



ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ
ΣΧΟΛΗ ΘΕΤΙΚΩΝ ΕΠΙΣΤΗΜΩΝ
ΤΜΗΜΑ ΠΛΗΡΟΦΟΡΙΚΗΣ ΜΕ ΕΦΑΡΜΟΓΕΣ
ΣΤΗ ΒΙΟΙΑΤΡΙΚΗ

**Κατασκευή συστήματος καταγραφής ηλεκτροφυσιολογικών
μετρήσεων για διάγνωση ήπιας νοητικής διαταραχής και συναφών
νευρολογικών διαταραχών**

Στυλιανός Χατζηχρόνης

ΠΤΥΧΙΑΚΗ ΕΡΓΑΣΙΑ
Επιβλέποντες
Αλεξίου Αθανάσιος
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Λαμία, 2016

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Με ατομική μου ευθύνη και γνωρίζοντας τις κυρώσεις ⁽¹⁾, που προβλέπονται από της διατάξεις της παρ. 6 του άρθρου 22 του Ν. 1599/1986, δηλώνω ότι:

1. Δεν παραθέτω κομμάτια βιβλίων ή άρθρων ή εργασιών άλλων αυτολεξεί **χωρίς να τα περικλείω σε εισαγωγικά** και χωρίς να αναφέρω το συγγραφέα, τη χρονολογία, τη σελίδα. Η αυτολεξεί παράθεση χωρίς εισαγωγικά χωρίς αναφορά στην πηγή, είναι λογοκλοπή. Πέραν της αυτολεξεί παράθεσης, λογοκλοπή θεωρείται και η παράφραση εδαφίων από έργα άλλων, συμπεριλαμβανομένων και έργων συμφοιτητών μου, καθώς και η παράθεση στοιχείων που άλλοι συνέλεξαν ή επεξεργάστηκαν, χωρίς αναφορά στην πηγή. Αναφέρω πάντοτε με πληρότητα την πηγή κάτω από τον πίνακα ή σχέδιο, όπως στα παραθέματα.
2. Δέχομαι ότι η αυτολεξεί **παράθεση χωρίς εισαγωγικά**, ακόμα κι αν συνοδεύεται από αναφορά στην πηγή σε κάποιο άλλο σημείο του κειμένου ή στο τέλος του, είναι αντιγραφή. Η αναφορά στην πηγή στο τέλος π.χ. μιας παραγράφου ή μιας σελίδας, δεν δικαιολογεί συρραφή εδαφίων έργου άλλου συγγραφέα, έστω και παραφρασμένων, και παρουσίασή τους ως δική μου εργασία.
3. Δέχομαι ότι υπάρχει επίσης περιορισμός στο μέγεθος και στη συχνότητα των παραθεμάτων που μπορώ να εντάξω στην εργασία μου εντός εισαγωγικών. Κάθε μεγάλο παράθεμα (π.χ. σε πίνακα ή πλαίσιο, κλπ), προϋποθέτει ειδικές ρυθμίσεις, και όταν δημοσιεύεται προϋποθέτει την άδεια του συγγραφέα ή του εκδότη. Το ίδιο και οι πίνακες και τα σχέδια
4. Δέχομαι όλες τις συνέπειες σε περίπτωση λογοκλοπής ή αντιγραφής.

Ημερομηνία 21/09/2016

Ο Δηλών

(Υπογραφή)

(1) «Όποιος εν γνώσει του δηλώνει ψευδή γεγονότα ή αρνείται ή αποκρύπτει τα αληθινά με έγγραφη υπεύθυνη δήλωση του άρθρου 8 παρ. 4 Ν. 1599/1986 τιμωρείται με φυλάκιση τουλάχιστον τριών μηνών. Εάν ο υπαίτιος αυτών των πράξεων σκόπευε να προσπορίσει στον εαυτόν του ή σε άλλον περιουσιακό όφελος βλάπτοντας τρίτον ή σκόπευε να βλάψει άλλον, τιμωρείται με κάθειρξη μέχρι 10 ετών.

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ΠΕΡΙΛΗΨΗ ΣΤΑ ΕΛΛΗΝΙΚΑ

Η Ηλεκτροεγκεφαλογραφία (EEG) είναι μια ευρέως χρησιμοποιούμενη τεχνική η οποία εστιάζεται στην καταγραφή των ηλεκτρικών σημάτων που προέρχονται από το εσωτερικό του εγκεφάλου. Η απεικονιστική εξέταση EEG εφευρέθηκε ως σύστημα από το Hans Berger το 1929 και στόχος του ήταν η καταγραφή των νευρολογικών διαδικασιών στο εσωτερικό της κεφαλής. Αργότερα χρησιμοποιήθηκε για τη διάγνωση ασθενειών που συνδέονται με την εγκεφαλική λειτουργία και διαταραχές του Κεντρικού Νευρικού Συστήματος, όπως ο Αυτισμός, η νόσος του Parkinson κλπ. Στην ουσία η EEG είναι μια διαδικασία που συνίσταται στην παρατήρηση των ηλεκτροφυσιολογικών σημάτων του εγκεφάλου με τη χρήση ειδικών ηλεκτροδίων που τοποθετούνται στην κεφαλή, στην επεξεργασία των σημάτων αυτών με κατάλληλα φίλτρα και στην αποτύπωσή τους στο πεδίο του χρόνου και της συχνότητας, με στόχο την εξαγωγή χρήσιμων συμπερασμάτων. Υπάρχουν πολλά είδη συστημάτων EEG με πολλαπλά κανάλια και ηλεκτρόδια, όμως το πιο διαδεδομένο και ευρέως χρησιμοποιούμενο τόσο ερευνητικά όσο και διαγνωστικά, είναι το 10-20 σύστημα το οποίο και προτείνεται από την παγκόσμια ομοσπονδία Κλινικής Νευροφυσιολογίας. Στην παρούσα πτυχιακή εργασία σχεδιάστηκε και προγραμματίστηκε λογισμικό, για τη σύνδεση συσκευής EEG με 8 κανάλια στο σύστημα 10-20 σε ένα προσωπικό υπολογιστή με σκοπό, την καταγραφή, επεξεργασία και απεικόνιση των σημάτων του εγκεφάλου. Το συγκεκριμένο λογισμικό διαθέτει μια σειρά λειτουργιών, όπως οπτικοποίηση των σημάτων και αναπαράσταση σε τρισδιάστατο μοντέλο εγκεφάλου, εφαρμογή φίλτρων, διαχωρισμό ομάδων συχνοτήτων, σύγκριση πολλαπλών καταγραφών (control group και autism

group) για την εκτέλεση στατιστικών τεστ, καθώς και ένα τμήμα 'Art Therapy' για την μετατροπή των εγκεφαλικών σημάτων σε ήχους και την ταυτόχρονη χρήση ενός εξειδικευμένου μενού ζωγραφικής ειδικά σχεδιασμένο για άτομα με Αυτισμό (η σχεδίαση αυτή υλοποιήθηκε σε συνεργασία με την Ελληνική Εταιρεία Προστασίας Ατόμων με Αυτισμό). Η εργασία, περιλαμβάνει βιβλιογραφική ανασκόπηση σχετική με την EEG, περιγραφή του νέου λογισμικού και παράρτημα με τμήμα του εφαρμοζόμενου κώδικα.

INTRODUCTION

The World Health Organization has reported nowadays, approximately 35 million people suffering from various form of dementia worldwide. This number is increasing at an alarming rate and is costing heavily to the pockets of individuals, family and the government. This figure, as high as it seems, may be a low estimate because many researchers believe that a significant number of cases go undiagnosed and unreported. The incidence of new cases, however, is known to increase dramatically with age. With increasing number of individuals over 65 years of age, combined with new diagnostic approaches helping to identify more number of cases; the number of diagnosed cases of dementia is expected to double by 2050. In the light of prevailing economic depression, only few major projects and collaborative programs are devoted to Active and Healthy Ageing worldwide. Their attempt is mainly to improve the sustainability and efficiency of social and health care systems, and boost citizens and markets to respond to and win the challenge. While prevention, screening and early diagnosis is the key for healthy growth and development, many IT multidisciplinary applications have already been used for care and cure of dementia in elderly population. Mild Cognitive Impairment (MCI) as well as neurological diseases and related disorders are conceptually defined by subjectively noticeable impairments of cognitive function whereby the changes are not severe enough to interfere with the patient's normal daily routine. The transition between normal cognition and dementia is characterized by alterations both in the brain (structural and functional) as well as the behavioral level.

EEG is known as the safe method of identifying, amplifying, processing and emulating signals that located in specific spots on the surface of head. In these spots electric activity occurs, which is identified as EEG signals and it is created by inner brain structures. The measurement is accomplished through metal electrodes. After

the identification, the signal is processed and amplified in order to be recorded and virtualized [1-5]. EEG was firstly created and established in 1924 by the German Psychiatrist Hans Berger, who also discovered the alpha waves. This EEG system known as *the recording of "brain waves"*, actually recorded any potential difference activity in the surface of the head [1,5-6]. Till the end of the 20th century, many systems were created such as the 10-20 system and the 10-5 system, where higher resolutions in signal and reduction in noise were also included [2-4]. There are several types of waves identified in the head's surface and each category gives an analytically description for the functionality of the brain. These waves are created from the neurons located in the scalp [1,5]. Brain is consists of a neuronal grid, where neurons are complicatedly connected and spread signals, from the one brain area to the other. These signals are mainly consisted of ion current and in that way nervous system works. This current mainly includes Na^{++} , K^{+} , Ca^{++} and Cl^{-} ions [1,7,9]. Brain cells are in fact neurons (Figure1) and each neuron is consisted of nerve dendrites (Figure2) and the axon.

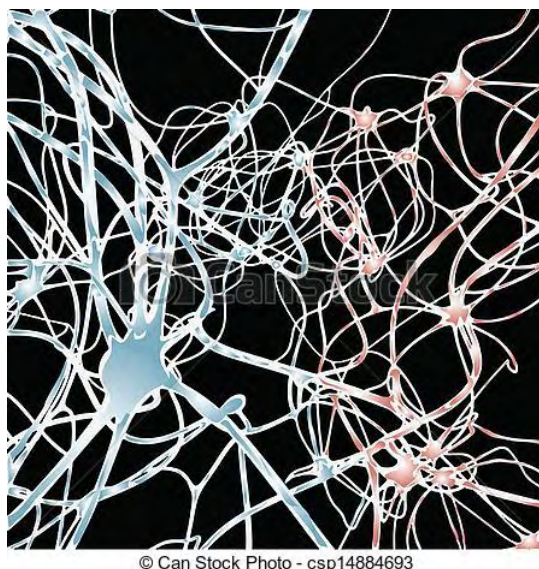


Figure1: The structure of neurons, taken from www.dreamstime.com

Axon is a long extension of the nerve cell. The edge of the axon is a membrane called presynaptic membrane, which is connected with metasynaptic membranes of other nerve cells. In the presynaptic membranes synapses are produced, which participate in the ion signal transmission, between a presynaptic membrane and a metasynaptic membrane [1,7,9].

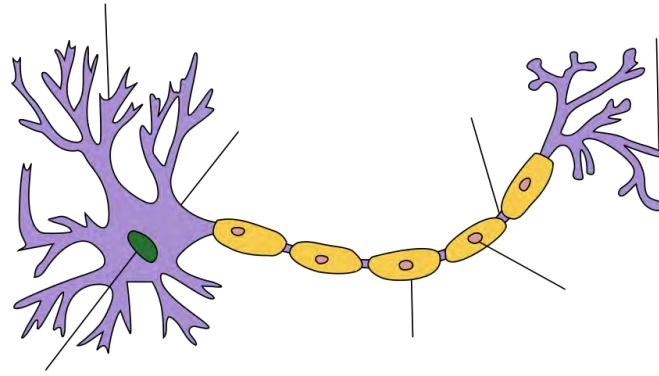


Figure 2: The structure of neurites, taken from wikipedia.org

Dendrites are long and thin prominences of the nerve cells that create ramifications. Dendrites are able to continue the transmission of the signal in order to reach the nerve cell using the metasynaptic membranes. The connection of the presynaptic and metasynaptic membranes is processed by neurotransmitters, which are created by the neurons. Dendrites, axon and nerve cell are enclosed by a cell membrane. The cell membrane is composed by a double lipid chain. Those lipids are mainly phospholipids, which have a hydrophilic heads and hydrophobic tails (Figure 3). Is the cell exposed to wet environment the tails tend to avoid and draw away from water, while hydrophilic heads separate them [7].

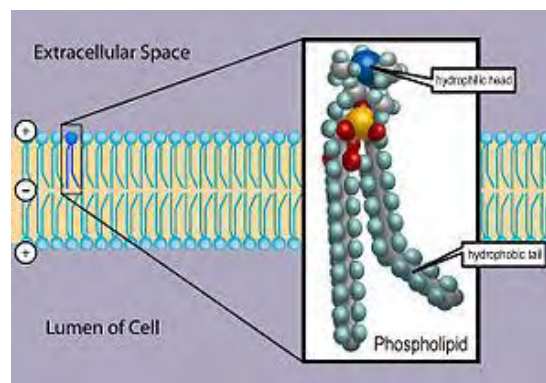


Figure 3: Phospholipids with their hydrophobic heads and hydrophilic tails in the middle, taken from wikipedia.org

Certain proteins constructing this layer act as ion diodes, and their role to the functionality of the nerve system is major. They actually transmit the signal, through specific substances. There are diodes that their operation is controlled by the

transmembrane voltage, diodes that their operation is based on the existence of some chemical elements and diodes which are not affected by outside stimulus [7,8].

There is a potential difference in the cytoplasm and outside the cell. The voltage outside the membrane is positive, while inside is negative. This potential difference is called membrane potential. Usually the cell is on resting potential which means that it is under normal state. At this phase the membrane potential is steadily in 70mV and it is of main significance. The potential difference exists due to the fact that there is different quantity of ions in each side of the membrane. On the cytoplasm there is a greater negative quantity of ions than outside the membrane, which justifies the statement that the voltage is negative inside. When the voltage inside is increased there is depolarization, while in respective reduction there is hyper polarization. Through these equilibriums and their fluctuations, the signals are able to be transmitted as ion current successfully to another cells. So, the flow of the ion current through the membranes of the cells depends on the potential difference in each neuron cell. In that way the neurons are connected through potentials [7,8]. There are two kind of potentials, action potential and post synaptic potential. Action potential includes increase in the transmembrane potential of the neuron. Transmembrane potential is defined as the summary of the outer incentives that dendrites receive. The process involves increase of the potential greater than -50mV to reach 30mV approximately and then a gradual reset to resting potential. There are three stages:

- i) Neuron activation and depolarization
- ii) Repolarization
- iii) Hyperpolarization

Post synaptic potential is related to the transference of incentives from a presynaptic membrane to a metasynaptic membrane. In depolarization postsynaptic potentials that tend to increase the probability of generating action potential are known as inhibitory PSP - IPSP. Respectively potentials that tend to decrease the probability of generating action potential are called excitatory PSP - EPSP. This transmembrane ion current that flows and dispersed in the regions of the head can also be found on its surface. This ion current that derived from the activity of the neurons are in fact the signals that EEG identify through the electrodes on the surface of the head. The electrodes are placed in specific points and identify ion current from the inner activity of the head and external factors [7].

