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Electrical field modelling of transcranial direct current stimulation

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Abstract

Transcranial Direct Current Stimulation (tDCS) is a technology for neurotransmission that provides direct current to relatively intensive cortical areas in order to modulate internal brain activity. There have been inaccuracies in tDCS findings identified by recent studies. In this study, we present a modelling pipeline for computer based tDCS analysis for studying different electrode montages and different sizes (1 x 6 cm^2) and (5 x 7 cm^2) of electrodes to find out the outcomes. The assumption is that a given brain region's stimulation would be stable in different montages. The total simulation current flow and electric field distribution within the brain were determined for the four most widely used tDCS montages: F3-F4, F3-FP2, FP1-FP2 and C4-FP2, using the COMETS2 software tool. The effect of the size of the electrodes is simulated for tDCS in F3-FP2 mounts in small (1 x 6 cm^2) and wide (5 x 7 cm^2) rectangular electrodes. The current flow is calculated in order to examine the impact of the mounting setup for current density and electric field. Regional as well as localized current densities in the electrode sites have been considered for each of the various mounting setups.

Keywords

Transcranial direct current stimulation (tDCS), direct current, COMETS2, current density, electric field, electrode size, computer simulation.

Foreword

The idea for this thesis formed from my personal interests in human brain. I was planning to work in brain treatment planning. So, I contacted with Tuomas Neuvonen from Sooma Medical about my interest in their company. Lucky enough that I got invitation to his company to visit the office. Doing this thesis on my own opened me a wide variety of opportunities and helped me to complement my skills on a subject that I personally find interesting.

Firstly, I would like to thank Tuomas Neuvonen to give me such opportunity to work in Sooma Medical and supervisor Maria Kivistö, Sooma Medical and supervisor, Professor Timo Jämsä, for his mentorship, guidance, and support in all my endeavors, academic and otherwise. My master's thesis could not have been done without the support and assistance of those respected people, especially Professor Timo Jämsä. You took a chance on a graduation with very little experience, and I will be forever grateful for the patience and kindness you showed me.

I would like to thank the Professors, my families and my friends who have helped me and whom I can always rely upon before or after my studies. Finally, I want to thank all the fantastic friends that I met during my studies. You made this unforgettable part of my life, and I appreciate all the wonderful times we have shared over these last years!

Helsinki, 14.03.2021

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Md Shofiqul Islam

Abbreviations and Symbols used

COMETS	Computation of Electric Field Due to Transcranial Current Stimulation
CES	Cranial Electrotherapy Stimulation
CSF	Cerebrospinal Fluid
DC	Direct Current
EEG	Electroencephalography
FDA	Food and Drug Administration
MDD	Major Depressive Disorder
MEP	Motor Evoked Potential
tDCS	Transcranial Direct Current stimulation
tACS	Transcranial Alternative Current Stimulation
TMS	Transcranial Magnetic Stimulation

Table of Contents

1 Introduction

Transcranial direct-current stimulation (tDCS) is stimulation with electric current that has physiological effects on both animals and humans. A few years earlier, some experimental study demonstrated that the brain of man uses a technology called "direct current polarization" It later became clear that this same technique could be used to noninvasively modify human cortical activity. Low direct current through the brain induced cortical excitement through the build electric field. This method is noninvasive, and there is no need for an operation to act on a surgical procedure inside the human body. When the cortical excitability is modulated, behavioral changes have been observed. There is much evidence that using a technique of using brain stimulation called tDCS, which is a method to stimulate the brain, may have beneficial effects for a wide range of mental disorders[1,2].

tDCS is also being implemented in the developing brain as a new therapeutic method, while mechanistic work in adults in the past fifteen years has less studied within pediatrics[1]. In recent years, computer models have led to understanding how direct current behaves but have several drawbacks though helpful[4]. For example, tissue conductivity is based on assumptions. However, various assumptions can lead to very different results in electrical field quantities[5]. Other elements which alter electric fields include registration errors, anatomical variations, and interindividual variability.

In order to validate tDCS in humans' more effectively, it is essential to investigate the current flow in a structural model that represents the human brain microanatomy and its various anatomical comparison conductivities[6]. Animal experiments do not translate current delivery into the human brain. In the meantime, the attempts at electrical stimulation were limited with the discrepancies between living and dead tissues. However, previous research used accurately documented modeling of electroencephalography (EEG) sources using real-skull phantom heads[7]. Materials of different conductivity have also been used to model human skull geometries into practical electrical stimulation facials[8]. The brain is a complex and unique organ with many different roles. Head models must be realistic and take the anatomical variability into account, so that accurate measurement methods on phantom heads can help to estimate a current diffusion in vivo across various conductivities of the tissue[9].

This thesis aimed to simulate tDCS using computational system analysis. The study investigates the effects of different electrode positioning and electrode size on current distribution and electric field distribution in tDCS using the COMETS2[10]. MATLAB tools and discusses shortly of computer based tDCS clinical applications, limitation, and future possibilities. Each analysis contains necessary background information, results of the simulation, its implications, as well as references to additional studies and materials that can be used when performing similar experiments.

2 Background

In this chapter, we discuss below about history and principle of tDCS and how the electrical stimulation is introduced in medical treatment, finally we will follow some related tDCS work.

2.1 History of electric stimulation

The history of electric stimulation has been proven scientifically meaningful, until today. Historically, it has been used for the treatment of diseases for centuries[2]. The concept began with animal electricity used as a source of energy for electrical stimulation. Around 3000 BC, the ancient Egyptians discovered the strength of the nile catfish, but it is not obvious enough that it could be experimented medically[2]. A few hundred years later, around 400 to 300 BC, Plato and Aristoteles acknowledged their capacity to generate healing effects from their electrical discharge, and the first evidence of electrical stimulation comes into mind[3–5]. In AD 43, the first electrical stimulation evidence came when Scribonius Largus suggested that live torpedo fish could ease the patient's headache in the Roman empire[6]. It is possibly the first known homo sapiens who were immune to torpedo fish control. And eventually, an observational torpedo fish was explored by a Muslim physician in Persia, called Ibn Sidah[7].

Electric fish stimulation at that time is well known worldwide and spread across Africa, where the Jesuits claimed that the local people used cat-fish to extract animals from the bodies of mankind in Early Modern Abyssinia[1]. Fish electricity was perhaps the most common form of electrical stimulation in over ten centuries, but effect calculation was not considered very seriously. So, then in 1660, a German physicist Guericke designed a frictional crank-controlled system[9]. A number of scientists, including Italian anatomist Leopold Marco Caldani and later on used this system to stimulate the muscles of sheep and frogs in 1756, and its variants were known to be the pretty new stimulator system[11]. Possibly the first hospital in 1767 to purchase electrostatic equipment was the Middlesex Hospital in England[12]. Ewald Georg von Kleist, the first condenser to be invented in 1745, was the Leyden jar[13]. This device can store electrical charges generated by an electrostatic generator.

The Leyden jar for therapeutic electrical electrification was used together by experimenters, such as 1755, Anton de Haen, and the 1757 Franklin experimenter[14]. Torpedo fish was extensively studied by the Scottish surgeon and medicine expertise John Hunter in 1773[15]. These investigations were carried out at John Walsh's request, which showed that the shock created by torpedo fish resulted from electricity generation. These kinds of spices or fish have an electrical organ that generates three-dimensional dipole fields around their bodies controlling by the brain and which can decrease charge single-cycle pulses between below 1 Hz and about 65 Hz [16].

Direct current (DC) is the movement of electric charge that does not change over time, which produces continuous signals, unlike fish electrical control and electrical power[17]. Around 11th century, DC generator was invented in a Persian civilization [18]. However, additional sources give the invention to the Arsacid (247 BC), which was called the Galvanic cell (Baghdad Battery)[19]. This discovery was forgotten early in the 20th century when it was found in Iraq and possibly used for medical purposes by archeologist Wilhelm Köning. During the 18th century, the DC battery was invented by Italian physician Galvani in 1780, and his nephew, Giovanni Aldini, was one of the first to use animal electricity for clinical use, Galvani is well-known for bioelectomagnetics[20].

