iOT device design for rapid detection of Alzheimer inducing P. gingivalis bacteria

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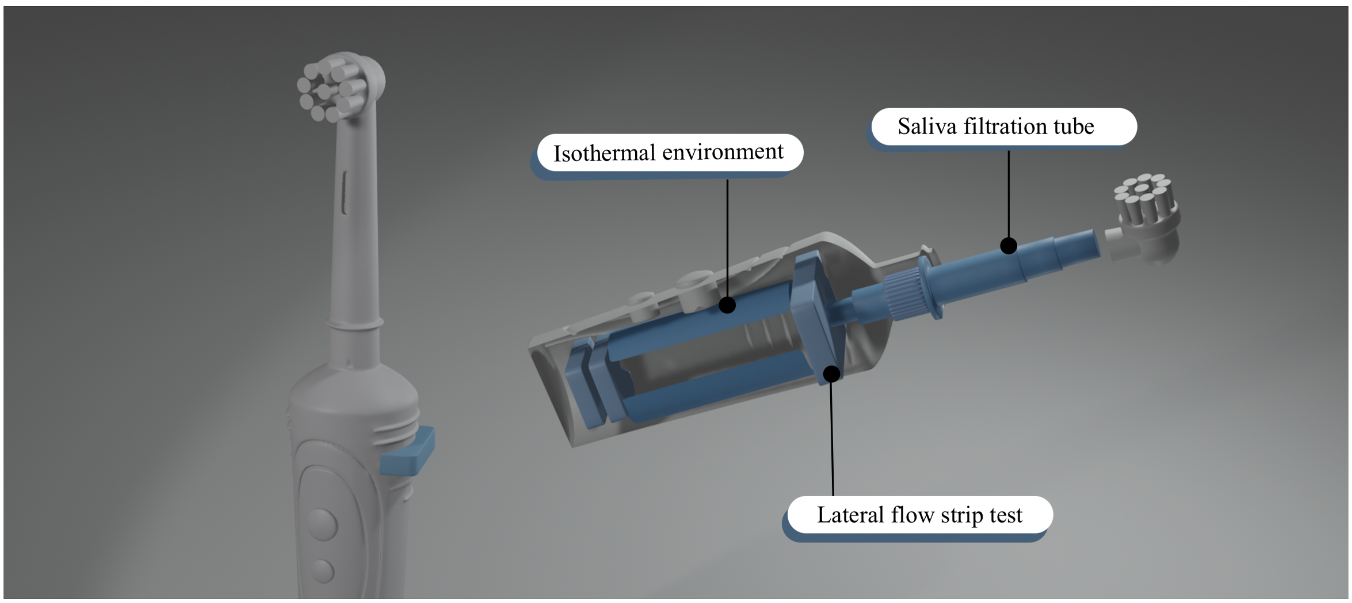

Figure 1: IoT-Enabled Toothbrush with Embedded P. gingivalis Bacteria Test for Alzheimer's Disease Risk Assessment.

ABSTRACT

Regular monitoring of cognitive health to detect early signs of decline is essential for the diagnosis of Alzheimer and other forms of dementia. However, cognitive testing is usually carried out in healthcare settings by physicians and other professionals, which limits accessibility, or via self-reported tests that can be burdensome for older adults to regularly undertake. Dental plaque microbes, including P. gingivalis, have been linked to Alzheimer's disease pathology, prompting the exploration of a brain-oral connection. Recent advancements in P. gingivalis detection, such as Isothermal Amplification and Lateral Flow Strip Techniques, open avenues for early diagnosis with a potential to integrate low-burden reliable screening in care pathways. This paper proposes an IoT device for timely Alzheimer's-linked oral pathology detection, addressing a critical research gap in accessible testing. We introduce an electric toothbrush prototype with bacteria-sampling capabilities, capitalizing on daily habits to self-monitor oral health dynamics.

CCS CONCEPTS

• **Applied computing → Health informatics**.

KEYWORDS

IoT Device, Oral Health Monitoring, Alzheimer's Disease, Bacterial Biomarkers, Healthcare Technology

