traditional power-consuming miniature water pumps, relying entirely on the capillary force generated by precise microchannel geometric structures to achieve autonomous fluid transport, accomplishing "zero power consumption" in the fluid control process; at the electronic circuit level, microcontrollers and RF modules with nanoampere-level standby currents were strictly selected, ensuring long-term operation in a wearable environment.

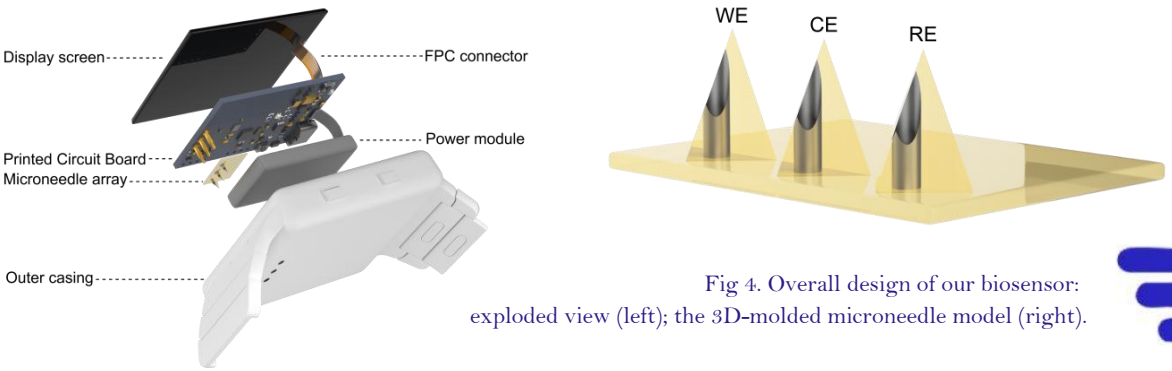


Fig 4. Overall design of our biosensor: exploded view (left); the 3D-molded microneedle model (right).

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3.1.2. Technical feasibility of wearable sensor

To prove the efficiency of our biorecognition strategy, we confirmed the signal amplification from the engeneering enzyme CoDH. The utilization of this enzyme resulted in a significant enhancement of the measured current compared to that obtained with tyrosinase. With the enzyme layers immobilized, the sensor demonstrated a progressive increase in the CV peak value with rising analyte concentration, yielding a linear calibration curve.

To enhance the stability of the electrode, we investigated two distinct strategies: use of protein crosslinkers and immobilization via metal-organic frameworks (MOFs). Preliminary experimental results indicate that both strategies exhibit significant potential for application in biosensing platforms.

To cope with the challenges faced by wearable devices in daily environments, such as temperature fluctuations, mechanical stress, and sweat erosion, this system has carried out rigorous design in its mechanical structure and underlying hardware. At the mechanical level, the system adopts a highly reliable geometric connection structure and comprehensive waterproof and sweatproof packaging, greatly enhancing the connection stability among the microneedles, fluidics, and circuit modules. On the core electronic signal chain, the system is built around an ultra-stable digital-to-analog converter (DAC8563) and a microcontroller based on FRAM architecture (MSP430FR2433). This hardware combination not only possesses extremely low temperature drift characteristics but can also continuously maintain calibration accuracy in the event of battery aging or environmental temperature changes, defending against system drift from the physical sourc and providing a solid hardware foundation for robust wireless connectivity.

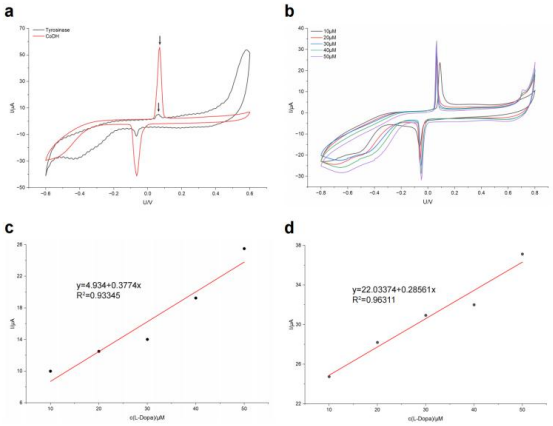


Fig 5. Electrochemical performance of the bisensor:

(a) Comparison of using CoDH with Tyrase.

(b) Calibration curve of detecting with CoDH.

(c, d) Linear response while deteting with CoDH and Tyrase.

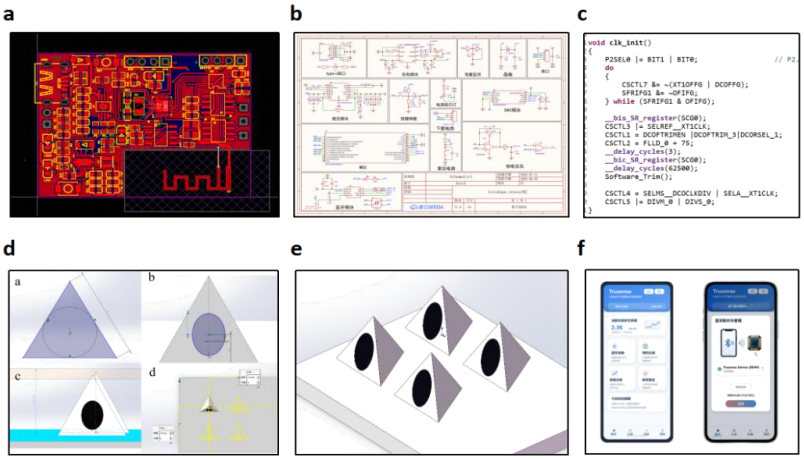


Fig 6. Design of the instrument: (a-b) Circuit schematic and PCB layout. (c)Code snippet. (d-e) 3D model of the microneedle. (f)Upper computer.

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3.2. Reliability of sensor output

3.2.1. Technological novelty of reliability concept

To ensure measurement accuracy, a critical prerequisite for subsequent analysis, we implemented a baseline subtraction method. This procedure isolates the true Faradaic current--generated by the electrochemical reaction of interest--from the non-Faradaic background current. The baseline, identified as the segment of the CV curve with a relatively small and constant slope, is computationally removed to yield accurate peak current values.

To further enhance enzyme stability, we integrated a decay function into our calibration model to compensate for the inevitable decay in enzyme activity. This corrects for signal drift, extending the sensor' s reliable operational lifetime even as enzyme activity diminishes.