ANALYSIS OF EEG SYSTEMS

Electroencephalography is a method that involves identification of the electric activity of the head through the use of electrodes that placed in the surface of the pate. For EEG measurements special electrodes, amplifiers with filters, analog to digital converter and recording device are required. Signals are affected by potentials that emanated from cells (neurons mainly) of the head. Those potentials give specific signals which are ranging from $1\mu\text{V}$ to $100\mu\text{V}$ are amplified and recorded to be depicted and examined. Also, those signals are affected by outer factors and needed to be filtered. Meanwhile achieving the optimal resolution a greater number of electrodes are necessary. The recording can be achieved through certain methods known as systems. A EEG system is in fact the mapping of the pate, which is needed for the right positioning of the electrodes in their corresponding regions [3,4]. So, different systems of EEG were created for such purposes with variety in the quantity of the electrodes and the regions of the scalp examined [1,7,8]. Despite the fact that, all these systems have such differences, the stages of recording and amplifying is quite common. First, each electrode interacting with the ion current that comes from the neurons of the head, transform the ion current into electrode current that flows in the wires to end up to recording. The electrodes usually are made from Ag, AgCl [7]. Those electrolytes are stabilized either using glue or a ring between the skin and the electrode. Their diameter is ranging from 5mm to 10 mm. To get optimal signal from the head, cleaning is needed by using liquor. In that way reduction in resistance is succeeded reaching a level lower than $5\text{k}\Omega$, which is necessary for a sufficient signal transmission. During the contact of the electrode with the skin ions are moved. As a result of this after a short period of time a balance is created depending on the quantity of ions in both electrode and its electrolyte. In that state both quantities remain static because of a the potential difference that is created. This potential difference interferes in the movement of the ions by hampering them. Its sensitivity is regulated by the quantity of the ions. Any alteration in those quantities that may exist, affects directly this potential difference. In other words, when a signal in the cerebrum is being spotted ,that means that there is a change in the quantities of the ions in both electrolyte and the electrode. That would cause an alternation in the potential difference (either reduction or increase). In any case the value of the ion current identified by the electrodes shall be different depending on the changes that happened and as a result of that the transformed current emanated from the ion current would

have its respective value. However, the electrodes are also sensitive in other factors such as electrodes' thermal alterations. To avoid such an interfere it is wise Ag or AgCl electrodes to be used with a combination of Cl^- electrolytes. In that way movement of the ions is enhanced [1,7,8].

SYSTEMS AND MAPPING

Quite many EEG methods were created through the years, but the most common one is the 10-20 system. The 10-20 system or international 10-20 system, is widely used and recognized through the scientific community for clinical and research purposes [9-11]. It is the only one that is recommended by the International Federation of Clinical Neurophysiology. It is created by Jasper in 1958 and it is actually a brain map, which analyses the placement of 21 electrodes on the surface of the head [4,5,7]. The two reference points are the nasion, which is located at the top of the nose right before the start of the forehead and the inion, which is a bony lump located on the back of the head [3,4]. The distance of the two ears or the distance between nasion and inion is used for the placement of the electrodes. There is a 20% of this distance between two electrodes. In addition, the electrodes that are beside the ears are placed in 10% of that distance away from the ears. The placement of the electrodes depends on the scalp of each patient too [8]. Each electrode receives the ion activity from a specific underlined area of the brain. In that way a sufficient identification of the electrical activity in each area of the brain is feasible.

The designation of each electrode is determined by its respective underlined region. There are five main lobes with their corresponding letters, F letter for Frontal lobe, T for Temporal, C for Central (central lobe does not exist, it is used in that case only for measurement purposes), P for Parietal and O for Occipital. There is also the Fp Frontopolar, which are the spots above the nasion in a corresponding ear distance of 10%. Each electrodes' name is defined by the letters mentioned and a number which gives a background for the hemisphere location. Left hemisphere's locations are described by the numbers 1,3,5,7, right hemisphere's locations by 2,4,6,8 and z is used for the electrodes placed in the center of the head [10].

Electrode	Lobe
F	Frontal
T	Temporal
C	Central
P	Parietal
O	Occipital

Table 1: In this table the main regions of brain are described

Additionally, Fp electrodes are placed above the nasion in a 10% nasion-inion interval. Fp1 is placed in the left hemisphere and Fp2 in the right hemisphere. Also O electrodes are placed above the inion in a 10% nasion-interval. O1 is placed in the left hemisphere and O2 in the right hemisphere.

There is an arc that connects the nasion with the inion. That arc is osculated on the surface of the head and it is located precisely in the virtual bisector of the hemispheres. In this arc three electrodes are placed, which actually are in the middle of the head. The Fz electrode is located 30% away from the nasion along the arc. The Cz is located precisely in the top of the head, which is 20% away from Fz and Pz electrode. The Fz electrode is located 30% away from the inion along the arc.

There is also a corresponding arc that connects the two ears and passes through the peak of the head. In that arc, electrodes are placed, which are T3 in the left hemisphere abstained 10% from the left ear, as well as T4 in the right one abstained 10% from the right ear. C3 electrode has 20% distance from the T3 and C4 has 20% from T4 as well. Both C3 and C4 have an interval of 20% from the Cz electrode.

Between the Fp1 and T3 another arc exists, where the F7 electrode is placed with intervals of 10% from Fp1 and T3. F8, T6, T5 electrodes are placed in the same way between their respective electrodes Fp2 and T4, T4 and O2, T3 and O1. The electrode F3/F4/P3/P4 is placed in a 25% inion-nasion distance between the F7, Fz/F8, Fz/T5, Pz/T6, Pz. Also, A1 and A2 electrodes are placed on the ears of the patient or alternatively in the nasion and in the inion. In both cases 10% distances from the nearest electrodes are required.

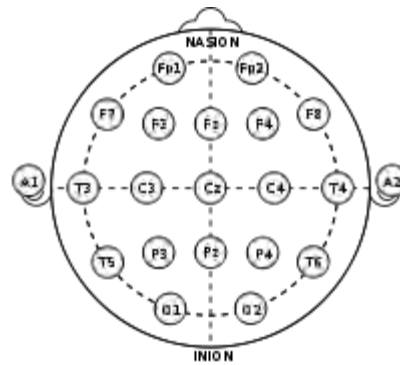


Figure 4: The 10-20 System consisting of 21 electrodes, taken from wikipedia.com

In Figure 4 we can see the 10-20 system mapping (Figure 4), but apart from this there are other systems such as the 10-10 system, which include additional electrodes to achieve higher resolution in the signals detected. There are more complicated systems with 32, 64, 128, 256 and even 512 electrodes. It is mentioned for optimal spatial resolution 64 electrodes are needed and even 97% noise reduction is obtainable.

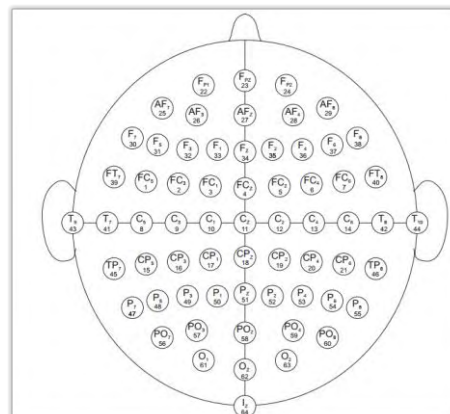


Figure 5: A 10-10 EEG system consisted of more electrodes than the 10-20 system for a greater resolution, taken from <http://www.physionet.org/>

IDENTIFICATION OF THE SIGNAL

In any case the method that signals are being processed from this state is quite common for all these systems. It is mentioned that the electrodes that are placed on the head have potentials that created from the electric activity in the head. As a result of that, each electrode has a potential. Any potential difference that may existed between two electrodes are the signals that the EEG receives. Those signals are amplified and filtered.

All EEG amplifiers are "differential", which means that they measure the signal taken between two inputs. The amplifier takes the difference between the measurements, and amplifies the result. Therefore, all EEG measurements require two electrodes per channel. The second electrode is used as a "ground" electrode. Depending on how these electrodes are located on the head, either "unipolar" or "bipolar" recording is possible. Each channel requires two recording electrodes, designated "active" and "indifferent" (or "reference"). If the amplifier provides separate connections for each channel, then bipolar recording is possible on each channel. However, some amplifiers only provide a single reference for all channels. In this case, bipolar recording is not possible for all channels. For the unipolar recording, one electrode (active) is placed on the designated scalp location, and the other (indifferent) is placed in a "neutral" location such as an ear. In this case, the indifferent electrode is located where there is little or no brain activity to record. The EEG recording is primarily a reflection of the brain activity beneath the active electrode. In bipolar recording, both electrodes are placed on scalp locations, and the EEG recording reflects the difference between them. Therefore, it reflects the activity in an area that is between the two sites. This provides a more accurate representation of the brain activity in a specific area, and is more sensitive to localized activity. For example, beta will be more pronounced using a bipolar recording, and theta will be less pronounced, because it is a more widespread activity, and will be cancelled out by a bipolar recording.

FILTERING AND AMPLIFYING

Brain signals have a range from approximately 1 Hz to 60 Hz, so there is a great need of amplification in order to be compatible with the devices used. There are requirements though that need to be met. First, it is necessary to ensure that any malfunction shall not affect the patient or any equipment. Therefore, an amplifier that protects patient from any electric shock and electric equipment from any malfunction in voltage especially when it comes to terms of high voltage. Then, the amplifier should include filters that reduce superimpose noise and any interferences, for a better signal identification and processing. Also, the signals shall not be affected by the amplifier.

In the EEG, amplification factors of 10^5 are mainly used. The signal is processed firstly by low noise preamplifiers. The signals have a range from $1\mu\text{V}$ to $100\mu\text{V}$, so the preamplifier requires its inner noise to be in the range of nV. Circuits of differential amplifiers are used to reach 120 dB CMRR(common mode rejection ratio) [1,7]. Then the signal is processed by an A/D converter and a digital voltmeter. In that way transformed into digital form, in order to be used by devices. The depiction, the processing and the saving of the signal is available, as well as the on line measurement of the patient condition. Usually, the A/D converter and digital voltmeter are in form of an integrated card that is connected with the computer. Rarely, the signal is depicted in paper in analog form by a recording machine [1,7].

BRAIN WAVES

The waves of the brain, known also as 'brain waves' are actually the waves noticed through EEG recording. They are discovered by the English physician Richard Carton in 1875, before EEG invention [12]. Any type of brain activity could be represented by a wave. The separation of those waves is based on their spectral content.

Those waves are Delta (δ), Theta (Θ), Alpha (α), Beta (β), Gamma (γ) and Mu (μ) and they are also known as rhythms (Delta rhythm, alpha rhythm etc.) [1,7,8,10,13]. Unfortunately, there are disagreements in what ranges of those rhythms should be, but their separation is based on the glossary of terms most commonly used by clinical electroencephalographers and proposal for the report form for the EEG recordings recommended by the IFCN [10]. The following matrix shows analytically the bands of the waves and their corresponding frequencies. For practical purposes the lower frequency limit is 0.5Hz.

Bands	Frequency
Delta	0.5- 4 Hz
Theta	4-8 Hz
Alpha	8-13 Hz
Beta	14 - 40 Hz
Gamma	Greater than 40 Hz
Mu	7-11 Hz

Table 2:Table of the EEG bands recommended by IFCN

Each rhythm is related to operations of the brain and each rhythmic activity gives a background of the functionality in certain brain regions. Also, all the rhythms affect each other and giving a description of the whole brain activity.

Alpha rhythm represents waves that their frequency is ranged from 4Hz to 8 Hz. The name and Alpha is originated by the Greek letter α , as well as its symbolism (α wave). The duration of an alpha wave is 1/8-1/13s. It is mainly noticed in adults. Higher levels of alpha waves are found in artists, musicians and creative thinkers in general. Usually higher frequencies of alpha waves are noticed in female individuals rather than males [10,13]. There are two sub categories of Alpha waves. The normal Alpha is the most known and studied rhythm. In the adults the amplitude of the rhythm varies, but it does not exceed the threshold of 50 μ V. Alpha waves can be found in everywhere in the brain as all areas examined have a characteristic alpha wave. However, in regions such as occipital and posterior lobes where the amplitude is about 50 μ V, alpha rhythm can easily be detected and observed. The amplitude is affected by the concentration of the patient. Alpha rhythm is in fact the resting state of the mind. For optimal identification of those waves, each individual should have his eyes closed and be in a relaxing state. It is related to inhibition control of certain regions of the brain. It is also associated with alpha coma. Although, much of progress has been done, yet the origins of the alpha waves are still unknown [1,7,8,10,13].

Beta rhythm symbolized as β rhythm (Greek letter β), has a frequency band of 14Hz to 40 Hz. The amplitude of a beta wave ranges from 5 to 10 μ V. It can be detected in parental and frontal lobes. Beta rhythm is noticed when the patient is alerted, focused or attentive. There are three categories of beta: low beta, mid beta and high beta. Right amount of beta waves leads to the optimal integration of processes, while higher one leads to extreme anxiety and stress. Also, its activity is related to memory retrieving, benzodiazepines and it is reinforced by stimulants or drugs [1,7,8,10,13].

Gamma rhythm known as γ rhythm (Greek letter γ), includes the highest frequencies that EEG identifies, which are greatest than 40 Hz. It is located in the Somatosensory cortex. When electroencephalography was still analog the frequencies that were

included in the EEG process were less than 25 Hz. With the development of digital EEG further frequencies studied and so Gamma waves. They are detected in Gamma rhythm is associated with optimal functionality of the brain, sleep, will, high concentration and meditation. There are also high frequencies in the brain spotted by researchers, who defined them as separate rhythm known as Lambda and Epsilon rhythms [1,7,8,10,13].

Delta rhythm known as the δ rhythm (Greek letter δ), is the rhythm that includes the lowest frequencies noticed by the EEG in the brain. The threshold is 4Hz. Delta wave has a duration of 1/4 seconds approximately. Delta waves are related to the most unconscious state of mind in contrast with the waves mentioned. During deep sleep (REM) alpha waves are weaken, so theta and delta waves are dominant. Delta rhythm is also noticeable in coma and is mainly detected in cerebral cortex. Delta waves reinforce the release of anti-aging hormones [1,7,8,10,13].

