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Aptheimer: Design of Aptasensor with Carbon Electrodes and Prediction Algorithm for the Early Pseudo Diagnosis of Alzheimer's Disease

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***Abstract*– Alzheimer's is a neurodegenerative disease that is constantly growing in Peru. It affects more than 200,000 elderly people. This fact highlights the importance of creating diagnostic methods that are more accessible and efficient. Considering this, a novel approach proposes a biosensor to identify biomarkers, such as beta-amyloid and phosphorylated tau, in blood samples. The aptasensor works together with a prediction algorithm based on clinical data. The procedure involves acquiring aptamers, choosing carbon electrodes, and using a convolutional neural network model to detect Alzheimer's in the early stages. This system is expected to provide an accurate pseudo-diagnosis, reducing the need for invasive procedures and improving the clinical treatment of the disease, which at the same time will improve the quality of life of patients and their families.**

Keywords—Aptasensor, Carbon Electrodes, Alzheimer's Disease, Predictive Algorithm, Biomarkers, Convolutional neural networks

I. Introduction

Alzheimer's disease is a neurodegenerative disease that primarily affects older adults and is characterized by a progressive loss of memory and other cognitive functions. In Peru, the prevalence of this disease has been increasing, becoming a significant public health problem. According to data from the Ministry of Health (MINSA) in 2019, more than 200,000 Peruvian older adults suffer from Alzheimer's. [1] This situation represents a considerable challenge for the health system and for the families of patients, who must face both the emotional and economic aspects associated with caring for people with this condition.

The increase in Alzheimer's incidence in Peru not only places a greater burden on the health system but also highlights the urgency of creating more effective and available diagnostic and treatment methods. Given the above situation, it is crucial to investigate new procedures that can increase early identification and therapy of Alzheimer's, with a special focus on making these advances available to the inhabitants of Peru.

Biomedical engineering is central to this work, providing solutions such as creating biosensors to identify biomarkers in the blood, which could change how the disease is diagnosed. In this way, the union of cutting-edge technology and a patient-centered approach could significantly impact the battle against Alzheimer's in Peru and regions with similar problems.

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II. Current Alzheimer's detection systems in Peru

Early detection and diagnosis of Alzheimer's disease are essential to improve the quality of life of patients and their families. Yet, the widespread use of these tests is hindered by the availability and cost constraints, as well as the deficiency of expert practitioners. This section explains the most frequent diagnostic instruments, outlining their uses and key features. This examination offers a summary of the status of diagnostic methods for Alzheimer's disease.

A. Neuropsychological Tests

These assessments evaluate memory, reasoning, problem-solving, speech, and other mental skills. A commonly used tool to assess the degree of cognitive impairment is The Mini-Mental State Examination (MMSE). This brief assessment takes 5 to 10 minutes to complete and is intended to detect cognitive difficulties. It evaluates 7 different domains: visual copying, naming and following directions in language, knowledge of date, day, and season in temporal orientation, current location and direction home in spatial orientation, concentration and simple calculations in attention and calculation, and repeating three words in short-term memory. [2] It is important to note that the orientation questions were grouped in the original version and the visual construction was seen as part of the language.

B. Cerebral Imaging Techniques

Imaging has advanced in the diagnosis of Alzheimer's disease by shifting from ruling out surgical causes of cognitive decline to pinpointing characteristic patterns and amyloid deposits. [3] Imaging techniques such as Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), and Computed Tomography (CT) are utilized to identify brain structural and functional alterations linked to Alzheimer's

disease. Abnormal β-amyloid deposits have been detected in certain older adults with normal cognitive function, using a specific ligand for identification. The connection between these deposits and the level of impairment is uncertain in individuals with mild cognitive impairment or in the early stages of Alzheimer's disease. Some individuals with slight cognitive decline display the same build-up of deposits seen in early Alzheimer's, while others with the condition have lower levels. [4] Despite these difficulties, imaging continues to be a critical tool in identifying Alzheimer's.