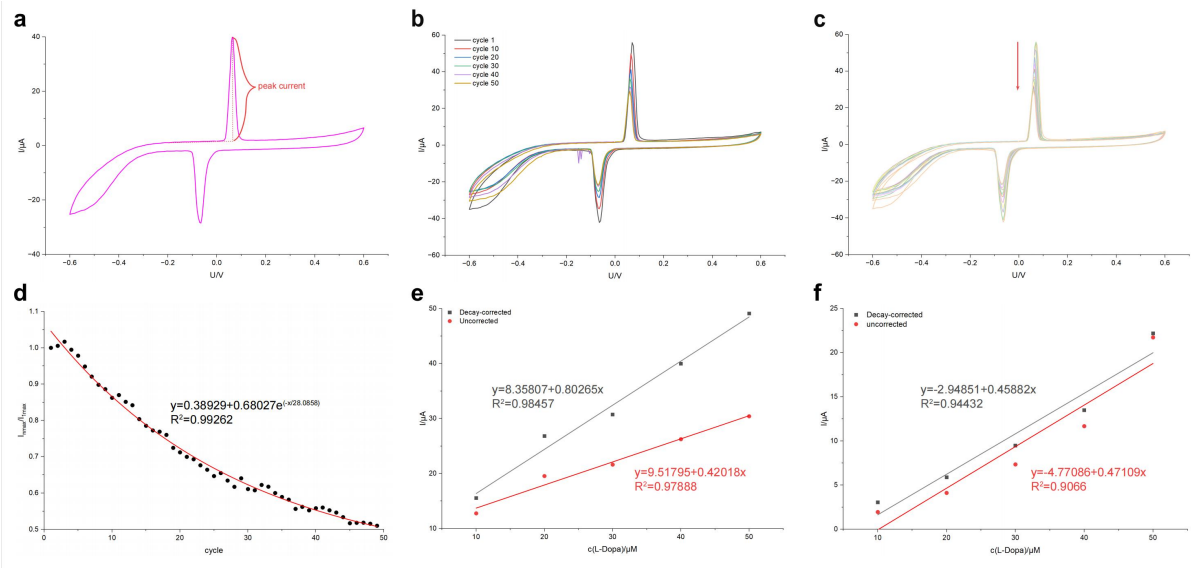


Fig 6. Stability Analysis and Signal Correction for Long-Term Reliability: (a) Baseline correction. (b) Cycle stability. (c) Long-term decay. (d) Decay curve fitting. (e, f) Corrected calibration in PBS and AIF.

3.2.2. Technical feasibility of reliability concept

We evaluated the on-board AD and DA modules, both of which demonstrated with high accuracy. Cyclic-voltammetry scans obtained with our self-developed in-house electrochemical workstation for L-Dopa sensing closely matched those recorded with a commercial workstation, exhibiting identical peak potentials and current magnitudes. In addition, deliberate disturbances--such as shifting the electrodes during 10 measurement--did not degrade signal stability, further confirming the robustness and usability of the system.

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We neat verified the stability of the enzyme with crosslinker. For each examples, we extracted data from the 10th CV cycle of each measurement, followed by automated baseline subtraction using our custom algorithm. The resulting baseline-corrected peak currents were then used to construct all calibration curves. To address long-term performance, we characterized signal attenuation over 50 repeated measurements in a single solution. It was observed that the electrochemical signal decreased steadily and continuously, eventually stabilizing at approximately 60-70% of its initial value. Meanwhile, the characteristic shape of the voltammogram remained unchanged, indicating the underlying electrochemical process was stable. The predictable signal decay was then fitted to a mathematical decay function:

$$y = 0.68e^{-\frac{x}{28.08}} + 0.39$$

Applying this function to calibrate the raw data computationally corrected for signal drift. This process significantly improved the linearity (R^2) of the final calibration curves in both PBS and AIF serum medium.

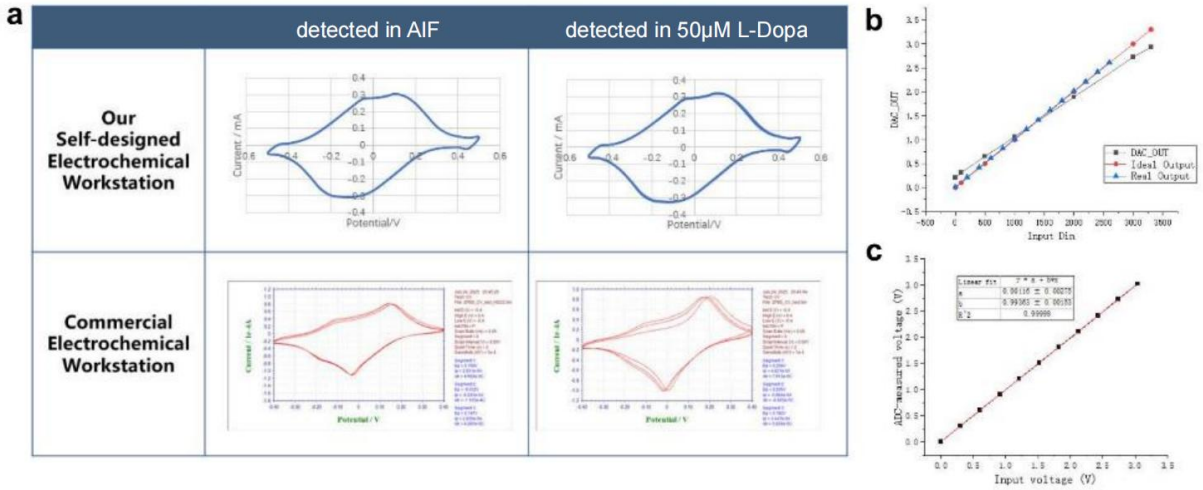


Fig 7. Characterization of hardware accuracy :

(a) Comparison of CV test results between a commercial electrochemical workstation and our self-designed circuit. (b) Accuracy test of the DA module. (c) Accuracy test of the AD module

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3.3. Original contributions

By the supervisor

I have superised the Zhejiang University SensUs team, TruSense, over the past few years, including this year. Early in their work, the students settled on a wearable biosensor concept foe continous L-Dopa monitoring, with their core design archored in a microneedle-based sampling system. To meet the competition' s requirements for noninvasive, long-term operation, they resolved to integrated hollow microneedles with a engeneering enzyme cascade and electrochemical detection.

The fusion of hollow microneedle sampling with a Au/CoDH/Nafion electrode is highly innovative, particularly in its compact, user-friendly form with real-time data transmission. I can confirm that the entire technical approach was independently chosen by the team. They reviewed literature to develop enzyme engeneering and immobolization methods, refined microfluidic and circuit designs, and built the companion app, They proactively sought expert input from various departments and developed every system component, including sampling, detection, electronics, and software, on their own, receiving only equipment usage guidance and safety training.

In conclusion, this deligent and independent team has developed a novel wearable biosensor for continuous L-Dopa monitoring.