Theta rhythm (θ rhythm) includes a band of 5-8 Hz. It is a slow wave such as Delta wave and it is noticed in adults in a relax state of sleep while dreaming. Too much amount of Theta rhythm shows negative feelings like depression, while right amount endure creativity [1,7,8,10,13].

Mu rhythm, whose band is 7-11 Hz is located in sensory motor cortex and it is highly associated with autism. Also , many neurons are synchronized to create a wave that is noticeable through EEG and is called Mu rhythm desynchronization [8,10].

Coherence

The formula that is usually used for the comparison of the signals is called Coherence.

The coherence formula is given by the formula:

$$C_{xy} = \frac{|\langle s_{xy}(f) \rangle|^2}{|\langle s_{xx}(f) \rangle| |\langle s_{yy}(f) \rangle|}$$

Coherence is used to compare two signals in order to find any similarity in frequencies. Coherence is a normalization of the cross-spectral density. The values are varied from 0 to 1. Numerator is the power-spectral density and denominator is the

power spectrum of x and y signal. A variety of conclusions can be reached depending the hypo coherence (low coherence) or hypercoherence (high coherence) of signals. The majority of them are listed below.

Electrode number	Brain Part	Function Brain
FP1	The anterior pole of left frontal lobe(Prefrontal cortex)	Logical attention, orchestrate network, decision making, working memory, task completion, interactions planning
FP2	The anterior pole of right frontal lobe(Prefrontal cortex)	Emotional attention, judgment, sense of self self-control restraint of impulses
Fz	Frontal lobe	motor planning of both lower extremities (BLE) and midline, walking, running, kicking
F3	Left middle frontal gyrus	Motor planning right upper extremity (RUE), Fine motor coordination, mood elevation
F4	Right middle frontal gyrus	Motor planning left upper extremity (LUE), Fine motor coordination (left hand)
F7	Pars triangularis of left inferior frontal gyrus	Verbal Expression, speech fluency mood regulation (cognitive)
F8	Pars triangularis of right inferior frontal gyrus	Emotional expression, drawing (right hand) mood regulation (endogenous)
T3	Left middle temporal gyrus	Logical (verbal) memory

		formation and storage, phonological processing, hearing (bilateral) suppression of tinnitus
T4	Right middle temporal gyrus	Emotional (nonverbal memory formation and storage ,hearing (bilateral), suppression of tinnitus, autobiographical memory storage
T5	Left middle temporal gyrus superior temporal gyrus inferior temporal gyrus	Logical (verbal) understanding, word recognition Auditory Processing
T6	Right middle temporal gyrus superior temporal gyrus inferior temporal gyrus	Emotional understanding, facial recognition symbol recognition auditory processing
01	Left occipital pole	Visual processing right half of space, pattern recognition, color, perception, movement perception, black/white perception, edge perception
02	Right occipital pole	Visual processing left half of space, pattern recognition, color perception, movement perception, black/white perception, edge perception
Cz	Precentral gyrus	Sensorimotor integration both lower extremities (BLE) and midline, ambulation
C3	Left Precentral sulcus, postcentral	Sensorimotor integration right upper extremity

	sulcus	(RUE), alerting responses handwriting (right hand)
C4	Right Precentral sulcus, postcentral sulcus	Sensorimotor integration left upper extremity (LUE), calming, handwriting(left hand)
Pz	Between central sulcus and parieto-occipital sulcus	perception midline, spatial relations, praxis route finding
P3	Angular gyrus of left inferior parietal lobule	Perception (cognitive processing) right half of space, spatial relations sensations, multimodal sensations, calculations, praxis, reasoning (verbal)
P4	Angular gyrus of left inferior parietal lobule	Perception (cognitive processing) left half of space, Spatial Relations Multimodal Interactions Praxis Reasoning (nonverbal)

Table 3: Regions and functionality. (Adopted from, A Modular Activation/Coherence Approach to Evaluating Clinical/QEEG Correlations and for Guiding Neurofeedback Training:Modular Insufficiencies, Modular Excesses, Disconnections and Hyperconnections)

Coherence	Result of Hypocoherence	Result of Hypercoherence
Fp1 and Fp2	Less efficient integration of logical/emotional attention	Lack of flexibility of integrating logical/emotional attention
Fp1 and Pz	Logical attention/midline perception	Lack of flexibility of logical attention/midline perception
Fp2 and Pz	Less efficient emotional attention/midline perception	Lack of flexibility of emotional attention/midline perception

Fz and T3	Less efficient logical memory/midline motor actions	Lack of flexibility of logical memory/midline motor actions
Fz and T4	Less efficient emotional memory/midline motor actions	Lack of flexibility of emotional memory/midline motor actions
Fz and T5	Less efficient logical memory/midline motor actions	Lack of flexibility of logical memory/midline motor actions
Fz and T6	Less efficient emotional memory/midline motor actions	Lack of flexibility of emotional memory /midline motor actions
Fz and Cz	Less efficient midline motor action/midline sensorimotor integration	Lack of flexibility of midline motor action/midline sensorimotor integration
F3 and F4	Less efficient motor actions RUE/motor actions LUE	Lack of flexibility motor actions RUE/motor actions LUE
F3 and F7	Less efficient verbal/motor actions R	Lack of flexibility of verbal/motor actions R
F3 and F8	Less emotional expression/motor actions RUE	Lack of flexibility of emotional expression/motor actions RUE
F3 and O1	Less efficient motor actions RUE/visual sensations R	Lack of flexibility of logical memory/midline motor actions
F3 and O2	Less efficient motor actions RUE/visual sensations L	Lack of flexibility of emotional memory/midline motor actions

F4 and F7	Less efficient verbal/motor actions L	Lack of flexibility of verbal/motor actions L
F4 and F8	Less emotional expression/motor actions LUE	Lack of flexibility of emotional expression/motor actions LUE
F4 and O1	Less efficient motor actions LUE/visual sensations R	Lack of flexibility of motor actions LUE/visual sensations R
F4 and O2	Less efficient motor actions LUE/visual sensations L	Lack of flexibility of motor actions LUE/visual sensations L
F7 and F8	Less efficient verbal/emotional expression	Lack of flexibility of verbal/emotional expression
F7 and C3	Less efficient verbal/sensorimotor integration RUE	Lack of flexibility of verbal/sensorimotor integration RUE
F7 and C4	Less efficient emotional expression/sensorimotor integration LUE	Lack of flexibility of emotional expression/sensorimotor integration LUE
F8 and C3	Less efficient emotional expression/sensorimotor integration RUE	Lack of flexibility of emotional expression/sensorimotor integration RUE
F8 and C4	Less efficient emotional expression/sensorimotor integration LUE	Lack of flexibility of emotional expression/sensorimotor integration LUE
T3 and T4	Less efficient logical memory/emotional memory	Lack of flexibility of logical memory/emotional memory
T3 and Cz	Less efficient logical memory/midline sensorimotor	Lack of flexibility of logical memory/midline sensorimotor

	integration	integration
T3 and Pz	Less efficient logical memory/midline perception	Lack of flexibility of logical memory/midline perception
T4 and Cz	Less efficient emotional memory/midline sensorimotor integration	Lack of flexibility of emotional memory/midline sensorimotor integration
T4 and Pz	Less efficient logical memory/midline perception	Lack of flexibility of logical memory/midline perception
T5 and T6	Less efficient logical memory/emotional memory	Lack of flexibility of logical memory/emotional memory
T5 and Cz	Less efficient logical memory/midline sensorimotor integration	Lack of flexibility of logical memory/midline sensorimotor integration
T5 and P3	Less efficient logical memory/perception R	Lack of flexibility of logical memory/perception R
T5 and P4	Less efficient logical memory/perceptions L	Lack of flexibility of logical memory/perception L
T6 and Cz	Less efficient emotional memory/midline sensorimotor integration	Lack of flexibility of emotional memory/midline sensorimotor integration
T6 and P3	Less efficient emotional memory/perceptions R	Lack of flexibility of emotional memory/perceptions R
T6 and P4	Less efficient emotional memory/perceptions L	Lack of flexibility of emotional memory/perceptions L
O1 and O2	Less efficient visual sensations R/visual sensations L	Lack of flexibility of visual sensations L/visual sensations R
O1 and C3	Less efficient sensorimotor integration RUE/visual	Lack of flexibility of sensorimotor integration

	sensations R	RUE/visual sensations R
O1 and C4	Less efficient sensorimotor integration LUE/visual sensations	Lack of flexibility of sensorimotor integration LUE/visual sensations
O2 and C3	Less efficient sensorimotor integration RUE/visual sensations L	Lack of flexibility of sensorimotor integration RUE/visual sensations L
O2 and C4	Less efficient sensorimotor integration LUE/visual sensations	Lack of flexibility of sensorimotor integration LUE/visual sensations
C3 and C4	Less efficient sensorimotor integration RUE/sensorimotor integration L	Lack of flexibility of sensorimotor integration RUE/sensormotor integration L
P3 and P4	Less efficient perceptions R/perceptions L	Lack of flexibility of perceptions R/perceptions L

Table 4: Coherence and results of hypercoherence and hypo-coherence. (Adopted from A Modular Activation/Coherence Approach to Evaluating Clinical/QEEG Correlations and for Guiding Neurofeedback Training: Modular Insufficiencies, Modular Excesses, Disconnections and Hyperconnections)

EEG FOR PHYSIOLOGICAL PURPOSES

EEG includes event related potentials(ERP), which are in fact any voltage fluctuations that generated by any sensory, motor, cognitive event identified in the surface of the scalp or other external factors [7,14]. There are two kinds of ERP, Evoked Potentials (EP) and Emitted potentials. Evoked Potentials are associated with mental with any outer stimulus, while Emitted potentials with mental activity. Also, Evoked Potentials vary. There are Visual Evoked Potentials (VEP), Auditory Evoked Potentials (AEP) and Somatosensory Evoked Potentials (SEP) [7,14,15].

Through EEG a great analysis of diseases such as Autism, Alzheimer's, Parkinson's, Schizophrenia is obtainable. Abnormalities in EEG signals show correlations with

such diseases. For example, alteration in alpha .gamma waves and desynchronization are highly associated with Bradykinesia and Parkinson [16,17,18].

Furthermore, EEG is associated with modern technologies. It is used in Sologenetics, which includes activation of inner brain structures in *Caenorhabditis elegans* [20]. Experiments showed that the brain cells are able to controlled by waves, so a manipulation of cellular function in vivo can be achieved. Also, the technology of the insight exists, which is a wireless device that is placed on the head and through recording of brain waves a transformation of signals into data is achieved. An application of this technology is called Brain driver and its purpose is to drive a car mentally. Also, epoch is used to identify brain waves and transform them into computer commands in order to play a computer game. Muse is a device familiar to epoch ,which involves mobile phone's control. DAPRAS prosthetic arm is placed into a disarmed human and can be controlled by the brain. In addition, orbit helicopter is a flying device commanded by thought.

A single EEG routine-EEG protocol

Requirements

- EGG electrodes and a centimeter tape measure is required for calculating the distances between the electrodes, in order to find their corresponding positions, unless there is a headset for the EEG routine.
- There are also sub dermal needles, but there are not recommended due to the discomfort process and risk.
- Conductive EEG gel.
- The basic laboratory equipment of recording EEG.
- A total haircut is recommended for the optimal touch of the electrodes to get the optimal signal, otherwise calipers or hair clips shall be required.
- Having either pencil or pen to mark the spots.
- Cleaning the head before the routine.
- Skin preparation for ensuring low impedance and optimal contact of the electrodes.
- Cleaning the equipment after the process.
- The patient should not drink any substance that includes caffeine at least 8 hours before the routine.

- Fasting is not allowed in the previous night of the test because low levels of sugar in the blood may affect the results.
- The process is fulfilled by the EEG technician.

Preparation

- The doctor gives details to the patient about the reduction of the sleep one night before the test. In certain cases adults may not be allowed to sleep more than 4 hours(6 hours for children), if the test requires the patient to sleep during the routine.
- If any medical illness occurs, the doctor shall prepare the patient with special preparation.

Placing the electrodes

- When the electrodes are placed, their corresponding spots are calculated by measuring the distance of the nasion and theinion through the vertex.
- The 10% of the distance is used to mark a spot above the nasion. This is the Fpz mark, which is in fact located between F1 and F2 and it is used only for the process of measurement in the 10-20 system.
- The next is 20% above Fpz, which is the Fz mark.
- Following the same pattern in the 20% distance from Fz (top of the head) Cz electrode is located.
- In the 20% distance from the Cz spot the Pz electrode is located
- In the 20% distance from the Pz electrode there is the Oz spot, which must have a distance of 10% from inion. Oz is in fact used in international 10-20 system as mark between the O1 and O2.
- Using the Cz, another line of electrodes exists in the head, vertically located in relation to the previous line of electrodes mentioned with familiar distances.
- 10% distance from the left ear T3 exists, then 30% distance C3, in the middle is Cz, then C4 and 10% from the right ear there is T4 electrode.
- A1 is located on the left ear,A2 is spotted on the right.
- Using the Oz and Fpz a cycle exists. The electrodes in the cycle are the F1 right and F2 left from the Fpz in a 10% distance.
- F7 is 20% from the F1 and 20% from T3

- F8 is 20% from the F2 and 20% from T4
- T5 is 20% from the O1 and 20% from T3
- T6 is 20% from the O2 and 20% from T4
- Then the distance of the O1 and Fp1 is measured
- There is two arcs .The one contain Fp1, O1 and C3, while the other Fp1, O2, C4.
- Between Fp1 and C3 there is the F3 in a 25% distance of O1 and Fp1 from Fp1
- Between C3 and O1 there is the P3 in a 25% distance of O1 and Fp1 from O1.
- Between Fp2 and C4 there is the F4 in a 25% distance of O1 and Fp1 from Fp2.
- Between C4 and O2 there is the P3 in a 25% distance of O1 and Fp1 from O2.
- Last check if the electrodes are anatomically placed properly.
- In case of head deformities anatomy is used to change the spots of the electrodes.

Description of a single EEG routine

- A routine EEG recording lasts for about 20 to 40 minutes.
- The patient would normally be sitting on a chair or lie in a bed.
- During the test, the patient has to rest quietly and open or close your eyes from time to time. In most cases, it will be asked to breathe in and out deeply (known as hyperventilation) for a few minutes.
- The routine ends with a flashing light placed near the patient in order to spot any affection in the brain activity.

Sleep EEG

- It is used to test sleep disorders.
- During the test the patient is sleeping and may asked not to sleep last night.

Ambulatory EEG

- The brain activity is recorded throughout some period of time using special equipment that is attached to the electrodes in order to let the patient to do other activities without electrodes cumber him.

