

Introduction

Parkinson's Disease (PD) is a progressive neurodegenerative disorder affecting over 10 million people globally, with cases projected to nearly double by 2030. Currently, a definitive diagnosis is only possible after significant, irreversible neuronal loss has occurred. Standard diagnostic tools—including neurological exams and DaTscan imaging—are often expensive, invasive, and inaccessible to many populations. By the time motor symptoms like tremors or rigidity appear, patients have typically lost 60–80% of their dopamine-producing neurons. This creates a critical unmet need for a noninvasive, low-cost screening tool capable of detecting PD in its prodromal (pre-symptomatic) phase. Recent studies indicate that specific volatile organic compounds (VOCs) trapped in earwax differ markedly between PD patients and healthy controls. This research develops a chemical sensing strip and AI- based analysis pipeline to detect these Parkinson's-linked VOCs noninvasively.

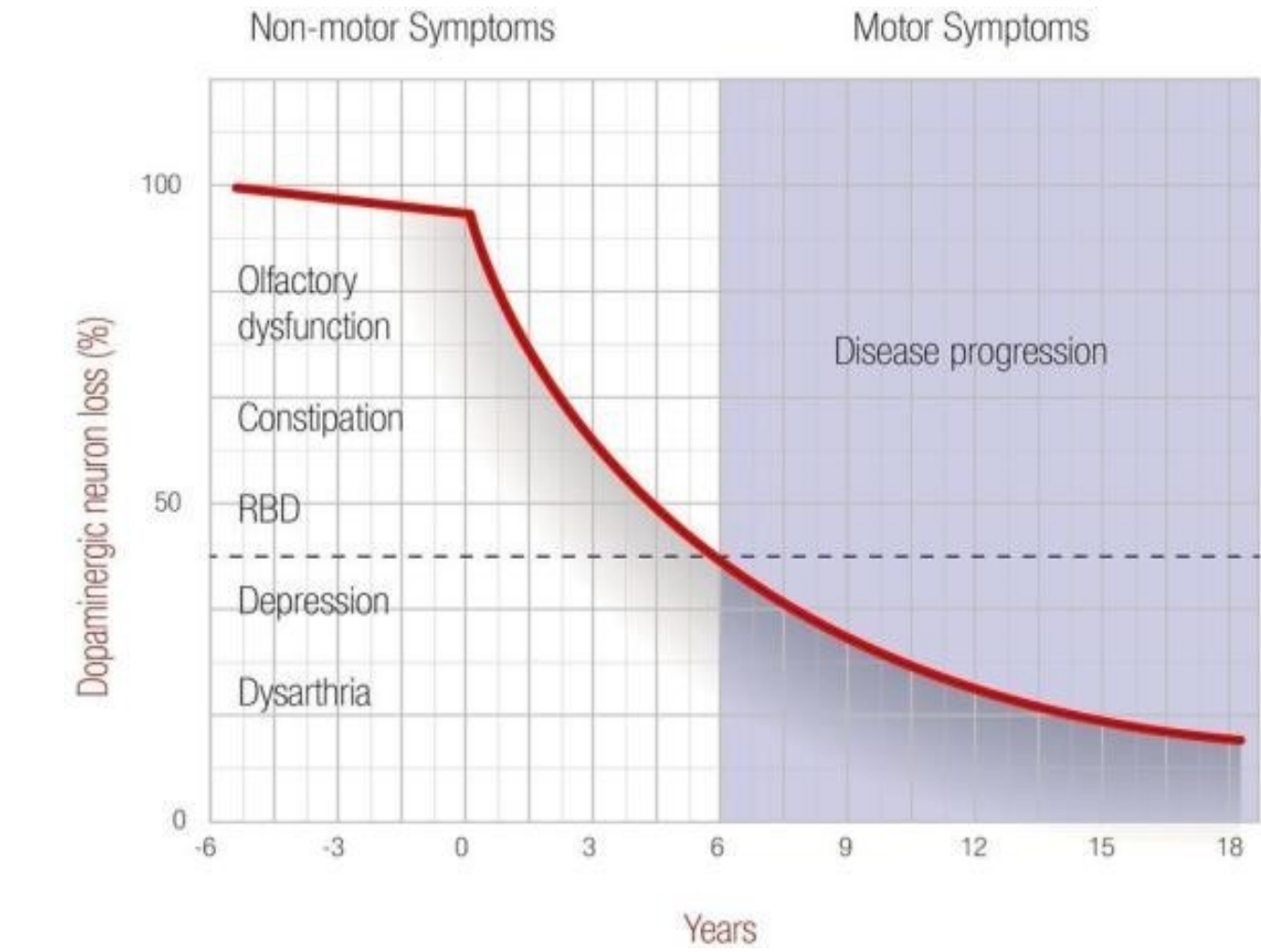


Figure 1: The Diagnostic Gap in Parkinson's Disease. Clinical diagnosis (red) typically occurs only after a 60- 80% loss of dopamine-producing neurons. Our research targets the prodromal phase (green), using earwax VOCs to enable detection years before the onset of motor symptoms.

Synthetic Earwax Creation

To eliminate the inherent biosafety risks and variability associated with human biological samples, a synthetic earwax matrix was engineered to replicate the lipid-rich composition and volatile organic compound (VOC) retention of natural cerumen. This standardized substrate was developed by blending 3.5 g of anhydrous lanolin, 3.0 g of beeswax, 2.2 g of light mineral oil, and precise amounts of oleic acid, palmitic acid, and squalene. The preparation involved heating these components to 65–70°C for approximately seven minutes to achieve a homogeneous melt, followed by a controlled cooling phase before refrigerated storage.

