EEG for detecting and diagnosing Alzheimer's Disease

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Abstract - **This paper presents the design of the signal processing unit of the EEG circuit aimed at improving the accuracy and reliability of EEG as a diagnostic tool in general and for early diagnosis of Alzheimer's disease (AD). Our circuit design removes power line noise and unnecessary brain waves, such as δ and θ waves, from the electrode signals and amplifies brain signals from microvolts to volts. As a result, EEG signals slow down in AD patients, with increased power in low frequencies and decreased power in higher frequencies. The circuit design methodology, data acquisition, signal processing, and algorithm development are provided throughout this paper. Results show that the circuit effectively removes power line noise and unnecessary brain waves, leading to more reliable AD detection through nonlinear dynamical analysis and spectral analysis. Furthermore, by improving the accuracy of EEG signal processing, the circuit designed has the potential to enable earlier detection of AD, thus contributing to better outcomes for patients.**

I. Introduction

Alzheimer's disease (AD) is a progressive neurological disorder affecting millions worldwide. AD symptoms include cognitive decline, memory loss, and changes in behavior and personality. Although there is no immediate cure for AD, early detection and intervention can improve patient outcomes and delay the progression of the disease. Electroencephalography (EEG) is a non-invasive technique that measures and records the brain's electrical activity, providing valuable information about brain function and abnormalities.

EEG is used in diagnosing and monitoring neurological disorders, including AD. Studies have shown that changes in brain wave patterns, specifically the slowing down of α and β waves, can be an early indicator of AD. EEG signals slow down in AD, with increased power in low frequencies and decreased power in higher frequencies. In addition, γ frequency band power increases in AD patients, and transient oscillations occur more often at low frequencies, indicating further slowing down. In this research paper, we propose designing and developing an EEG circuit to detect this slowing down of α and β waves. The designed six-stage circuit filters and amplifies raw EEG signals to be processed and analyzed by computers.

The potential impacts of this work are significant. Early detection and intervention can improve patient outcomes, delay the progression of AD, and reduce the economic and social burden on individuals, families, and society. Furthermore, developing an accurate and reliable EEG system can have long-lasting and vast impacts on Brain-Computer Interfacing. Ultimately, our research aims to contribute to developing practical and accessible diagnostic tools for AD.

II. Physiology

The fundamental mechanisms underlying AD involve the Amyloid Precursor Protein's (APP) expression in the brain. Although APP's complete function is unknown, its movement throughout the body is not. Under normal circumstances, APP is cleaved by α-secretase and β-secretase to generate a waste product cleared efficiently by the body. However, in AD patients, APP is cleaved by γ-secretase and β-secretase, forming a 42 amino-acid long polypeptide chain known as Amyloid β (Aβ). Aβ contains "sticky ends," which cause multiple Aβ proteins to stick to one another, forming oligomers, a neurotoxic plaque in the brain that builds up over time.

