

Challenges and Opportunities in Instrumentation and Use of High-Density EEG for Underserved Regions

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Abstract. Electroencephalography (EEG) is a non-invasive method of measuring electrical signals from the brain. However, traditional clinical EEG uses only 10-40 electrodes for diagnosis which limits its potential as an imaging modality. High-density (HD) EEG, as well as the more recent Ultra-High-Density (UHD) EEG, are imaging platforms that can be used to image the brain using various techniques to solve inverse problems. These platforms comprise a measurement device and algorithms for data analysis. Recent studies have provided promising evidence that increasing the density of electrodes can improve resolution up to at least approximately 1,000 electrodes for whole-scalp coverage. Both HD and UHD-EEG can be made inexpensive and portable; therefore, perhaps most importantly, accessible to many parts of the world. However, there are remaining challenges that can hinder HD- and UHD-EEG development and use. Here, we discuss these challenges and present the approaches our research program has developed to overcome them.

Keywords: High-resolution brain imaging; neural inference; high-density EEG

1 Introduction

Electroencephalography, or EEG, is a technique used to measure electrical signals produced by activity in the brain. EEG measurements are made by a technician, and have classically been used to diagnose neurological disorders (e.g. epilepsy, brain injuries, stroke, sleep disorders, etc.), interface machines with the brain, as well as study the brain activity noninvasively. The miniaturization of electronics has allowed EEG systems to use more electrodes, and has opened the possibility of using EEG as a portable imaging technology, even if the obtained spatial resolution is lower than that of less portable technologies (e.g. Magnetoencephalography, MEG, and functional Magnetic Resonance Imaging, fMRI). Roughly, a system that packs 64-256 electrodes on the scalp is referred to as a **high density** (HD)-EEG, and even higher-density systems, reaching as many as 1,000 electrodes, are possible and considered Ultra-High-Density

(UHD)-EEG. Recently, our research has established, both theoretically [1, 2] and experimentally [3], that an UHD-EEG system provides higher spatial resolution of neural signals than its lower density counterparts.

HD-EEG systems are non-invasive, and require only inexpensive sensors and electronic circuits, making them a low-cost solution for diagnosis of neural disorders, interfacing with the brain, and neuroscientific studies. On the spectrum of available imaging technologies, shown in Table 1, there are three main parameters that we consider for comparison: temporal resolution, spatial resolution and cost. For instance, fMRI provides very high spatial resolution images, but these are obtained very slowly (> 1 second), making conditions such as seizures hard to detect and/or localize. On the other hand, MEG has the same temporal resolution as EEG and a high spatial resolution, but MEG systems cost millions of US dollars; and only a few hundred machines are in use across the world. Moreover, both fMRI and MEG systems are non-portable because they require bulky shielding from earth's magnetic field and, typically, superconducting subsystems that necessitate coolants such as liquid helium. In contrast, HD-EEG can be made relatively inexpensively *and* portable, and thus can be accessible to many more communities around the world.

While HD-EEG demonstrates a great deal of promise as a viable brain imaging modality, there are a number of emerging obstacles that limit the scope of its use in clinical settings, particularly in developing countries with limited resources. In this paper, we do not intend to provide a comprehensive survey of how HD/UHD-EEG has developed. Instead, it is a biased perspective on how our team has been pursuing research and advancement of high-resolution EEG inference, and understanding its implications in clinical science. We provide an overview of some of the challenges we observed in instrumentation and platform development of HD/UHD-EEG, and briefly discuss how we have addressed or are trying to address these issues. More detailed literature review on HD/UHD-EEG can be found in [1, 3].

Table 1: Available Imaging Technologies versus High Density EEG (HD-EEG)

Imaging Modality	Cost of the Machine (USD)	Temporal Resolution (seconds)	Spatial Resolution (mm)
Magnetic Resonance Imaging (MRI)	\$0.5M - \$3M	200 - 1000	0.5 - 2.8
Functional MRI (fMRI)	\$0.5M - \$3M	0.05 - 5	2 - 4
Computed Tomography (CT)	\$50,000 - \$0.5M	0.1 - 1	0 - 1.5
Positron Emission Tomography (PET)	\$100,000 - \$0.5M	10 - 1000	2.5 - 5
Functional Near Infra-Red Spectroscopy (fNIRS)	\$15,000 - \$0.2M	0.1 - 1	5 - 10
Magnetoencephalography (MEG)	\$1M - \$2M	0.5m – 1m	5 - 28
Electroencephalography (EEG)	\$3000 - \$10,000	0.5m – 1m	55 - 120
High Density-EEG? (anticipated)	\$3000 - \$10,000	0.5m – 1m	5 - 20