The experimental protocol for simulating Parkinson's Disease focused on the targeted introduction of pentanal to the synthetic matrix. One-gram samples of the wax were gently warmed to a semi-solid state at 35–40°C to facilitate the integration of a 1 mg/mL spiking solution. This process allowed for the creation of three distinct experimental conditions: a 0-ppm control, a 3 ppm "PD-like" concentration, and a 30 ppm "non-PD" reference. Once spiked, the samples were mixed and allowed to equilibrate at 4°C for one hour to ensure a stable and representative headspace for subsequent analysis.

Utilizing a synthetic matrix offers significant advantages for high-fidelity testing and machine learning applications. By removing external variables such as individual diet, hygiene habits, and medication use, the model provides a consistent "ground-truth" for calibration and sensor validation. Furthermore, the use of an engineered substrate enables safe, repeatable trials, generating the robust datasets necessary for training diagnostic algorithms without the ethical or logistical constraints of clinical human sampling.

Colorimetric Analysis Extraction

After each exposure, the test strips were photographed immediately to prevent fading or further color change. To ensure consistency, every image was taken on a plain white background, from the same distance and angle, under stable lighting. Any photos with glare, shadows, or blur were excluded to avoid distorted color measurements. Analysis focused only on the reaction zone, the specific area where the reagent produced a color change, and this region was selected the same way each time to maintain fairness across samples. Multiple color readings were collected from that area to reduce error caused by small uneven spots on the paper. Each image's measurements were then paired with its known concentration and correct group label, creating a clean and organized dataset for calibration and model testing.