Luigi Lanzarini, a middle age farmer with a major depression disorder, was associated with DC psychiatric care in Bologna, Italy, on May 17, 1801, and counted first time of the effects of currents upon his head [21]. The mood of the human dramatically saturated, and Lazarini getting well within few weeks later. The idea of Aldini was the absolutely milestone that explore of the era of neurological and psychological direct current stimulation. The two scientists, Hellwag and Jacobi, revealed the use of transcranial DC (also defining the first sign of visual perception by transcranial DC) in the year 1802[21]. Since 1880, German psychiatrists discovered of electrotherapy, and it is early stage of tDCS method, especially applied for brain stimulation treatments on patients. In this period, research protocols for experimental designs in more outstanding groups were popular[22]. For his experiment in 1870, Arndt, for example, used 12 psychotic patients. Although his reports are very detailed, they do not provide exact data on the intensity of the current applied[22].

There were contradictory studies, some with positive and others with unfavorable results and an incomprehension of operative values, and electrotherapy was consistently only proposed as an achievement. Several other researchers used DC during 19th and early 20th centuries for the treatment of brain disorder with variability in theory, vague explanations, little qualitative details, and confused polarization findings contributed to conflicting or nonsensical outcomes. DC stimulation was discontinued since the thirties[23]. DC reappeared in electro sleep therapy in 1957 and DC bias was introduced around 1960–1963. The anodic charge turn out to an increase in mood and motor activity, while cathodic polarization induced silence and apathy[24,25]. In 1970s stimulation of the DC was again discontinued, because of new invented psychiatric medication, following with some research projects[26]. In 1998, Priori and his research team found magnet stimulation upon cortex excitability[27]. In recent days, tDCS instruments have been introduced with superior power over stimulation parameters. Study on tDCS addressing neurological and psychological conditions is presently being performed, with uses in depression, epilepsy, chronic pain and addiction[28,29].

2.2 Principle of transcranial direct current stimulation

tDCS refers to stimulating the scalp by the electrodes with weak direct current. Typically, the direct current required for electrodes is provided by about 12-volt batteries. The device is generated as a direct operating current source with a maximum direct current of 1 milliamps to 2 millamps[30]. The electrical supply is connected to two electrodes, anode, and cathode. The cathode is a positive electrode, and the anode is a negative electrode. Current flow is directed to various brain areas, depending on the position of the anode and cathode electrodes on the head[30]. tDCS is simple and it is easy to maintain the appropriate stimulation. The tDCS is equipped with a powered battery (Fig. 1). The tDCS device can control stimulus duration and intensity. The electrodes are attached on the scalp, normally using an elastic strap, headcaps, head gears etc[31].

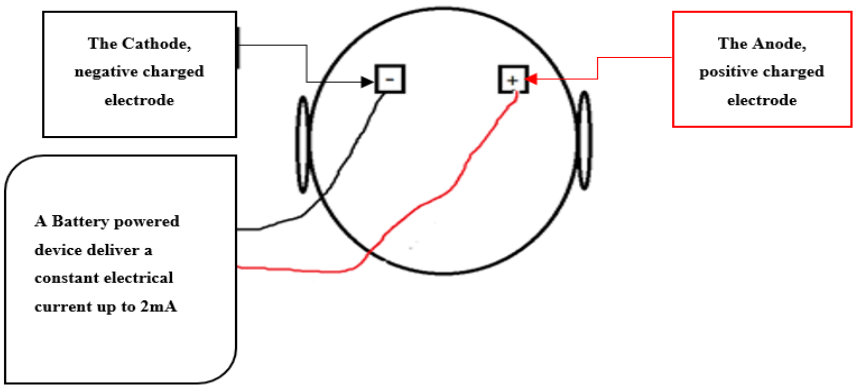


Figure1: Scheme of tDCS showing the head and the electrodes.

A low direct current is not strong enough to activate the neuron's potential but rather influences the existing active neuronal pattern. The action potential is part of the activation of the neuron process. As neurotransmitters happen during the action potential, positively charged ions are able to enter the neuron, called hyperpolarization, while the cell membrane discharges negatively charged molecules, called depolarization[31]. In different directions, anodal and cathodal electrodes induce differences in brain activity. It should be acknowledged that direct transcranial stimulation does not induce neurons to react immediately. The internal flow induces a negative electrical field and the external electrical flow generates a positive field in Figure 2 [32].

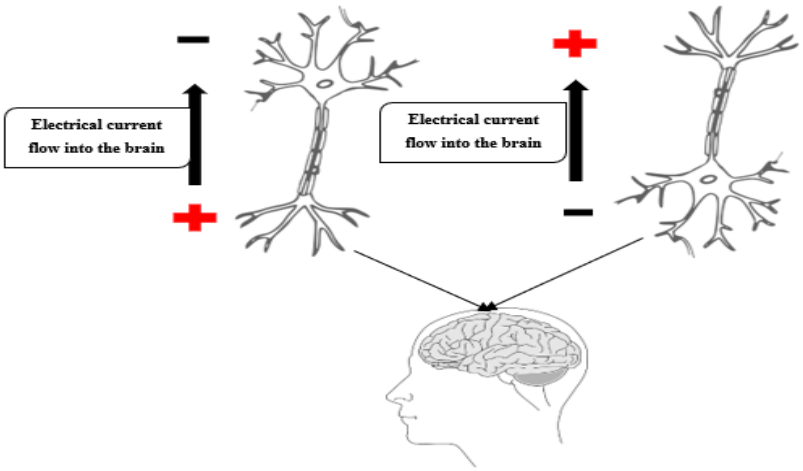


Figure 2: Schematic of active transcranial stimulation of human brain. Anodal activation is depolarized and enhancing excitation of the neuronal membrane and cathodal activation hyperpolarizes and reduces the excitability of the synaptic membrane. Adopted from www.dreamstime.com[33].

The tDCS changes neuronic firing in the brain through synaptic plasticity and functional neuronal contact, and this is the conduct basis for practice training. Practice is also compatible with tDCS. Training facilitates brain functions that are self-learning, but tDCS causes similar results at the same time. Depression, hypertension, chronic pain, and concentration, are medical applications where tDCS is currently being researched[34]. tDCS may also be used for reasons other than medical wellbeing, such as accelerated learning[35], meditation and relaxing[36].

tDCS health risks are still being investigated, but the side effects found up to now are minor and electrode-related [37,38]. This involves temporary skin dryness, itching, and tingling. Other reported health risks of tDCS can include headaches and dizziness. All those side effects are almost at the same level as sham stimulation if tDCS is not applied appropriately. Other side effects such as temporary, non-dangerous light flash phosphene can occur[39]. If electrodes are put too near to the eye, it may happen.

In addition, improper tDCS administration may cause skin burns. No clinical evidence of permanent injury or continuous side effects exists from tDCS. Both tDCS tolerability and protection findings should therefore be recognized in supervised clinical trials using special equipment and tightly regulated techniques, such as the restriction of established distances and exercise volumes. Many people have also experienced a tingly, scratching, or hot sensation in tDCS.

These are not uncomfortable feelings, and they disappear when stimulation ends. Increasing the accuracy of a system depends on good system procedures, good equipment, and use of tDCS current parameters, which in turn results in tolerable use of tDCS[30]. The results of decades of research support the argument that the process involved in the proper use of tDCS is affective.

2.2.1 Current density and electric field in tDCS

In this study, each layer of the head and brain as well as other parts of the model were passive conductors of all the current the applied. The basic formula used for the electrical field analysis is the electrostatic Laplace equation of the electric current with the corresponding boundary electrode conditions to simulate the current distribution.

$$\nabla.(\sigma\nabla\varphi) = 0 \quad \text{.....(1)}$$

Where, σ is the electrical conductivity and φ is the electric potential.

We use the direct solver of continuous positive voltage on the anode and negative voltage on the cathode for test simulations. Then we verify the limit state of normal electric current density components as equation (1) by using the solution details. We also used computer-based model until the entire tDCS unit is filed in equation (1) in the process. This voltage is called a true voltage providing both the relevant maximum value of the current applied through the scalp and the consistent distribution of potential within the scalp's electrode field. The following constraints were also performed to validate current consistency of the normal variable in current density on all internal surfaces. The distributions of electric field (E) and current density (J) are accomplished by the following relationships at all points of the dielectric solution.

$$E = -\nabla\varphi \quad \text{..... (2)}$$

and,

$$J = \sigma E \quad \text{..... (3)}$$

Where, J is a normal component of the electric current density.

Electric field intensity (E) is used frequently in tDCS research where current density is correlated with E as in Equation (3), where J = current density, E = electrical field intensity (V/m), and σ = tissue conductivity.