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1 INTRODUCTION

Alzheimer's disease is a distressing neurodegenerative condition that imposes a significant healthcare burden on individuals and society as a whole. Detecting this debilitating disease as early as possible is of paramount importance, yet recieving a timely diagnosis remains a challenging endeavor especially for those who face barriers accessing healthcare services [2]. This is where the authors see potential in self monitoring iOT devices built into daily routine which enable timely identification of worrisome bioindicator developments. Microbes within dental plaque such as *P. gingivalis* have been linked with the formation of pathology characteristic for an Alzheimer's disease [3]. Although the direct mechanism of causality has not yet been fully understood it became evident to the scientific community that there is a direct brain-oral connection, as *P. gingivalis* bacteria are consistently present in the brain tissues of Alzheimer's patients [13]. Recently, a novel rapid detection method for *P. gingivalis* based on Isothermal Amplification and Lateral Flow Strip Methods has been proposed by a team of scientists at Lianyungang City Hospital [5]. Leveraging these rapid testing methodologies open the door to the use of bioindicators as a preventative measure to flag the need for further diagnostic tests within the context of long-term cognitive health monitoring. This paper builds upon recent *P. gingivalis* rapid detection advancements and proposes a design of an iOT-enabled toothbrush device with integrated bacteria sampling technology. The habitual daily usage of toothbrushes by patients gives a unique opportunity to sample and create a temporal understanding of the oral health without the need of complex laboratory instruments.

2 RELATED WORKS

2.1 P. gingivalis and Alzheimer's disease

A growing body of research such as [4], [12] and [9] has explored the intriguing link between Porphyromonas gingivalis (P. gingivalis), a bacterium associated with gum disease, and Alzheimer's disease, a neurodegenerative condition characterized by cognitive decline and memory loss. Recent studies have suggested that chronic oral infections, including periodontal disease caused by P. gingivalis, may contribute to an increased risk of Alzheimer's disease. P. gingivalis can release toxic proteins known as gingipains, which can enter the bloodstream and potentially reach the brain. In the brain, these gingipains may trigger inflammation and the accumulation of beta-amyloid plaques, one of the hallmarks of Alzheimer's disease[4]. While more research is needed to fully establish the causal relationship between P. gingivalis and Alzheimer's, these findings underscore the importance of oral health as a potential factor in cognitive decline and the need for maintaining good dental hygiene as part of a holistic approach to brain health and Alzheimer's disease prevention.

2.2 Isothermal Amplification and rapid testing

To perform a lateral flow strip assay the DNA sample needs to be amplified. Recombinase Polymerase Amplification (RPA) is a molecular biology technique used to make multiple copies of a specific DNA sequence at a constant temperature, without the need for a thermal cycling process, as required in Polymerase Chain Reaction. This method offers advantages such as simplicity, rapidity, and the ability to perform DNA amplification in resource-limited settings. The amplified DNA in turn increases the sensitivity of lateral flow strip (LFS) assays and minimizes the risk of false negative test. [11].

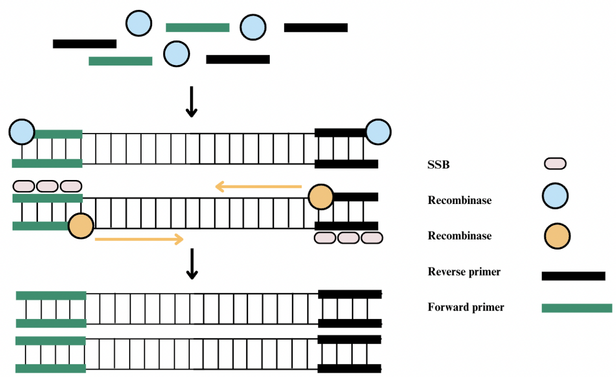

Figure 2: DNA amplification

In the RPA process three core enzymes—recombinase, single-stranded DNA-binding protein (SSB), and strand-displacing polymerase—work in tandem with forward and reverse primers to orchestrate the precise and efficient amplification of target DNA or RNA sequences. Recombinase enzymes play a pivotal role by binding to the target sequence and initiating the process of strand exchange, creating single-stranded regions essential for primer annealing. These enzymes facilitate the formation of recombinase nucleoprotein filaments and joint molecules. Single-stranded DNA-binding proteins further stabilize the single-stranded regions by preventing their re-annealing, ensuring that primers can effectively anneal to their complementary sequences. Strand-displacing polymerases are responsible for DNA synthesis, extending the primers and amplifying the target sequence in a highly specific and efficient manner.

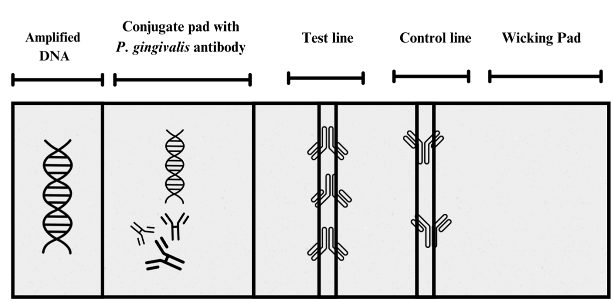

Figure 3: Lateral flow strip with RPA amplified DNA sample

Once the amplified sample is ready, the next step is the Lateral Flow Strip diagnostic. It consists of a strip with immobilized antibodies specific to P. gingivalis. When an oral sample is applied, any P. gingivalis present binds to the antibodies, forming complexes. As the sample flows along the strip, these complexes encounter a test line with immobilized antibodies, causing a visible line to appear if P. gingivalis is present. A control line further validates the test's accuracy.