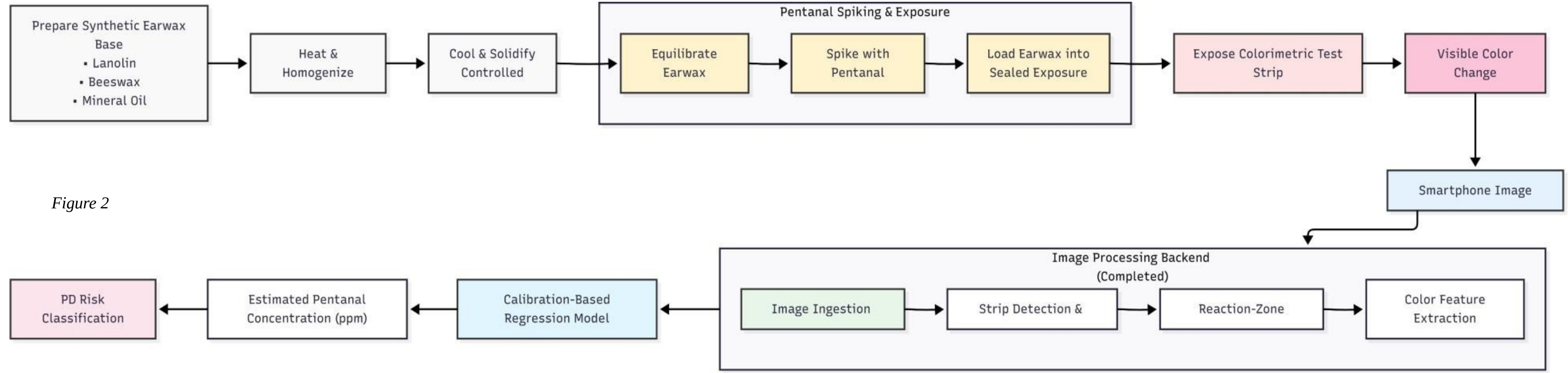
This standardized imaging process was critical because the predictive model depends on subtle differences in color intensity. Even small variations in lighting or angle could introduce noise into the dataset. By tightly controlling how images were captured and processed, the system ensured that changes in numerical values reflected real chemical differences rather than environmental inconsistencies. This improved both the reliability of the regression model and the overall accuracy of the final classification results.

Validation & Calibration Refinement

Calibration was performed by plotting extracted color intensity features against known pentanal concentrations to build a mapping from color space to ppm estimates. To test generalization, blinded samples were analyzed using the full pipeline without revealing labels until after prediction. Model performance was evaluated using classification accuracy and standard diagnostic metrics (precision/recall and error patterns across concentration groups). The completed system achieved ~90% accuracy and was deployed in an iPhone-based workflow that guides image capture, runs automated analysis, and returns a PD-like vs non-PD result with confidence. Future refinement focuses on expanding calibration points and stress-testing against lighting/camera variability to reduce uncertainty—improving robustness without redesigning the chemistry or pipeline.

A Low-Cost Colorimetric Sensor Strip for Detecting Parkinsons-Linked VOCs in Earwax

Chemistry & AI Diagnostic Pipeline



AI Quantitative Prediction

After the reaction zone is isolated, the system converts the image into structured numerical data rather than treating it as a simple photograph. Each pixel in the reaction area contains measurable RGB intensity values, which are also transformed into HSV to capture both raw intensity and perceptual color information. Using OpenCV and NumPy, the program computes statistical summaries across the region, including mean RGB, mean HSV, and normalized color ratios to reduce lighting variability. These values are combined into a feature vector that quantitatively represents the chemical response of the strip. Each feature vector is paired with its known pentanal concentration (0 ppm, 3 ppm, or 30 ppm), forming a labeled dataset for supervised learning.

For quantitative prediction, Ridge regression with L2 regularization is used to model the relationship between color features and pentanal concentration. The model learns weighted coefficients by minimizing prediction error while penalizing large coefficients to reduce overfitting and improve stability, particularly because RGB and HSV channels are correlated. This produces a continuous ppm estimate that can generalize beyond calibration points. Logistic regression is then applied to convert predicted concentrations into a probability-based PD-like or Non-PD classification. Model performance is evaluated using cross-validation, Mean Absolute Error (MAE) for regression accuracy, and classification metrics including accuracy, precision, recall, F1-score, and ROC-AUC to ensure reliability across unseen samples.

Biomarker Selection & Chemical Sensing

The biomarker strategy focused on VOCs reported to differ between PD and healthy controls in ear-canal secretion studies. VOCs are attractive targets because they can be detected without blood draws, imaging, or complex clinical procedures, and because they can be measured through chemical reactivity rather than expensive instrumentation. Among reported candidates, this project prioritized pentanal as a primary target because it is an aldehyde compound that is chemically well- suited for low-cost colorimetric detection.