Video telemetry EEG

- The patient is recorded into a video and all signals are transferred wirelessly to a computer.

After the test

- The equipment is cleaned and the patient is free to go, unless it is a sleep EEG test.
- The results are announced after some days of analyzing.

THE EXPERIMENTAL PROCEDURE - THE NEW SOFTWARE

In this section, experiments over brain signals are fully analyzed. The whole process includes the implementation and use of a new software that detects, displays and analyze EEG signals. These signals are compared and handled in terms of music and color. Also, with the appropriate statistical tests an automatic routine of comparing signals from Autism Spectrum Disorder patients and control group is added to expedite the research over Autism.

SETUP

The used EEG device is the OPENBCI 32bit Board Kit. The inputs and outputs of the software are adapted in OPENBCI's protocol. The device has negative and positive inputs for electrodes and without any extension it used for an 8-channel measurement. Apart from EEG signals it can be used for detecting other signals on the surface of the skin. For this thesis the kit was used for the 8-channel EEG experiments. In addition, the device is not directly connected with the computer, but there is a bluetooth module that handles the connection within. Through that module the software send and receive commands from the OPENBCI Board Kit.

For the experiments conductive Gel for electrodes and Gold cup electrodes were used for optimal resolution. Each electrodes must be put strictly in the correct position and kept steady during the test to minimize any interference or noise.

THE SOFTWARE

The software is based on the combination of the programming languages Java and Processing. In fact, Processing is quite too similar to Java, but it more oriented in visual effects, painting and arts in general. It can be mixed with Java as an extended Applet (PApplet). Processing was chosen for its orientation to imaging and Java for its libraries and its compatibility with Processing. When the program is initially executed, the index screen includes a window that is divided into four quadrants (Figure 6). Each quadrant has different functionality depending on the current data. In the top right group the EEG signals are displayed either in a live mode or can be imported from a playback (saved) file. In the top left side, there is a rotated 3D representation of the human brain connected with the different electrodes, while in the down left there are multiple selections for painting especially designed for autism patients. In the downright group there are a number of selections for the user related to the transformation of EEG data to sound sculptures.

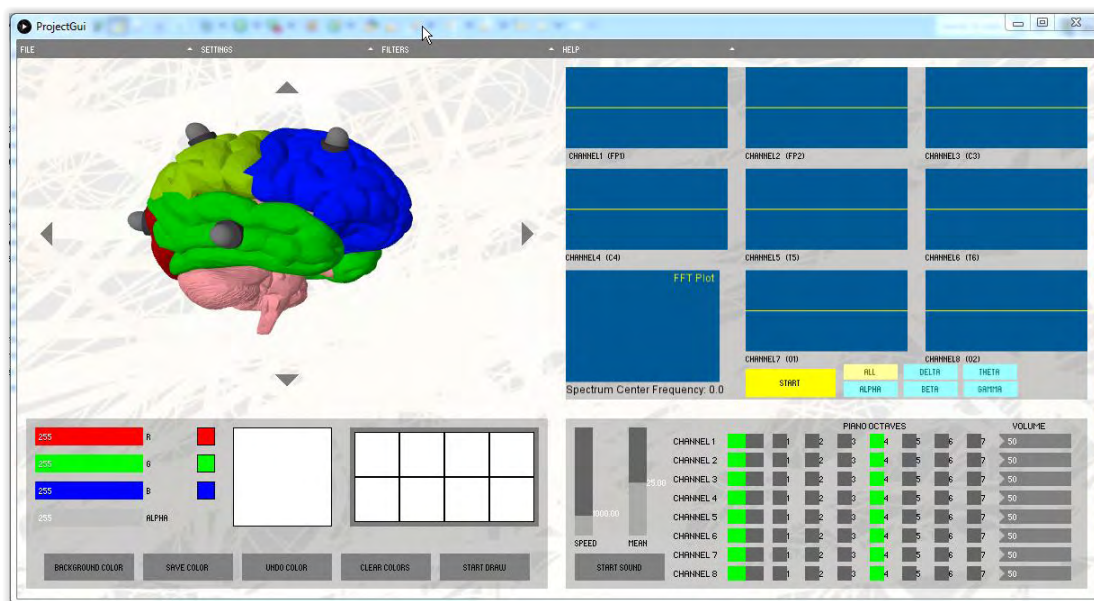


Figure 6: The initial program framework. Each quadrant has a different functionality

DOCUMENTATION OF THE PROGRAM

FUNCTIONALITY MODULES

The top right group displays the data derived from each channel as well as an FFT plot depending on the selected filters and settings. To start and stop the stream,

clicking on the "START" Button is required as well as to stop the streaming. Also, in this group a filter-bands exists. If the user wants to display the signal in the range of Delta band (0 - 4Hz), he can simply push the button "Delta" (Figure 9). On the same way he can push the other buttons to see the corresponding filtered signals (Figure10), (Figure11), (Figure12). In addition, each channel has its corresponding electrode, which is mentioned under each plot [Channel 1(Fp1), Channel2(Fp2), Channel3(C3) , Channel4(C4), Channel5(T5), Channel6(T6), Channel7(O1), Channel8(O2)]. This configuration for channels and electrodes is highly recommended while each channel has its corresponding brain region displayed in the top left window, and any mismatch will lead to a disarray.

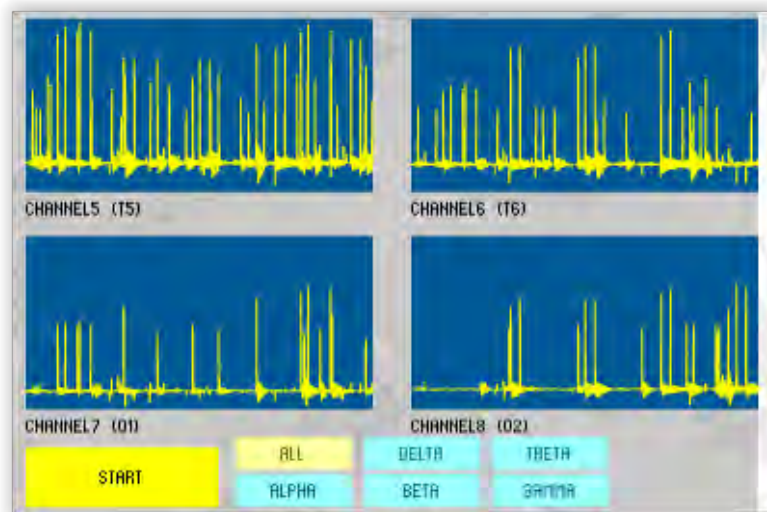


Figure 7: Channels in action while filtered data with Bandpass Filter 0.3Hz - 50Hz and Notch 50Hz are displayed. No band filter is used.

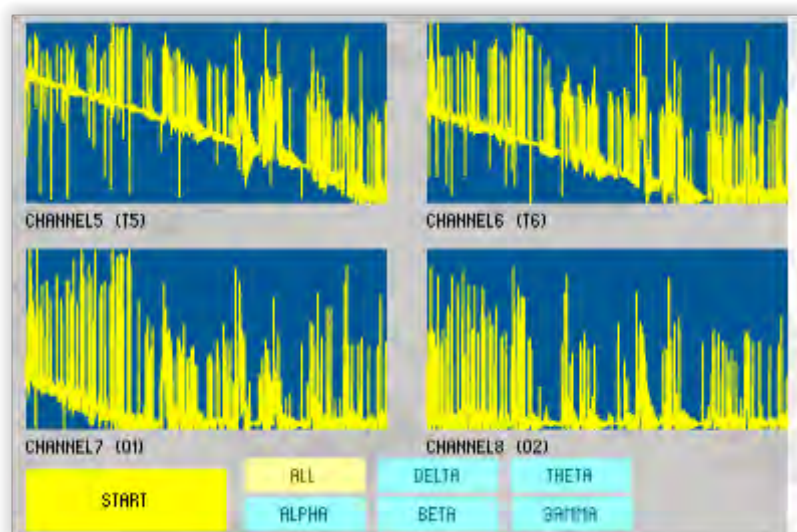


Figure 8: Channels in action with no electrodes connected while filtered data with Bandpass Filter 0.3Hz - 50Hz and Notch 50Hz are displayed. No band filter is used.

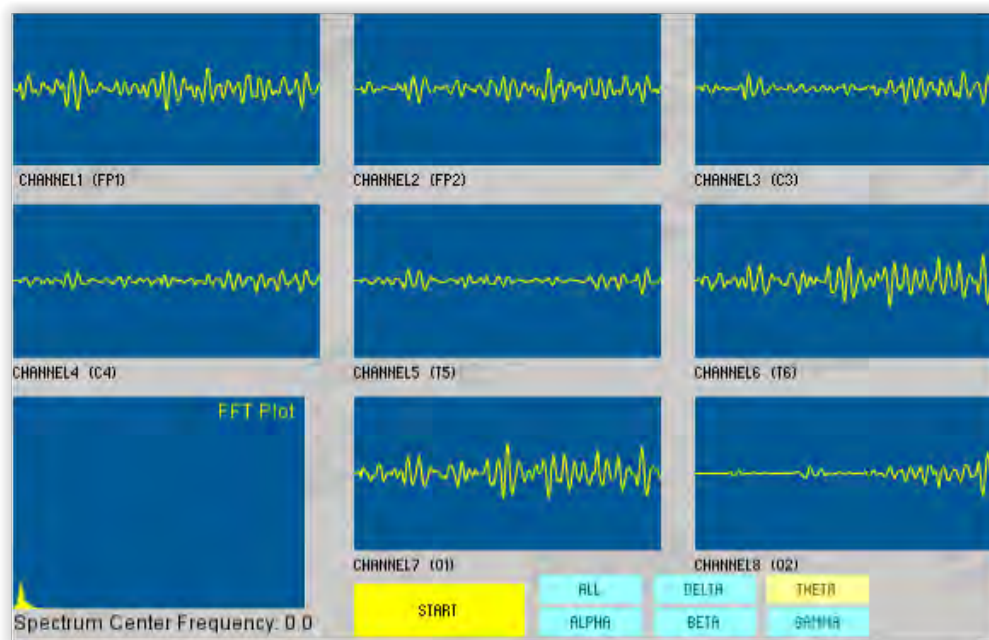


Figure 9: Channels in action with the use of Gamma Band filter, Bandpass Filter 0.3Hz - 50Hz and Notch 50Hz.

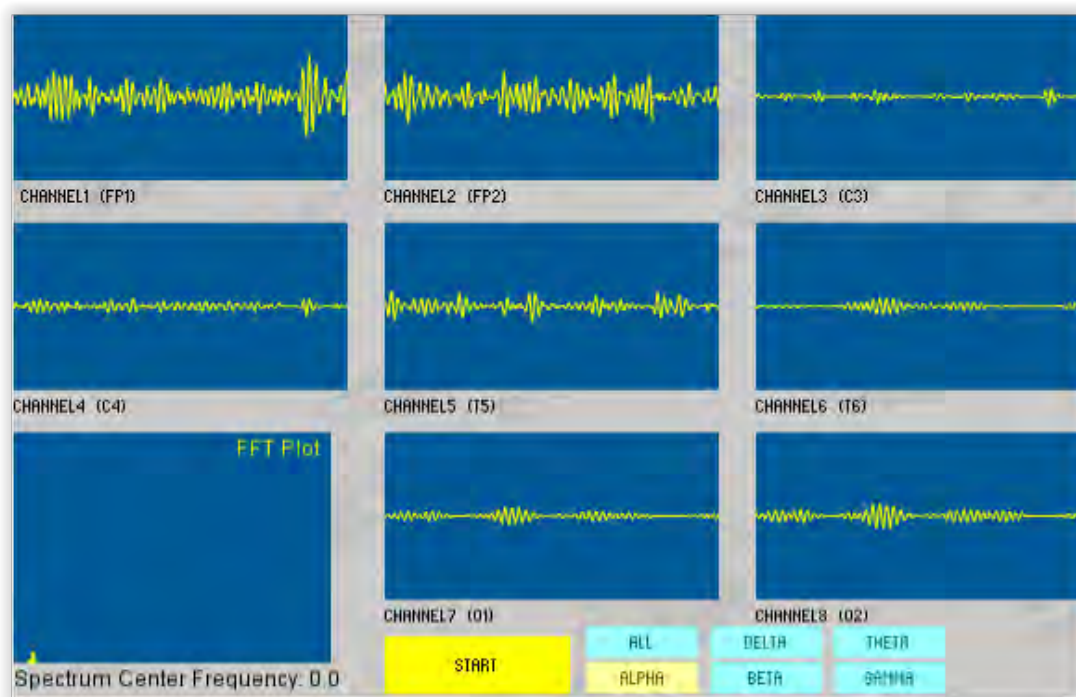


Figure 10: Channels in action with the use of Alpha Band filter, Bandpass Filter 0.3Hz - 50Hz and Notch 50Hz.

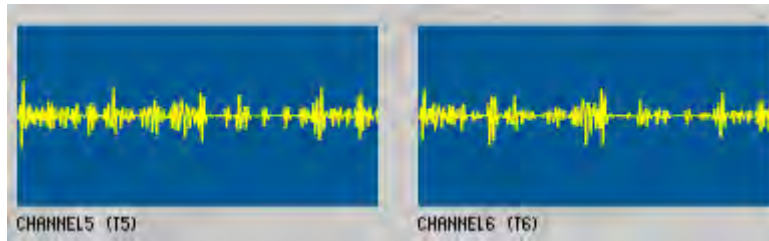


Figure 11: Channels in action with the use of Gamma Band filter, Bandpass Filter 0.3Hz - 50Hz and Notch 50Hz.

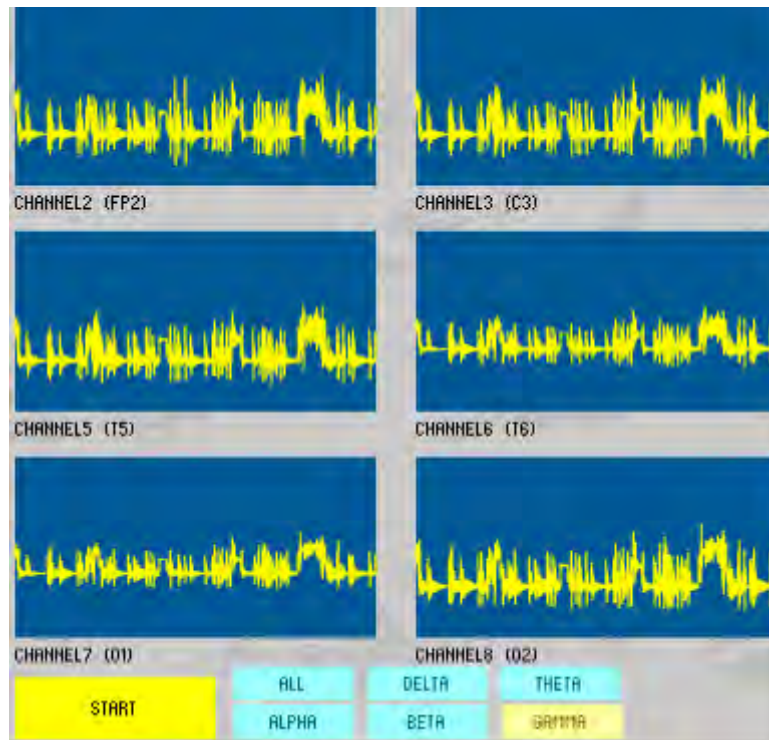


Figure 12: Channels in action with the use of Gamma Band filter, Bandpass Filter 0.3Hz-50Hz and Notch 50Hz.