C. Lumbar Puncture Test

Lumbar puncture, a safe and minimally invasive procedure, allows analysis of the cerebrospinal fluid surrounding the spinal cord and detects abnormalities that indicate neurodegenerative diseases. While lumbar puncture is mostly safe, it can have various complications. Post-puncture headache (PDPH) is the most prevalent, impacting up to 40% of patients and having a duration of fewer than 5 days to multiple weeks. Additional issues that can arise include cranial nerve problems like blurry vision or ringing in the ears caused by low pressure within the skull; irritation of nerve roots and lower back pain, which in rare instances may cause lasting sensory or motor damage; and infections stemming from a dirty needle or an infection at the puncture site. Hemorrhagic events, like subdural or subarachnoid hematomas and epidural hemorrhages, may also happen, though they are uncommon. Occasionally, puncturing can result in brain or spinal herniation due to a sudden drop in cerebrospinal fluid pressure, and issues related to the stylet, like inserting a skin plug incorrectly into the intrathecal area. [5] Cerebrospinal fluid (CSF) analyses are used to measure levels of specific proteins, such as beta-amyloid and phosphorylated tau. In Alzheimer's disease, these biomarkers are indicative of the presence of senile plaques and neurofibrillary tangles, hallmarks of the disease.

D. Genetic Testing

The purpose of genetic testing is to identify the genes that are linked with a higher possibility of being afflicted with Alzheimer's disease. A vast amount of genetic research has established that the primary genetic contributor to this disorder is the ε4 allele of the APOE gene.[6] Despite being an important hereditary risk factor, clinical practice does not frequently employ genetic tests for the detection of this allelic form. Instead, it is mainly utilized in research and clinical trials aimed at enhancing comprehension of the genetics underlying Alzheimer's, leading to the production of specific interventions. These tests can yield valuable insights into one's genetic predisposition toward the development of Alzheimer's; thereby enabling understanding about its meaning and potential threats.

In general, tests for Alzheimer's disease have two main drawbacks: they are not frequently used in standard clinical settings, and they can cause adverse effects in patients. Advanced diagnostic methods, such as a lumbar puncture to analyze cerebrospinal fluid, are effective in detecting specific biomarkers, but they carry risks such as headaches, infections, or bleeding. Likewise, imaging techniques such as MRI and positron emission tomography (PET) provide valuable information about brain alterations, but they can be expensive and not available in all healthcare centers. The limitations underscore the need to develop simpler and less invasive screening methods to improve the ability to accurately identify Alzheimer's disease in its early stages.

III. IMPORTANT BIOMARKERS IN ALZHEIMER'S DISEASE

Biological markers are real biological signals that can be measured and analyzed objectively to determine diseases inside the human body. Early detection of the disease, as well as tracking its development, is mainly done through biomarkers in Alzheimer's disease. So far, β-amyloid (1-42), total tau, and phospho-tau-181 are the most reliable biomarkers for detecting Alzheimer's disease with accuracy. This allows the disease to be detected early, before symptoms appear, making it easier to start treatment and manage it promptly. [7] This discovery has changed how we diagnose this neurodegenerative condition due to the existence of some unique Alzheimer's biomarkers. Not only do these markers help us confirm cases of Alzheimer's disease but they also differentiate it from different types of dementia. The importance of this stage cannot be overemphasized because there are times when symptoms are so mild that they may go undetected or even be mistaken for normal aging processes or other mental disorders.

A. Beta-amyloid

Beta-amyloid is a protein fragment derived from the amyloid precursor protein (APP), which is in cell membranes. The precursor protein is degraded into smaller fragments, with beta-amyloid being a major component. In Alzheimer's disease, beta-amyloid fragments tend to cluster together and create amyloid plaques in the brain. These plaques are viewed as one of the most defining and unique discoveries of the illness. The build-up of amyloid plaques in the brain negatively affects the function of neurons. These plaques disrupt neuron communication, impacting synaptic transmission and leading to gradual neuronal demise. The interruption of communication between neurons and the death of nerve cells leads to cognitive decline and memory deficits linked to Alzheimer's disease [8].

Evaluating beta-amyloid levels in both cerebrospinal fluid (CSF) and blood has become a crucial method for detecting the disease in its early stages. Evaluating beta-amyloid levels is essential for determining the existence and impact of amyloid plaques in the brain, assisting in early detection and treatment of the disease. According to research conducted by the University of Zaragoza in Spain, the plasma Aβ42/Aβ40 ratio, which indicates the proportion between the levels of beta-

amyloid peptides 42 and 40, has shown an accuracy of 81% in predicting beta-amyloid accumulation in the cerebral cortex. This ratio is 110% higher than the presence of amyloid load in healthy control subjects [9]. Thus, the Aβ42/Aβ40 ratio could be an inexpensive and non-invasive way to identify early amyloid load in the cerebral cortex, which would facilitate diagnosis and selection of participants for clinical studies.