2 Background

2.1 Origin, Measurement and Uses of EEG

EEG signals primarily originate from synchronized synaptic activity of neurons in the brain. The signal that is measured by an electrode placed on the scalp is the sum of positive and negative charges within the brain. A typical clinical EEG measurement system is non-invasive and uses anywhere from 10 to 40 electrodes spread across the scalp. Commonly, these systems use “wet” electrodes (i.e., where electrode-skin contact is gel-based) to reduce impedance of the electrode skin contact. EEG recording electrodes in clinical settings often involve abrasion of the skin to remove the epidermal layer because it has a higher impedance than the underlying tissue. Disinfection as well as sterilization is required for EEG electrodes because of the abrasion under CDC guidelines.

EEG systems are used for observing different types of brain signals such as temporal EEG signatures, frequency-domain signatures, event related potentials (ERP) [4], and steady-state visually evoked potentials (SSVEPs) [5]. A common use-case of EEG is in the detection of epileptic seizures which appear as rapidly oscillating waves; indeed, EEG is the gold standard in epilepsy diagnosis. Further, source localization techniques using EEG are used to identify the foci of seizures, so that they can be surgically removed. In neuroscience, EEG is used to study the neural mechanism underlying cognitive processes such as attention, learning, reading, memory, etc. ERPs and SSVEPs are recorded from the continuous stream of EEG data which allows characterization of brain processes triggered by the specific events. More recently, the use of EEG has become prevalent in Brain Machine Interfaces (BMI) [6]. In this section, we briefly describe existing methods of EEG measurement and the applications of high-density EEG.

2.2 High-Density EEG

EEG signals propagate through cerebrospinal fluid, skull and finally the scalp, where they are measured. Low electrode count EEG systems do not measure high spatial frequency signals from the brain because they get severely attenuated through these layers, which act as spatial low-pass filters [1, 7].

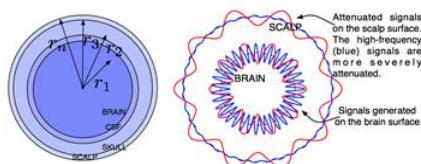


Fig. 1. Computer simulations of a spherical head model depicting the low pass filtering of spatial high frequency signals that originate in the brain. High-density EEG increases the number of electrodes over scalp to reliably reconstruct high spatial frequency signals from within the brain.

The main advantage of EEG over other imaging systems such as fMRI and fNIRS (functional Near InfraRed Spectroscopy) is that EEG has a much higher temporal resolution. By increasing the number of electrodes, we aim to improve the spatial resolution as well, thereby creating a new neuroimaging modality in HD/UHD-EEG. The combination of high temporal and spatial resolution allows a myriad of new applications. For instance, HD-EEG may allow improved reliability of detecting a phenomenon known as Cortical Spreading Depolarization (CSD). CSDs are waves of neural silencing that spread slowly across the brain surface and manifest in the presence of a traumatic brain injury, stroke, hemorrhages, and even migraines [8].

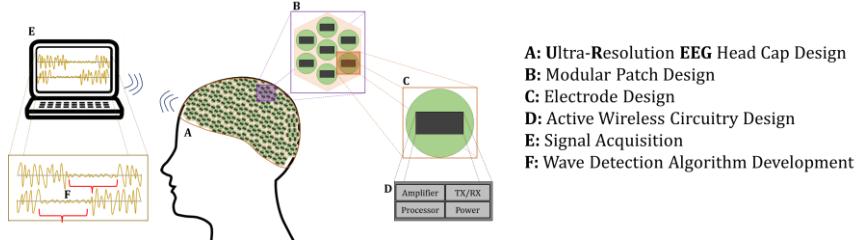


Fig. 2. High Density Electroencephalography platform design: The EEG signal is measured from a high density cap (A) consisting of more than 500 electrodes. These electrodes are modularized into patches (B). Each electrode needs to have a low impedance interface to the scalp (C). The signal-to-noise ratio of the measurement increases if the electrodes are active (D). Once the signal has been acquired, anomalies are detected using novel algorithms (F).