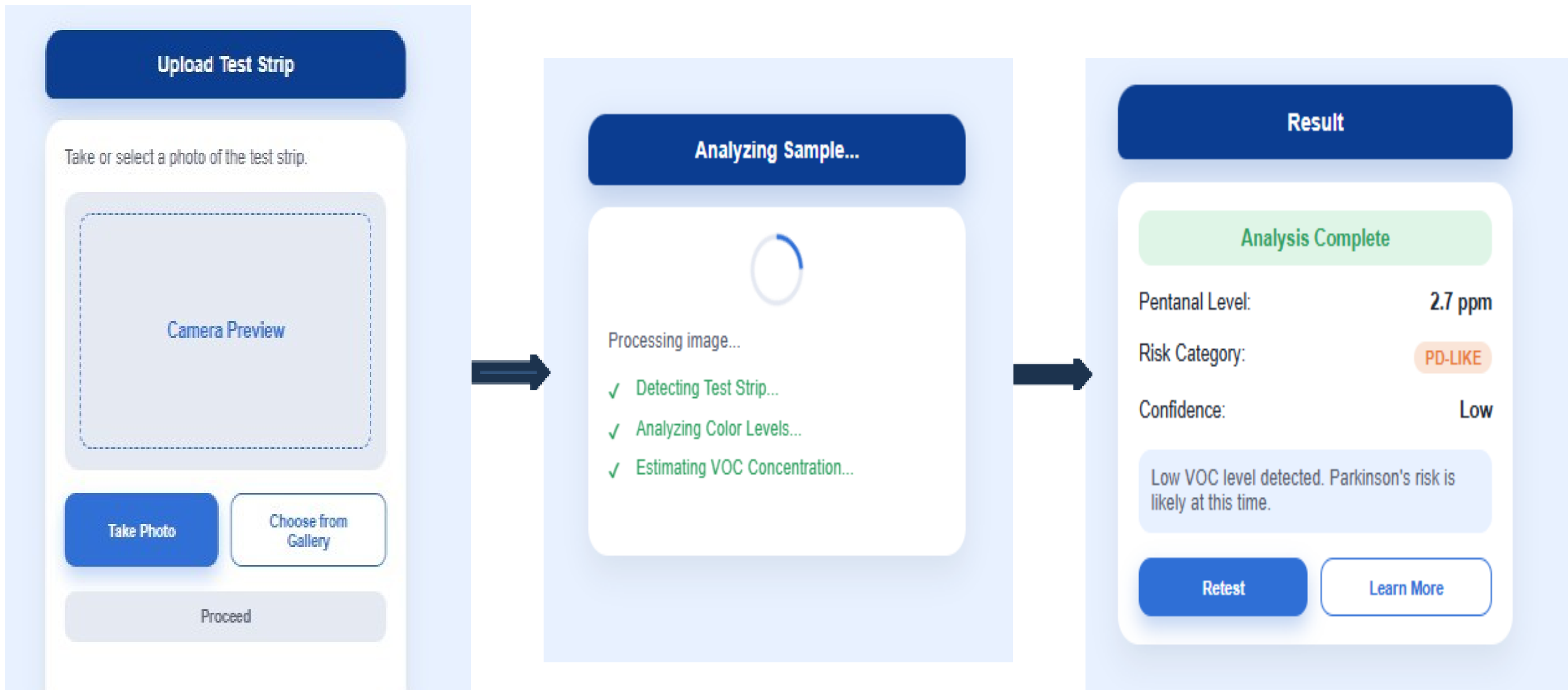
Aldehydes can be detected through selective reagents that produce visible color changes, enabling a low-cost sensing pathway. The chemical sensing approach used a reagent-treated paper strip designed to react with aldehyde vapors released into the vial headspace above the earwax sample. This “headspace exposure” method reduces contamination and allows the reaction to occur primarily in the sensing zone rather than directly in the wax matrix.

Key design reasons for this approach:

- Non-contact sensing: strip does not need to touch wax → cleaner images and more consistent reaction zone.
- Optical measurability: the output is visible color intensity, which can be quantified through simple imaging.
- Scalability: paper strips and small vials are inexpensive and repeatable for large datasets.
- Compatibility with AI: the result is a standardized image classification/regression problem.