B. Phosphorylated Tau protein

Tau protein that has been phosphorylated is found in abundance in neurons within the brain. Tau interacts with microtubules in neurons, ensuring their stability and facilitating transport within axons. In Alzheimer's disease, tau proteins undergo abnormal phosphorylation when their normal function is to support microtubules in neurons. This atypically phosphorylated tau variant clumps together to create neurofibrillary tangles within nerve cells. These neurofibrillary tangles block the passage of essential nutrients into neurons, causing cell dysfunction and ultimately cell demise. Another important biomarker for the detection of AD involves assessing the levels of phosphorylated tau found in the cerebrospinal fluid. Recent research suggests that it may be feasible to detect p-Tau181, a type of tau protein phosphorylated on threonine 181, in blood and cerebrospinal fluid as a biomarker for Alzheimer's disease. [10]

IV. METHODOLOGY

To effectively address the issue of Alzheimer's detection, an Empathy Diagram, and a Business Model Canvas will be developed. The Empathy Diagram will allow for a deep understanding of users' experiences and emotions, which is crucial to identifying their needs, frustrations, and aspirations about Alzheimer's diagnosis. This tool will help design a solution that accurately addresses their concerns and improves their experience with the product.

The Business Model Canvas will be used to structure all key aspects of the project. The Canvas will include the following elements:

A. *Key Activities:* The process involves the development of specific aptamers, followed by the binding of these aptamers to electrodes. The biosensor is then validated using plasma samples. Next, the multiple linear regression algorithm is implemented, and the collected data are analyzed. Finally, the results are evaluated by experts.
B. *Key Resources:* The system includes compatible aptamers, screen-printed electrodes, a microcontroller for signal detection, hardware comprising electronic and mechanical components, data analysis software, and a database.
C. *Value Proposition:* Blood extraction is used to collect analytes instead of lumbar puncture. This approach reduces diagnostic times, eliminates the need for imaging tests that involve ionizing radiation, and ensures that the biosensor is accessible in pharmacies.
D. Customer Relationship: Discounts or benefits for patients who undergo regular testing, incentivizing the continuous use of the biosensor, as well as workshops and seminars on Alzheimer's and the biosensor.
E. *Channels:* Pharmacies, clinics, and hospitals, online sales, and social media.
F. *Customer Segments:* Patients with Alzheimer's disease, caregivers of individuals with suspected Alzheimer's, healthcare professionals, and pharmacies and medical device distributors.
G. *Revenue Streams:* Sale of biosensors, diagnostic services, collaborations with clinics, research and development funding, and fees for training and workshops.
H. *Cost Structure:* Development of aptamers, biosensor manufacturing (materials and labor), electronic components (microcontrollers, electrodes, etc.), data analysis and management software, validation and clinical testing, marketing and product promotion, and user training and education.

To ensure the successful implementation of the biosensor in real-world scenarios, it is essential to address scalability from the outset of development. This involves planning for large-scale production, and ensuring that manufacturing processes are efficient and sustainable. Selecting high-quality yet cost-effective materials is key to balancing cost and performance, facilitating mass production without compromising the device's accuracy. Additionally, developing a distribution strategy that allows for the efficient and cost-effective delivery of the biosensor to pharmacies, clinics, and hospitals will be crucial. Utilizing online sales platforms and establishing partnerships with medical device distributors can further enhance the product's reach. By planning for scalability from the beginning, the aim is not only to reduce costs but also to ensure that this innovative diagnostic tool is accessible to those who need it most.

On the other hand, the biosensor's mechanism of action is based on two key components: the biosensor itself, developed with specific aptamers, and the associated predictive algorithm. The biosensor, designed to detect biomarkers through aptamers, provides essential electrochemical data. These data, in turn, are analyzed by the predictive algorithm, which uses advanced techniques to interpret the information and generate accurate predictions. This synergistic combination ensures accurate and efficient detection of Alzheimer 's-related pathological conditions.