Yong Wang

By captains

Our team has developed a fully integrated wearable biosensing system for the continuous monitoring of levodopa concentration in interstitial fluid (ISF). The system features a custom-designed hollow microneedle patch, functionalized in-house with our own sensing inks with an engineered enzyme complex, and this is also our key innovation. To ensure long-term operational accuracy and reliability, we developed two key software components: a baseline subtraction algorithm to extract true Faradaic current, and a software-derived compensation function to dynamically correct for enzyme activity decay. On the hardware side, our team designed highly integrated, ultra-low-power electronics and communication links in-house. Built around an ultra-low-power MCU, high-precision ADC, and low-noise precision op-amp, we constructed a centimeter-scale micro electrochemical workstation, with strictly standardized cross-wiring between the MCU and Bluetooth module to ensure stable transmission under complex motion. The system integrates passive microfluidics and, after three iterations of hardware and firmware, has been miniaturized to smartwatch size. Combined with a custom housing and dedicated mobile app, it achieves the design goals of stability and compactness, providing patients with a comfortable, long-lasting wearable experience.

Zhe hao Song Wang Yuqing

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3.4. Bonus criteria Innovation

Besides the two core modules of "Wearable Sensor" and "Reliability of Sensor Output," this project explores additional dimensions covering system integration, engineering iteration, interdisciplinary collaboration, clinical translation planning and user experience design.

Our team finished three rounds of hardware revision and firmware upgrades on schedule, solving engineering trade-offs between integration density, thermal management, electromagnetic compatibility and wearing comfort, and miniaturized the device to a 3.3cm*4.6cm smartwatch-scale size. The core innovation is the systematic iterative method for multi-constraint optimal solutions, which enables the key upgrade from conceptual prototype to practical wearable device.

With biological electrodes, microfluidic chips, circuits and mobile software developed independently by respective teams, we implemented cross-module system integration to tackle interface matching, timing synchronization, signal integrity and workflow coherence. Regarding system integration as a vital technical challenge, we realized comprehensive mastery of complex system engineering beyond single-module advantages.

We also proposed a long-term post-competition development roadmap: improving sensor performance and clinical detection accuracy, launching small-batch validation production and optimizing products with user feedback. This closed-loop strategy transforms laboratory research to product-oriented development, highlighting forward-looking layout for full "lab-to-clinic" translation.

During technical development, we recognized our limitations and introduced interdisciplinary expertise, including biochemical engineering resources, wearable electronics guidance, medical experts' clinical optimization advice and enzyme engineering technical support. The integrated interdisciplinary knowledge complements our team' s capabilities and constitutes a key innovative feature of the project.

Beyond basic APP measurement and calibration functions, we optimized user experience for clinical scenarios by designing real-time data visualization, medication tracking and concentration alert functions, and simplifying interface and operation logic. These upgrades convert abstract electrochemical signals into user-friendly patient management tools, realizing the shift from functional implementation to user-centered value creation.

4. TP award: Translation potential

4.1. Customer interviews

4.1.1. Identification of potential stakeholders

We interviewed four groups of stakeholders in total. The core group, Parkinson' s patients and their families, are the product' s primary end users. The second group includes clinicians and neurologists, who are relevant to clinical demand validation, dose optimization, and sensor safety and accuracy assessment. The third group comprises senior R&D experts from peer enterprises, whose research aligns closely with the team' s work and the product' s technical development. The fourth group consists of government regulatory staff handling follow-up matters such as product launch approval and medical insurance inclusion.

Sakeholders	Num	Specific Description
Patients /Families	3/3	● Mr. Shi, 78-year-old male, 15-year diagnosis, with relatively well-managed disease course. ● Ms. Xiu, 65-year-old female, motor complications induced by long-term excessive medication ● Mr. Sun, middle-aged male, 6-year diagnosis, medication-compliant yet under substantial pressure balancing work, family and treatment.
Clinicians /Neurologists	2	● Dr. Ni Jie, Associate Chief Physician, The First Affiliated Hospital of Zhejiang University School of Medicine. ● Dr. Liu Ye, Associate Chief Physician, Shanghai Jiao Tong University Affiliated First People's Hospital.
R&D experts	1	● Wouter Nijenhuis,from Palmsens,Electrical Engineer
Regulators	2	● Staff from the NMPA and the NHSA

4.1.2. Interview approach and execution

We used tailored interview methods for different stakeholders. Patient interviewees (family of team members and alumni) were interviewed at home. Physicians, industry experts and government officials were sourced via team connections, Palmsens and official government portals respectively. See Appendix A4.1.2 for the interview outline.

Stakeholders	Approach
Patients /Families	① **Face-to-face interviews** with each patient together with their family members. ② **Semi-structured interviews:** A core interview outline is prepared in advance. During interviews, we flexibly adjust the order of questions and raise follow-up inquiries according to how the conversation proceeds. ③ **MOM test technique:** No interview outline or work laptop is placed on the table to build a more relaxed communication atmosphere. Our team acts as active listeners, focusing on interviewees' past experiences and existing challenges.
Physicians /R&D experts	**One-on-one** online **semi-structured interviews.**
Regulators	Consult via official government service portals with **standardized questions.**

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4.1.3. Interview results and conclusions

Stakeholders	Conclusions
Patients /Families	**①Challenges voiced by interviewed patients confirm the clinical value of continuous levodopa blood-drug concentration monitoring.** ● **Medication management**: Patients struggle to distinguish under-dosing from over-dosing.Symptom fluctuations make patients prone to subjective guesswork and trigger anxiety; one patient resorted to risky self-adjustment, harming physical and mental health. **Real-time monitoring eases medication anxiety and avoids dosing-related side effects.** ● **Motor function**: Motor symptoms affect daily life unevenly. Impacts are mild for stable, retired home-bound elderly patients. Those with high activity needs expect optimized medication to **better control motor symptoms for normal living and reduce family care burdens** **②User Requirements for the Monitoring Device：** 1）Accurate measurements and reliable technology； 2）Non-invasive/minimally-invasive, safe and comfortable to wear； 3）Prefer small, discrete patches over wristbands； 4）Reject frequent consumable changes; 7-14-day interval is acceptable； 5）Affordable pricing; insurance reimbursement is preferred
Clinicians /Neurologists	**①Validates the clinical value of continuous levodopa-concentration monitoring devices:** Parkinson's dose adjustment currently depends largely on clinical observation and physician experience without quantitative metrics. Routine hospital blood sampling cannot track rapid levodopa concentration swings and is clinically impractical. Real-time drug-level data helps clinicians differentiate poor treatment outcomes stemming from ineffective regimens or suboptimal adherence, enabling data-driven instead of experience-driven Parkinson's management. **②Extensive validation remains necessary for personalized dosing guidance derived from levodopa concentration profiles:**.An inter-individual drug-response clinical concentration-symptom correlation database is urgently required. For clinical translation, animal studies and pilot trials must address long-term wear safety and detection accuracy. Sensor outputs should closely match blood drug concentrations, with metabolic interferences suppressed to ensure clinical reliability.
R&D experts	**①Compared with wristbands, the patch-type design is preferred.**Patch-type designs are preferred for weak electrochemical signal acquisition to mitigate motion artifacts induced by ill-fitting wristbands. Eliminating on-device screens and other components cuts power draw, allocating hardware and battery capacity exclusively to high-precision electrochemical sensing. **②Local interaction on the patch should be streamlined and diverse medication-reminder options shall be provided for different user groups.** **③From the hardware charging perspective, the product monitoring cycle can be set to 7-14 days.**
Regulators	**①In China, this product tends to be classified as a Class III medical device.** ②Out-of-home C-mode monitoring lacks direct insurance reimbursement.