The top left group is a 3D brain model. This model has been created in the environment of Blender and then was added as an object in the software. The brain can be also viewed from all the possible directions depending the buttons that are chosen. The lamps on the surface of each region are used to show any brain abnormalities in the corresponding region. In normal state the light is green, while in significant dangerous values it turns red. Grey is the initialized color.

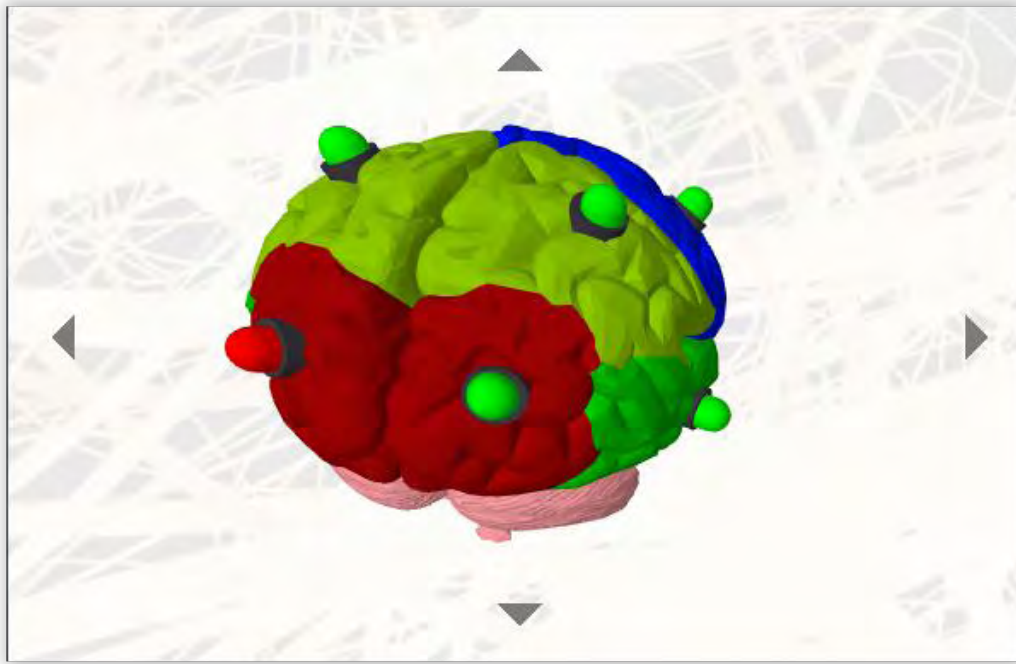


Figure 13: Brain in action with the lights working, the red light indicates the presence of an extreme value.

For the moment the threshold for each lamp is set to the most extreme values that are received. Thresholds shall be modified in the future depending the requirements and the purposes of that group.

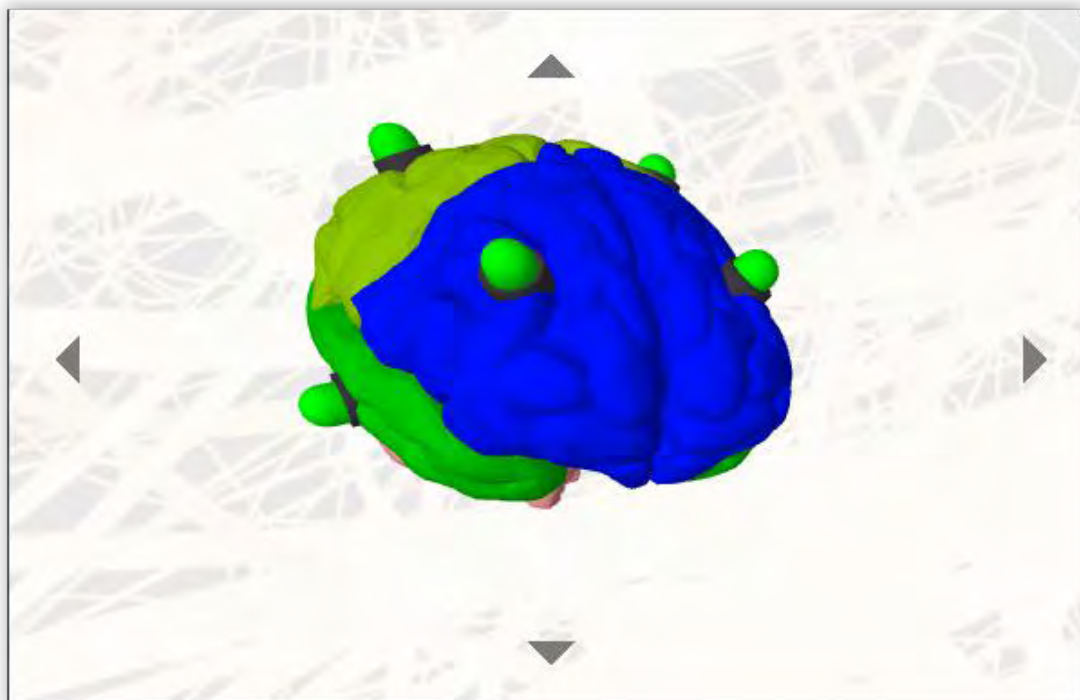


Figure 14: Brain in action with the lights working, in a normal EEG routine.

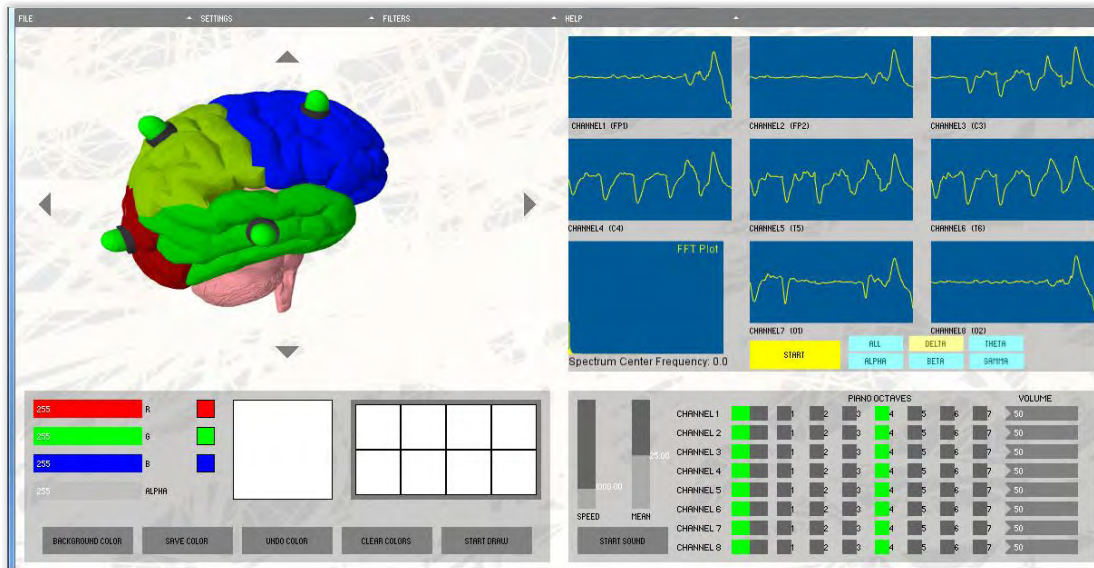


Figure 15: Painting module is located on the down left of the main window.

In the down left group there is the painting module, where users can select to display a second new window for the painting menu (Figure15), pushing the Start Draw button. In this section colors can be chosen individualized for each autistic patient. The doctor or any other involved medical staff, can select and save any color that the patient wants, prefers or feel at the moment 'peaceful'. Multiple colors are created using the RGB sliders and transparency slider ranging from eight or less colors.

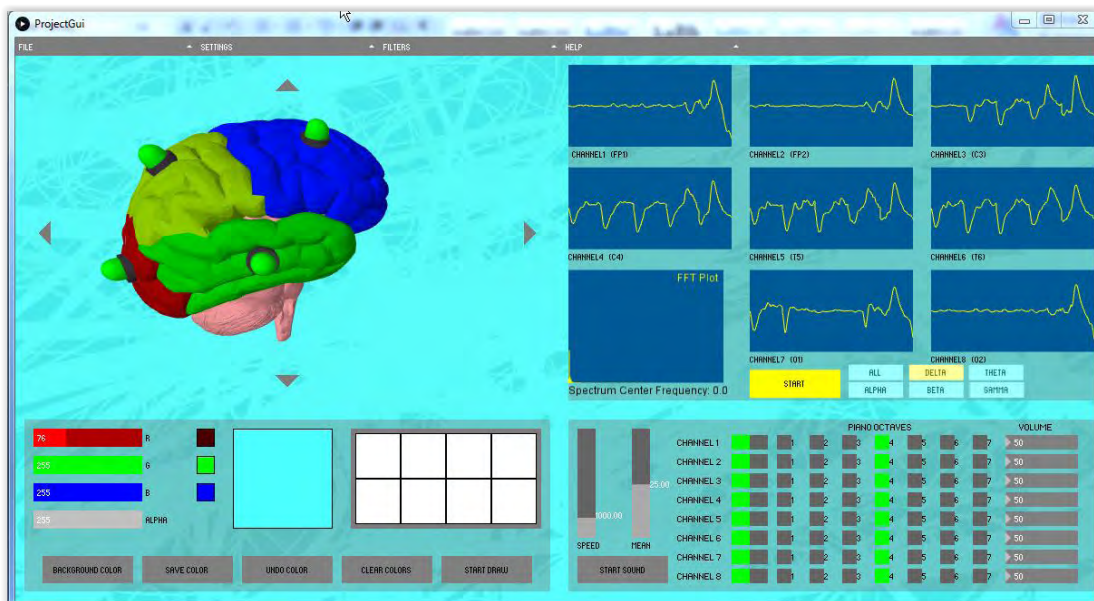


Figure 16: Sliders pushed to give a kind of blue color and then the BACKGROUND COLOR button was pushed to change the background color.

The button "BACKGROUND COLOR" change the background color of the program into the selected one (Figure16). The "SAVE COLOR" button save the color that shall be used in the upcoming window and store it in one of the 8 square (Figure17), while Undo deletes the last one added (Figure18).



Figure 17: This figure shows the way the colors are stored using save color button.

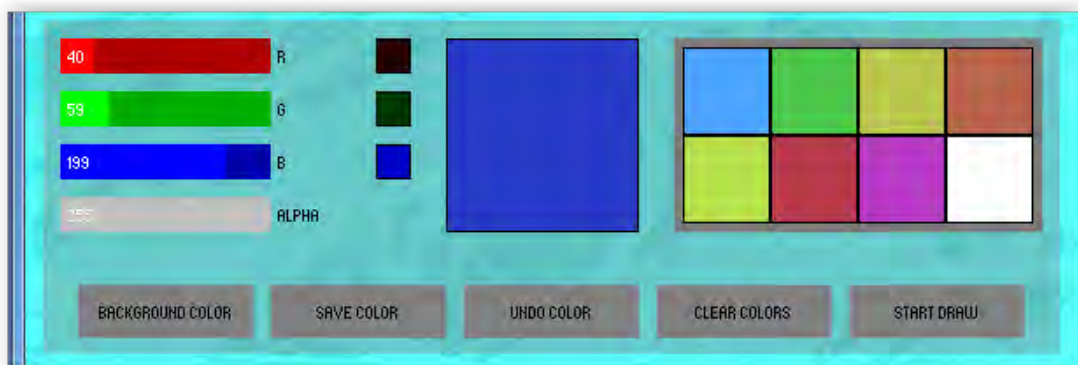


Figure 18: After electing the UNDO COLOR button the last color was deleted and was set in white

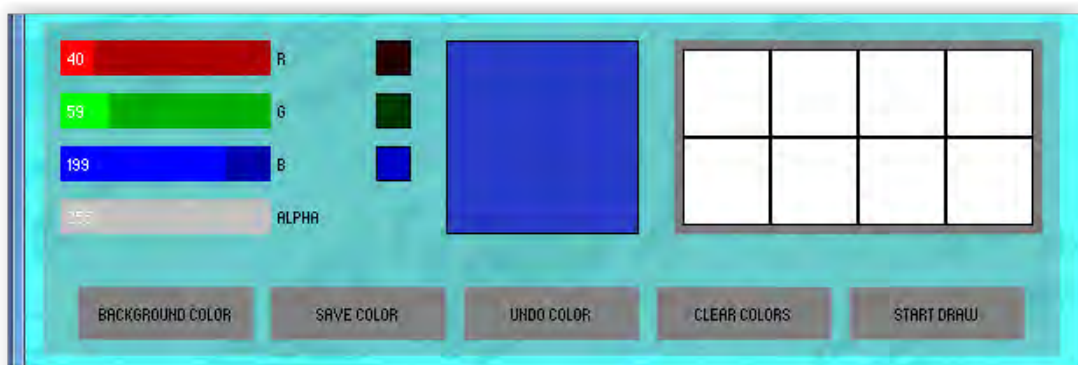


Figure 19: After pushing the CLEAR COLORS button

Button "CLEAR COLORS" delete all the stored colors (Figure19). When the user is ready pushes the button "START DRAW" and the second window opens. This

window is simplified in order to be more flexible for autistic patients. Cycle is selected to paint cycles, while squares or pencil can be also selected. Their size can be also customized. There is also an eraser, undo action defined as left arrow, redo action as right arrow and right icon as clear screen (Figure 20, Figure 21).



Figure 20: After pushing START DRAW button with the selected colors shown.

