An update on the project: ***Development of an Automatic Instrument for Schizophrenia(SZ) Diagnosis*** , for the MCIP Innovation Prize 2022.

February 28, 2023

1 Summary

As stated in the proposal document, this project came about as a result of the lack of a pre-psychotic objective scientific instrument to diagnose schizophrenia (SZ), this poses a large social threat as exiting nosologyis based on psychiatric evaluation requires active psychosis after which epidemiology becomes difficult and expensive to manage, thus the need to develop an instrument for early detection of SZ This project aims to develop a classifier for early detection of schizophrenics using the auditory steady state response (ASSR), fuzzy entropy and mismatch negativity (MMN) features from electroencephalogram (EEG) data of subjects.

In order to achieve the aforemntioned aim, data has been acquired from a total of 31 subjects divided into the healthy controls (HCs) and SZ patients, of which 13 are HCs and 18 are SZ patients After dropping null EEG recordings, the resulting data was made up of 10 SZ patients and 12 HCs, a total of 22 subjects out of 31. Data acquisition is done using the contek KT-2400 and KT-1018 devices of sampling rates 200Hz and 100Hz respectively. The KT-1018 was used mainly in testing of the developed software for data acquisition called Generis. Data acquisition (DAQ) and the Generis software are discussed within section 2 of this document.

First outlook at data processing produced EEG spatial and time-domain resulsts. Valid data from the 22 subjects have been subjected to a different data preprocessing and data processing pipeline producing results in the time, time-frequency domain and giving measures of disorderliness of spatial collapsed spatio-temporal series. These methods are discussed under section 3 of this document.

After processing, plots of results showed certain distinct characteristics between the HCs and SZ patients. These differences are discussed under section **??** of this document and figures describing such differences are shown in section **??** of this document.

This report also documents the milestones achieved, the challenges faced and the next steps towards achieving the aim of this project. This steps definitely do include more DAQ and making data processing more robust.

2 Data Acquisition

This section will discuss the EEG devices used for acquisition, the acquisition protocol, phases of DAQ protocol and their modalities. Lastly this section will briefly review the Generis software developed for DAQ, as an holistic approach in explaining this software can be time consuming as it took two programmers to design this software, I being one of the two.

2.1 Devices

DAQ was done using two EEG devices from the same manufacturer named the KT2400 and KT1018 from contek devices, each having 24 electrode channels and 18 electrode channels respectively.

The KT-1018 is a 16 channel EEG device with a sampling rate of 100 Hz per electrode channel. Its electrodes are distributed between the frontal, central, temporal, occipital and parietal lobes. The device has an analog to digital conversion (ADC) resolution of 12bits with a minimum input impedance of 10 MΩ and a patient leak current of 10 µA. Its noise parameters are good enough for the use case of this project which include a maximum noise level of 5 µV peak to peak, a minimum common mode rejection ratio of 90 dB and a minimum 50 Hz interference suppression level of 30 dB.

The KT-2400 is a 19 channel EEG device with similar noise performance characteristics to the KT-1018. it also has similar resolution and amplifier, sensor electrical parameters. It differs from the KT-1018 in it being a 19 EEG electrode channel EEG device and having a sampling rate of 200 Hz per channel.

The two devices have similar performance and similar behaviour in terms of communication protocol and mode settings. The KT-1018 was used in developing the Generis software initially and was expanded to cater for the KT-2400 later on. All data analysed were acquired using the KT-2400 device.

2.2 Acquisition Protocol

There is the need to define a protocol to be followed during acquisition, for easy identification, interpretaion, analysis and classification of data acquired. The EEG data is acquired in four phases, the order of which is defined for each subject by the acquisition protocol shown in figure 1.

Figure 1: Order of data phases in acquisition protocol

The time frame of acquisition for each phase is still conventional. It has been allowed to vary based on judgement of the electrophysiologist in charge of session. The time values shown in figure 1 is that which is most common among subjects trials. The method of delivery of the cue and instructions in each phase are defined by that phase. This is currently being updated based on suggestions from the electrophysiologists.

During the first and second rest phases, the subject receives an instruction to remain calm, avoid any form of movements and notify the clinicians and electrophysiologist of any inconvenience by means of speech. Instructions are delivered through the sound media output of device running the Generis software and displayed on the screen of the device. The auditory based instruction modality is language specific covering English, yoruba, hausa and pidgin, igbo yet to be covered. There is no need for any sort of special cue in these phases. The subject is expected to adhere to these instructions all through these phases. But in the case of the subject being a SZ patient, such subject might not fully understand the instructions and act against instructions, there is the need to annotate such points in time in the EEG data as artifact periods. This is currently being catered for by the the design of an hardware annotator.