* Conclusions are supported by stakeholder interview excerpts compiled in Appendix A.4.1.3

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4.2. Design of validation study

4.2.1. Selection of the problem

Targeted for the daily home-use scenario of patients with Parkinson' s disease, this sensor addresses practical challenges in patients' medication management and motor function. It facilitates more precise drug administration, eases patients' psychological concerns regarding dosage, and avoids safety risks and adverse outcomes arising from self-initiated medication adjustment. Meanwhile, it alleviates motor symptoms caused by mistimed or insufficient dosing, enhancing patients' mobility and quality of life. Technically, the sensor enables real-time monitoring of in-vivo levodopa concentrations to support the personalized optimization of medication regimens. Its form factor satisfies user requirements for comfortable wear, compact size and ease-of-use.

4.2.2. Conceptual design and use case

This coin-sized patch-style wearable L-DOPA detector is intended for long-term daily wear by Parkinson' s patients. Integrating microneedle arrays and an electrochemical sensing system, it adheres to the abdomen or upper arm. Its microneedles painlessly penetrate the stratum corneum to continuously measure L-DOPA concentrations in subcutaneous interstitial fluid. Detection data is transmitted via Bluetooth to a mobile APP. The modular design enables long-term reuse of core electronic components; the battery is recharged and the microneedle patch replaced bi-weekly.



The APP displays real-time L-DOPA concentration-time curves and corresponding data. These quantitative results offer objective references for clinicians to adjust medication regimens, overcoming the high subjectivity of conventional empirical dosing and supporting personalized precise therapy for Parkinson' s disease. Once the correlation between drug concentration and patient symptoms is established and concentration-guided medication adjustment matures, the APP can be extended with smart medication reminders. Pre-set individual safety concentration thresholds trigger automatic reminders for medication intake when levels fall below the therapeutic range and dose-reduction alerts upon overexposure to avoid medication risks. Multi-mode notifications including pop-ups, ringtones and vibrations for patients and caregivers ensure timely and standardized dosing. The device stabilizes in-vivo L-DOPA levels, reduces discomfort caused by drug fluctuations, eases medication-related anxiety, improves motor symptoms, and enhances self-care capacity and overall quality of life for Parkinson' s patients.

4.2.3. Validation study design

Critical aspects of the solution include clinical, end-user and technical dimensions.

From a clinical perspective, the study seeks to validate ISF-sensor accuracy for levodopa measurement, construct patient-specific concentration-motor-symptom association models, and show that real-time-monitoring-guided individualized dose titration alleviates motor symptoms. Full implementation details are included in the Appendix A4.2.3.

Stage	Population	Study Content	Primary Endpoints
I	Healthy volunteers (10 – 15 cases)	Paired comparison of sensor ISF concentration with venous blood HPLC-ECD over 4-6 hours after a single oral dose of levodopa	ISF-blood correlation coefficient, MARD, pharmacokinetic parameter consistency; confirmation that the sensor captures dynamic concentration changes
II	Patients (30 – 40 cases)	Patients wear the sensor at home for 4 weeks; the device screen displays real-time concentration values; patients record daily on-off diaries (simultaneously noting the current concentration reading); patients strictly follow their original prescription without changing the dosing regimen throughout this period	establishment of a preliminary individualized concentration-behavior correlation model; accuracy of patient-recorded concentration-symptom correspondence
III	Patients (≥60 cases)	After individualized modeling based on Stage II data, conduct a randomized controlled validation: the control group continues with the original prescription; the intervention group receives adjusted individualized dosing regimens by researchers based on the concentration-behavior curves; both groups continue wearing the device for another 4 weeks and record symptom data	Changes in UPDRS-III scores, proportion of "on" time, proportion of "off" time, frequency and severity of dyskinesia;magnitude of clinical benefit in the intervention group compared to the control group

From an end-user perspective: verify users' genuine product demand, willingness to pay, long-term-wear comfort, and medication-related-anxiety relief.

We produce a product promotional video to present the product' s value, functions, usage and other relevant information. Collect feedback from viewers via questionnaires to obtain data including video view rate, product-demand level, and acceptable price range. Within one week after the video was released on Xiaohongshu, a widely-influential social-media platform in China, it accumulated 1,286 views. Among the 81 valid questionnaires collected, 76.54% of respondents stated that they were relatively or highly willing to purchase the device for themselves or their family members. The price range of 300-500 RMB per month was the most widely accepted. Meanwhile, upon completion of product usage in Phase III of the clinical trial, questionnaires will be distributed for patients to rate wearing comfort and anxiety relief on a scale of 1 to 10. A mean score above 7 for a given indicator will be regarded as indicative of satisfactory corresponding performance.

From a technical perspective, four major aspects will be examined: in-vitro analytical specificity, in-vivo concentration consistency and time lag, 72-hour long-term signal drift, interfacial adhesion and skin biocompatibility, as well as stable low-power power supply and signal acquisition. Full implementation details are included in the Appendix A.4.2.3.