A typical HD-EEG system is shown in Fig. 2. There is considerable effort involved in designing electrodes, the high-density head cap, scaling the active electrodes to a wireless portable system, and designing effective algorithms for studying the measured data. In Section 3, we briefly discuss some of the impediments that limit the development of HD-EEG, as well as a description of our approach to address each of these challenges.

3 HD-EEG: Implementation Challenges

Designing HD-EEG systems should be holistic, invariably involving an interdisciplinary approach. Our research simultaneously approaches issues fundamental understanding, algorithms, neuroscientific validation, instrumentation, and scalability.

3.1 Electrodes and Gel Developments

In order to measure electrical signals from the brain, electrodes should have good contact with the skin [9]. The range of EEG voltage is small (order of 10 microvolts), and for a high signal-to-noise (SNR) ratio, the electrode-skin impedance must be low (order of 5 kilo-Ohms). Because the skin is a hydrated material, a low impedance is often obtained by a combination of abrading the skin, and using a conducting gel between the electrode and the scalp. Dry metal electrodes that are often used in many consumer EEG systems have high impedance and hence low signal-to-noise ratio.

Wet electrodes dry up for chronic use. Conditions such as epilepsy require long term EEG monitoring to detect the onset of a seizure. One of the main challenges here is the frequent drying up of the electrode gel, resulting in a non-conducting crystalline residue at the electrode-skin interface. Because there is an increase in impedance, the measured signal is unreliable. With HD-EEG, it is impractical to repeatedly apply gel to 500+ electrode locations.

Our approach: We believe this is one of the most underappreciated research challenges for practical, long-term use of low and high density EEG systems, and requires bringing together expertise from several disciplines. Our research has explored the development of new materials that can remain hydrated for extended time.

Different hair types prevent reliable measurement. The goal of HD-EEG is to have an easily accessible diagnostic imaging modality. Therefore, it is important to consider the social aspects of getting a reliable EEG measurement. While patients in critical care might have their heads shaved in order to get access to the scalp, patients who have come for a preliminary EEG measurement may not wish to do so. Existing EEG systems do not work reliably thick, coarse, curly, or long hair. Moreover, strands of hair between two electrodes can enable gel flow between them through the capillary effect, thereby shorting two electrodes. A high-density EEG makes the hair issue more of a challenge.

Our approach: Our research is trying to look at the problem of hair under the EEG electrode from a different perspective. Instead of only designing an EEG device that works with the hair, we can also modify the hair to work with the device. The key idea is to maximize the contact made by the EEG electrodes with the scalp by altering the position of the hair (Fig. 3).



Fig. 3. Curly hair types provide a very poor electrode-skin impedance (*left*). Modification of hair structure can provide reliable methods of obtaining stable EEG measurements.

Identification of bridged electrodes for high densities. One major problem with high-density electrode arrays and caps is the bridging that occurs between adjacent electrodes, implying that these two electrodes electrically behave as one large electrode. It is pertinent to identify which electrodes are bridged during measurement so that there is no loss of spatial information from the EEG signal.

Our approach: We have been able to successfully prototype arrays with pre-load our high-density arrays with high viscosity conductive gels (Ten20 Conductive paste).

These instrumentation methods are supplemented with algorithms to identify bridged electrodes after data acquisition through correlation studies [10].

Electrode configuration and caps for high density arrays. Traditional EEG locations are based on the 10-20, 10-10 or 5-10 electrode placement protocols [11]. With high-density EEG, individually preparing 300+ electrodes with these protocols is impractical. Moreover, injured parts of the head cannot be covered up by an electrode cap. There also needs to be a way to apply pressure on the scalp so that the electrodes do not move. If there is movement, that could mean shorting of adjacent electrodes, lowering spatial resolution.

Our approach: A way to approach this is through modularization over existing electrode locations. Designing high-density electrode patches will ensure that areas of the scalp that do not need to be measured can be left out, as in the case of a brain injury. An interlocked grid pattern allows us to fasten different portions of the cap quickly, and these modules can be pre-loaded with high viscosity electrode gels. Moreover, our research has shown that using hierarchical referencing techniques within these electrode modules [12] enables low power active circuitry at the electrode site (Fig. 4).