Mobile App

A fully functional iPhone application was developed to translate the laboratory-based sensing system into a portable, real-world screening workflow. The app allows users to capture or upload an image of the exposed Schiff's reagent test strip under guided alignment conditions to improve consistency. Once submitted, the backend image-processing pipeline automatically detects the strip, isolates the reaction zone, and extracts calibrated color features for quantitative analysis. These features are processed through a trained regression model that estimates pentanal concentration in parts per million (ppm). The estimated concentration is then interpreted using a clinically motivated threshold to classify the sample as PD-like or non- PD. The Results screen clearly displays the predicted pentanal level, risk category, and model confidence, providing transparent and interpretable output rather than a black-box score. The complete end-to-end system from chemical sensing to AI-based interpretation achieved approximately 90% classification accuracy in controlled testing. This demonstrates the feasibility of a low-cost, scalable, smartphone-compatible screening approach that can be further refined through expanded calibration and clinical validation.



Hypothesis

This study tested the hypothesis that PD-linked VOCs in earwax can be translated into a measurable optical signal and accurately interpreted by an AI model.

Chemical hypothesis: If an aldehyde VOC target associated with PD (e.g., pentanal) is present in the earwax headspace, then exposing a paper strip treated with an aldehyde- reactive reagent will produce a reproducible color change. Furthermore, the magnitude of the color change will scale with VOC concentration, creating a graded signal suitable for quantitative measurement.

Computational hypothesis: If strip images are captured under controlled, standardized conditions, then extracted color features (RGB/HSV intensity values, histograms, and normalized ratios) will correlate strongly with VOC concentration. A supervised ML model trained on labeled strip images will classify samples into PD-like vs non-PD VOC ranges with high accuracy.

Deployment hypothesis: If the imaging + ML pipeline is implemented inside a mobile workflow, then smartphone-based testing can deliver rapid screening results in a portable format without specialized lab-grade optical equipment.



Experimental Setup & Vapor Exposure

Time standardization: Exposure duration was A sealed headspace exposure system was engineered to translate VOC concentrations within the synthetic matrix into a controlled vapor environment. Each sample vial functioned as a miniature reaction chamber, allowing targets to partition from the wax into the air above. Filter-paper strips, prepared with a standardized reagent volume, were suspended at a fixed geometry to maintain a consistent distance from the substrate. This orientation ensured that the reagent zone remained within the headspace without direct contact with the wax, thereby improving image quality and reducing variability caused by strip placement.

To simulate realistic biological conditions and accelerate chemical equilibrium, vials were sealed and incubated at a physiologically relevant temperature. Exposure duration was strictly timed to ensure all samples underwent an identical reaction window. Immediately following exposure, strips were photographed under fixed lighting and at a standardized angle and distance. This rigorous control of the background environment, vial mass, and imaging focal length produced a repeatable dataset suitable for both chemical calibration and high-accuracy AI model training.



A sealed glass vial containing a uniform artificial earwax matrix at the base is used to simulate VOC emission. Volatile organic compounds (VOCs) released from the sample diffuse into the headspace and are captured by a suspended adsorbent paper strip. The interaction is visualized by highlighted molecules, illustrating a non-invasive headspace sampling approach for chemical detection and analysis.

Conclusions

This project demonstrates a practical proof of concept for low-cost PD screening using earwax VOC signatures. A Schiff's reagent-based colorimetric strip produced a concentration-dependent aldehyde signal in a synthetic earwax matrix, enabling consistent imaging and quantitative feature extraction. A complete AI vision pipeline was implemented to detect the strip, isolate the reaction zone, extract explainable color features, and generate VOC concentration estimates that feed a PD-like classification model. The system reached approximately 90% accuracy and was successfully translated into a smartphone workflow, supporting the feasibility of portable, scalable screening. With broader calibration, larger datasets, and clinical validation, this approach could evolve into an accessible early-risk screening tool to support earlier medical evaluation and intervention