4.3. Bonus criteria Translation Potential

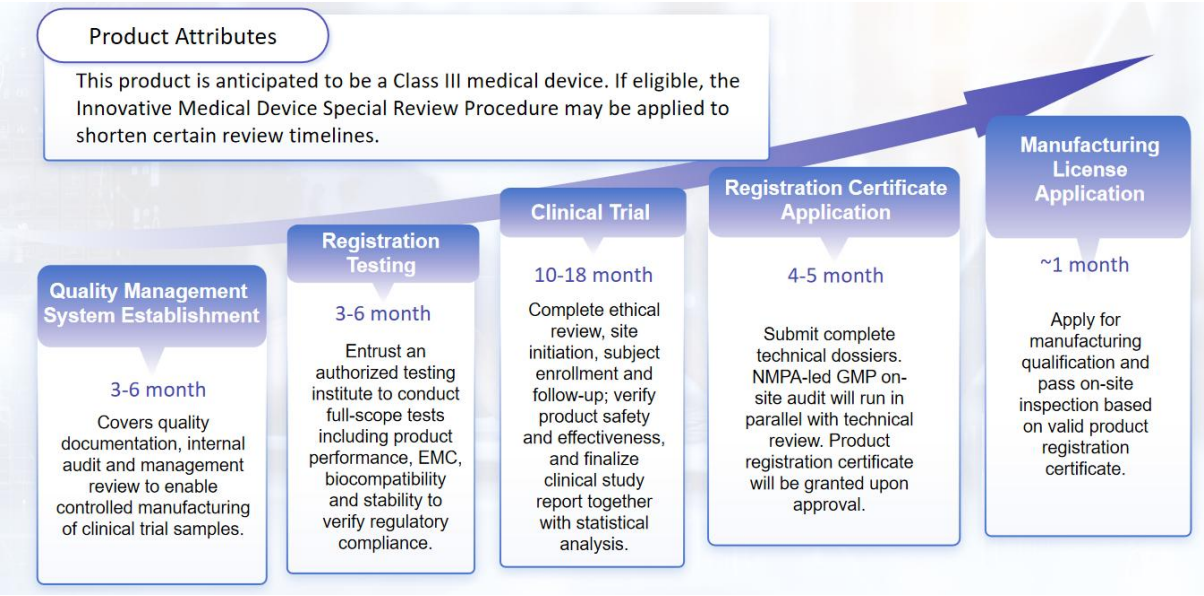
4.3.1. Profit-making Model

Our main products comprise two parts: the detector and test patches. The main detector allows long-term use upon the user' s initial purchase. Test patches are consumables that require regular replacement. The projected retail price of the main detector ranges from RMB 800 to 1,200. Each test patch is priced at RMB 150-180 with a service life of half a month. The average monthly usage cost stands at RMB 300-500, which matches surveyed users' expectations while maintaining profit margins. Meanwhile, we will establish a patch recycling mechanism. Users may mail back used patches to obtain discounts on new replacements. This measure reduces users' usage costs, enables the recycling and reuse of recoverable resources, and enhances user stickiness.

4.3.2. Promotion Strategy

For the To-C strategy, we will launch official flagship stores on Tmall, JD.com and Douyin E-commerce to directly engage patients and their families via store livestreams and short-video promotions. We will partner with Parkinson' s patient communities and forums, inviting patient KOLs to share user experiences for word-of-mouth marketing, building a closed-loop service ecosystem that links communities with end users. We will integrate data with mainstream health management apps including Huawei Health and Apple Health to broaden user coverage. To gain trust among elderly users, we will promote product science popularization through TV and radio health programs. We will also cooperate with pharmacy chains such as Laobaixing Pharmacy and Yifeng Pharmacy to set up offline experience zones, allowing users to test product wearability and app operations in real usage scenarios.

4.3.3. Go-to-Market Path



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5. Team and support

5.1. Contributions of the team members

Supervisor & captains:

Yong Wang (team supervisor): Provided profession guidance on advanced biochemical strategies, including enzyme engineering and immobolization, while being deeply committed to our academic and personal development.

Zhehao Song (team captain): Oversaw the project's overall progress and led the design and validation of the core biorecognition strategy.

Yuqing Wang (team captain): Responsible for the overall electronic circuit design of the miniature electrochemical workstation, conducted the smartwatch prototype conceptual modeling.

Biology group:

Yueyang Lu: Actively explored strategies of enzyme engineering and successfully validated a engineering enzyme complex.

Luming Xu: Actively coordinated the integration efforts across the three groups, making a contribution to consolidating our product from scattered components into a cohesive whole.

Xuanmo Li: Managed the enzyme stablization strategy and optimized experimental procedure.

Fangzhou Lv: Successfully constructed an optimal anti-interference coating on the enzyme.

Zian Gong: Enhance the complex system to improve the detection current.

Yufei Zhang: Engaged in strategy discussions and contributed to protein expression.

Instrument group:

Yuhang Wang: Focused on embedded software development. Spearheaded the implementation of the cyclic voltammetry (CV) function, driving the precise execution of electrochemical sensing algorithms and ensuring accurate signal acquisition at the firmware level.

Jiadui Zhang: Co-developed the embedded software architecture, focusing on system scheduling and low-power management. Furthermore, designed the 3D model for the microneedle patch.

Zeyu Ying: Engineered the box testing model and the passive microfluidic system. Designed the internal micro-channels to achieve zero-power fluid transport through capillary action, ensuring reliable sample delivery to the sensing electrodes.

Xiaoxue Liu: Designed the user interface and interaction flow for the smart mobile application.

Developed key interactive features such as real-time concentration curve visualization, medication tracking, and out-of-bounds alerts to optimize the user experience for patients.

Translation group

Pinghe Zhu: Oversees customer interviews, validation study and business-model design.

Ruiyao Tang: Leads patient engagement, interviews, product-concept prototyping and market validation.

Zhehong Ren: Leads physician outreach, interviews and the design of clinical validation study protocol.

5.2. People who have given support

Professor Fan Yang: Provided the laboratory space, equipment, and reagents that were essential for the successful completion of our project.

Professor Liujing Zhuang: As an expert in wearable biosensors, Professor Zhuang provided invaluable guidance on our hardware design, helping us overcome development challenges and sharing her experience in biorecognition element modification.

Professor Yuqi Zhang: As our medical consultant, Professor Zhang guided the team on how to construct new proteins through 3D simulation, and also gave us advices and share her insights regarding experimental procedures and process optimization.

Dr. Jianghao Ren & Chaolei Zhang: Provide significant help and guidance in the construction and expression of engineered enzymes.

5.3. Sponsors and partners

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浙江大学教育基金会 Zhejiang University Education Foundation

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浙江大学 医学院 SCHOOL OF MEDICINE ZHEJIANG UNIVERSITY

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6. Final remarks

We are very excited to connect with other teams during the competition in Eindhoven. Through the SensUs platform, we aim to learn from and share with teams from across the world, exploring topics such as technical innovation, industrial translation, and sustainable development.
The competition is not the end, but a new beginning. In the future, we hope to improve our product design so that TruSense sensors can move from lab-based research to real-world application, truly benefiting the public. To achieve this, we will continue to enhance the sensor's performance in real-world conditions, improve the detection and prediction accuracy of the supporting app, and produce small batches of sensors for testing and validation. Based on real-world use and user feedback, we will iterate the product further.