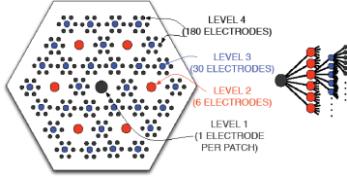


Fig. 4. Hierarchical referencing for HD-EEG electrode arrays: Modularization of EEG electrode arrays enables the use of hierarchical referencing [9]. The method decreases the length of wires routing from the electrode to the back-end circuit, thereby increasing the signal-to-noise ratio of the measurement.

3.2 Algorithm and Neuroscientific Development

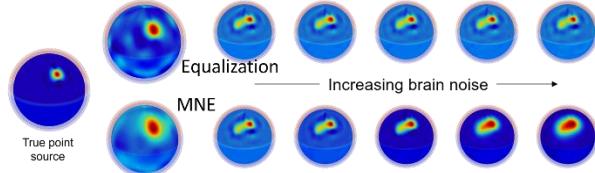
We have thus far highlighted the most relevant obstacles that stands in the way of *instrumenting* a high-density EEG measurement device. The device by itself is limited in its use without the accompanying algorithms that process the data obtained from the EEG sensors, using validation from neuroscientific studies.

Design of detection algorithms with HD-EEG. Traditional EEG and MEG imaging systems use a combination of algorithms to analyze data. It is often useful to project data in brain space (instead of sensor space) by use of one of many “source localization” or imaging algorithms. Use of “surface Laplacian,” a spatial filter that approximately projects scalp signal on to the dura has been shown to be useful [7]. However, the precision of these techniques is limited, particularly for lower density systems.

Our approach: For high-density EEG, our simulation-based results [1] demonstrate that increasing sensor count will increase resolution and narrow the region of uncertainty, i.e., the width of the point-spread-function in reconstructing a single dipole [2]. It is

plausible that to best exploit the information provided by HD-EEG, novel algorithms would be needed, and this warrants further study.

Fig. 5. Localization of seizure foci in a spherical head model of the brain using novel algorithms



with high-density EEG in the presence of simulated brain noise. The image shows a simulation of a true point source seizure focus, which is more accurately determined by the equalization based algorithm as opposed to the minimum norm estimate (MNE) algorithm [2].

Neuroscientific validation of HD-EEG. Traditionally, EEG has been used for low-spatial precision measures such as event-related potentials (ERPs), frequency-domain power (e.g., power in alpha, beta, gamma, delta bands and their ratios), coherence measures, steady-state visually evoked potentials (SSVEPs), etc. While source-localization and imaging techniques have been around for many decades, only recently have they been adopted in practice, and their use continues to be limited. Scientifically validated research with high-density EEG is scarce.

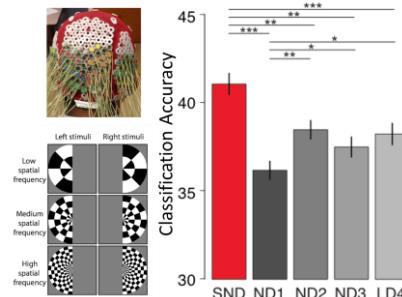


Fig. 6. High-density EEG (SND) improves classification of high spatial resolution images beyond different configurations of Nyquist rate (ND) spatial sampling [3].

Our approach: Our recent work [3] has established that HD-EEG, with sub-cm spacing of electrodes, offers higher spatial resolution than existing systems, superseding even those with 128 or 256 electrodes in 10-20 arrangement. Our simulations also reveal that HD-EEG's localization accuracy will increase with greater electrode counts. Further experimental validation is needed to quantify limits of HD-EEG in practice.

Clinical adaptation of HD-EEG in hospitals. Although research studies have used higher densities (72-128 electrodes), there are few validated studies for the clinical use of HD-EEG.

Our approach: Our aim here is to identify disorders that can benefit from higher spatiotemporal resolution monitoring. Disorders such as epilepsy, migraine, stroke, subarachnoid hemorrhage, and traumatic brain injury, can benefit from such monitoring. For example, for epilepsy, improved source localization, detect multiple seizure foci, or even improved depth inference, can alter treatment approaches [13]. For other disorders as mentioned above, detecting wave of Cortical Spreading Depolarizations (CSDs) can help understand the severity of the disorder, and also help manage and treat it [8]. CSDs are narrow waves of neural silencing that spread slowly on the cortical surface, and only recently was it shown that they can be detected using low-density EEGs, although the reliability of this detection was low [14], especially for narrower waves. In a recent study, our team demonstrated through rigorous simulations that even narrower CSDs can be detected reliably using HD-EEGs by stitching together data across time and space [15]. We expect other such biomarkers to be discovered in near future where HD-EEG is applicable, which can lead to novel HD-EEG designs and solutions for diagnoses and treatments.