A. Aptamer-based Biosensor

1) *Obtaining Aptamers using the SELEX Method:* A comprehensive process will be undertaken to develop a specialized library of aptamers. Initially, a diverse collection of random aptamers will be synthesized using advanced oligonucleotide synthesis techniques. This synthetic library will then be exposed to Tau-P or Aβ, which will be immobilized on a solid support matrix. This step facilitates the selective binding of aptamers that demonstrate high affinity for the targeted biomarkers. Following incubation, rigorous washing procedures will be employed to remove any aptamers that did not bind to the biomarkers, ensuring that only those with strong and specific interactions are retained. The aptamers that successfully bind to the biomarkers will be eluted from the matrix and subsequently amplified through Polymerase Chain Reaction (PCR) to generate enough of these specific aptamers. The entire process of selection and amplification will be iteratively repeated. This iterative approach ensures the enrichment of aptamers with the highest levels of affinity and specificity for Tau-P and Aβ. Through this method, we aim to isolate and optimize aptamers that can effectively recognize and bind to the targeted biomarkers, which are crucial for the development of a reliable pseudo-diagnostic biosensor.

2) *Selection of Carbon Electrodes:* Screen-printed carbon electrodes will be selected for their advantageous properties, including a large surface area, high conductivity, and excellent biocompatibility [11]. These features ensure enhanced sensitivity, improved electrochemical response, and an optimal interface for the immobilization of biomolecules. The extensive surface area of these electrodes allows for greater interaction with aptamers, thereby optimizing biomarker detection. Their high conductivity facilitates efficient electron transfer, enhancing the accuracy of electrochemical measurements. The biocompatibility of these electrodes is crucial to avoid adverse reactions during biomedical applications. Furthermore, these electrodes have been successfully utilized with aptamers in previous studies, reinforcing their suitability for our application. Their ability to provide reliable and reproducible performance in biomarker detection makes them an excellent choice for this research.

3) *Aptamer Immobilization via Chemical Adsorption:* The immobilization of aptamers will be achieved through chemical adsorption onto the carbon electrodes. This method involves the binding of aptamers to the electrode surface through non-covalent interactions, such as electrostatic forces and van der Waals interactions, which are facilitated by adjusting the pH and ionic strength of the solution. Before immobilization, the carbon electrodes will be thoroughly cleaned to ensure a pristine surface that enhances the binding efficiency of the aptamers. [12] The aptamers, which are specific to target biomarkers such as Tau-P or Aβ, will be prepared in a solution and introduced to the electrode surface. The adsorption process will be optimized to achieve a high density of aptamers on the electrode, which is crucial for maximizing the biosensor's sensitivity and specificity. After immobilization, the electrodes will be rinsed to remove any unbound aptamers, ensuring that only those aptamers that are specifically and stably attached remain on the electrode surface. This approach is expected to provide a robust and reliable platform for the subsequent detection of biomarkers.

4) *Sample Collection:* A blood sample will be obtained from an elderly patient using a standard venipuncture method, ensuring compliance with established ethical and biosafety protocols. The blood sample will then be processed through centrifugation to separate the plasma from the blood cells. The plasma, which contains the relevant biomarkers, will be used for further interaction with the biosensor. This process guarantees that the sample is properly prepared for accurate detection and analysis of the targeted biomarkers, supporting the effective use of the biosensor for diagnostic purposes.

5) *Target Sequence Hybridization:* The biosensor will be utilized to detect specific biomarkers in the plasma sample. The plasma sample, containing the biomarkers of interest, will be incubated with the biosensor at a controlled temperature, allowing the biomarkers to bind to the aptamers immobilized on the electrode surface. This interaction is facilitated through a carefully calibrated process to ensure optimal binding efficiency. The specific binding of biomarkers to the aptamers will be monitored to assess the presence and concentration of the target biomarkers.

6) *Measurement of Biomarker*s: The technique of cyclic voltammetry will be utilized to assess the changes in electrical current resulting from the binding of Tau-P and Aβ to the aptamers immobilized on the electrode. This method involves applying a carefully selected voltage range to achieve optimal electrochemical response. By doing so, it enables precise differentiation of biomarker concentrations, providing detailed insights into the levels of Tau-P and Aβ present in the sample. This approach ensures accurate measurement and analysis, crucial for reliable diagnostic results.