In the arithmetic phase, instructions are again given via auditory and now visual means after which a series of arithmetic task are dictated to the subject by the software in his/her selected language and also displayed on the screen. A fixed time is allowed to pass during which the subject is expected to attempt the task and give any answer. An incorrect answer is of no consequence as the arithmetic task, acts as an activation energy for the cognitive channels of the brain, so their state which is indicative of SZ status can be investigated. This phase uses no annotations and as such, the point in time at which the subject receives(understands) an arithmetic task and gives his/her answer is unknown. This is also catered for in the ongoing design of the hardware annotator.

The auditory stimuli phase instructions are similar to that of the rest phase. During this phase, the subject listens to a sequence of tones each, with the component tones having different parameters. There is the 1 kHz standard tone, the 3 kHz frequency deviant tone and the duration deviant tone. While listening to these tones, the subject passively wacthes a random clip to divert the subjects attention from the tone sequence. Each tone stimuli class lasts for a minimum of 100 ms.

Implementation of these phases, their cues, instrucions and annotations is achieved and managed by the Generis software which will be discussed next.

The EEG data from the auditory stimuli phase is to be used in computing the MMN response. Fuzzy entropy and ASSR paraneters are to be computed for EEG data of all phases and compared for notable differences between the HCs and the SZ patients.

2.3 Generis Softwware

The Generis DAQ software was designed for the following reasons:

- For communication with contek firmware to receive EEG data stream.
- For control of switching between phases and visual/auditory presentation of stimuli and instructions.
- For annotating EEG data event occurence in time.
- For taking in subject, clinician and electrophysiologist feedback/annotation.
- For time synchronization of annotation stream, feedback stream and EEG stream.
- For subject info management.

The Generis software is mnade up of components parts which interact with themselves to achieve the purpose of the built software which can be summarized as event occurence tracking and recording of EEG data. Figure 2 shows the architecture of the system of which each box represents a component part of the software.

- Cue generator: The cue generator according to the appropriate phase of DAQ generates cues or instructions information which is passed to the annotator.
- Annotator: The annotator based on phase of execution, time of phase and data from the cue genertor generates time/string(marker) information to be attached to the EEG recording and stored in its file, the European data format (EDF) file.

- USB Driver: This is responsible for fetching the EEG data in its raw binary form. This interacts with the firmware on the contek device.
- edf maker: This components receives the EEG data from the USB driver, alongside the sample number from the onset of recording and saves it into a variable within the generated EDF filed called *eeg_data* and uses the information from the annotator and sample number from recording onset to append to a variable called *eeg_markers* in the generated EDF file. Onset of events are represented by their appropriate string and their time of occurence in EEG recording.
- Audio/Video module: The audio module based on phase of DAQ and input gotten from annotator selects what pre-recorded audio file of stimuli or instruction is to be played using the laptops media sound output. During the auditory stimuli phase of acquisition, random image clips are combined into frames of a video for the subject to watch. This is implemented by the video module.
- GUI: This is the Graphical user interface (GUI) module which implements what is seen by the eclectrophysiologist and subject during recording. It allows the electrophysiologist set the recording parameters such as dration for each phase, subject info such as age, religion, language, etc.. It also allows the electrophysiologist select EEG recording device to be used. KT-1018 or KT-2400. It has three sub-components namely:
  - Instruction screen: which just displays audio and non-audio instructions in textual form.
  - Settings screen whch allows clinician/electrophysiologist to interact with software so as to define parameters of recording.
  - EEG display screen which justs plots the acquired EEG data in real time.

The flowchart of the USB driver for acquisition of one sample of data is shown in figure 12. Figures 9 through 11 shows various interfaces of the Generis software.

3 Processing

This section discusses both the preprocessing and processing(feature-computation) of the acquired EEG data. Some results are discussed here with the figures displayed under section 7 of this document.

3.1 Preprocessing

Data preprocessing pipeline has been developed to be flexible in order to allow for results comparison between the various sequence of methods chosen. The adopted data preprocessing architecture is shown in figure 4.

In order to have a first outlook of the acquired data, preprocessing was carried out on the EEG data of the first three subjects. Montage plots and time-series plot of electrodes of the temporal lobe were generated, the time-series plot being from the auditory stimui phase EEG data. To generate the montage plots, three preprocssing path were tried. One made use of 1-70Hz bandpass filtering alone, another combined edge interpolation,another combined edge-interpolation and baseline correction. Taking the first as the standard, it was observed that without baseline correction, edge-inerpolation inverted the spatial domain information shown by the montage plot, while baseline-correction alongside edge-interpolation helped recover this information. The figures describing these results are shown in figures 5. The baseline correction was thus adopted in generating the time-series plot from the auditory-stimuli phase. One of such plot for an electrode in the temporal lobe is shown in figure 6, in which the average for each tone class in the auditory stimuli phase is plotted.

3.2 Feature-computation

On the 22 subjects whose data were valid, processing(feature computation) was carried out, still maintaining the, preprocessing path of baseline correction and 1-70Hz filtering, this time around montage plots were not generated, rather short time fourier transform (STFT) spectrograms for each phase and fuzzy-entropy values of the frontal lobes regions, parietal/central lobes, parietal/occipital lobes, temporal/occipital lobes were generated for each phase per subject. A 100 ms time-series of the average of tone stimuli classes fromt the auditroy stimuli class was generated for each electrode region in the temporal lobe.