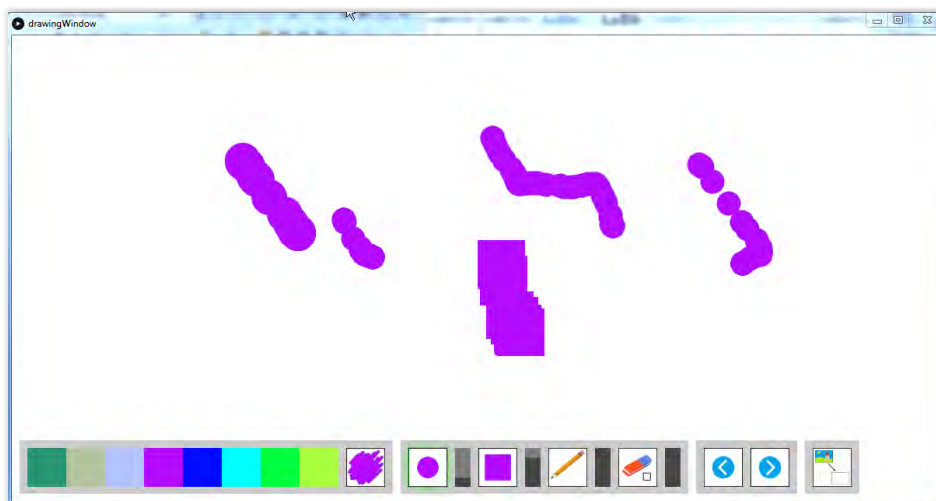


Figure 21: Cycle is selected to paint cycles, while squares or pencil can be also selected. Their size can be also customized. There is also an eraser, undo action defined as left arrow, redo action as right arrow and right icon as clear screen.

The last downright group is related to sound (Figure 22). In fact, it gets the frequencies from 0hZ to 60Hz and choose the one with the highest amplitude in the FFF plot to be played as sound. Most common note are coming from the Delta band because highest amplitudes are noticed in this band. Sometimes, also highest amplitude exists in the Theta band and rarely in others. There are selection in terms of octave of the note played and volume can be controlled. Also, there is a selection for

handling the channels and choosing which of them shall be heard. Speed of the notes is configured and the bar Mean can be used to find mean amongst frequencies with highest amplitudes.

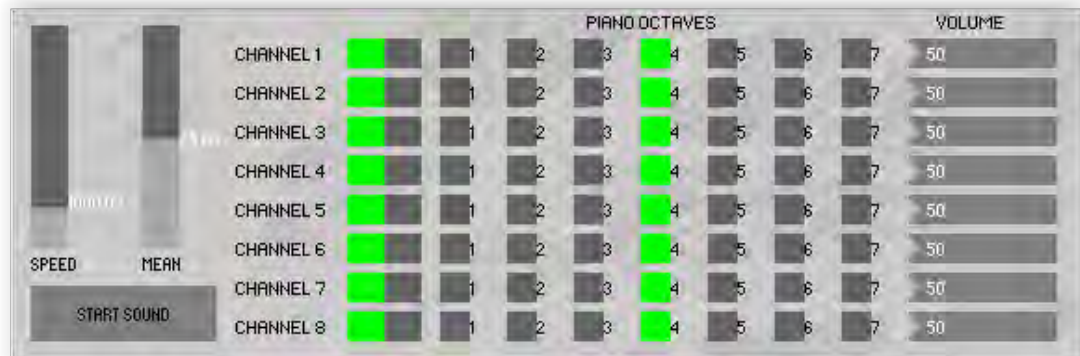


Figure 22: The sound group where each frequency is played as a midi note

EXTRA MENU

Apart from the main functions there are also the menus that play important role in the connection with the board kit, the data processing and accomplish other necessary functions. In the main menu and in the Menu FILE, there are the options of AUTISM TEST, where a new window is opened to perform tests for multiple patients, NEW PROJECT which initialize the program to start a new recording, OPEN FILE where a previous recording can be inserted into the program. This recording is in form of a text file (Figure 25).

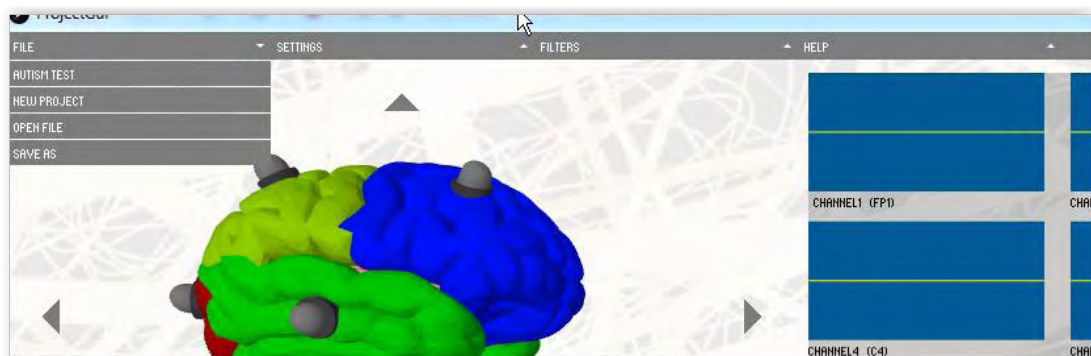


Figure 23: From the main menu, the file bar is selected. The options are AUTISM TEST, NEWPROJECT, OPEN FILE, SAVE AS, SAVE, EXIT as also shown in **Figure 24)**

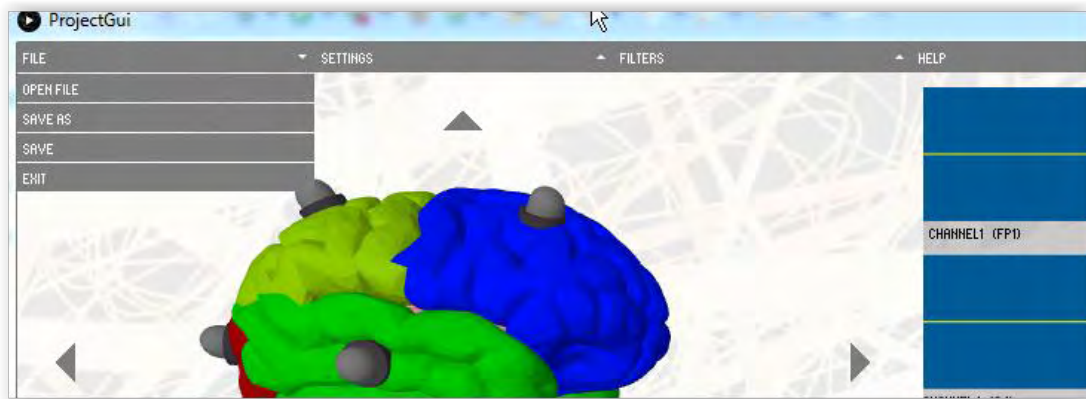


Figure 24: From the main menu, the file bar is selected. The options are AUTISM TEST, NEWPROJECT, OPEN FILE, SAVE AS, SAVE, EXIT as shown in **Figure 23**

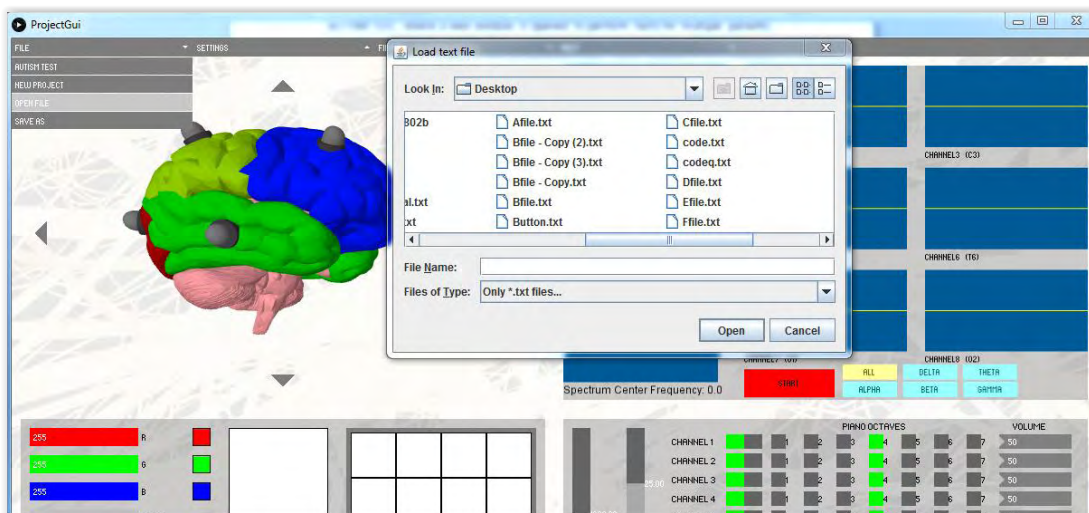


Figure2 5: When the option OPEN FILE is selected fileChooser will be appeared in order to load a file in the program

In the third option SAVE AS a live recording can be saved in a *.txt file for a future use. The option SAVE overwrites a file to save this recording and option EXIT closes the program (FIGURE 23).

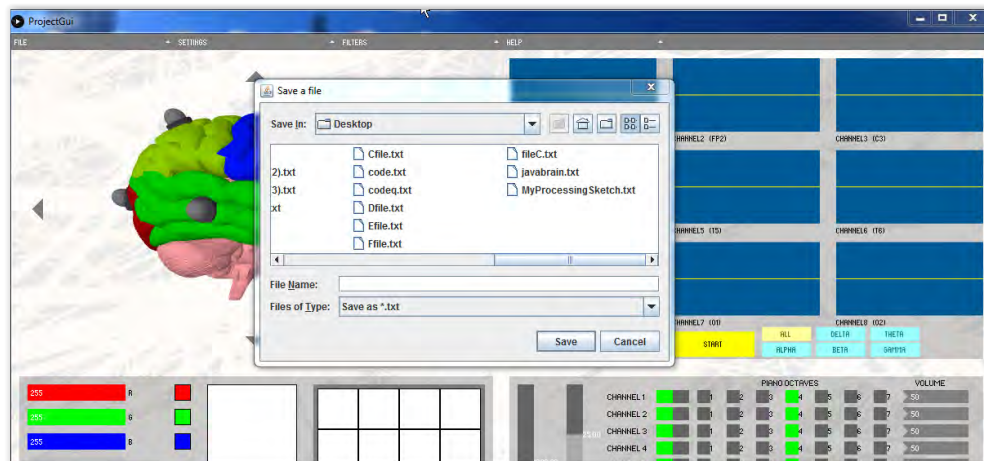


Figure 26: When the option SAVE AS is selected a new window will be appeared in order to save the recording as a *.txt file

In the SETTINGS menu, there are choices that change the settings of the EEG recording. IMPEDANCE - and IMPEDANCE + are set to off and by clicking they can be set to ON. If they are set to ON then the impedance is tested in negative pins or positive pins. In the option Gain program sends signal to the OpenBci board kit to set the gain as shown in the menu. The default gain is x24, while it can be changed to x1,x2,x4,x6,x8,x12,x24. The option INPUT TYPE is set to NORMAL for normal EEG recordings and also can be set SHORTED, BIAS_MEAS, MVDD, TEMP, TEST, BIAS_DRP, BIAS_DRN as described in the OpenBCI protocol. BIAS option is a trigger to set ON or OFF the Ground Pin. BIAS is the ground pin of the openbci board Kit. SRB1 is the reference electrode and it is located in the Upper row of pins. SRB1 can be set to OFF or ON. SRB2 is the default reference electrode and it is located in the down row of pin in the openbci kit. It can also be set to OFF or ON. All these settings send signal to Board kit as show in the Openbci protocol.



Figure 27: Settings include IMPEDANCE+, IMPEDANCE-,GAIN, INPUT_TYPE, BIAS, SRB1, SRB2

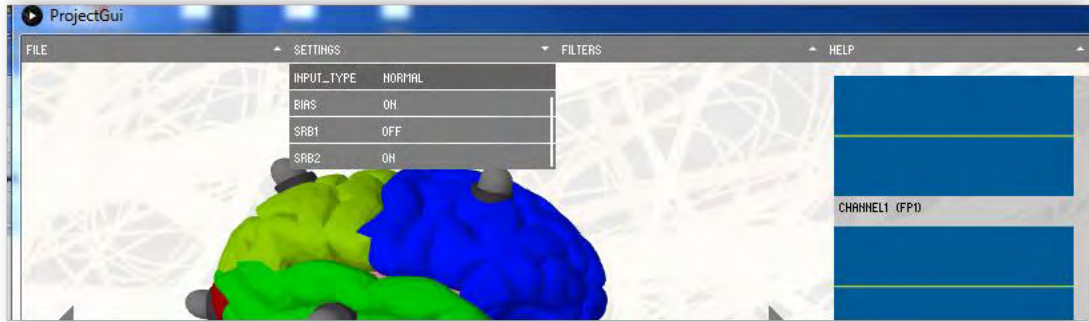


Figure28

In the option FILTERS (Figure 29) there are the main selections that filters the data. There is a Bandpass and a Notch filter. The option BandPass 0.3-50 Hz and Notch 50Hz are set as the default filters. Bandpass contains extra options such as 1 - 50Hz, 7 - 13hz, 15 - 50Hz, 5 - 50Hz and No BandPass Filter. Notch filter has also as option a 60Hz Notch filter and No Notch filter. The filters are functions within the program and they are not configured by the openbci board kit such as settings.

In the option Help there is the Documentation button which includes documentation about the program and the button About for information about the program. (Figure 30).