The application of tDCS induces polarizing currents and its effects depend greatly on the length and intensity of the applied current flow. This is commonly defined as direct current stimulation. The current density is defined by the transversal unit current flow[40], and the current density J is defined as:

$$J = \frac{I}{A} \quad \text{.....(4)}$$

Where A is area, and I is the electrical current.

Equation 4 shows that the rise of the electrode's surface area with a specific current decreases the resulting current density. In tDCS, the electrical current density is roughly 0.5 A/m^2 for 5x7 cm^2 rectangular pad electrodes. By lowering the surface area, the current density increases by the same current in turn. If the current density is high, the stimulation is larger and greater than for a low current density. The increased current density often induces longer side effects after stimulation. The presence of extremely high current results in increased to inflammation of the skin because of pain and other undesirable side effects.

2.2.2 Mechanism of action

The effect of small electric threshold areas on neurons and neuronal networks remains a common investigation. Besides, long-term chronic stimulation produces parallel action pathways. The high frequency repeated transcranial magnet stimulation of the prefrontal cortex will stimulate release of dopamine within the caudate nucleus[41]. Frontal cortex tDCS can also activate similar procedures. In vivo human and animal experiments on functionary brain processes have been studied. Human studies have been primarily focused on tDCS mediated metabolic change in brain tissue, assessed by resonance measurements and subsequent improvements in the recording of neuronal activity[42,43]. The key mechanism of action is at the neuronal level, a tDCS-polarity-dependent switching of the membrane potential. Although anodal Direct Current Stimulation (DCS) normally increases cortical behaviors and excitabilities, cathodal DCS has opposite effects[7,44,45].As a result, tDCS produces electrical field that remains active for up to an hour [46,47].

Applying these techniques are not strictly due to changes in electrical neuronal membrane potential. The tDCS also affects the excitability of the brain by modulating intracortical

and corticospinal neurons[48]. The results of tDCS may be like the effects found a vivo study[49], which applied anodal cortex stimulation and showed permanent increases in the ability to excite postsynaptic[50].

Studies with peripheral nerve and backbone stimulation have shown that DC effects are also monosynaptic with possible temporary changes to the protein channel density located under the stimulating electrode[51]. Activity also showed that DC effects are no synaptic and that they can include temporary changes in the protein channel density underneath the stimulating electrode. Because all polar molecules are displaced by the continuous electric field, and most neurotransmitters and receptors in the brain have electrical properties, tDCS may also affect neuronal activity, causing sustained neurochemical changes[51,52]. Negative influences are sometimes found, besides the direct tDCS effects mentioned previously.

These changes can be seen in distant cortical and subcortical regions driven by connection. The results basically indicate the neural process of the tDCS whereby the anodal current transfers the remaining membrane potential of previous and post-synaptic neuronal towards depolarization, resulting in hyperexcitation and a neuronal hypo-excitation leading in the cathodic current transferring the membrane potentials from the other direction[53,54]. While most early tDCS studies in the motor cortex were conducted, the tDCS not only causes long-term changes in the motor evocative capacity but also influences the somatosensory and visually vocative full potential[55]. This behavior depends on the region Ferrucci[56] and Galea[57] stimulated, proof that tDCS can affect the human brain.

The magnitude and role of the current induced in cortical tissues are an important feature of the discussion of tDCS mechanisms. In order to address this problem, several modeling studies have been carried out and will be addressed in a later section. At last, frequent electric fields impact various tissues, such as vessels, connective tissue and pathophysiological processes, such as swelling, cell migration, and vascular motility. Moreover, their effects on cytoskeletons, mitochondria and, membranes can be observed. This also helps tDCS to affect the nervous system's non-neuronal components[58]. Once

again, the DCS operating mechanisms have yet to be fully understood, which can have major impacts on potential clinical applications. The processes probably have numerous synaptic and non-synaptic effects on neurons and non-neuronal tissue and organs of the central nervous system.

2.3 Clinical applications of transcranial direct current stimulation

2.3.1 Depression

The neurotechnology of tDCS has shown positive results to improvement of depression treatment[59]. Sooma Medical, one of the most established and influential companies in Finland for depression treatment[60]. According to the WHO, Major depressive disorder (MDD) is one of the world's most severe public health concerns. It presents with signs of depression, such as feelings of sadness, dissatisfaction, weak concentration, exhaustion, and low self-esteem[61].There are common pathophysiological features in MDD, which include imbalances in the behavior of the left and right prefrontal cortex, and abnormal neural networks in the cortex-subcortex area. left dorsolateral prefrontal cortex (DLPFC) hypoactivity and hyperactivity are evident in MDD[62].

Since the balance of cortical activities in the DLPFC appears to be linked to depressive symptoms, distributing tDCS to treat depression is a proposed theory[63]. The main target of anodal stimulation is the left DLPFC/F3 area in the international 10–20 system for electroencephalography (EEG)[64]. Where the cathodal electrode is positioned varies in each trial. Some studies use the supraorbital area as an example of F4[65].

Scientists observed that low levels of prefrontal tDCS increased cognitive function in patients with MDD for at least three weeks[66]. Other research indicates that in addition to its general clinical results, transcranial direct current stimulation (tDCS) to the prefrontal cortex is beneficial for cognitive functions, as well as the processing of emotional information[67]. tDCS in which current is applied (active) has both positive impact on clinical symptoms and focus, as well as increased working memory measured by the Symbol Digit Modalities Test[68].

A new research has noted that the number of published studies evaluating clinical effects of tDCS for treating depression is higher than for the next most-studied psychiatric disorder, schizophrenia, as well as for all medication. According to preliminary data, tDCS is successful in treating depression as well as post-traumatic stress disorder[69].

2.3.2 Other Applications

tDCS has also investigated many other applications such as Cognition, Parkinson's disease, dementia, and schizophrenia and other problems related to the brain. Researchers have also raised concerns about possible long-term adverse effects because of lack of knowledge of understandability of tDCS, but they have accepted its application. Despite the significant perspectives of tDCS neurotechnology, we searched for 'transcranial direct current stimulation' in the academic literature and found 5,850 papers published it. This demonstrates widespread sharing of information, and research on this subject is still going on (Fig. 3). The methodology and designs of the analysis however vary significantly and do not favor a systematic method apart from treatment in depression[38,70].

The objective of this qualitative research is therefore on clinical trials performed in recent years (i.e., 2015-2021) with a sample size appropriate to determine at least decrease effects and a single or double-blind study design to evaluate the effects of tDCS. This study aimed to develop protocols for brain disorders, such as Parkinson's disease and schizophrenia, as well as depression, and to explain the effectiveness of various tests and testing procedures in those fields.

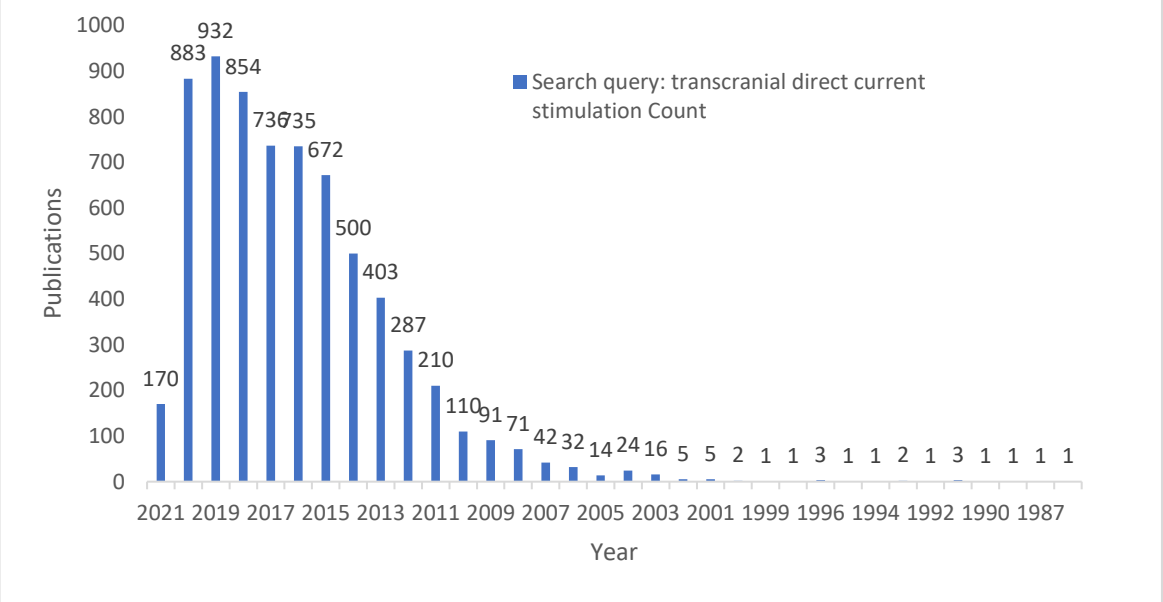


Figure 3: PubMed search on 21st February,2021 for "transcranial direct current stimulation" found 5,850 publications.