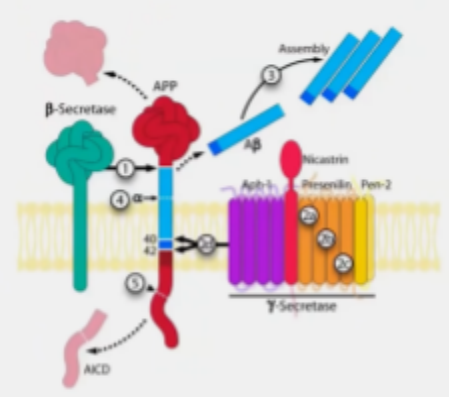


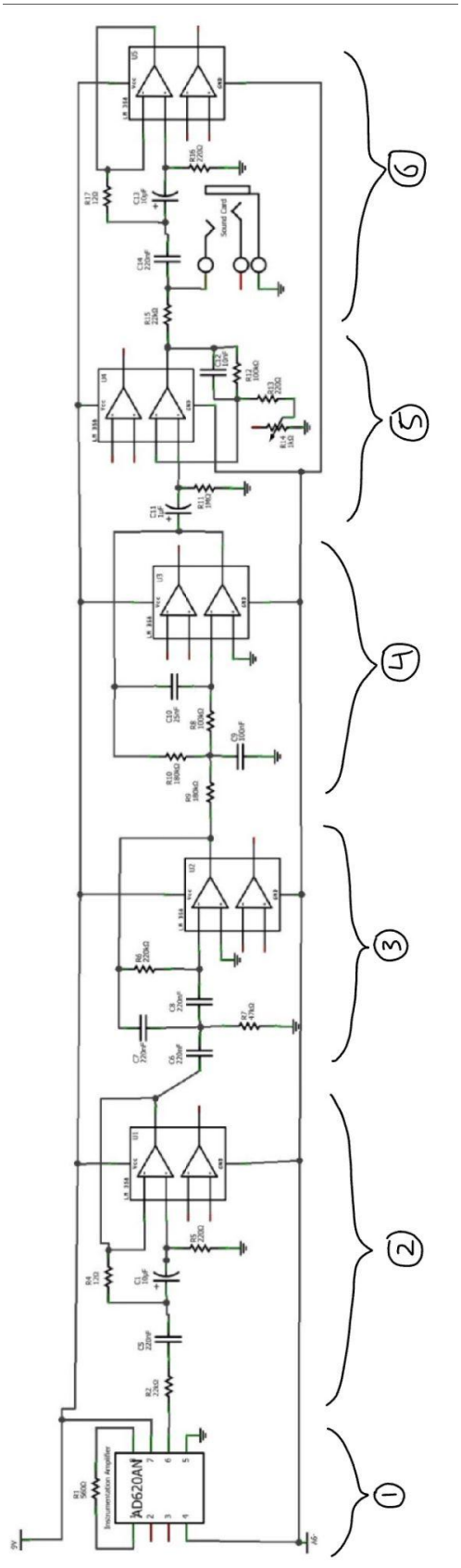
Fig. 1. Formation of Aβ from APP

Furthermore, Tau, a protein that forms microtubules within neurons, dissociates in AD patients, forming neurofibrillary tangles that cause cognitive dysfunction for AD patients. These cognitive dysfunctions can be detected in changes in the α and β waves picked up in our EEG circuit, detailed further below.

III. Methods

The bioinstrument used is a six-stage EEG circuit that takes in signals from three electrodes and outputs an amplified and filtered signal ready for analysis. The purpose of the circuit is to filter out unwanted signals and amplify the signal enough to make it simple to work with; raw EEG signals are on the order of μV, which is too small for many processing machines and software to use. The circuit components used are a ± 9V power supply, electrodes, wires, resistors, capacitors, a potentiometer, an instrumentation amplifier, and operational amplifiers. The inputs to the circuit are two active electrodes connected to different regions on the head, while the third electrode is grounded to act as a reference.

The circuit's first stage is an instrumentation amplifier intended to amplify the signals enough to read them. The amplifier used is an AD620AN with a gain formula of $1 + 49400 / R_G$. In order to have a gain of roughly 90 V/V, one can use a resistor of 560Ω, yielding a gain of 89.2 V/V. This gain is not high enough to output a usable signal, but the gain



cannot be made much higher because the common-mode voltage gain increases with the differential gain. Therefore, only part of the gain is assigned to the instrumentation amplifier to reduce common-mode voltage gain. The other portion is resolved with an operational amplifier in stage 5.

The second stage is a 60 Hz notch filter. The powerlines in the United States have a signal frequency of roughly 60 Hz, which can disrupt the desired EEG signal. Because of this, the designed notch filter diminishes the amplitude of 60 Hz signals while enabling other signals to flow through. It could be a better notch filter, so some frequencies around 60 Hz will also be filtered, but since α and β waves are the focus of this instrument, filtering out signals above 30 Hz will not affect the result.

The following two stages are a 7 Hz high-pass filter and a 31 Hz low-pass filter. These filters remove extraneous brain wave frequencies not being analyzed in this project. Because α and β waves are the only waves involved, only a frequency range of roughly 7-31 Hz is required. Other frequencies could disrupt the pertinent signal.

Stage 5 consists of a 1 Hz low-pass filter, a 160 Hz high-pass filter, and a variable gain operational amplifier system. The two filters remove additional unwanted noise. This component is optional but beneficial. The low-pass filter is the capacitor-resistor combination in front, and the high-pass filter is the parallel capacitor-resistor combination inside the operational amplifier's feedback loop. The other portion is the operational amplifier, which handles the remaining gain that stage 1 could not. The potentiometer in the system exists so that the user can control exactly how much gain they want. The gain formula for this system is $1+R_{12}/(R_{13}+R_{14})$, where R_{14} is the potentiometer. In this case, it is a 1kΩ potentiometer, so the resistance ranges from 0 - 1000Ω. For example, with a resistance of 0 Ω, the gain is 455 V/V, but when the resistance is 1000Ω, the gain is 83 V/V. This variable gain is essential because it gives the user control over how they want to amplify the signal; this can make post-processing and analysis easier as the output is flexible to the user's demands.

Stage 6 is another 60 Hz notch filter that functions the same as the filter in stage 2. The notch filter is in place so that any new 60 Hz noise not initially filtered out is filtered back out.

In the final stage of the bioinstrument, the output signal of the filter is ready to be sent to a computer to be processed more and analyzed to help make diagnoses. The overall gain ranges from 7403.6 - 40586 V/V depending on the potentiometer value. This circuit has many components, so it is also highly adjustable to fit a user's requirements. Any of the filter cutoffs can be changed to isolate different frequency ranges. For example, if one wanted to study θ waves, which have a frequency range of 4 - 8 Hz, the filters can be changed to fit this range. In addition, the potentiometer adds a high degree of variance, and it can also be changed to the user's preference. The overall goal of the instrument is to take in raw EEG signals from electrodes and output a non-noisy amplified signal that can be used to help make diagnoses in patients. It does this using a combination of passive and active filters and amplifiers.