So as to compute the STFT spectorgram, the data from each phase was epoched such that for each phase all epochs have same number of sample. The non-frontal electrodes were dropped. So as not to tamper with frequency, time-frequency , spatial domain information in the pursuit of eliminating statistical variabilities in time, spatial domain information, these epochs were not in any way averaged, rather a nine discrete frequency point spectrograms was computed for each epoch and the resultant epochs spectrogram for each phase was averaged to get the mean time-frequency domain activity. After this the non-frontal electrodes were dropped and the resulting spectrogram for frontal electrodes averaged for each phase, to get the effective frontal activity for each phase. This was done so as to compare differences in the response of cognitive areas during the arithmetic task phase and other phases. It was noticed that in HCs the arithmetic and auditory phase were spectrograms indicated more activity compared to the rest phases, while in SZ patients the spectrograms across all phases were more similar with the pattern in HCs also repeating in some SZ patients. Figures 7 and 8 show these differences.

A python library called EntropyHub was used in computing the fuzzy-entropy values for each subject. The library has a limitation on the minimum number of dimensions in the first axis. This meant that lobes having less than five electrodes could not have their entropies computed. For this reason the electrodes were grouped as follows:

- Frontal(F)
- Parietal/Control(P/C)
- Parietal/Occipital(P/O)
- Temporal/Occipital(O/T)

The electrode grouper transformer was first of all used to group the electrodes as stated above after which epoching of data from phases took place just as in the computation of the STFT. After this epoching the epochs were averaged in order to eliminate statistical variabilities in the time domain. After the epoch averaging, the fuzzy entroy was computed and for each phase of DAQ. This was done per subject. It was noticed that the fuzzy entropy was consistently higher during the arithmetic and auditory stimuli phases, mostly in the frontal cortex in HCs. This held in few SZ patients with more deviations from this observation in SZ patients. To highight this difference, the average entropies among HCs and glsplszPtnt were computed and compared. This is shown in figure 3 which showed that the observation holds for HCs across all cortical regions, is attenuated in glsplszPtnt and is most prominently observed in the frontal lobe(cortex). Figures 7 and 8 show these differences between a HC and a SZ patient.

Some challenges were encountered during the processing of the data, some of these challenges include:

- Subject response on unders:tanding and completion of arithmetic task not annotated in data.
- Time points of artifacts in data not annotated.
- Non-uniform phases duration across subjects.
- Resrtictions on minimum electrode axis dimensionality when computing fuzzy entropy for resulting in the combination of electrodes of brain lobes.

4 Preliminary Results

sec:results] As stated under 3.2, teh notable differences between the HCs and SZ patients are:

- Irregular similarity in STFT spectrogram of SZ patients across phases of DAQ. and obvious differences in SZ patients. ***figures 7 - 8***
- Consistently higher fuzzy entropy during arithmetic task and auditory stimuli in HCs mostly in the frontal cortex as opposed to fuzzy entropy pattern variations in SZ patients. ***figures 7, 8*** & **3**

Some patterns were also noticed in the time-series plot from the auditory stimuli phase in the electrodes of the temporal lobe. These patterns are illustrated in figures 7 & 8. The dark-blue plots represent the average of the 1 kHz standard tone, the green represents the duration deviant tone and the red the 3 kHz frequency deviant tone. The patterns noticed are:

- More evident MMN in SZ patients.
- Random nature of duration deviant tone signal in SZ patients.
- Increased synchrony between standard tone and frequenct devainr in HCs.

5 Challenges

Various challenges have been faced during the course of this project. These challenges will not be discussed explicitly but will be highlighted here.

- Timing and Mobility:subject availaniliy, transporation and time management.
- Subject recruitment: subject reluctance, lack of motivation from subjects, skewed pwepective of HCs.
- Communication: language specific cue implementation(volunteer), verbal interactions still used.
- Resources: Per subject disposable headset, subject/clinincian feedback annotator, dedicated system for DAQ sessions.
- Data processing results as stated in section 3.2.

6 Next Steps

The next steps towards achieving the goal of this project are as follows

- Evaluate results of other pre-processing paths on already existing data, and select path resulting in most discriminable features.
- First outlook at classification using an ensemble on existing data.
- Development of audio cues for the igbo language.
- Development of hand-held annotators/feedback systems for clinician and subject.
- Algorithm for time-evolving montages.
- Standardization of time frame for each phase of data acquisition.
- Design of handheld annotator device for feedback from clinicians and subject.
- Acquire data from 70-90 more subjects.