The tDCS is often paired with some other preparation or exercise. tDCS has been CE marked in several countries around the world, including in Europe, for the depression medication [71–76], but not in USA approved by FDA yet[27,77]. tDCS is usually combined with some other kind of exercise or training, but this depends on the clinical practice in each country. Clinical trials have shown concern promise with tDCS therapies. The number of treatments possibly needed to assess benefit and evaluate optimum dose is an important challenge when undertaking the necessary clinical trials.

Scientific proof from both basic and clinical research indicates that tDCS can have systematic effects to produce clinically important effects throughout many routines. While a few long-term studies have proven the efficacy of tDCS therapies, other experiments have shown that they have value as well [78]. Descripted evidence shows that tDCS is safe and can successfully treat depression. Compared to traditional drug treatment, tDCS has fewer, non-harmful side effects [79]. The tDCS clinical care has traditionally been restricted to this limited set of guidelines for stimulation that represents both the safety issues and the restriction of advanced and common clinical stimulus devices. There are dose variables that influence clinical outcomes, also within tDCS therapy.

From today, there is still no scientific evidence supporting the claim that tDCS can improve cognitive abilities in people who are not under clinical distress[80]. In several studies, small yet significant cognitive improvements have been found[59]. Parkinson's disease can be displayed clinically and tDCS is helpful in treating certain motor and cognitive indications, since they appear in this condition, e.g., through retrograde cortical stimulation of degraded dopamine middle of brain structures, in the various cortical areas such as motor, frontal and prefrontal cortex. In addition, memory output corresponds to frontal volume of dopamine[81].

The application of tDCS in neuroscience has mainly focused on attempts to connect various parts of the brain to various cognitive and behavioral functions[82]. Research has focused on the cerebellum, being below the skull, due to its high neuron density, and its close connections to the two main centers for motor and cognitive functions[56]. Since most

of these studies focus on the cerebellum, the hypothesis is that tDCS influences only on the motor, cognitive, and affective systems, and it is also reasonable that it functions as a direct facilitator of affect the nerve cell activity[23].

The tDCS is cost efficient, reliable, and scientifically proven. Even though a large amount of research has been done, there is still limited understanding about how mood and cognitive brain functions effect the brain. Significant, comprehensive three-phase clinical evaluations and a more systematic approach to generate all elements of an electric stimulation, including polarity, intensity, and the number of times it can be performed out is still needed. The studies above indicated the clinical effects of tDCS, including the use of brain imaging and electrode interfaces. There will be further opportunity for exploration with regards to tDCS and learning memory, and its clinical applications for the treatment of memory loss and brain injury.

2.5 Clinically meaningful dose sizes

One of the most critical aspects of tDCS is efficient dose size. A dose of tDCS shall consist of various parameters, including the current intensity and duration, number and size of the electrodes and the brain area of the electrode placement and target [51]. In comparison to reliably detectable pharmacological therapies, tDCS does not have a specific dose completion indicator. To avoid transmission of incorrect dosages, stimulating devices should have precautions.

The technology for tDCS in the home environment should allow for the control of stimulation dosage. This can be accomplished by preprogrammed stimulation parameters in equipment and electronic codes that activate configured stimulation parameters for certain treatment sessions or through electronic time-sensitive lock that activates tDCS implementation in a previously defined timeframe of the recommended dose. For instance, a moment switch will allow for a 20-minute stimulus during 6am and 6pm, once a day in required intensity[79]. The typical tDCS doses are applied with 30 minutes of stimulation, amperage strength within 0.5 to 2 mA range supplied through two electrodes with area of 25 to 35 cm^2 [27].

Consequently, there are several exceptions and researchers can consult the growing literature when designing new studies to explore clinical issues. The dosage size is important that should be tested in laboratory conditions prior to use in clinical trials in home environments. Under the medical use, parameters of the earlier unproven technology stimulation dosing should be avoided. The specific patient dosage can be tailored to patient's needs in the direction of the clinician. For example, a long-term titrated dose schedule can consist of consecutive regular sessions with a pattern of application that is less frequent in time. The use of tDCS with research to help direct the clinical application continues to be an open issue of dosage and titration.

3 Modelling of tDCS effects

tDCS modeling is a non-invasive brain stimulation technique that uses low amplitude direct current to modulate brain simulation. Several researchers are still interested in applying this technique to the treatment of neurological disorders due to its potential non-pharmacological, non-invasive, painless, and reversible solution. Different electrode montages result in different current flow patterns through the brain, which enables tDCS to be modified to different functions[82]. The effects of tDCS can be analyzed by various approaches. The most popular method is indirectly to calculate whether a certain tDCS polarity modulates a certain behavior. Therefore, to learn about the results of tDCS, you must first select the distribution where you'll evaluate the parameters. It is understood that the basic assumptions of the tDCS interface design are that the excitability of the anode or cathode increasing or decreasing, studied in terms of the current flow pattern[83].

It is important to note that when analyzing the effects of these simulations, the rate of current flow in any certain brain area does not simply equate to the degree of brains modulation in a linear way. It does seem therefore rational to predict that certain current flow areas are more directly or indirectly influenced because of stimulation while the direct effects of stimulation are spared regions with little or no current flows. The tDCS computer model varies from focus sphere models to individualized high-resolution models that are based on the magnetic resonance imaging (MRI) of an individual. Reasonable information depends on the computer tools available, and the clinical question posed.

Whatever the complexity, both models share the key outcome of accurate prediction of brain activity across transcranial stimulation into substantially controlled clinical practice[27]. The tDCS devices, applied through a constant current source, are used in most clinical trials, but with the aid of models, there are infinite variations in the dosage and mounting processes. The current is transmitted through a standard area of 25 to 35 cm^2 by cap electrodes but can differ depending on the scalp surface order of magnitude[84]. The applied intensity of the total current is usually 0.5 to $2mA$. Steps to enhance the specificities of tDCS have been suggested, including the use of large sponges and

extrusion electrodes, to advance investigation, additional studies are needed to assess the roles of electrode installation in neurological and positioning activation.

For this reason, modeling methods are essential and for instance, modeling studies generally concluded that the return electrode location plays a profound role to modulate the general current flow [85]. Changes in the location of the return electrode including cerebral and extracephalic positions impact the current stream around the suspected target area directly under the active electrode for a fixed active electrode position on the heads. In addition to evaluating the effects of skin shunting and action in deep brain structures, the complete electrode range design modulates subtly the cortical current flow [86].

Computer modeling may again provide useful information on this method. Modern modelling studies indicate that individual anatomical differences can impact cortical flows. There is no similar reason to titrate the tDCS dose compared to transcranial magnetic stimulation (TMS) that uses motor evoked potentials (MEP) to indicate its capacity. A similar concern is the improvement in tDCS dosing montages for people with skull defects or lesions related to stroke. These individuals may be tDCS therapy candidates, but deficiencies or accidents are likely to change the current circulation.

As obvious reasons, any cerebrospinal fluid (CSF) defect or injury, including those associated with the stroke or traumatic brain injury, can ideally shorten current flow [87]. One of the challenges in administering tDCS is finding ways to apply the current to different regions of the brain while minimizing the chance of serious safety issues like existing heat sources. Modeling effects indicates that large cortical areas, especially between and under the electrode, can reach significant amounts of current in typical tDCS[83]. The tDCS modeling experiments have also shown that electrode mounting is important for shifting the current through the skin[84].

The installing of electrodes is critically correlated with how much current is shut through the skin, how much the brain is delivered and what the objectives are. The general theme of modeling efforts is that all specifics and characteristics of electrode mounting have an effect on current flow through clinical progress in applying simplifying rules in the field

of dosage design, so that it would apply certain analyzing rules somewhere within a restricted range of parameters. For instance, an average current density can be a useful method for normalizing specific results of neurophysiology like TMS evoked MEPs, when we consider the entire spectrum of possible electrode mounts no universal relationship between current and brain densities[32,84].