3.3 Scalability and Accessibility

A successful technology platform needs to be scalable to be useful to society. One of the most attractive features of HD-EEG is that it can be made low-cost and portable. Miniaturization of electronics has made scalability complex, but not impossible.

Design of a wireless HD-EEG device. Traditional EEG devices attach long shielded lead wires to each scalp electrode, and the wire bundle extends back to instrumentation with amplifiers and analog-to-digital converters (ADCs). Some newer EEG systems utilize small pre-amplifier circuits on top of each electrode to boost the EEG signals before sending them through the wires, reducing the effects of noise [16]. But all of these systems require the subject to be tethered to the measurement system, and restrict movement.

Our approach: We are developing a wearable EEG system with wireless data transfer capabilities. Wearability requires miniaturized electrodes, amplifier and ADC circuitry, wireless radio, power, and packaging, while maintaining costs that are competitive with existing EEG systems. We are using off-the-shelf amplifier, ADC chips, off-the-shelf wireless radios, and utilizing our group’s experience in ultra-small circuit boards and assembly techniques to make the overall EEG system lightweight, wearable, and cost-competitive.

FDA Device Classification. Although the HD-EEG portable platform is non-invasive, it can be used to diagnose significant brain illnesses, and introduces an element of criticality to its device classification.

Our approach: Because it is non-invasive, it will likely be a Class II device according to the US FDA. Our initial discussions with regulatory consultants with regulatory consultants regarding this device suggest that it may qualify for a 510(k) clearance, i.e., it is substantially equivalent to a similar legally marketed device. However, it remains to be understood what clinical trials may be necessary.

4 Discussion and Conclusions

The development of a new medical technology is exciting because of the potential it has to improve the quality of life to the people who use it. Electroencephalography (EEG) is a classical and well accepted modality used for brain imaging. For example, in the case of epilepsy, which affects 1 in 17 people in developing countries [17], EEG is one of the three pillars that guide its treatment (along with structural MRI and patient semiology). Our research has shown that traditional EEG is limited in its scope because only 10-40 electrodes are regularly used in clinics. Increasing the spatial resolution to about 500+ electrodes, while utilizing the high temporal resolution of EEG is the reason to advance to High Density EEG (HD-EEG).

HD-EEG is a non-invasive, low-cost and portable imaging technology that can be used globally to diagnose disorders such as epilepsy, stroke and traumatic brain disorders. These conditions often go unnoticed early on due to lack of resources, only to become more severe later. Other imaging techniques such as (functional) Magnetic Resonance Imaging (fMRI), Magnetoencephalography (MEG) are very equipment intensive and expensive and are not easily accessible to a large section of world population. HD-EEG can be made portable and inexpensive because the accompanying electronics is a well-matured field, and has been applied judiciously in several biomedical devices such as pacemakers and fitness monitors. Scaling a 40 electrode system to a 500+ one, while maintaining the same surface area (i.e., the human scalp) is a challenge we are addressing through both engineering and algorithmic improvements. This paper highlighted a few pertinent points of interest that arise when designing a HD-EEG system. We described factors in electrode and gel design - which included issues such as having a portable HD-EEG device work with different types of hair without bridging. We also emphasized a critical need for simultaneous development of algorithms and neuroscientific verification to process the data that is acquired.

The study of EEG measurements for diagnostics is embedded in clinical training all around the world. Subsequently, HD-EEG is conducive to massive adoption as compared to other more recent modalities because of familiarity, training, immense historical knowledge and data, while delivering resolutions comparable to or even superseding competing modalities. Development of HD-EEG is an immense interdisciplinary effort by engineers, clinicians and neuroscientists. HD-EEG is appealing because the challenges outlined in this article are not fundamentally insurmountable, and ongoing research continues to make significant strides in overcoming them to achieve unparalleled efficiency for low-cost imaging platforms.

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