7 Figures

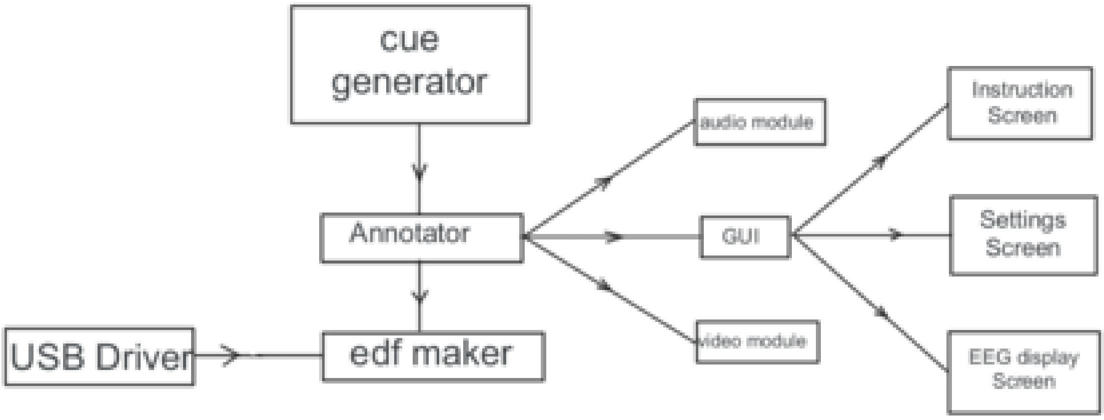


Figure 2: Architecture of Generis, showing relationship betwwen software components.

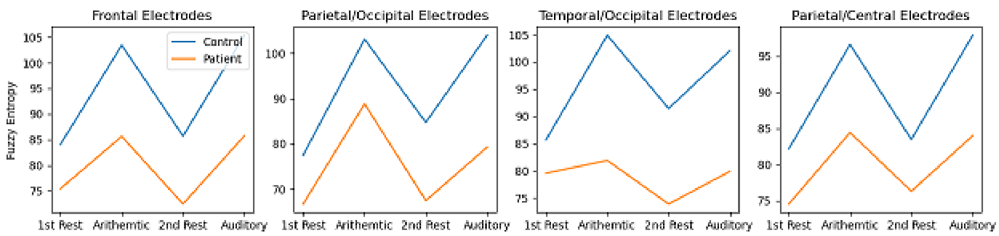


Figure 3: comparing fuzzy-entropy amonng subjects and controls

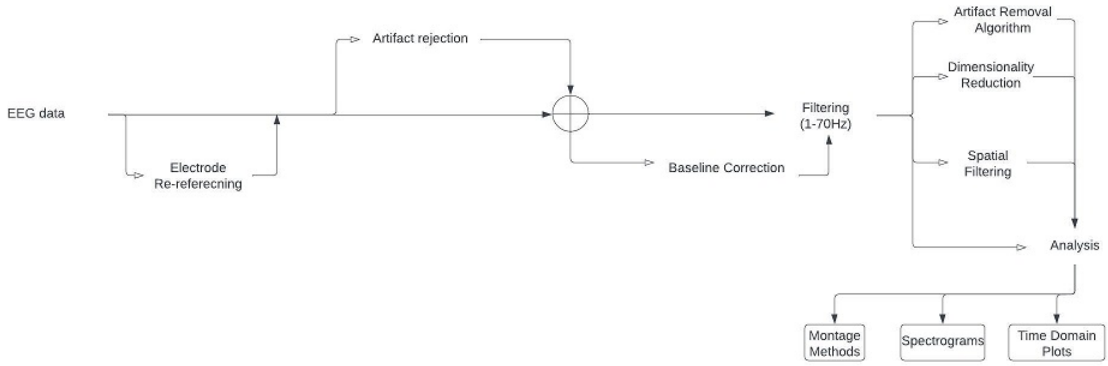
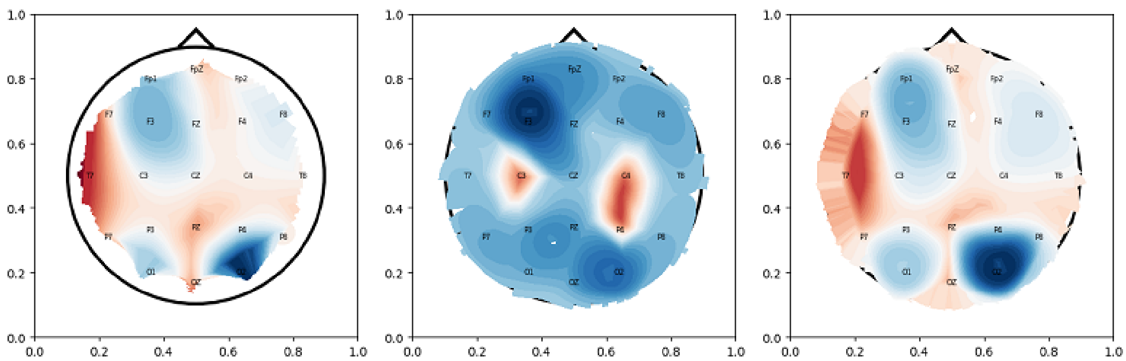