Gyri and sulci geometry have recently been modeled and shown that power can be focused on the edge of gyri[84]. Consequently, in the activated region the results cannot be homogenous. In-depth understanding of the complexity of current flow through the head that reinforces the use of computer models to aid the design of the tDCS dose[88] instead of merely relying on certain heuristic rules such as increasing anode excitability. As well as estimating brain current movement, modelling studies also provide insights into the design of electrodes through prediction of flux patterns through the skin. Modelling experiments have reflected the fact that the current is not uniformly transferred by the skin but appears to focus along the edges of the electrodes or on the skin[84].

The electrode configuration may be simple saline-drenched elastic or Sponge pads and designed for stimulation pads with unique types and materials. The modeling shows that reducing the salinity of the patches decreases the current peak at the edges even when total current and average current density are calculated[89]. In short, modeling studies can play a key role in developing tDCS technology and approaches of the next decade. The cutting - edge technology still has some limitations. These include a stimulated focus area, penetration depth, and control of the position. Technologies using electrode arrays[90] such as the high definition tDCS (HD-tDCS)[91] and other such technologies have recently been proposed, for example, simultaneous EEG monitoring during tDCS to change the dose, and parameters. In the end, clinical monitoring and effectiveness will increase when we start to combine new technologies with transcranial stimulation techniques.

Finally, a technical note. Whilst it has become clear that more and more accurate and complicated models have been produced[88,92,93], certain universal technical problems should still be taken into consideration for high-precision models, starting with high resolution anatomical scans (for example 1 mm). The validity and reliability of tissue

measurements masks and conductivity levels integrated inhomogeneity and anisotropy limits any finite-element human head model. Because it is concerned with the nature of precision, the discussion points out that the final finite element mass approach to solving uses the cortical surface, but then it shows that sulci and gyri are also added to provide an additional understanding of tissue anatomy and current flow factors to refine the segmentation.

Irregularities which are not present in the environment are particularly important because of the limited scan resolution, especially both unnatural perforations in planar tissue such as holes in brain fluid, in which skull contacts the brains and microstructures such as incomplete or vowed vessels may cause severe aberrations. Importance will obviously decrease prediction accuracy without proper develop self - awareness. An incorrect combination of these variables may lead to distortions of the flow of brain current of the magnitude or to a greater amount of unregulated extra complexity. We therefore suggest that the approach that is most suitable to deal with the clinical issue essentially relies on the clinical question. Since the brain and the electrode are interaction-free, the neuronal tissue also has less chance of a void, electrochemical damage or heating. In addition, for standard tDCS protocols, experimental and modeling studies indicate no major temperature changes[88,92,94].

4 Methods

4.1 Finite Element Model (FEM)

The FEM is a computational way to address partial differential equations in two or three space variables, including problems of boundary value. The FEM divides a complex structure into smaller, simpler ways called finite components, to solve complexity. To obtain the desired solution, space modeling is done by constructing a mesh of the object and assigning it a numerical domain: the numerical domain to use in the solution. So, FEM boundary value problem formulation can generate an algebraic equation system. Finite elements, such as whole numbers and sets, are modeled by simpler equations, and then the entire problem is modeled by adding equations that use these simpler ones. Once the FEM has constructed over the number of iterations required, it continues to develop an approximate solution using non-linear methods that generate from the differential by minimizing the related error function.

The following phases are part of a modeling problem:

1. Preprocessing
2. Processing
3. Post-processing

The data and structures that define the problem statement are specified in the preprocessing phase. The processing contains the finite element decertification, the material properties, the solution parameters, matrix rigidity, vectors power etc. Borders will be determined, and the system will be resolved using equation (1). The findings from the treatment section are examined in the post-processing phase. Stresses can be measured here, and data can be displayed. We will concentrate mainly on the processing portion in this paper. Many of the pre- and post-processing operations are adopted using COMETS2 toolbox in MATLAB.

4.2 COMETS2 toolbox

COMETS2 stands for Computation of Electric Field due to Transcranial Current Stimulation 2.[10] It is a new edition of previous COMETS toolbox designed by the Computational Neuro Engineering team, Dongseo University, Korea. It can be used for calculating the three-dimensional electrical field created by tDCS. It has extended into underlying existing conductivity stimulating mechanisms and includes the production of new electrode assemblies and has increased field concentrations in targeted brain areas.

COMETS2 has easy and interactive user interfaces, and users can simulate various electrode sizes, electrode orientation and configurations without having to encode MATLAB scripts[95]. It has several functionalities:

tDCS research toolbox based on Windows GUI
Realistic head model (more realistic than in COMETS1: now CSF (Cerebrospinal fluid)-brain interface is considered)
Sponge electrode pads automatically created
Repeated research fast computing technique
For professional users, their own head models can be used

With COMETS2 it is possible to compute the distribution of the three-dimensional cortical current by the system of electrostatic finite elements. COMETS2 is a proven model for computerized tDCS evaluations[3]. Because of semi electrical conductivity of the head compartments and the edge effect, the modulated cortical areas cannot be exactly predicted.

Realistic 3D simulations can enable researchers to identify electrodes in areas where stimulating currents are enhanced in the targeted brain[96,97]. To evaluate the current density and electric field distribution inside the human head of the tDCS, 3D FEM is adopted.

4.3 tDCS parameters

In any functional neuroimaging or treatment, we need the basic anatomical structure of human brain to study the density, placement, stimulation length and number of sessions in tDCS protocols.

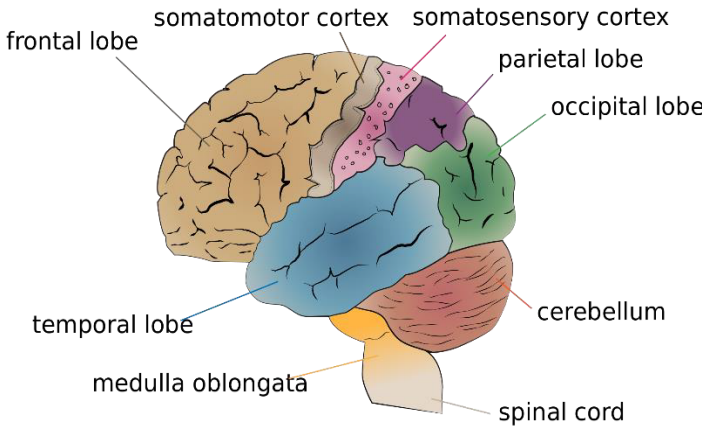


Figure 3: Lobes of human brain. Adopted from Wikipedia[98].

The parameters of tDCS vary widely and many variables are recognizable. The considerations are electrode size and position, magnitude, stimulation duration, amount of practice sessions a day and interval of sessions. There are different levels of electric power, which can be modified to cause varying physiological effects. The area of interest is stimulated with a selected electrode configuration, depending on the desired target. In one scenario, stimulation could concentrate on the prefrontal cortex if the application is for aggression[99]. Process should be needed to stimulate neurons in the target area to follow up behavioral changes triggered by stimulation. Instead, bihemispheric montages may be used, where the location of both target electrodes is necessary to control one region cathodic currents downwards and the parallel zone in the opposite hemisphere upward anodal current.

The target area should be on the cortical surface, as deep brain regions cannot be reached with scalp electrodes. Modelling experiments have shown that even if electrode mounting remains coherent, the current distribution can vary across subjects due to anatomical features such as skull thickness and composition[100]. In this thesis, we used computational

model-based test, but for clinical studies tDCS parameters must be consider seriously. After all, regardless of what kind of cortical positioning system is used, surrounding areas could be stimulated as well, which may trigger unspecified performance changes.

4.4 Montage selection

The assemblies analyzed in this study were simulated in the windows operating system based on the MATLAB tDCS toolbox for tDCS simulation in COMETS2[10]. Motor cortical (i.e., anode) in position A and supraorbital (i.e., cathode) in position B have been the most popular for simulation analysis in tDCS. The electrode's polarity anode or cathode refers to the M1 electrode. M1 anode modulates chronic pain-related sensory function. Just one motor cortex is activated, which is to use bilateral mounting for bilateral pain syndromes[101].

In this thesis, we divided ten cortical brain areas into regions based on established anatomical maps. The segmented regions are frontal left and right, parietal right and left, temporal left and right, and occipital left and right. For the analysis, we were considering specific tDCS assemblies, F3-F4[102], F3-FP2[103], FP1-FP2[104], and C4-FP2[105]. The anode placement is in four montages in separate regions of the cortex (F3-F4 parietal lobe, FP1-FP2 prefrontal cortex, FP3-FP2 frontal lobe, and C4-FP2 motor cortex).