III. Results

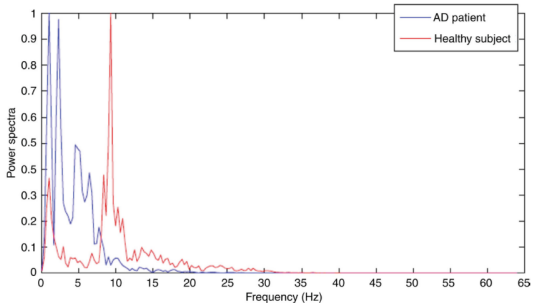


Figure 2.4 ***Comparison between a mild AD patient and a healthy subject using power spectrum.*** The graph is presented for Fz electrode [12].

Taking a discrete Fourier transform of the raw data, we can create power spectra and analyze it. In AD patients, EEG signals slow down as there is an increase of power in low frequencies (typically δ and θ waves) and a decrease in power in high frequencies (typically α and β waves). The picture above shows a shift in the band frequency to that of slower frequencies. Looking at the amplitude envelopes, we see less synchronization in AD patients. Lesser synchronization is where the amplitude is fractured into a few smaller peaks rather than seeing a single peak, as in healthy patients. In addition, the reduction

in complexity as an entropy measure is also visible. Essentially the flux of information seen in the EEG signal is reduced in AD patients.

Looking at Non-linear Dynamical Analysis (NDA) of EEG data has shown decreased complexity of EEG patterns and reduced functional connections in patients with AD. This concept benefits research as it can help better understand AD in patients and the signs to look for in early diagnostics. AD patients tend to have patterns that are less complex when compared to healthy patients. This consequence may occur due to problems arising from coupled neurons. These actions result in neural activity and dynamics becoming simpler than healthy people's neural activities. One of the assumptions made with NDA is that EEG signals are "generated by non-linear deterministic processes with non-linear coupling interactions between neuronal populations." (Hornero 2009). This signal implies that neurons will act in a way controlled by threshold and saturation levels. Many large networks of interconnected neurons exhibit local nonlinear interactions in the brain. The result is that the interconnected neurons will slowly build up an energy value until a threshold value is met, followed by bursts of energy redistribution. As a result, AD patients have lower correlation dimensional values than control subjects.

Furthermore, "lower [correlation dimensions] have been found in patients with increased severity of dementia and suggest that a reduced [correlation dimensions] may be associated with an increase in the proportion of lower frequency components in the AD patients' EEGs." (Hornero 2009). As a result, we expect to see simpler patterns/dynamics leading to slowing, where we see more frequent low-pass signals.

IV. Discussion

Various electrode types have been used in recording EEG signals. These include disposable gel, reusable discs, headband/electrode caps, and saline-based and needle electrodes. Gel electrodes are the best option if the goal is to diagnose someone with AD and their stage most accurately. The advantages of gel electrodes include the availability of high-density recording, a measure of how many electrodes are being used. The more electrodes, the higher the resolution and the more accurately they can predict the stage of the AD patient. Other advantages include having high signal quality and being much less susceptible to movement artifacts and interference than water and dry electrodes. Stable measurements require an extended amount of EEG data, making gel electrodes reliable. They are compatible with ring electrodes as alternative measurement solutions and integrable with other research equipment such as NFIRS and TMS. Disadvantages with gel electrodes include discomfort when slightly scratching the skin to gain impedance. An EEG procedure takes a long time to set up and clean, and the patient also must be clean and not have greasy hair. The gel can dry out after about 5 hours. However, this does not concern us since the typical EEG measurement can be done in 20-40 minutes, thus making gel electrodes the preferable electrode type for this project.

As far as limitations go, it is currently hard to access EEG data of AD patients since databases are private, like ECG or other biomedical data. Due to this, it is also "hard to systematically benchmark and assess the existing methods for diagnosing AD from EEG signals" (Dauwels). Unfortunately, EEG does not incorporate biophysical knowledge in its measurements of AD. In summary, the numbers do not explain what is physiologically happening in the brain. Nevertheless, EEG data analysis can be used to predict better and diagnose AD. However, conclusions should be made by combining EEG signals with imaging modalities such as MRI, SPECT, and TMS.

Furthermore, "The correlation between AD risk factors (e.g., the high plasma concentration of homocysteine) and EEG characteristics need to be investigated in greater detail" (Dauwels). The relationship between memory loss and EEG abnormalities is also not well studied. For this reason, the next step is to determine how EEG signals correlate to the progression of AD and dementia. On the plus side, EEG has many degrees of freedom and can be measured while the patient is at rest, performing memory tasks, or being stimulated with auditory, tactile, and visual stimulation.

Acknowledgements

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