7) *Calibration via Curve*: Standard solutions of Tau-P and Aβ will be prepared, with known concentrations covering the relevant range for Alzheimer's disease diagnosis. Each of these solutions will be used to measure the electrochemical response of the biosensor, with multiple readings taken to ensure reliable results. The data obtained will be used to generate detailed calibration curves that correlate the measured changes in electrical current with the known concentrations of Tau-P and Aβ. These curves will serve as a critical reference for determining the concentrations of biomarkers in patient samples, allowing for accurate and reliable assessment of biomarker levels in the context of Alzheimer's pseudo-diagnosis.

B. Predictive algorithm

The predictive algorithm will be implemented using the data generated by the electrode during the measurement of the sample signal. This integration between the biological component and the predictive algorithm is crucial for the success of the system. The data is derived from the interaction between the biosensor, which detects and measures biomarkers present in the blood sample, and the algorithm, which processes this information to make predictions.

This data encompasses quantitative information about the concentrations of specific biomarkers, as well as variations in the signal that reflect both normal physiological and pathological conditions. Such information is vital for assessing the patient's health status and for identifying patterns that may indicate the presence of a disease. Once collected, this data is organized into a structured dataset. This dataset will serve as the input for the predictive algorithm. The algorithm will use this dataset to analyze biomarker concentrations and differences between physiological and pathological conditions, identifying patterns and correlations indicative of the patient's condition.

A dataset with information like gender, age, MMSE score, CSF biomarkers (β-amyloid and phosphorylated tau), and APOE4 allele presence will simulate data from biosensor electrodes. This dataset will solely be utilized for algorithm testing before sensor evaluation takes place. In simple terms, it will function as a representation of the anticipated outcomes of the biosensor before obtaining actual data from the device. The dataset serves only for testing the algorithm's effectiveness, with no additional role in the process. The following describes the detailed process for implementing the algorithm.

1) *Data Preprocessing:* The numerical features ("Age," "MMSE," "CSF Amyloid," "CSF Total Tau," "CSF Phosphorylated Tau") will be scaled to a comparable range using Z-score normalization. This ensures that all features have similar magnitudes and prevents any single feature from disproportionately influencing the learning process. Conversely, categorical features ("Sex," "APOE4") will be encoded using methods such as one-hot encoding or embedding techniques. This approach allows the model to learn complex relationships between categorical variables and numerical features. Subsequently, all preprocessed features will be combined into a multidimensional tensor for each sample, representing individual patients. This tensor will serve as the input to the convolutional neural network (CNN), facilitating the analysis and pattern recognition necessary for effective predictions and insights.

2) *Prediction Model:* The architecture of the convolutional neural network (CNN) will be designed as follows. The CNN model is designed to analyze tabular data and detect patterns related to Alzheimer's disease. Its architecture starts with an input layer that processes patient-specific data, such as the biomarker levels. Next, a series of 1D convolutional layers will be applied. These layers use filters that slide across the features to capture important patterns and relationships between the different variables. The convolutional layers allow the model to detect interactions between biomarkers and clinical features that may indicate Alzheimer's progression. As the model progresses through these layers, the filters will increase in size and number of channels, allowing the model to learn both simple patterns (e.g., a single biomarker anomaly) and more complex relationships (e.g., combinations of biomarkers that predict disease progression). Each convolutional layer is followed by a ReLU activation function, which introduces non-linearity to the model, allowing it to learn more complex patterns that go beyond simple linear relationships. Batch normalization is also used at each layer to help stabilize learning and speed up the training process by ensuring the output of each layer has a stable distribution of values. To reduce the size of the data while retaining the most important information, the model includes max-pooling layers. These layers take the highest value from small sections of the data, effectively reducing its dimensionality. This makes the network more efficient and less prone to overfitting (where the model becomes too specific to the training data). An attention mechanism is integrated into the model to focus on the most relevant features for Alzheimer's prediction. The attention mechanism assigns higher weights to key variables, such as specific biomarkers that are critical in diagnosing or predicting disease progression. This ensures the model doesn't overlook important features in the data. At the end of the convolutional layers, a global average pooling layer is applied. This layer summarizes the information from the convolutional layers by taking the average of each feature map. By doing so, the model reduces the number of parameters without using a fully connected layer, helping to avoid overfitting. Finally, the extracted features are passed through fully connected dense layers, which further transform the data into higher-level representations. These layers will progressively reduce in size to compress the information into a more compact and informative representation. Dropout is applied to these layers to randomly deactivate a portion of neurons during training, preventing the model from becoming too reliant on any single neuron and helping reduce overfitting. The model ends with an output layer, where a sigmoid activation function will provide the final classification.