This not only introduces high current variability caused across various brain regions, but also improves understanding of current flows in these areas. The elements are positioned with the COMETS2 toolbox on the standard 10-20 electrode configuration. A 1 mA or 1.5 mA direct current is injected into the cortical surface using either a 5 x 7 cm^2 or 1 x 6 cm^2 electrode pad during each electrical assembly simulation.

The cathode location defines the direction of current flow although this effect is predicted. Mostly as measure, the neuroanatomical location of these clusters is identical when the cathode position in the supraorbital is fixed and the anode position changes from F3 to F4 (see Fig 4). In cases of a coexistence of two routes and the minimum overlap in the existing distribution of two assemblies, the cathodes can be in two separate directions.

5 Results

In this chapter, we present the distribution of current density and electric field in different montages, and the effect of the electrode shape and size on current density, using COMETS2 computer-based MATLAB model software.

5.1 Current density distribution in different montages

A 1.0 mA DC current was applied directly for computer-based simulations (COMETS2) for four separate electrode montages (F3-F4, F3-FP2, FP1-FP2, and C4-FP2). The maximum current density values in ten brain areas are shown in Table 1. The current density distributions are represented in the Figure 4.

Table 1. The maximum current density values calculated in ten brain areas. The highest values of each montage are marked with bold and the lowest values with red.

Brain Region	**Maximum Current Density $J(A/m^2)$**			
Montages	F3-F4	F3-FP2	FP1-FP2	C4-FP2
Left Frontal	0.06	**0.21**	0.12	0.2
Right Frontal	0.02	0.12	**0.20**	0.24
Left Temporal	0.08	0.03	0.04	**0.26**
Right Temporal	**0.24**	0.06	**0.25**	0.07
Left Parietal	0.16	0.08	0.06	0.06
Right Parietal	0.07	0.05	0.07	0.04
Left Occipital	0.12	0.02	0.03	**0.27**
Right Occipital	0.03	0.04	0.05	0.03
Left Motor	0.15	**0.17**	0.19	0.06
Right Motor	**0.19**	0.10	0.13	0.14

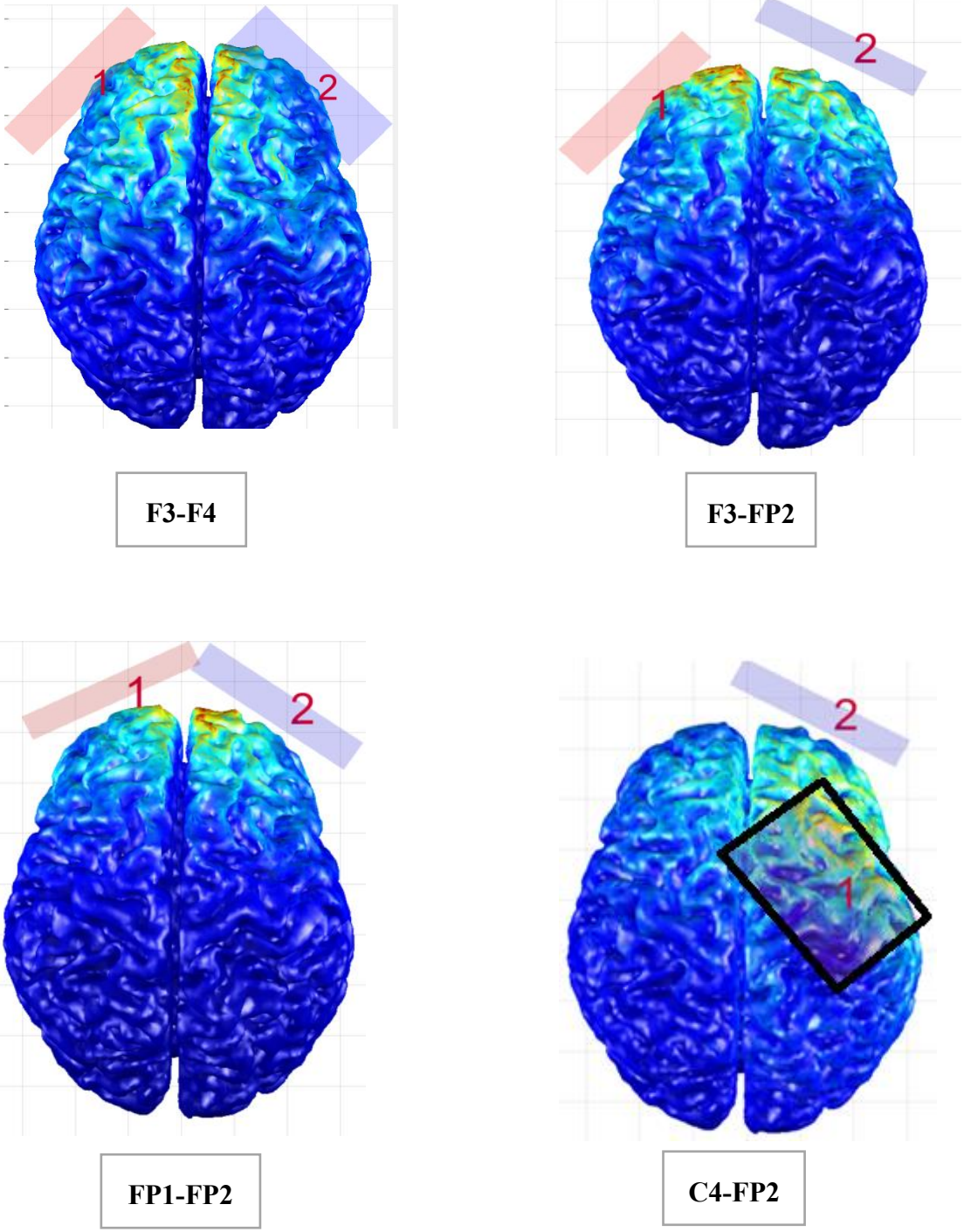


Figure 4. Current density distribution with 1mA DC electrode current in four different montages (F3-F4, F3-FP2, FP1-FP2, and C4-FP2). The position 1 is at anodal and position 2 is cathodal and all the montages show the areas of high current density marked in red and the areas of low current density marked in blue.

F3-F4 montage: For the F3-F4 montages, current density peaks of between 0.24 Am^{-2} and 0.19 Am^{-2} are calculated and both found through simulated regions in the Right Temporal region and Right Motor region. The smallest demonstrated current densities of 0.03 Am^{-2} and 0.02 Am^{-2} is found in Right Occipital and Right Frontal regions of the brain.

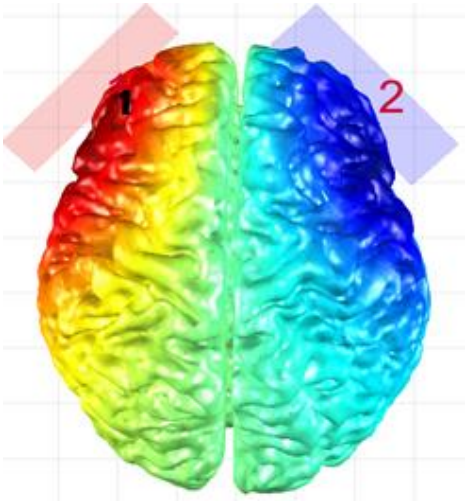
F3-FP2 Montage: The largest current density maximum values of 0.21 Am^{-2} and 0.17 Am^{-2} is found for the montage F3-FP2 across Left Frontal and Left Motor regions, respectively. The smallest current densities of 0.02 Am^{-2} and 0.04 Am^{-2} is found in Left Occipital and Right Occipital regions of the brain, respectively.

FP1-FP2 Montage: The largest current density values of 0.20 Am^{-2} and 0.25 Am^{-2} is found through Right Frontal and Right Temporal for the montage FP1-FP2. The smallest values of 0.04 Am^{-2} and 0.03 Am^{-2} is found around simulation regions of the brain in Left Temporal and Left Occipital.