Figure 4: data preprocessing architecture



(a) montage from 1-70hz bandpass filtering

(b) montage from filtering & edge-interpolation

(c) montage from filtering, edge-interpolation & baseline-correction

Figure 5: montage plots, first outlook

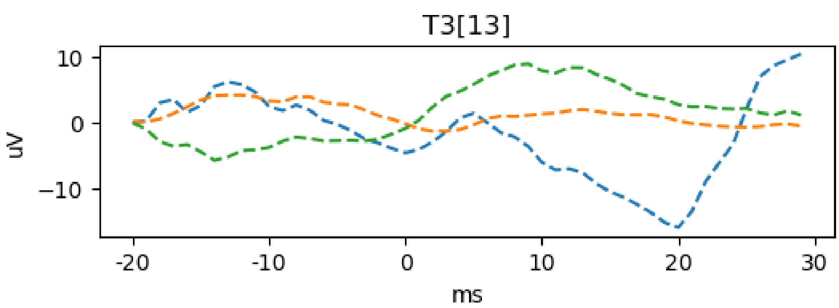


Figure 6: plot of tone averages from auditory stimli phase during 1st outlook of data

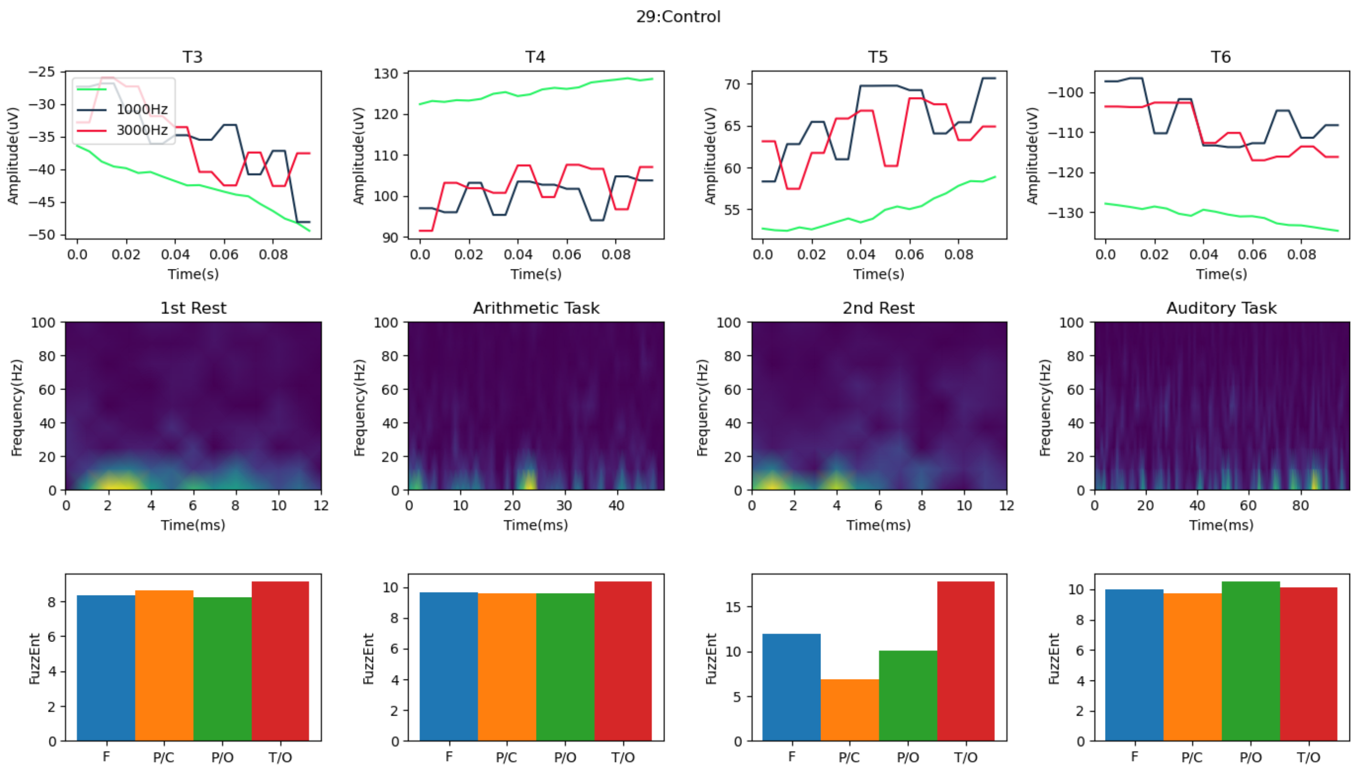


Figure 7: feature computation from HC