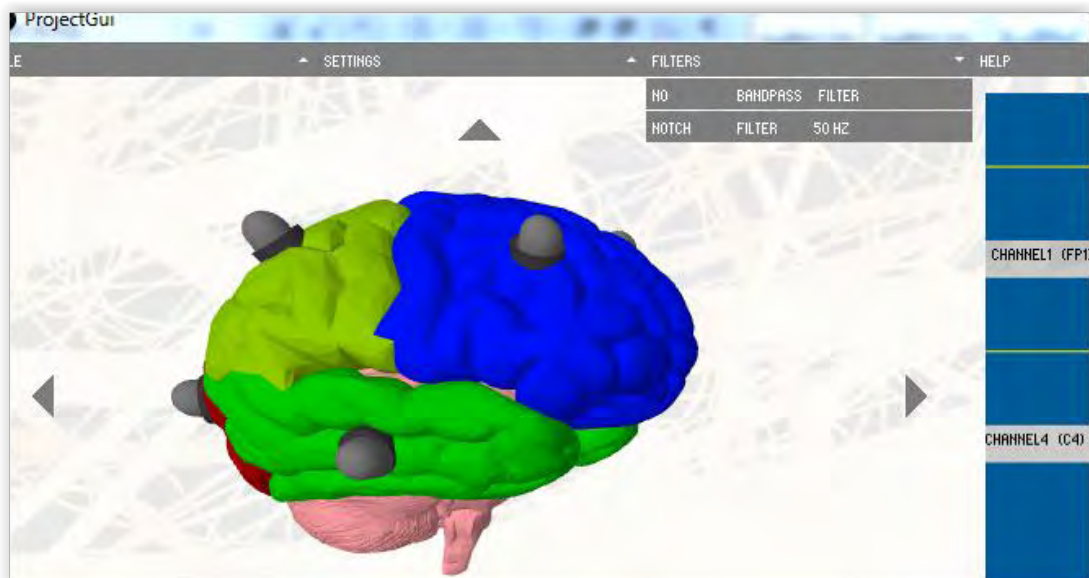


Figure 29: FILTERS OPTION

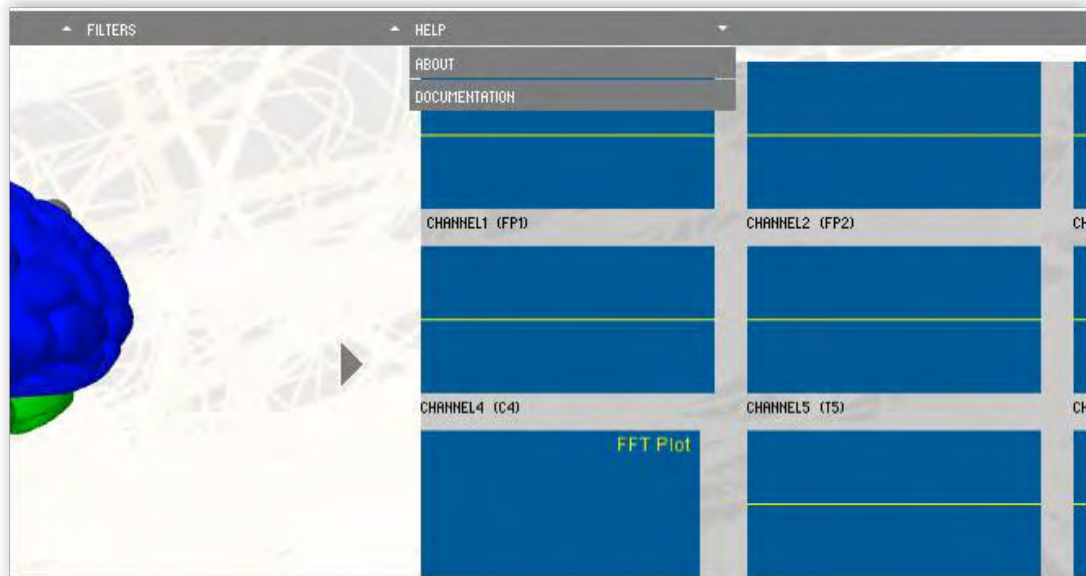


Figure 30: HELP OPTION

STATISTICAL TESTS MODULE



Figure 30: The enabled window when the option Autism Test from File menu is selected

In this new opened window there is a standalone application for testing EEG samples and find any significant differences through the use of statistical tests. Those statistical test are U-test the (non parametric test) and t-Test for data with normal distribution. Also, a primitive test of normality, the W/S test is used to choose between t-Test and U-test. A There are few limitations for the number of samples used, however the arrays of critical values have lack of cases and so the number of samples must be carefully chosen. In the main menu AUTISM SAMPLES of this window files of ASD patient can be added by clicking the ADD ADS PATIENT

button to load multiple txt files from recording at once. The same routine is applied for the Control Group by pushing button ADD CONTROL GROUP. EXIT button exits the program. The Button BEGIN TEST starts the test for the files given. The number of patient files are shown next to the number of ADS files labeling. The number of normal EEG recordings files are shown next to the number of ControlGroup files labeling. When the test is completed an array with results shall appear next to the menu (Figure 31).

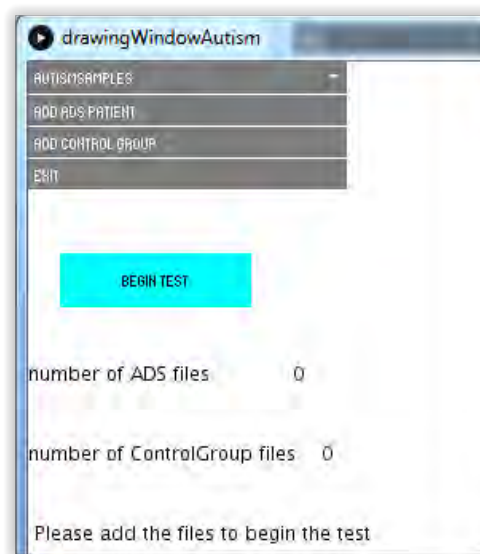


Figure 31: The menu of the statistical tests module

EXTRA SETTINGS

The baud rate is 115200 while sample rate is 250Hz automatically opens and the streaming between the board kit and the program is achieved. The board Kit in fact receives signals from the electrodes connected in the head and transforms them to bits. Then data are transferred in the bluetooth device, which also send them into the port. The data sent actually are packets. Each packet contains a header and then the rest bytes are each channels info. The end of the packet includes the footer.

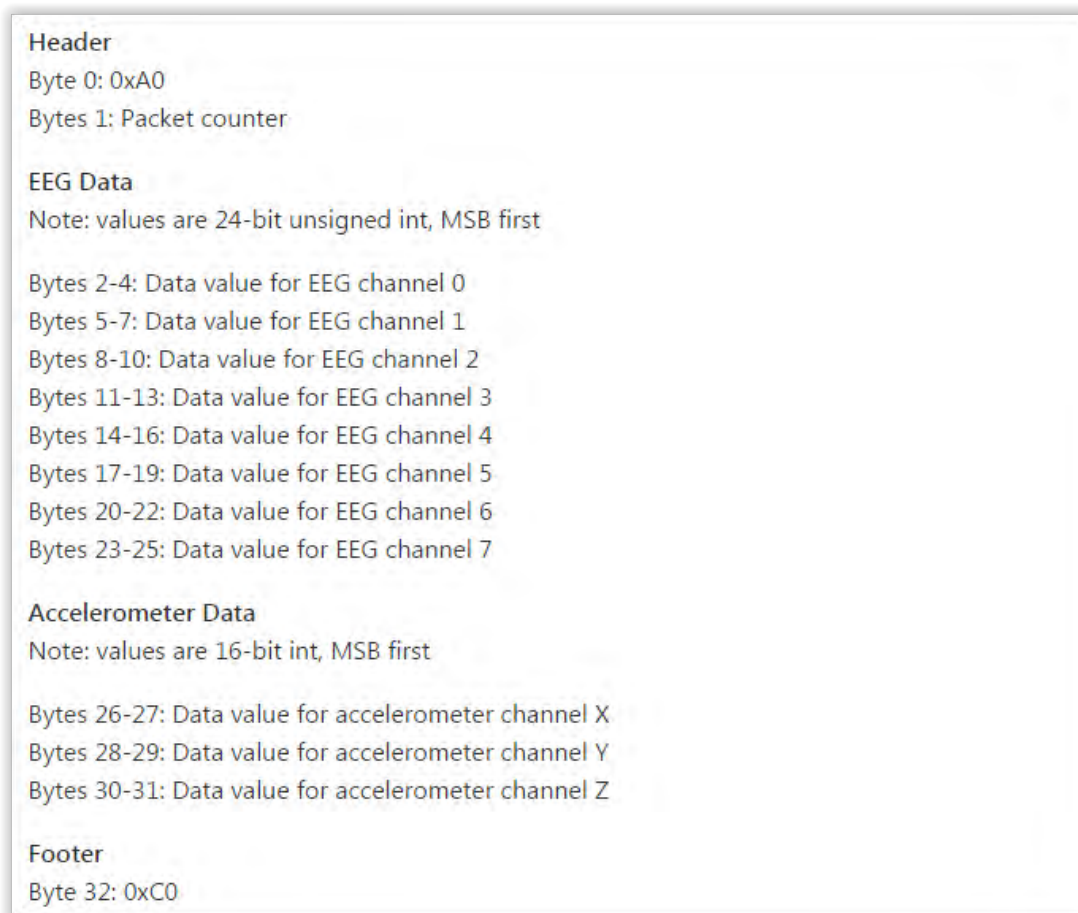


Figure 32: In this figure the packet is analyzed: Header includes two bytes, Footer the last byte, while other bytes are the EEG data

The program receives a 24-bit unsigned integer which must be converted to a 32-bit signed integer (Figure 32) and sends coded signals.

```
int interpret24bitAsInt32(byte[] byteArray) {  
    int newInt = (  
        ((0xFF & byteArray[0]) << 16) |  
        ((0xFF & byteArray[1]) << 8) |  
        (0xFF & byteArray[2])  
    );  
    if ((newInt & 0x00800000) > 0) {  
        newInt |= 0xFF000000;  
    } else {  
        newInt &= 0x00FFFFFF;  
    }  
    return newInt;  
}
```

Figure 33: The code that transforms 24 bit unsigned integer to 32 bit unsigned integer as shown in the github.com

Apart from that after this whole process the data which were sent are still not Volts. To transform those bits in Volts a scale factor with formula $(\text{Volts}/\text{count}) = 4.5 \text{ Volts} / \text{gain} / (2^{23} - 1)$ is recommended, but also in the OpenBCI program the formula of scale factor = $V_{\text{ref}} / ((\text{pow}(2,23)-1)) / \text{gain} * 1000000$ is used.

EXECUTING THE PROGRAM

The program has two main functionalities. One is the recording, filtering, displaying and saving in a file the EEG signals taken from an individual and the other is the comparison of multiple files from healthy subjects and patients using appropriate statistical tests to extract information about significant differences between the groups.

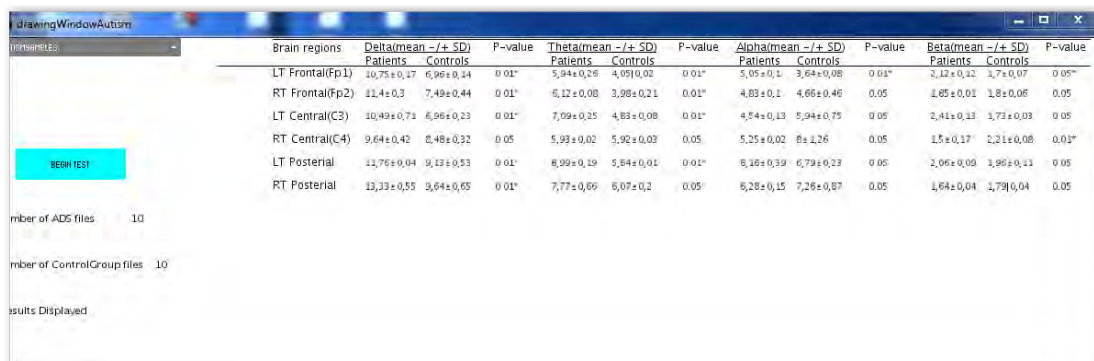
PHASE A

The program starts the recording by simply pushing start button. Then the serial port that bluetooth module is connected. After receiving through serialEvent function the data and transforming them into Volts or μVs depending the scale factor, raw EEG data are available for filtering. The filters that are used are Notch filters and Bandpass filters. Those filters are constructed by Butterworth filters, which were extracted from matlab. Then the data are displayed in the frame. The rate that the data are displayed in the screen is 250f equal to the sample rate. SerialEvent and displaying in processing are two non-synchronically processes. To ensure that there is no conflict in the data stored in the array and the data copied from the array to the frame. A long buffer and flags are used for certain regions of the buffer to remove such conflict. It is also mentioned that 250 samples are displayed per frame. Each frame is refreshed in a slow rate and it is possible to pass packets of 250 samples altogether rather than refreshing 250 times a second. To avoid any additional delays the values of the arrays are not copied in the corresponding arrays that are used on display. In this state the use of the aliasing technique is used. Copying references from objects and arrays rather than whole arrays is way faster and heavy delays are avoided. Also, apart from filtering data library minim is used to perform any calculations and transformations are used to show the spectrum of the signal in a Hamming window. Having the data available in display the brain group and the sound group are also operating

simultaneously with the use of flags. Pushing the button Start the stream is stopped and pushing it again it will continue from where it stopped. Also, recording can be kept by saving the data as previously shown.

STATE B

The second state is independent from the first stages. It involves the comparison of the energy of delta, theta, alpha, beta bands from multiple recordings. In fact, the power in the regions of brain are compared in delta, theta, alpha and beta bands within. To find any significant differences the use of t-Test and U-test is required. The selection of t-Test or U-test is an automatic process as a primitive test of Normality for data is made to choose the most proper one. First, the user chooses files from control group and patients. After inserting them into the program by pushing the button BEGIN TEST and waiting a few seconds the results from statistical tests are shown.



Brain regions	Delta(mean +/- SD)		P-value	Theta(mean +/- SD)		P-value	Alpha(mean +/- SD)		P-value	Beta(mean +/- SD)		P-value
	Patients	Controls		Patients	Controls		Patients	Controls		Patients	Controls	
LT Frontal(Fp1)	10,75±0,47	6,96±0,44	0.01*	5,94±0,26	4,05±0,02	0.01*	5,05±0,1	3,64±0,08	0.01*	2,12±0,12	1,7±0,07	0.05**
RT Frontal(Fp2)	11,4±0,3	7,49±0,44	0.01*	6,12±0,08	3,08±0,21	0.01*	4,83±0,1	4,66±0,46	0.05	1,85±0,01	1,8±0,06	0.05
LT Central(C3)	10,49±0,71	6,96±0,23	0.01*	7,09±0,25	4,83±0,08	0.01*	4,54±0,13	5,94±0,75	0.05	2,41±0,13	1,73±0,03	0.05
RT Central(C4)	9,64±0,42	8,48±0,32	0.05	5,93±0,02	5,92±0,02	0.05	5,25±0,02	8±1,26	0.05	1,5±0,17	2,21±0,08	0.01*
LT Posterial	11,76±0,04	9,13±0,53	0.01*	8,99±0,19	5,84±0,01	0.01*	6,16±0,39	6,79±0,23	0.05	2,06±0,08	1,96±0,11	0.05
RT Posterial	13,33±0,55	9,64±0,65	0.01*	7,77±0,66	6,07±0,2	0.05	6,28±0,15	7,26±0,87	0.05	1,64±0,04	1,79±0,04	0.05

Figure 34: The results that are shown after the completion of the whole test.

An attempt to test the program has been made. Although, data from recordings are exist, due to the lack of ADS patients' recordings, data from the paper "Quantitative EEG in autistic children" was used [20]. In fact, a routine with selective data was created. Those data was used instead of the recordings. The data mentioned are random values that are chosen from a specific range of values. For example in Delta Band (Figure 35) in the LT Frontal region the Patients' mean absolute power is 10,75. The values that are stored in each patient in this field were chosen from the function random (9.2f,13.2f). That means that the values for this filed chosen were from the range of 0.2 -13.2. Each patient has a value for each field. In that way all fields for all patients are filled and the test was completed successfully. It is also mentioned that

the load of files in the program was performed in order to know the number of the participants in each group. However, the data used for the test were created from the sub routine mentioned. In this case, 10 files for ControlGroup and 10 files for ASD group were loaded.