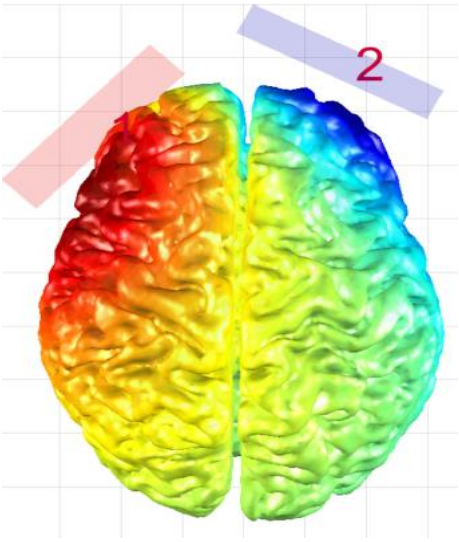
C4-FP2 Montage: In the montage C4-FP2, the highest current density of about *J* of 0.26 Am^{-2} and 0.27 Am^{-2}, Furthermore, the color matter changes of the Left Temporal and Left Occipital Areas were found to show unique alterations. The lowest current densities that are found in the current density 0.04 Am^{-2} and 0.03 Am^{-2} in Right Parietal and Right Occipital.

5.2 Electric field distribution in different electrode configurations

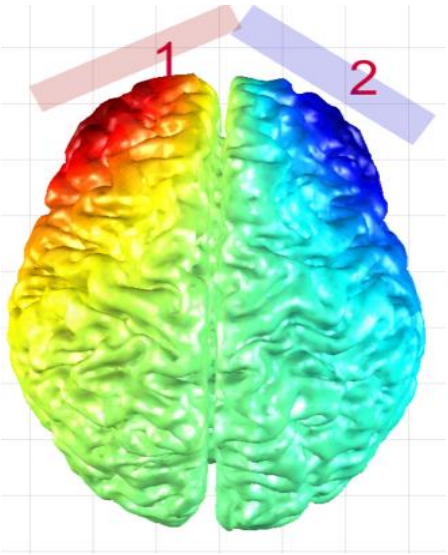
The electric field distribution of simulations with different electrode patterns of the experiment (F3-F4, F3-FP2, FP1-FP2, and C4-FP2) with 1.5 mA direct current are represented in Figure 5. The image outputs of interest, that represent the spatial pattern have been completed (see Fig. 5). The values for the maximum Electrical field density both 1 mA and 1.5 mA assign into the ten brain areas are found in Table 2. The electrical density distributions are represented in Figure 5.



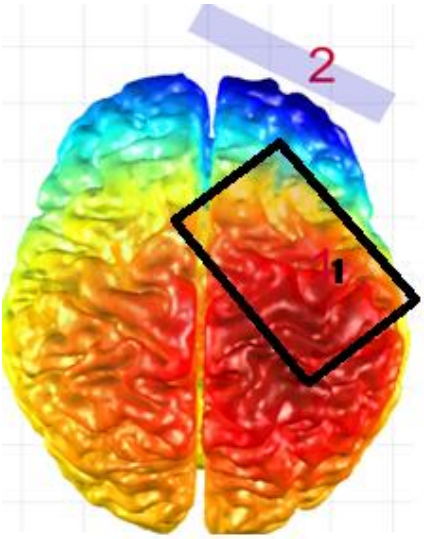
F3-F4



F3-FP2



FP1-FP2



C4-FP2

Figure 5: Electric field distribution with 1.5mA DC electrode current dose in four different montages (F3-F4, F3-FP2, FP1-FP2, and C4-FP2) with electrode size 5 × 7 cm^2. The position 1 is at anodal and position 2 is cathodal and all the montages show the areas of high electric field marked in red and the areas of low electric field marked in blue. The

local electric field values at the left and right motor cortex regions are shown for each montage.

It is important to determine the distribution of electric field intensities throughout the brain. In Table 2 presents the total electrical field in the left and right motor regions, as well as the range of fluctuation between these regions, for two separate currents (1 mA and 1.5 mA).

Table 2: The electric field values in ten brain areas calculated in the four electrode montages (F3-F4, F3-FP2, FP1-FP2, and C4-FP2)

Brain Region	Electrical Field V/m							
Montages		F3-F4		F3-FP2		FP1-FP2		C4-FP2
Assign Current	1 mA	1.5 mA	1 mA	1.5 mA	1 mA	1.5 mA	1 mA	**1.5 mA**
Left Frontal	0.203	0.219	0.225	0.268	0.233	0.261	0.048	**0.078**
Right Frontal	0.059	0.078	0.094	0.114	0.056	0.078	0.067	**0.086**
Left Temporal	0.213	0.236	0.203	0.234	0.246	0.276	0.178	**0.214**
Right Temporal	0.198	0.212	0.101	0.117	0.119	0.156	0.185	**0.234**
Left Parietal	0.243	0.274	0.284	0.312	0.243	0.273	0.293	**0.334**
Right Parietal	0.212	0.223	0.173	0.195	0.165	0.178	0.327	**0.356**
Left Occipital	0.223	0.268	0.159	0.178	0.178	0.195	0.213	**0.253**
Right Occipital	0.102	0.117	0.056	0.078	0.097	0.115	0.178	**0.217**
Left Motor	0.267	0.285	0.213	0.263	0.212	0.241	0.223	**0.274**
Right Motor	**0.228**	**0.241**	**0.187**	**0.219**	**0.175**	**0.207**	**0.215**	**0.267**

The highest electric field in the F3-F4 montage for 1 mA range 0.059 to 0.267 V/m and 1.5 mA range 0.078 to 0.285 V/m was found in the Left Motor 0.267 V/m (1 mA), 0.285 V/m (1.5 mA), and Left Occipital 0.223V/m (1 mA) and 0.268 V/m (1.5 mA), accordingly.

The electric field in the F3-FP2 montage resulted in the highest electric field in the Left Parietal of 0.284 (1mA) and 0.312 V/m (1.5mA), and in the Left Frontal of 0.225(1mA) and 0.268 V/m (1.5mA), and in the ten brain regions ranged from 0.056 V/m to 0.284

V/m for 1mA and from 0.078 V/m to 0.312 V/m for 1.5mA. The highest electric field for both amounts of current is 0.234(1mA) and 0.276 V/m(1.5mA) in the Left Temporal and 0.243(1mA) and 0.273 V/m (1.5 mA) in the Left Parietal, and the distribution of the ten brain regions for 1mA is 0.056V/m to 0.246 V/m and 1.5mA is 0.115 V/m to 0.276 V/m.

The electric field in C4-FP2 montage shows in the Left Parietal both current is 0.293 V/m (1mA) and 0.334 V/m (1.5 mA) and in the Right Parietal 0.327(1 mA) and 0.356 V/m (1.5 mA) (Table 2). The data for F3-FP2 and C4-FP2 indicate a large electric field magnitude, based on the results review above. ; more specifically, moved towards the right motor cortex both 1 mA and 1. mA (0.312 V/m (1.5 mA)in F3-FP2 to 0.356 V/m (1.5 mA) in C4-FP2) Figure 5 and Table 2).

5.3 Effect of electrode shape and size

The effect of electrode shape and size in tDCS is studied by comparing rectangular 5 x 7 cm^2 and rectangular 1 x 6 cm^2 electrodes, using two current magnitudes, 1mA and 1.5mA (Figure 7).

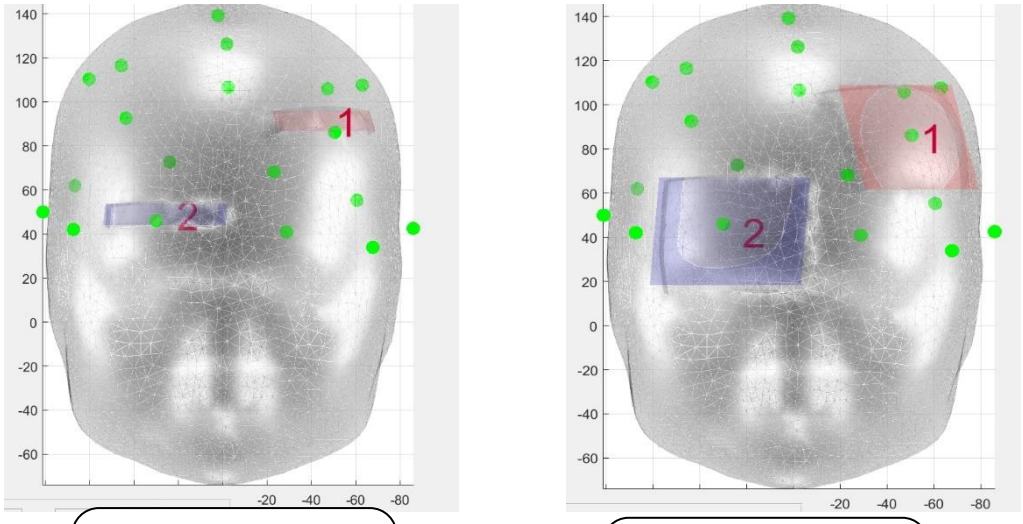


Fig 6. Schematic illustration of the area covered under the electrodes in the F3-FP2 montage with 1 x 6 cm^2 rectangular and 5 x 7 cm^2 rectangular electrodes

Table 3: Maximum current density with difference size electrodes.