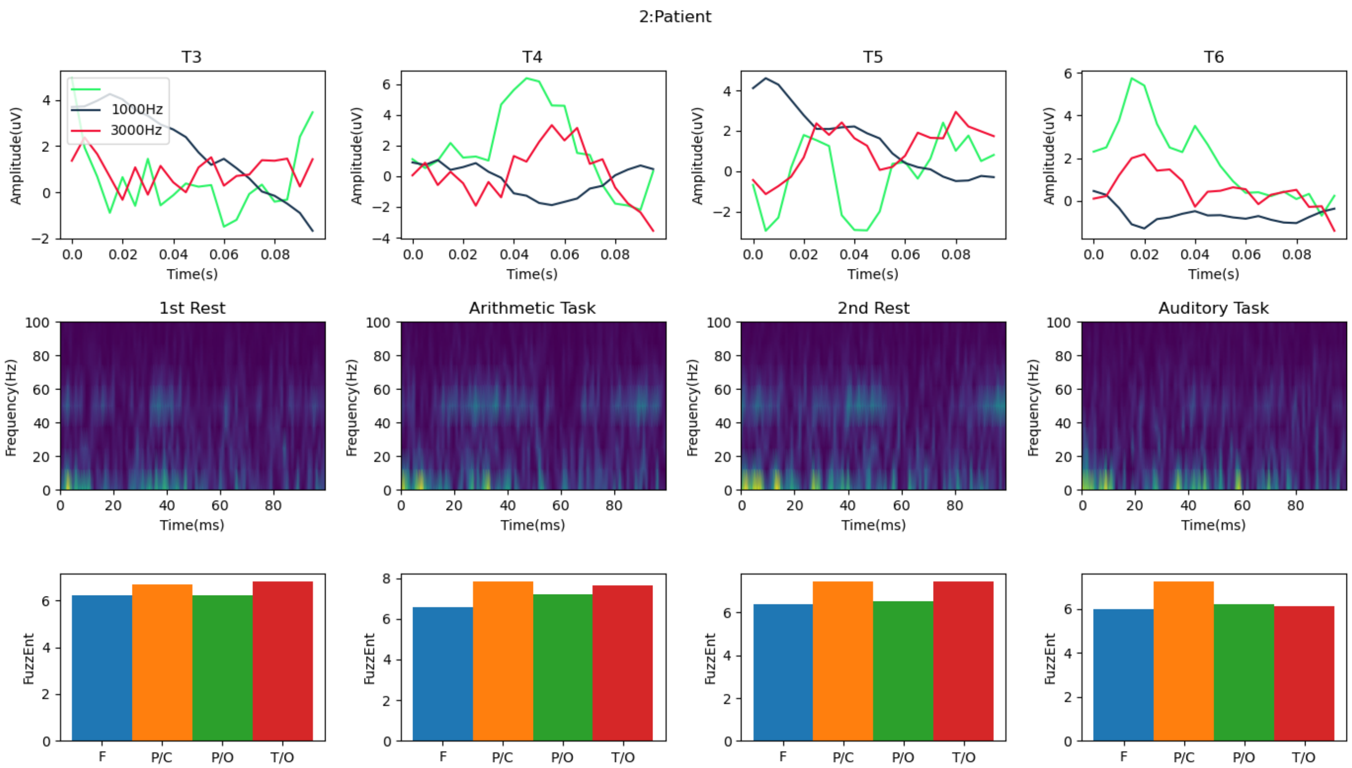


Figure 8: feature computation from SZ patient

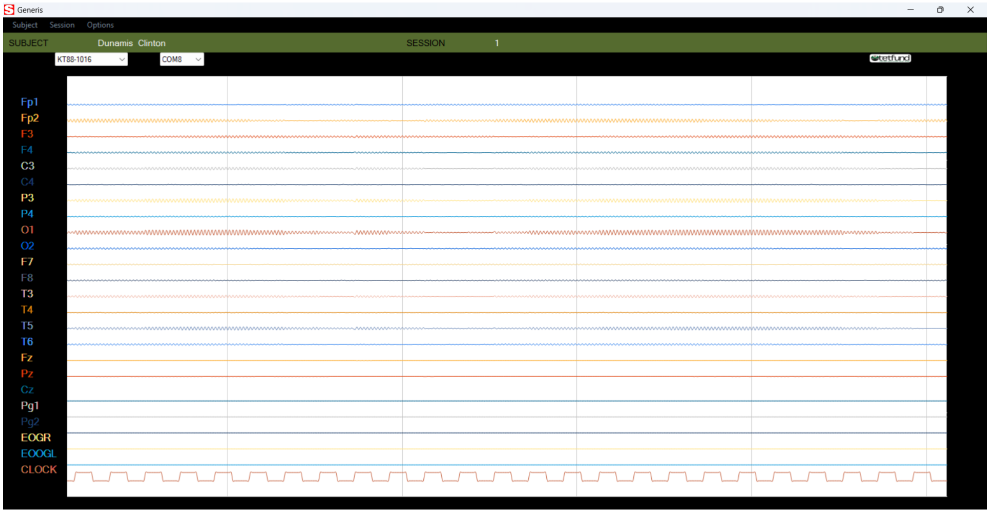


Figure 9: montage plots, first outlook

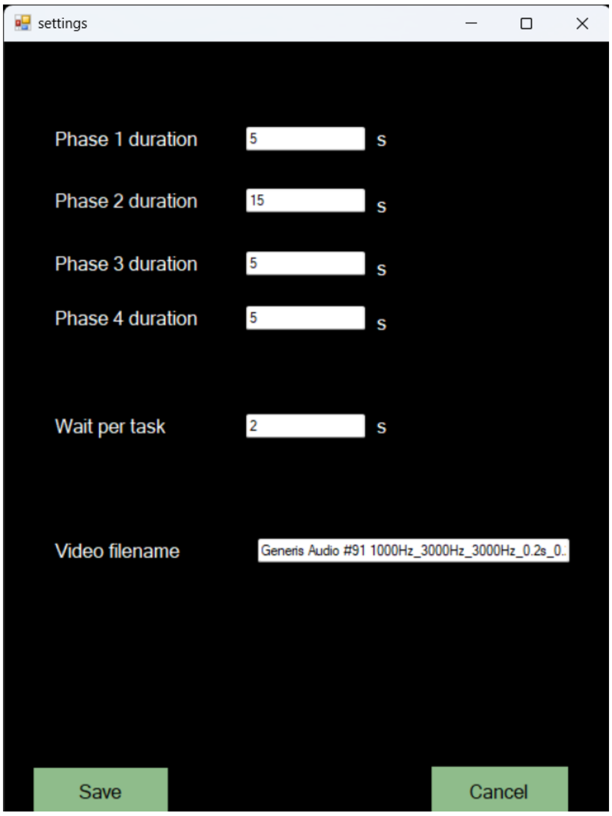