2.3 Self-monitoring iOT devices for cognitive decline detection

iOT-enabled devices for cognitive decline recognition can be categorized as PIR motion sensors, body-worn sensors, pressure sensors, video monitoring and sound recognition [10]. For instance, the study conducted by F. Ahamed utilizes smart video monitoring and a smart home setup in combination with predictive model for cognitive anomalies detection [1]. Another prominent body of research proposes a sleep tracker and investigates the interplay between sleep patterns and Alzheimer's disease pathology. The authors suggest a bidirectional relationship wherein insufficient sleep heightens the risk of Alzheimer's disease development, and within the context of the disease, sleep disturbances manifest forming a positive-feedback loop. This cyclic phenomenon is attributed to the accumulation of amyloid-β in the brain. Subsequent to the formation of amyloid plaques, sleep-wake functions and circadian rhythms are disrupted[7]. Many available iOT developed devices use the PAS architecture, which is a protocol developed for third party component communication and privacy implementation for monitoring medical devices [6]. Existence of a large prior research body, as well as established privacy protocol standards allow the proposed design to leverage the pre-existing insights.

3 PROPOSED IOT DEVICE DESIGN

The proposed device consists of saliva filtration, rapid testing data storage modules and a isothermal chamber. The sample of oral bacteria film is taken during brushing of the teeth and fall into the saliva filtration tube, where using mechanical filtration saliva will is extracted from the solution. Next, when the device is be put back to the charging station and connection with the charging port is detected the filtered saliva falls into the lateral flow strip once the isothermal chamber reaches the desired temperature. The test is extracted for 30 minutes and a photo of the test is taken by a embeded camera and using computer vision-based classification algorithm the test result is determined. A green light on the toothbrush outer body indicates lack of P.gingivalis bacteria and a red light indicates detection of bacteria in the tooth film. The device would be distributed by the healthcare practitioners and dentists, who would be able to answer patients questions and concerns regarding the device. The device would be designed with a 2 year lifespan and at distribution it would be equipped with multiple brush heads for hygiene maintenance. The replaceable parts such as the lateral flow strip test would be available in pharmacies.

3.1 Saliva filtration tube

Separating saliva and toothpaste is a challenging task due to their complex compositions. One approach is to exploit their differential solubility in water. Saliva, primarily composed of water and organic molecules, readily dissolves in aqueous solutions. Toothpaste, on the other hand, typically contains various components such as abrasives, thickeners, and fluoride compounds, with varying solubility characteristics. To separate them, one can first mix saliva and toothpaste with distilled water, which could be embeded inside the toothbrush and replaced every time testing takes place. By allowing the mixture to sit undisturbed, less soluble toothpaste components, such as abrasives, settle at the bottom while the soluble components dissolve in water. Subsequently, the clear liquid supernatant can be carefully decanted, effectively separating the more soluble toothpaste constituents from the saliva. Given that this process could be cumbersome and difficult to implement we identify the need for consideration of implementation of the *dry brushing mode*, where the user will use the toothbrush to scrape the dental film with the toothbrush prior to using the toothpaste. An alternative approach would be to test the sensitivity of the Lateral flow test to the presence of inpurities such as toothpaste, which we discuss in more details in the Limitation's section.

3.2 Rapid testing module

This module composes of the insertable lateral flow strip slide and the lower part of the saliva filtration tube where the solution for RPA is stored. Once the connection of the device with the charging port is detected the RPA process starts in the isothermal environment and once compleated the filtered and amplified saliva is released onto the lateral flow strip.

3.3 Data extraction

In the development of an IoT-enabled toothbrush for Alzheimer-linked bacteria sampling, effective data handling plays a crucial role across various layers of the IoT architecture. In the design of the data handling architecture we plan to subdivide it into the Perception layer, Network Layer and Application Layer. Perception Layer serves as the foundation for data collection through a myriad of sensors, including micro camera which captures the lateral flow test results, which later on is passed to the Network Layer, which handles data flow. For this device a cloud-based approach will be considered for handling data-intensive image classification tasks. We realize that this introduces the need for rigid privacy and communication protocols such as the PAS architecture and introduces potential latency problems [8]. The final Application layer handles data analytics using simple computer vision-based classification algorithm to determine the result of the test. The classification outcomes will be translated into easy to understand for the user visual-cues. A light embeded in the external body of the toothbrush will indicate presence of the *P. gingivalis* bacteria (red light) or absence of the bacteria (green light).