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8. Appendix

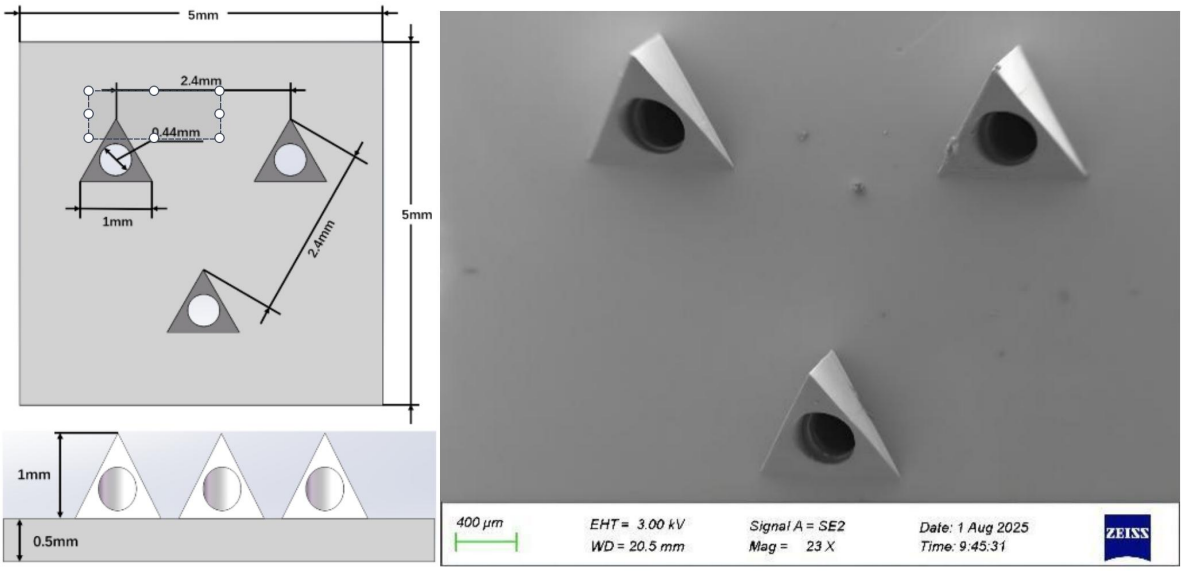


Fig S1. Microneedle dimensions (left) and a scanning electron microscopy (SEM) image of the microneedle patch before filling (right).

Enzyme Fusion Strategy

Enzyme Sequence

CoDH:

MITRRRFLQIGLGAGAMLAMGFTLQYILR
TGEVKRPETSAPVPPLIKEATYIEATASGY
MAEGVLNPTIILRRGQRVDMTLKNKLTEP
TIVHWHGFDVNWHNDAHPSFAITPGESY
NYSFDVVNRAGTYLYHPHPHGLTAKQFY
MGQLGLVIVEDSGSDLGFKYGVNDLPLVI
SDRRFIGGAPVYNPTPMEMIAGFLGNAVL
VNGVKDAVFKLSGGSYRLRLVNGSNARL
YMLSIVKKNGDVVPMRLIAVDQGFLARPI
EVRALFLAPAERAEVVVELGEGVYLLKNTP
IDPMHLEMGHGMQEALPEGSEYTIATFLV
EGKGEAVPVEALSDPPPEPPKPTRTRRFAL
SLSGMQWTINGMFWNASNPLFEHVSVE
GVELWEIVNDKASMPHPMHLAGFPMWI
IERKDSPRQVAELAVDNRGRLPTDLGLKD
TVLIWPGETVKIVVNFDAKKRGQLFPFAC
HNLEHEDGGMMINIAVK



Fig.S2. Prodiction of 3D model of CoDH

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A.4.1.2. Interview outline

Patient interview outline:

【Understanding patients' current medication routines and daily status】

1.Could you briefly describe the patient' s disease progression? (How long ago was the diagnosis? What medications is the patient currently taking?)

2.Approximately how many times per day does the patient take levodopa? At what general time points are doses administered?

3.Who is responsible for reminding or arranging medication intake? (Patient themself / family member / alarm clock / other means)

【Understanding patients' subjective experience and distress related to medication-effect fluctuations】

4.Has there ever been a situation where the patient skipped a dose because they felt well that day or symptoms were mild?

5.Have there been instances of delayed dosing or overdosing? What discomforts occurred afterwards?

6.Can the patient perceive in advance that the drug effect is wearing off? How do they tell that “the medication is no longer working”? (By physical sensations? By elapsed time?)

7.Have you noticed inconsistent drug effects from time to time? How frequent are these fluctuations between good and poor drug response?

8.How significantly do these fluctuations impact daily life? (e.g., going out, meals, sleep, mood, etc.)

【Understanding preference for device-related requirements】

9.If a device could measure the patient' s in-vivo levodopa concentration in real time to optimize medication regimens, would you consider it helpful?

10.Would you prefer an adhesive-patch-style wearable or a wrist-band-style wearable? Would you accept replacing the patch component every one or two weeks?

11.What are your biggest concerns regarding usage? (Pain? Price [what price range would you accept per replacement cycle]? Privacy? Safety? Wear-comfort? Water resistance?)

12.What kind of medication alert would you prefer the device to deliver? (Beep? Vibration? Light flash?)

Physicians interview outline:

1.In your daily clinical practice, what are the main challenges faced by Parkinson' s disease patients during levodopa treatment?

2.How do you generally determine a patient' s medication regimen (including drug dosage and dosing frequency) for a given period?

3.In your opinion, what are the limitations of existing monitoring and assessment tools for Parkinson' s disease (e.g., clinical rating scales, motion-monitoring devices)?

4.What Parkinson-related testing devices are currently available in hospitals that can specifically measure levodopa levels? What are the corresponding testing modalities?
5.Do you believe real-time monitoring is necessary, or is trend-tracking sufficient? Please explain your reasoning.
6.From your perspective, should levodopa threshold values be used primarily as a reference for medication adjustment or as a medication reminder?
7.Suppose the device is designed as a coin-sized patch similar to a real-time blood-glucose monitor, to be replaced every one or two weeks. What do you anticipate would be the most common difficulties for patients during use?

R&D experts interview outline:

【Product monitoring-duration considerations】

1.For the miniature biosensor hardware module under your R&D, how frequently does the battery require charging? How many years of monitoring can the hardware sustain?

【Product monitoring-duration considerations】

2.From a hardware-engineering perspective, which product form is more suitable: patch-type or wrist-band-type?

【User-interaction considerations】

3.What interactive functions should be retained on the patch unit?
4.How should alerts be implemented to confirm pre-wear and post-wear status?
5.How should medication reminders be delivered? Is integrating a vibration module on the patch feasible?

Regulators interview outline:

1.Which category of medical device this product most closely falls under?
2.What are the specific phases of the corresponding market-access procedure? What are the associated costs and timeline?
3.Is it possible for this product to be covered by medical insurance?