3) *Model Training:* To ensure the CNN generalizes well to new data, the dataset will be split into two subsets: training set and test set. The training set will teach the model to identify patterns in the data by adjusting its internal weights based on prediction accuracy. The test set will be used at the end to assess the model's generalization to unseen data, offering a realistic evaluation of its predictive power. During training, the Adam optimizer will adjust the model's weights, using an adaptive learning rate for faster convergence. The loss function will be

binary cross-entropy for binary classification tasks, such as predicting whether a patient has Alzheimer's disease. Regularization techniques like L2 and dropout will be applied to prevent overfitting. Additionally, early stopping will monitor performance and halt training when improvements cease, ensuring the model doesn't overfit the training data.

4) *Inference and Evaluation:* Once training is complete, the model's final performance will be evaluated on the test set. Various metrics will be used to assess how well the CNN performs. Accuracy will measure the percentage of correct predictions out of the total cases. Precision will determine how many of the predicted "Alzheimer's" cases were correct, while recall will assess how many true "Alzheimer's" cases were correctly identified by the model. The F1-score, which is the harmonic mean of precision and recall, will provide an overall effectiveness measure, particularly useful when dealing with imbalanced class distributions. Additionally, the AUC-ROC (Area Under the Receiver Operating Characteristic curve) will evaluate the model's ability to distinguish between different classes, such as predicting the likelihood of Alzheimer's progression. To ensure robustness, cross-validation can be employed, training and testing the model on multiple data subsets to provide a more reliable estimate of its performance and minimize bias.

The integration between the biosensor and the predictive algorithm allows the system to not only collect accurate and relevant data but also to effectively interpret it to make predictions based on biomarker analysis. This process ensures that the algorithm can provide accurate pseudo-diagnoses and forecasts, aiding in the early detection and monitoring of diseases.

V. Results

In this section, the findings from the research and development efforts are presented. The Empathy Map was utilized to gain deeper insights into the needs and experiences of both Alzheimer's patients and their caregivers. The results revealed crucial information about the challenges these individuals face, such as patients' difficulties in accessing accurate diagnostic tests and the emotional impact of the disease. Additionally, the map highlighted the caregivers' need for more accessible and less invasive diagnostic tools. This thorough understanding enabled the adaptation of the biosensor's design to address these critical issues, ensuring that the proposed solution is both relevant and effective in the daily lives of its users.

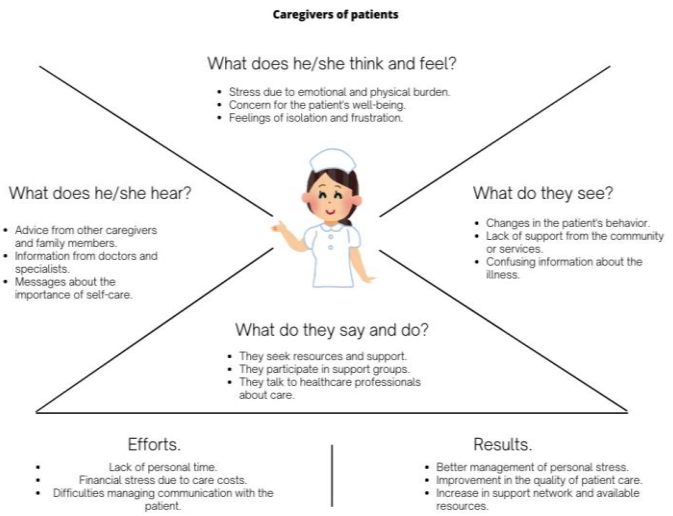

Fig. 1 Empathy Map for Alzheimer's Caregivers.