3.4 Isothermal module

The DNA amplification requires isothermal conditions. Therefore within the body of the toothbrush we embed a thermal control system based on the PID (Proportional-Integral-Derivative) control device, to maintain a constant temperature around 37-42°C optimal for P. gingivalis detection. The PID controller continuously computes the control output as a weighted sum of the proportional, integral, and derivative components. In context of the proposed device the Proportional Gain K_p represents how aggressively the device responds to differences between the desired temperature setpoint and the actual temperature inside the toothbrush, Internal Gain K_i stands for accumulation of past errors over time and the Derrivative Gain K_d, accounts for the rate of change of the error signal. It anticipates future error by calculating the rate at which the error is changing and adjusts the control output accordingly.

Control Output = $(K_p\cdot\text{Proportional})+(K_i\cdot\text{Integral})+(K_d\cdot\text{Derivative})$

Control Output is the dynamic signal generated by the PID controller to control the temperature, ensuring that it remains within the specified range for the successful amplification and detection of P. gingivalis DNA. The PID controller continuously calculates and updates this output to maintain precise and stable isothermal conditions, essential for accurate pathogen detection from the toothbrush.

3.5 Service design

The IoT-enabled toothbrush integrates into already established habit of tooth brushing and it translates complicated knowledge into a user-friendly experience. Device acquisition and onboarding can be done with the help of a primary care physician. The proposed device will be equipped with a straightforward LED indicator, featuring a small green or red light on the toothbrush that offers immediate detection results. A green signifies the absence of P. gingivalis bacteria, while red signifies its presence. The toothbrush will have a vibration function if P.gingivalis is present to further alert the user thereby improving accessibility of the device for the visually impaired.

4 TEMPORAL ANALYSIS OF RESULTS

To further mitigate the inaccuracies in predictions a regression-based composite measure derived from the average of lateral strip test results will be implemented. Brushing time reflects the duration of daily oral hygiene routines, while brushing frequency signifies how often individuals engage in these practices. The relationship between these independent variables and the oral health score can be modeled using a multiple linear regression equation, as depicted in equation below, where Y represents the oral health score, β_0 is the intercept, β_1 and β_2 are the regression coefficients for brushing time (X_1) and brushing frequency (X_2) respectively, and ϵ represents the error term. This regression model allows us to explore and quantify the potential impact of brushing behaviors on oral health outcomes.

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_p X_p + \epsilon \tag{1}$$

5 LIMITATIONS

The proposed IoT device necessitates replacement of the lateral flow strips for effective bacterial detection, as they cannot be reused. Regular maintenance and replacement of these strips are necessary for users to ensure reliable results, which could be inconvenient and add overall cost of using the device. Furthermore, bacterial sampling using IoT device relies on the isolation of saliva sample from the toothpaste. We identify the need for further testing of the proposed isolation technique for which we will use pure saliva samples with P. gingivalis bacteria, pure saliva without bacteria, saliva with toothpaste solution with P. givalis bacteria and a saliva with toothpaste and no bacteria present. Those samples will be tested using the RPA-LFS assay technique using TwistAmp DNA amplification kit and a Lateral Flow Test produced by Ustar BioTechnologies. We hope to verify with this experiment the impact of impurities on lateral strip test results. Another limitation of the device may also be susceptability to false positives and false negative results. Variations in the concentration of P. gingivalis in the oral cavity, cross-contamination, cross-reactivity, and sensitivity in detection methods may contribute to incorrect readings. For instance, there is still a possibility of IoT device cross-reacting with other oral bacteria that are irrelevant to AD (Alzheimer's Disease), which may result in false positives or false negatives. False positives may cause unnecessary concerns for users, while false negatives may lead to users not being able to detect Alzheimer's-linked oral pathologies at an early stage.

6 CONCLUSIONS AND FUTURE WORK

The development of an IoT-enabled toothbrush for the rapid detection of Alzheimer-linked P. gingivalis bacteria represents a significant step towards accessible and timely Alzheimer's disease diagnosis. Future developments of the IoT-enabled toothbrush should focus on addressing its limitations and creating a tangible prototype. Research efforts can be directed towards gathering user feedback and optimizing lateral flow strip technology to reduce the need for frequent replacements, thus enhancing cost-effectiveness and user-friendliness. Furthermore, exploring advanced machine learning algorithms for data analysis could improve the device's sensitivity and specificity. This would help mitigate the risk of false positives and false negatives, enhancing the device's overall accuracy. Collaborations with healthcare professionals and institutions are essential to validate the device's efficacy in clinical settings. Large-scale studies and longitudinal assessments can provide valuable data on its real-world impact on Alzheimer's disease detection and prevention.

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