Montage	**Maximum Current Density** $J(Am^{-2})$			
	1 x 6 cm^2 rectangular		5 x 7 cm^2 rectangular	
	1 mA	1.5 mA	1 mA	1.5 mA
F3-F4	0.15	0.42	0.08	0.27
F3-FP2	0.14	0.43	0.10	0.24
FP1-FP2	0.17	0.47	0.07	0.23
C4-FP2	0.16	0.41	0.08	0.29

We simulated two different current magnitudes, 1 mA and 1.5 mA, implemented into two different size electrodes. The results of the simulation showed higher current density for the smaller electrode (1 x 6 cm^2) and lower current density for the bigger electrode (5 x 7 cm^2). The current density at the electrode lower edge increased significantly when increasing the current. About the same average current density was observed to similarly sized electrodes for different montages, and the rectangular electrodes had a relatively high peak current absorption.

In the FP1-FP2 montage, the highest maximum current density of 0.17 Am^{-2}. is also found with electrode (1 x 6 cm^2) size and 1mA current, and the highest maximum current density of 0.47 Am^{-2} is found with 1.5 mA current. In the (F3-FP2) montage, 1 mA implement current have this highest maximum current density of 0.10 Am^{-2}, while 1.5 mA had the highest maximum current density of 0.27 Am^{-2} (Table 3).

6 Discussion

This thesis presented electric model pipeline for using a COMETS2 MATLAB toolbox for creating computer-based simulation model that focuses on current density and electrical field density, using two different shape and size electrodes in four different electrode montages, to improve the optimization of tDCS brain stimulation techniques. In the montage configuration C4-FP2, the current density found highest current densities in Left Temporal (0.24 A/m^2) and at the Left Occipital (0.27 A/m^2). The F3-FP2 montage stimulated by the left frontier lobe (F3), induced highest current densities in left frontal (0.21A/m^2) and the left motor cortex (0.17 A/m^2).

Consequently, stimulation of the left frontal lobe at FP1 did not lead to the increase in *J* of the right cortex of the (F3-F4) assembly. However, due to the proximity of the cortex to the right temporal cortex, a higher current density of 0.25 A/m^2 was observed. It should be noticed that on all other montages, the activating frontal lobe increased current density values in the motor cortex.

A possible cause may be the similarity of the motor cortex and the frontal lobe areas for current flow. In C4-FP2, the stimulation site FP2 is more distant from C4 than F4 is from FP2 right motor cortex, so the *J* value is just 0.26 A/m^2 across the left temporal cortex. For the F3-F4 montage, the same seems to hold true. In the F3-F4 installation, the parietal lobe stimulation C4-FP2 provided higher current density throughout the motor cortex. eg. Left Temporal & Left Occipital. The fact that the parietal lobe sits between these two areas may clarify that.

A significant challenge for its application area in health and disease is the documented complexity of such physiological and behavioral outcomes, both between individuals and among research studies [80,87,106–108]. This discussion is that the current going into the brain relates directly to the effect of stimulation, so the difference in current supplied would be a significant crucial phenomenon in the impact of the stimulation.

It can be supposed that individual differences in anatomy can lead to significant differences in the electric field during tDCS. However, by using the current single head model for electrical stimulation, we were not able to simulate those individual differences.

In the electric field investigations in the montages F3-F4, F3-FP2, FP1-FP2, and C4-FP2, a few differences observed are studied. In this analysis, a high-resolution finite element head model and its derivatives were used. The tDCS studies have mostly used the classical electrode configurations F3-F4 and F3-FP2 to measure depression therapy to assess the function of the brain[109].

In this study, we investigated the model's competence using the computer based COMETS2 software. The results of different electrode placement (take one or two contact lands with each electrode) cannot be generalized to other types of electrode setups. As such, each montage, no matter how good they are, should be considered separately.

The above findings indicate that tDCS not only causes direct effects, but also can generate indirect effects that are not expected[53.] This seems to be showed in modifications of remote cortical and subcortical areas powered by connectivity[54]. Maybe no neuronal and evoked behavior is known to modulate tDCS, but also neuronal oscillation spontaneous. Model-based and in vivo experiments can be able to estimate that possible closely to understand the neuron networks can be more resilient to weak direct currents than isolated neurons[103-105].

The third investigations showed that under 5 x 7 cm^2 and 1 x 6 cm^2 rectangular electrode conditions, there is substantial difference in the increase in current excitability. Larger current densities are caused by small active sizes such as 1 x 6 cm^2 electrodes. The current density is higher with smaller electrodes that raises the enhanced area's spatial focus. This result shows the efficiency of tDCS in increasing excitability by concentrating the direct current under the active electrode. The tDCS in the 1 x 6 cm^2 electrode condition resulted in the maximum current density.

One explanation may be that the very large stimulation electrodes cover not only the region of interest, but also the adjacent functional areas of the cortical area, which does not enable the intended cortical area to be selectively stimulated[84]. On the other hand, the current concentrates at the edge of the electrodes based on modelling and imaging research, so using smaller electrodes would keep the electrode edge closer to the stimulation target area[106]. To address these limitations, it would be beneficial to precisely monitor the stimulation region by increasing the focus of DC stimulation with smaller electrode sizes to minimize unwanted sensitivity to other cortical areas (Fig 3.)

The montage and location of the electrode were kept constant, however due to the further proximity of the edges of the anode and the cathode, using smaller electrode sizes could minimize the percentage of shunted current and increase the amount of injected current passing through the scalp[84]. The tDCS resulted in a substantial increase in current density for both electrode sizes. This technique enables neuronal activity to be modulated in a non-invasive way. After the treatment, the side effects tend to be uncommon, mild and vanish. In depressed patients, several publications have reported toxic effects, including burns and mental health problems[107]. In the scientific literature, only one significant neurological complication has been identified[108.]

There are some limitations in the study. One of the drawbacks is the small sample size, which limits the generalization of results. This is a computer-based simulation study with just one brain model, stimulation parameters were considered constant, and no parametric study is performed. The simulations revealed that as observed in the literature, there is a large degree of similarity, and that no moderator shown on the study could justify this. The reporting bias is also evident in previous studies. Finally, many previous studies had different montages and small variation of electrode sizes. Moreover, this study could not include real clinical data due to the lack of time.

In future studies, both memory cognitive test and psychophysiological tests, e.g., event-related ability or neuroimaging, could be used to experimentally confirm the results. Insight into the cognitive and neurophysiological impact of tDCS will be given by a combination of such outcome tests. The possible influence of tDCS on neurobiological changes in computer-based analysis obviously needs to be explored and something should be done for healthy individuals also. It may also be helpful to calibrate the tDCS protocol for each participant in future. It is possible to apply a computer model to determine how individual variations would influence the current distribution. In addition, this estimation is computer-based analysis could be possible to implement in vivo analysis with many patients and different kind of brain diseases such as Parkinson's and Alzheimer's diseases. Also, future studies should be focused on circular shape that COMETS2 tool does not currently support.

7 Conclusions

This computer-based simulation study helps us to understand a basic 3D head phantom as a practical tool for pre-analysis how and what happen to the brain after applying direct current transcranial stimulation. Computer-based simulations were performed to assess different electrode configurations. The results characterize the variance in the findings of electrical stimulation study design. Variations in the electrical stimulation setup may lead to significant differences in the current and electric field distribution within the brain. Two current magnitude were applied to specific setups and compared to COMETS2 simulation results, showing the highest current densities shown in the C4-FP2 electrode setup. Also, the C4-FP2 montage showed the highest electric fields after tDCS stimulation. The study also demonstrated the effect of electrode size on current density. Applying larger electrodes with a lower current density may result in decreased cutaneous awareness.

A simulation-based approach that included various electrode arrangements provided current density distributions across the scalp, which is useful in understanding in vivo applications of tDCS in different electrode setups. We suggest that in future electrical stimulation procedures, imaging dependent electrode positioning is used, and that the procedure considers the possible effects of spatial differences in stimulating electrode positions. The positive preliminary outcomes, the non-invasiveness of tDCS, and support for its high tolerability demonstrate need for further research into this technique.

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