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A.4.1.3. Stakeholder interview excerpts

Patient 1	• **Described drug efficacy dependent on subjective "feelings," lacking objective data support.**The system requires concentration trend prediction to provide advance warning regarding the off-period. • **Difficult to distinguish between the underlying causes of a "poor condition" (insufficient drug efficacy, drug overdose, or other medical conditions)** . • **The pricing of expected products should be inclusive.**It would be better if they can be covered by medical insurance reimbursement.
Patient 2	• Safety margin progressively narrowed without their awareness; the risk of overdose remained entirely undetected until the onset of dystonia. Consequently, **there is a need for the test results to be accurate and the technology exhibits to have strong stability**,intercepting impulses for "self-rescue-style dose escalation" and enabling proactive alerts when the patient experiences a "feeling of well-being."
Patient 3	• **The "switching phenomenon" is entirely unpredictable.**Early warning of an approaching "off-period" enables users to live and work without safety risks. • **Does not require frequent replacement of consumables;** a component replacement interval of 7–14 days is acceptable. • **Prioritizes non-invasive or minimally invasive approaches; the equipment is lightweight, discreet, comfortable, and does not interfere with existing lifestyle habits.** • **The burden of home care is fully transferred, placing immense psychological pressure on spouses and children.** Remote notification to family members facilitates a transition
Doctor 1	• Affirms the clinical significance of a real-time monitoring product. Current dose adjustment relies solely on visual observation of clinical manifestations without any quantitative indicators; the hospital lacks relevant detection equipment to measure levodopa concentration in real time. • Cannot distinguish between "poor condition" due to insufficient efficacy or drug overdose; cannot confirm whether patients are taking medication on time and at the prescribed dosage. • Recommends conducting a pilot study to establish concentration–behavior correlation profiles. • Suggests that target users should be patients with prolonged medication duration and those experiencing "on–off" phenomena; if integrated with a drug delivery system, the scope could expand to include patients with poor adherence (which may exist in both early and late stages).
Doctor 2	• Emphasizes the limitations of traditional blood sampling: it cannot capture the full picture of rapid levodopa fluctuations, and repeated venipuncture increases patient discomfort. • Whether long-term contact of microneedle arrays with the skin may cause rashes or foreign body reactions; requires dermatological verification. • Accuracy: Sensor readings must maintain good consistency with blood test results; interference from metabolic pathways and adjuvant drugs, as well as time resolution challenges, need to be addressed. • Recommends systematically establishing calibration models through paired sampling across multiple time points in preclinical studies, clarifying the sensitivity and specificity of the detection.

R&D Expert	• Charging is generally required every 7-14 days: the main controller is removed when replacing the skin electrode patch and charged in the charging dock for 1-2 hours. With weekly charging, the battery can function properly for over 3 years. The hardware service life ranges from 2 to 3 years. • The patch-type form is preferred over the wristband-type. Electrochemical detection measures faint current at the pA-nA level. The patch adheres tightly to the upper arm or abdomen without relative movement. By contrast, wristbands tend to become loose, and motion-artifact noise can completely obscure genuine signals. In addition, the patch requires no screen or complex interactions. Its main controller stays in sleep mode most of the time, allowing hardware and battery resources to be fully dedicated to high-precision, low-power electrochemical sensing. • A dual-color LED and miniature beeper are recommended on the patch for pre- and post-wear status confirmation. A vibration motor is not advisable: vibration interferes with faint electrochemical signals, significantly increases power consumption and device size, and may cause user discomfort. For patients capable of self-care, medication reminders can be delivered via ringtones, vibration and pop-ups on mobile phones or wristbands. For elderly users unfamiliar with smartphones, alerts will be sent to community caregivers or remote family members.

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A.4.2.3. Full implementation details

User-end part: product promotional video link【http://xhslink.cn/o/9PGniZfh6uT】

Technical part:

Experimental Subjects and Sampling Design	In vitro/Ex vivo Group	Microfluidic artificial ISF simulation system (containing histones and common interferences)	
	In vivo Animal/Clinical Group	Parkinson's disease models (or subjects), continuous wearing for 72 hours. Simultaneous timed venous blood sampling (HPLC-MS to determine plasma levodopa concentration) to establish time-matched pairs	
Category	Indicator/Item	Experimental Condition/Design	Target Value/Evaluation Criteria
A. Analytical Performance and Specificity (In vitro/In situ)	Cross-interference Deviation Rate (Interference Ratio)	Add 20 μM L-Dopa at physiological concentrations (100 μM AA, 300 μM UA, 10 μM DA, 50 μM Carbidopa)	$\lvert \Delta I / I_0 \rvert < 5\%$
	Enzyme Stability and Response Time	Measure the 10%–90% step response time T_0	$T_0 < 30$ seconds
B. Biological Correlation and Delay Quantification (In vivo)	Consistency (Bland-Altman & CEG)	Verify MARD≤20% and ISF-blood correlation coefficient r≥0.75	MARD≤20% and r≥0.75
	Lag Time (T_lag)	Compare serum and ISF concentration curves after oral/bolus L-Dopa administration. Calculation formula: $T_{lag} = \text{argmax}_\tau R_{blood,ISF}(\tau)$	Total lag T_lag ≤ 12 min (physiological lag ≤ 8 min, sensor response lag ≤ 4 min)
C. 24–72 Hour Long-term Stability and Adhesion Tolerance	Signal Drift Rate	72 hours of continuous operation, signal detection based on standard solution	Drift rate < 0.4% / hour, 72-hour cumulative signal attenuation < 15%
	Calibration Strategy and Accuracy	Based on single-point/two-point calibration formula $C_{ISF} = S \cdot (I - I_0)$	Calibration frequency ≤ 1 time/24h, relative error MARD < 10% after in-situ calibration
	Interface Adhesion and Skin Tolerance	Adhesive tape peel strength retention after 72h of wearing (including simulated sweating/exercise shear force)	Peel strength retention ≥ 75%, shedding rate 0%; after removal, evaluated according to Draize protocol, Draize Score < 1.0 (no or very slight irritation)
D. Power Supply and Hardware System (SAP/Power)	Power Supply Stability	Full cycle (72h) output voltage fluctuation rate	$\Delta V / V_{nominal} < 2\%$
	Power Consumption and Acquisition	Average current consumption, sampling signal-to-noise ratio, wireless data packet loss rate at sampling frequency of 1 Hz (integrated filtering, 10s output one frame)	Average current consumption < 100 μA, sampling signal-to-noise ratio SNR > 35 dB, wireless data packet loss rate < 0.05%

Clinical part:

I. Trial Procedures

(1) Stage I: Healthy volunteers undergo intensive sampling over 6 hours after a single dose administration in a clinical research unit (0, 0.5, 1, 1.5, 2, 3, 4, 6 h).

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(2) Stage II: Patients wear the device at home for 4 weeks, with the patch replaced every 7 days. The device screen continuously displays real-time concentration values; patients record their current concentration readings simultaneously when documenting symptoms in their diaries. Throughout this period, the original prescription is strictly maintained without any dose adjustments based on sensor data. Study coordinators conduct weekly telephone follow-ups to confirm adherence. Patients return to the research center at Weeks 1, 2, and 4 for UPDRS assessments and venous blood sampling.

(3) Stage III: Individualized concentration–behavior curve modeling is completed based on Stage II data, and researchers (neurologists) review the model results to formulate personalized dosing recommendations. Subjects are then randomly assigned to two groups:

(a) Intervention group: Dosing regimen adjusted according to personalized recommendations; continued device wear for 4 weeks.

(b) Control group: Continued device wear for 4 weeks; original dosing regimen maintained unchanged.

Patients return to the center for assessment at Weeks 6 and 8, with final UPDRS assessment and venous blood sampling conducted at Week 8.