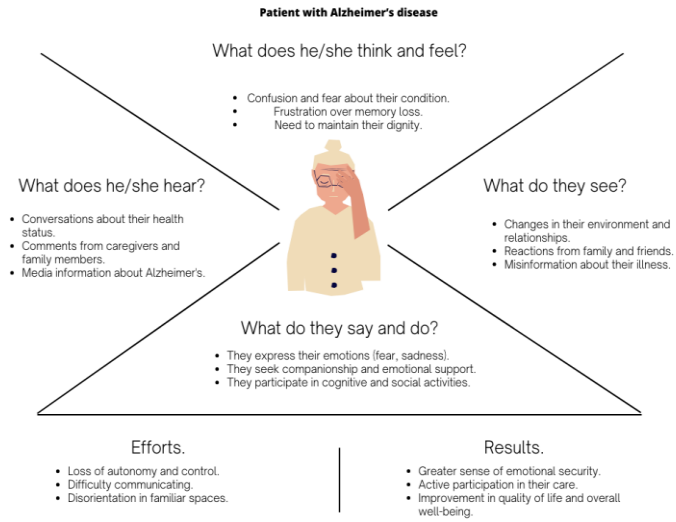

Fig. 2 Empathy Map for Alzheimer's Patients.

In turn, the Business Model Canvas provided a clear framework for the project's implementation. This model enabled the identification and organization of the essential business components, such as the value proposition, which emphasizes the advantage of using a blood sample instead of a lumbar puncture and the accessibility of the biosensor. It also defined distribution channels, customer relationships, and revenue streams, ensuring a solid strategy for marketing the biosensor. The detailed planning of the Canvas facilitated the identification of key resources and critical activities, as well as cost structuring and customer relationship management, providing a comprehensive foundation for the project's success.

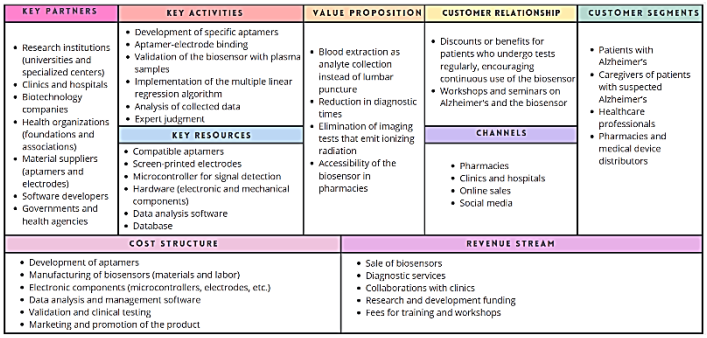

Fig. 3 Business Model Canvas for the Alzheimer's Detection Biosensor Project.

Additionally, the design of the biosensor has been completed, illustrating the integration of aptamers and electrodes for measuring relevant biomarkers in blood samples. This design outlines the functionality and detection process of the biosensor, ensuring its effectiveness in diagnostic applications.

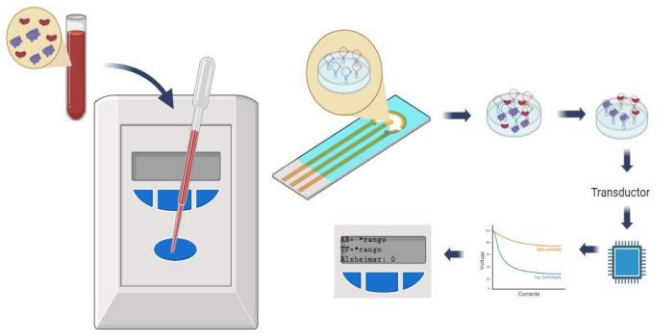

Fig. 4 Design of the Aptasensor Prototype Based on Carbon Electrodes.

In the final phase of the predictive algorithm evaluation, the performance of the model, which employs convolutional neural networks (CNNs), will be examined. While CNNs are traditionally designed for image processing tasks, they have demonstrated exceptional performance when applied to tabular data, as evidenced in this analysis.

The results demonstrate the performance of the model in both the training and testing phases. In the training phase, the model achieved a high precision of 0.96 for the No Alzheimer class and 0.97 for the Alzheimer class, indicating that the model is highly accurate in predicting true positive cases. The recall scores were also impressive, with values of 0.97 for No Alzheimer's and 0.95 for Alzheimer's, suggesting the model's effectiveness in identifying actual positive cases. The F1 scores, which balance precision and recall, were both strong, at 0.96 for No Alzheimer's and 0.96 for Alzheimer's, reflecting a robust overall performance.