Brain regions	Delta(mean +/- SD)		P-value	Theta(mean +/- SD)		P-value	Alpha(mean +/- SD)		P-value	Beta(mean +/- SD)		P-value
	Patients	Controls		Patients	Controls		Patients	Controls		Patients	Controls	
LT Frontal(Fp1)	10,75±0,17	6,96±0,14	0.01*	5,34±0,26	4,05±0,02	0.01*	5,05±0,1	3,64±0,08	0.01*	2,12±0,12	1,7±0,07	0.05*
RT Frontal(Fp2)	11,4±0,3	7,49±0,44	0.01*	6,12±0,08	3,98±0,21	0.01*	4,83±0,1	4,66±0,46	0.05	1,85±0,01	1,8±0,06	0.05
LT Central(C3)	10,49±0,71	6,96±0,23	0.01*	7,03±0,25	4,83±0,08	0.01*	4,54±0,13	5,34±0,75	0.05	2,41±0,13	1,73±0,03	0.05
RT Central(C4)	9,64±0,42	8,46±0,32	0.05	5,93±0,02	5,92±0,03	0.05	5,25±0,02	8±1,26	0.05	1,5±0,17	2,21±0,08	0.01*
LT Posterial	11,76±0,04	9,33±0,53	0.01*	8,99±0,19	5,84±0,01	0.01*	8,18±0,29	6,79±0,23	0.05	2,06±0,09	1,96±0,11	0.05
RT Posterial	13,33±0,55	9,64±0,65	0.01*	7,77±0,66	6,07±0,2	0.05	6,28±0,15	7,26±0,87	0.05	1,64±0,04	1,79±0,04	0.05

Figure 35: The results that are shown after the completion of the whole test with the use of the routine-data.

CONCLUSION

The results of the test showed that there are significant differences between ControlGroup and ASD patients. The use of U-test was dominant due to the lack of normal distribution in data. In Delta band there were differences between two groups in mean absolute power. In the regions of LT Frontal (Pvalue < 0.01), RT Frontal (Pvalue < 0.01), LT Central (Pvalue < 0.01), LT Posterial (Pvalue < 0.01) and RT Posterial (Pvalue < 0.01) significantly lower mean absolute power of the ASD group related to the ControlGroup was noticed.

In Theta Band LT Frontal (Pvalue < 0.01), RT Frontal (Pvalue < 0.01), LT Central (Pvalue < 0.01), LT Posterial (Pvalue < 0.01) ControlGroup developed higher mean absolute power related to the ASD group.

In Alpha Band the LT Frontal with Pvalue<0.01 was founded to be area of significance. ASD group has had lower mean absolute power, while the ControlGroup higher.

In Beta Band the LT Frontal (Pvalue < 0.05) and RT Central (Pvalue < 0.01) was founded to be areas of significance. ASD group has had lower mean absolute power than the ControlGroup in the LT Frontal Region, in contrast to the RT Central region where mean absolute power in ASD was higher than mean absolute power of ControlGroup.

In general this routine is flexible enough to examine difference for all kind of groups. Its functionality can be extended to compare multiple kind of groups with the same validity. It can be efficiently compare Parkinson and Epilepsy groups or any other related neurodegenerative disorder.

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Publications in the Thesis

Chatzichronis S et al (2016) Art Therapy Software for Treatment of Autism Spectrum Disorders. *Frontiers in Aging Neuroscience, Research Topic, Neuroscientific Research for Management of Dementia*, abstract accepted, *full paper under submission*

APPENDIX

APPENDIX_I

The code that handles the connection with the bluetooth module using the serial port.

```
public void serialEvent(Serial port) {
    if ( myPort.available() > 0 )
    {
        buff = port.read();
        byte byteRead =(byte) buff;
        validc[counterfromzero]++;
        if(BYTE_START == byteRead){
            counter=0;
            localCounter=0;
            channelCounter=0;
        }
        else if(BYTE_END == byteRead){
            if(counterfromzero==249){
                flagBuffer = 1;
                flagForDraw=true;
                flagForDraw2=true;
                flagFilterUsed1 = false;
            }
            else if(counterfromzero==499){
                flagBuffer = 2;
                flagForDraw=true;
                flagForDraw2=true;
                flagFilterUsed2 = false;
            }
            else if(counterfromzero==749){
                flagBuffer = 3;
                flagForDraw=true;
                flagForDraw2=true;
                flagFilterUsed3 = false;
                counterfromzero=-1;
            }
            counterfromzero++;
            counter=0;
            localCounter=0;
            channelCounter=0;

            println();
        }
        else
        {
            counter++;
            if( counter == 1 ){
                packetCounter = (int)buff;
                //Bytes 1: Packet counter
            }
            else if( counter < 26 ){
                bufferOfThree[localCounter] = byteRead;
                //store the byte in the buffer
            }
        }
        if( localCounter == 2 ){
            bufferData[channelCounter] = interpret24bitAsInt32(bufferOfThree);
        }
    }
}
```

```
        //24 to 32
        dataPacket[channelCounter][counterfromzero] =
scale_fac_uVolts_per_count * (float) bufferData[channelCounter]; //change
into volts
x.format("%f", dataPacket[channelCounter][counterfromzero]);

x.format("%s", " ");

print( dataPacket[channelCounter][counterfromzero]);
localCounter=0;
channelCounter++;
} else
localCounter++;
    }
}
}
}
```

APPENDIX II

The code that displays the 3D brain

```
controlP5.Group brainGroup =
mainAppGroups.addGroup("brainGroup",width/120,(height-20)/60+20,width/2-
2*width/120 );
    brainGroup.setBackgroundHeight(2*(height-20)/3 - 3*(height-
20)/60);

    brainGroup.hideBar();
    brainGroup.setColorForeground(black);
    brainGroup.setColorLabel(white);
    brainGroup.setColorBackground(color(255,255,255,0));
    brainGroup.setBackgroundColor(color(255,255,255,0));

    //Brain arrows for navigation
    PImage leftImage =
loadImage("C://Users//Stelios//proclipsing//ProjectGui//bin//data//arrows//
left2.png");

    Button left = buttons.addButton("leftButton");
    left.setSize(2*width/120,2*(height-20)/120);
    left.setPosition(0,16*(height-20)/60);
    left.setImage(leftImage);
    left.setGroup(brainGroup);
    left.updateSize();

    PImage rightImage =
loadImage("C://Users//Stelios//proclipsing//ProjectGui//bin//data//arrows//
right2.png");

    Button right = buttons.addButton("rightButton");
    right.setSize(2*width/120,2*(height-20)/120);
    right.setPosition(53*width/120,16*(height-20)/60);
    right.setImage(rightImage);
    right.setGroup(brainGroup);
    right.updateSize();
```

```
        PImage upImage =
loadImage("C://Users//Stelios//proclipsing//ProjectGui//bin//data//arrows//
up2.png");

        Button up = buttons.addButton("upButton");
        up.setSize(2*width/120,2*(height-20)/120);
        up.setPosition(26.5f*width/120,0);
        up.setImage(upImage);
        up.setGroup(brainGroup);
        up.updateSize();

        PImage downImage =
loadImage("C://Users//Stelios//proclipsing//ProjectGui//bin//data//arrows//
down2.png");

        Button down = buttons.addButton("downButton");
        down.setSize(2*width/120,2*(height-20)/120);
        down.setPosition(26.5f*width/120,32*(height-20)/60);
        down.setImage(downImage);
        down.setGroup(brainGroup);
        down.updateSize();

        groupShape = createShape(GROUP);

        model =
loadShape("C://Users//Stelios//proclipsing//ProjectGui//bin//data//models//
the_new_brain.obj");
        model.rotateX(PI);
        model.rotateY(PI);
```

APPENDIX_III

t-Test Code

```
float tCalculated = (mean1 - mean2)/ sqrt( SPsquare/numberFilesADS +
SPsquare/numberFilesControlGroup );

        float tCritical = arraytTest[df][5];
        tTestSignificant[currRegion][currBand] = false;

//critical value 0.0001
if( ((df>=1) && ( df< 30 )) || (df==30) ||(df == 120) ) {
    if( tCalculated > tCritical){
        //significant
        aValuetTest[currRegion][currBand] = 0.0001f;
        tTestSignificant[currRegion][currBand] = true;
    }
//critical value 0.002
if( tTestSignificant[currRegion][currBand] == false){
    tCritical = arraytTest[df][4];
    if( ((df>=1) && ( df< 30 )) || (df==30) ||(df == 120) ) {
        if( tCalculated > tCritical){
            //significant
            aValuetTest[currRegion][currBand] = 0.002f;
            tTestSignificant[currRegion][currBand] = true;
        }
    }
}
```

```

    }
}
    //critical value 0.005
if( tTestSignificant[currRegion][currBand] == false){
    tCritical = arraytTest[df][3];
    if( ((df>=1) && ( df< 30 )) || (df==30) ||(df == 120) ) {
        if( tCalculated > tCritical){
            //significant
            aValueTest[currRegion][currBand] = 0.005f;
            tTestSignificant[currRegion][currBand] = true;
        }
    }
}
    //critical value 0.01
if( tTestSignificant[currRegion][currBand] == false){
    tCritical = arraytTest[df][2];
    if( ((df>=1) && ( df< 30 )) || (df==30) ||(df == 120) ) {
        if( tCalculated > tCritical){
            //significant
            aValueTest[currRegion][currBand] = 0.01f;
            tTestSignificant[currRegion][currBand] = true;
        }
    }
}
//critical value 0.02
if( tTestSignificant[currRegion][currBand] == false){
    tCritical = arraytTest[df][1];
    if( ((df>=1) && ( df< 30 )) || (df==30) ||(df == 120) ) {
        if( tCalculated > tCritical){
            //significant
            aValueTest[currRegion][currBand] = 0.02f;
            tTestSignificant[currRegion][currBand] = true;
        }
    }
}
//critical value 0.05
if( tTestSignificant[currRegion][currBand] == false){
    tCritical = arraytTest[df][0];
    if( ((df>=1) && ( df< 30 )) || (df==30) ||(df == 120) ) {
        if( tCalculated > tCritical){
            //significant
            aValueTest[currRegion][currBand] = 0.05f;
            tTestSignificant[currRegion][currBand] = true;
        }
    }
}
}
}
}
else{
    System.out.println("False Inputs");
}
}

```

APPENDIX_IV

Code from U-test

```
for(int tr = 0; tr< numberFilesADS+numberFilesControlGroup;tr++ ){
    tempSum=0;
    int cccc=tr;
    float compare = theLongArray[cccc][0];
    if(tr<(numberFilesADS+numberFilesControlGroup-1)){
        do //check if there are elements of the same value
        {
            tempSum++;
            cccc++;
        }while((theLongArray[cccc][0] ==
compare)&&(cccc<(numberFilesADS+numberFilesControlGroup-1)));

        if(cccc == numberFilesADS+numberFilesControlGroup-1){
            if(theLongArray[cccc][0] == theLongArray[cccc-1][0]){
                tempSum++;
                cccc++;
            }
            int hold = tr+1;

            float variable=0;

            while( hold <=cccc){
                variable = variable + hold;
                hold++;
            }

            while(tr<cccc){
                theLongArray[tr][2]= variable/tempSum;
                tr++;
            }
            tr--;

        }
        else{
            theLongArray[tr][2] = tr+1;
        }
    }
}

float Ta=0,Tb=0;
for(int i=0;i<numberFilesADS + numberFilesControlGroup;i++){
    if(theLongArray[i][1] == 1){
        Ta = theLongArray[i][2] +Ta;
    }
    else{
        Tb = theLongArray[i][2] +Tb;
    }
}
```



```
    }  
  }  
  
  float Ua = Ta - (numberFilesADS*(numberFilesADS + 1))/2;  
  float Ub = Tb - (numberFilesControlGroup*(numberFilesControlGroup + 1))/2;  
  
  float Testvalue;  
  
  if(Ua < Ub){  
    Testvalue = Ua;  
  }  
  else{  
    Testvalue = Ub;  
  }  
  uTestSignificant[currRegion][currBand] = false;  
  
  //0.01  
  float Ucritical = arrayUtest2[numberFilesADS-2][numberFilesControlGroup-5];  
  if( Testvalue < Ucritical ){  
    //singificant  
    PvalueU[currRegion][currBand] = "0.01*";  
    uTestSignificant[currRegion][currBand] = true;  
    aValueUtest[currRegion][currBand] = 0.01f;  
  }  
  
  //0.05  
  if(uTestSignificant[currRegion][currBand] == false){  
    Ucritical = arrayUtest1[numberFilesADS-2][numberFilesControlGroup-5];  
    if( Testvalue < Ucritical ){  
      //singificant  
      uTestSignificant[currRegion][currBand] = true;  
      [currRegion][currBand] = "0.05*";  
    }  
    else{  
      PvalueU[currRegion][currBand] = "0.05";  
    }  
  }  
  aValueUtest[currRegion][currBand] = 0.05f;  
}
```

APPENDIX_VI

Code for using forward Fourier

```
fftBuff[currChannel] = new FFT(Nfft, fs_Hz);

fftBuff[currChannel].window(FFT.HAMMING);
fooData = dataPacket[currChannel];
fooData = Arrays.copyOfRange(fooData, fooData.length-Nfft, fooData.length);

fftBuff[currChannel].forward(fooData);
fftLin.forward( fooData );
fftLog.forward( fooData );
```

APPENDIX_VII

Code for displaying plot j

```
myChart[j] = spectroMyGroup.addChart(dataset[j])
    .setPosition(j*width/6,0 )
    .setSize(180, 90 )
    .setRange(-0.2f, 0.2f)
    .setView(Chart.LINE)
    .setStrokeWeight(1.5f)
    ;

myChart[j].addDataSet(dataset[j]);
myChart[j].setData(dataset[j], new float[1250]);
```

APPENDIX_VIII

Code from the the option Settings of the menu

```
settingsList = scrollList.addScrollableList("Settings");
settingsList.setPosition(201,0);
settingsList.setSize(200, 100);
settingsList.setBarHeight(20);
settingsList.setItemHeight(20);
settingsList.addItem(settingsAdds);
settingsList.setType(ScrollableList.LIST);
settingsList.isBarVisible();
settingsList.setColorBackground(backColorScroll);
settingsList.setColorActive(activeColorScroll);
settingsList.setColorForeground(foreColorScroll);
settingsList.close();
```