II. Subject Eligibility Criteria

(1) Inclusion Criteria:

(a) Confirmed diagnosis of Parkinson's disease;

(b) Age 40–80 years;

(c) Receiving a stable levodopa regimen for ⩾4 weeks with no anticipated major regimen adjustments during the study period;

(d) Possess basic self-care and diary-recording capabilities;

(e) Provide informed consent and voluntarily participate.

(2) Exclusion Criteria:

(a) Allergy to patch materials;

(b) Skin infection or damage at the application site;

(c) Severe cognitive impairment preventing cooperation with the study;

(d) Anticipated need for hospitalization or changes to the levodopa regimen during the study period;

(e) Pregnancy or lactation.

III. Ethics and Informed Consent

The study protocol must be approved by the Institutional Review Board (IRB)/Ethics Committee. All subjects provide written informed consent, with clear disclosure that the device displays data only and does not provide medication guidance, and that no treatment changes will be made during Stage II; Stage III may involve dose adjustments for subjects in the intervention group. The study must be registered with the Chinese Clinical Trial Registry (ChiCTR).

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IV. Critical Aspects and Measurement Endpoints

(1) Correlation between interstitial fluid levodopa concentration and plasma drug concentration: Paired sampling is used to validate the consistency between microneedle-extracted ISF concentrations and venous blood concentrations. Pearson correlation coefficients and Bland-Altman limits of agreement are calculated to establish a translational model from ISF concentration to plasma concentration. Long-term stability of concentration measurement forms the foundation for data-driven dose optimization with this product.

Reliability of concentration–behavior response curves and inter-individual variability:
Through combined analysis of patient self-rated "on-off" diaries and neurologist-administered MDS-UPDRS-III assessments, a multidimensional symptom quantification index system is established. After aligning sensor concentration time series with symptom indicator time series, time-series analysis and mixed-effects models are employed to construct individualized concentration–behavior response curves for each subject, identifying each patient's optimal therapeutic concentration window. On this basis, the degree of variation in concentration–behavior curve morphology across different patients (e.g., threshold concentration, coefficient of variation of optimal concentration window width) is further analyzed to assess the limitations of "one-size-fits-all" prescribing and to validate the necessity and feasibility of individualized dosing regimens.

Patient awareness and recording accuracy of concentration–symptom associations:
The device screen displays real-time concentration readings to patients, enabling them to correlate their subjectively perceived symptom states with objective concentration values. The accuracy with which patients synchronously record the current concentration display value when documenting symptoms in their diaries is verified (recording accuracy $\geqslant$85% considered as meeting the target).

Closed-loop validation of data accumulation and dosing regimen optimization:
Based on longitudinal data accumulated in Stage II, an individualized dosing recommendation report is generated for each subject, reviewed by researchers/neurologists and compared against the subject's original prescription, with clinical effects validated through the randomized controlled design in Stage III.

Long-term enzymatic stability and sensor operational lifespan:
The effective operational lifespan of the sensor under real-world use conditions is determined to establish a reasonable replacement cycle for consumable patches (target: 7–14 days), which serves as a technical prerequisite for long-term data accumulation.

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Wear tolerance and dermal safety:
Adhesion retention rate, skin irritation, and comfort scores during prolonged continuous wear are evaluated to ensure the product supports long-term daily use.

V. Measurement Methods and Data Acquisition
(1) Sensor continuous monitoring and data display:
The patch extracts interstitial fluid via microneedle arrays; the MSP430 platform performs electrochemical detection, with concentration data and timestamps stored locally on the device. The device incorporates an integrated micro-screen that displays real-time concentration values. Concentration units are presented in a patient-understandable format (e.g., "Concentration Level 1–5" or "Relative Concentration Percentage"), with the specific display format determined based on user surveys after Stage I.

(2) Multi-modal symptom recording:
(a) Patient self-assessment uses daily paper or electronic diaries to record the timing and severity of "on" periods, "off" periods, and dyskinesia, with the current concentration value displayed on the device screen transcribed simultaneously with each diary entry.
(b) Neurologist-administered MDS-UPDRS-III assessments are conducted at enrollment, at the end of Stage II (Week 4), and at the end of Stage III (Week 8).

(3) Gold-standard blood concentration comparison:
(a) Intensive sampling comparison is performed in Stage I;
(b) In Stages II and III, venous blood samples are collected at enrollment and at Weeks 2, 4, and 8 for HPLC-ECD analysis, enabling sparse calibration and validation against sensor data.

(4) Concentration–behavior modeling approach: Machine learning methods (Random Forest/Gradient Boosting) are employed, using concentration–time series as predictor variables and symptom indicators as response variables, to establish individualized dose–effect relationship models.

VI. Data and Safety Management
All sensor data, diary data, and IMU data are anonymized and uploaded to the research data platform, accessible only to the research team. If the device displays persistently abnormal concentrations or if patients report severe symptoms, researchers contact the patient by telephone within 24 hours and provide medical advice. Emergency response rules for both intervention and control groups must be clearly defined in the SOP in advance.

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VII. Success Criteria and Iteration Mechanism

(1) Technical success criteria:

Stage I validation achieves MARD $\leqslant$ 20% and ISF–blood correlation coefficient r $\geqslant$ 0.75; sensor signal attenuation $\leqslant$ 30% over 7 days of continuous operation.

Data quality and modeling success criteria:

At the end of Stage II, $\geqslant$ 85% of subjects achieve diary concentration recording accuracy $\geqslant$ 85%; $\geqslant$ 75% of subjects can establish a statistically significant ($p < 0.05$) individualized concentration–behavior association model; the coefficient of variation of the optimal concentration window across individuals is $\geqslant$ 30% (demonstrating the necessity of individualized adjustment).

Clinical validation success criteria:

In Stage III, the intervention group shows a mean reduction of $\geqslant$ 3 points on UPDRS-III compared to the control group (minimum clinically important difference, MCID), or an increase in "on" time proportion of $\geqslant$ 15%, without significant worsening of dyskinesia.

Commercialization preparation criteria:

Upon completion of Stage III, the complete individualized data modeling methodology and validation results are compiled to form a service process SOP of "sensor monitoring → data accumulation → individualized modeling → dosing recommendations." The final display format of the device screen is optimized based on user feedback from Stages I and II.

(5) Iteration mechanism:

(a) If Stage I does not meet the technical criteria, the sensor design is returned for optimization.

(b) If Stage II modeling success rate is $< 75\%$ or inter-individual differences are not significant, the effectiveness of symptom quantification methods is re-evaluated or the data accumulation period is extended.

(c) If Stage III does not meet clinical validation criteria, the modeling algorithm is optimized.

(d) Upon completion of all validation stages, a comprehensive real-world evidence report and individualized dosing modeling solution is compiled to serve as core supporting material for product commercialization and physician partnership efforts.

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