In the testing phase (see Table I), the model maintained solid performance with precision values of 0.88 for No Alzheimer's and 0.90 for Alzheimer's. The recall scores slightly decreased to 0.85 for No Alzheimer's but improved to 0.93 for Alzheimer's, indicating a strong ability to detect Alzheimer's cases even when tested on new data. The F1 scores also showed good balance, with values of 0.86 for No Alzheimer's and 0.91 for Alzheimer's. The total accuracy of 0.92 in the testing phase signifies that the model generalizes well to unseen data, maintaining a high level of effectiveness in distinguishing between the two classes. Overall, these results highlight the model's reliability and its potential applicability in real-world scenarios for Alzheimer's detection.

TABLE I. TESTING PHASE

Metric	Class	Training Phase	Testing Phase
Precision	No Alzheimer	0.96	0.88
	Alzheimer	0.97	0.90
Recall	No Alzheimer	0.97	0.85
	Alzheimer	0.95	0.93
F1 Score	No Alzheimer	0.96	0.86
	Alzheimer	0.96	0.91
Support	No Alzheimer	64	27
	Alzheimer	73	32
Total Support		137	59
Total Accuracy		0.98	0.92

VI. CONCLUSIONS

The Empathy Map revealed crucial insights into the needs and experiences of both Alzheimer's patients and their caregivers. Significant concerns were identified, such as the difficulty in accessing accurate tests and the emotional impact of the disease on patients. For caregivers, the need for more accessible and less invasive diagnostic tools was emphasized. This understanding enabled the adaptation of the biosensor design to address these critical issues, ensuring that the proposed solution is relevant and effective in the daily lives of its users.

The Business Model Canvas provided a clear framework for implementing the project by identifying and organizing the essential business components. It highlighted the value proposition of using blood samples instead of lumbar punctures and the accessibility of the biosensor. The Canvas outlined distribution channels, customer relationships, and revenue streams, ensuring a robust strategy for marketing the biosensor. This detailed planning facilitated the identification of key resources and critical activities, cost structuring, and customer relationship management, establishing a comprehensive foundation for the project's success.

Additionally, the design of the biosensor was completed, demonstrating the integration of aptamers and electrodes to measure relevant biomarkers in blood samples. The design detailed the functionality and detection process of the biosensor, ensuring its effectiveness in diagnosis. The biosensor development included aptamer selection via the SELEX method, choice of electrodes for optimal performance, aptamer immobilization on carbon electrodes, and calibration with standard solutions to ensure precise biomarker detection.

The proposed approach for Alzheimer's detection encompasses everything from data preprocessing to model evaluation. Initially, data is prepared through normalization and encoding of features to ensure consistent analysis. A convolutional neural network is employed to extract relevant patterns and highlight significant features, enhancing the identification of Alzheimer's progression.

The model is trained by dividing the data into training, validation, and test sets, using the Adam optimizer to adjust weights and prevent overfitting. Finally, performance is evaluated using specific metrics and prediction visualization, ensuring the model's accuracy, reliability, and applicability in clinical settings for early disease detection. The model achieved a 92% accuracy, demonstrating its strong performance and potential for practical use

Lastly, based on all the information presented, there are significant ethical considerations related to the implementation of biosensors and predictive algorithms. A primary concern is data privacy, as the biosensor will manage sensitive patient information, including biomarkers and personal health data. It is essential to implement robust data protection measures to ensure secure storage and handling of this information. Informed consent is also vital; patients must be fully aware of how their data will be used, the potential risks involved, and their rights regarding data access and deletion. Clear communication about the biosensor's capabilities and limitations, along with transparent data usage policies, will foster trust among users and promote ethical practices in biomedical engineering. Addressing these ethical considerations not only protects patient rights but also enhances the credibility and acceptance of the biosensor in clinical settings.

Therefore, Aptheimer offers a cost-effective and non-invasive alternative for the preliminary pseudo detection of Alzheimer's disease, eliminating the need for expensive tests and invasive procedures. This device has the potential to revolutionize the way Alzheimer's is diagnosed, providing tangible hope to millions affected by this devastating condition.

It is important to emphasize that Aptheimer is intended for pseudo-diagnosis, meaning it does not replace a comprehensive evaluation conducted by neurology experts. A definitive diagnosis requires expert clinical judgment and validation. However, the model has demonstrated an accuracy of 92%, indicating its high reliability in early detection.

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