Figure 10: Confifuring session settings

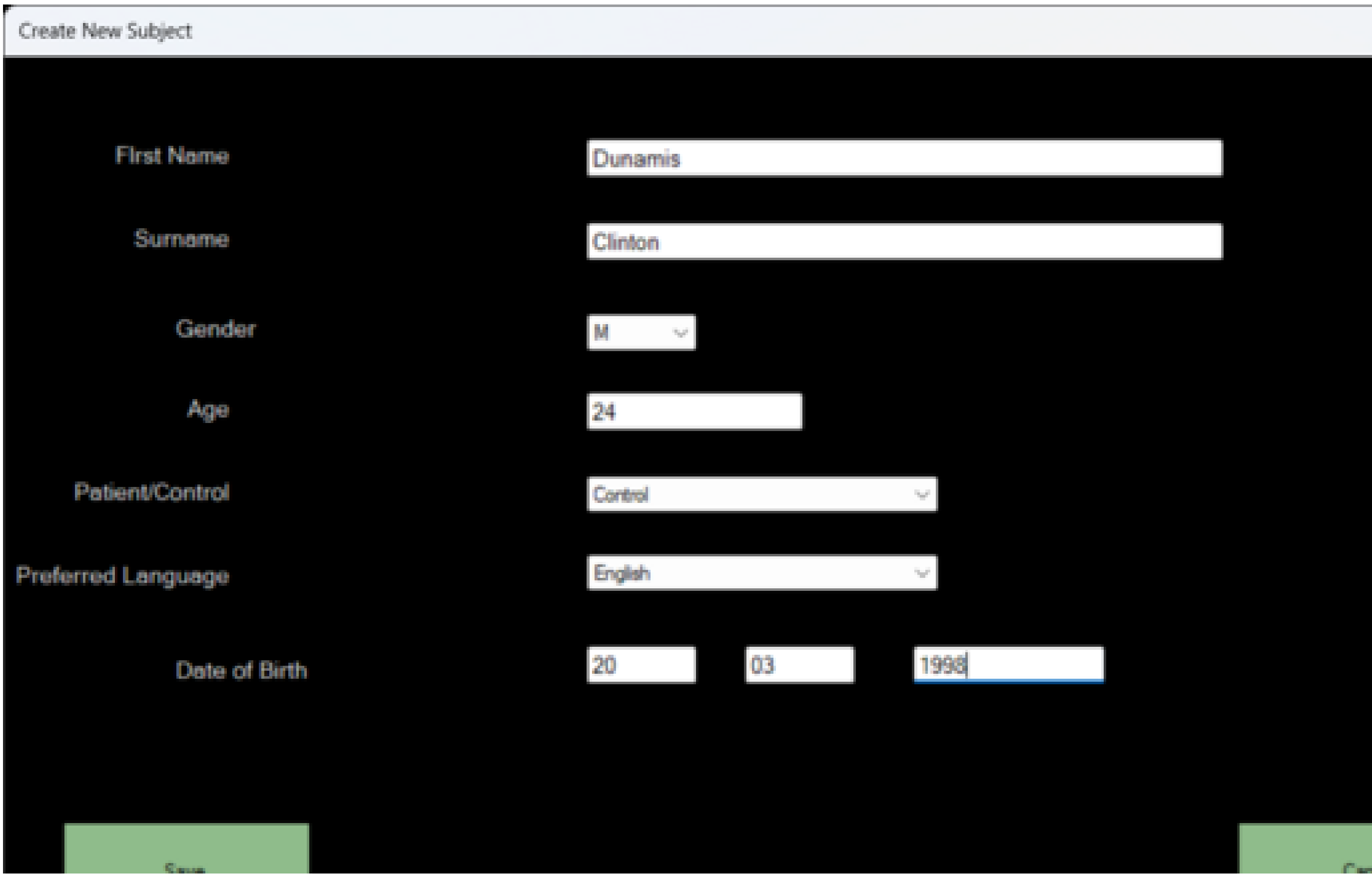


Figure 11: Create subject screen

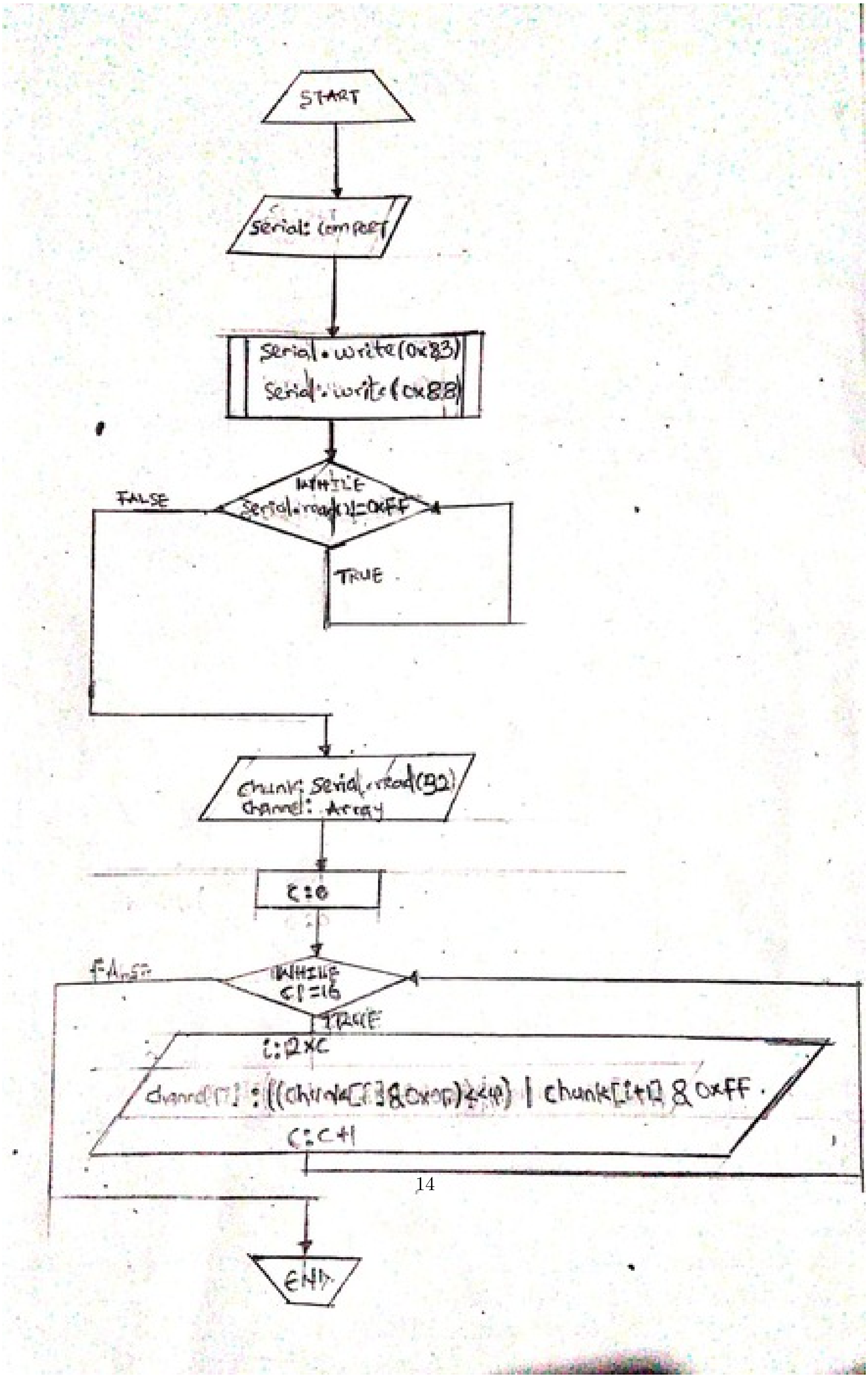


Figure 12: acquiring one sample of eeg data from