Decoding Upper-Limb Kinematics from Electrocorticography

Ewan Scott Nurse
ORCID: 0000-0001-8981-0074

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Department of Biomedical Engineering
Melbourne School of Engineering
The University of Melbourne
Abstract

Brain-computer interfaces (BCIs) are technologies for assisting individuals with motor impairments. Activity from the brain is recorded and then processed by a computer to control assistive devices. The prominent method for recording neural activity uses microelectrodes that penetrate the cortex to record from localized populations of neurons. This causes a severe inflammatory response, making this method unsuitable after approximately 1-2 years. Electrocorticography (ECoG), a method of recording potentials from the cortical surface, is a prudent alternative that shows promise as the basis of a clinically viable BCI. This thesis investigates aspects of ECoG relevant to the translation of BCI devices: signal longevity, motor information encoding, and decoding intended movement.

Data was assessed from a first-in-human ECoG device trial to quantify changes in ECoG over multiple years. The mean power, calculated daily, was steady for all patients. It was demonstrated that the device could consistently record ECoG signal statistically distinct from noise up to approximately 100 Hz for the duration of the study. Therefore, long-term implanted ECoG can be expected to record movement-related high-gamma signals from humans for many years without deterioration of signal.

ECoG was recorded from patients undertaking a two-dimensional center-out task. This data was used to generate encoder-decoder directional tuning models to describe and predict arm movement direction from ECoG. All four patients demonstrated channels that were significantly tuned to the direction of motion. Significant tuning was found across the cortex and was not focused on primary motor areas. Decoding significantly above chance with a population-vector approach was achieved in three of the four patients. Decoding accuracy was significantly improved by weighting the population vector by each channel’s tuning signal-to-noise ratio. Hence, directional tuning exists in
high-frequency ECoG during movement preparation, and movement angle can be decoded using population vector methods.

Having confirmed the existence of direction-related information in the recorded data, artificial neural network models were created to decode intended movement direction. A convolutional neural network (CNN) model had significantly higher decoding accuracy than a fully connected model for all four patients for decoding movement direction. Training models on data from all patients and testing on a single patient improved decoding performance for all but the best performing patient with the CNN model. Decoding using data from multiple time-points with a CNN model and averaging the results boosted accuracy when using the mode of the outputs. Overall, it was demonstrated that artificial neural network models can decode intended movement direction from ECoG recordings of a two-dimensional center-out task.

This thesis presents results that demonstrate ECoG has the desired signal properties for a clinically-relevant BCI. ECoG is shown to be robust over multiple years, encode direction-related information and can be decoded with high accuracy.
Declaration

I hereby declare that this thesis comprises only my original work towards the degree of Doctor of Philosophy at the University of Melbourne. All work included in this thesis, except where acknowledged in the Statement of Authorship, is my original work. All other work has been duly acknowledged.

This thesis is fewer than the maximum word limit of 100,000 words exclusive of tables, figures, bibliographies and appendices.

Signed: Ewan Nurse

December 2017
Statement of Authorship

I hereby declare that this thesis and the work presented in it are original and generated by me as the result of my own investigations. Except where acknowledged below, I was responsible for the experimental design, data collection, data analysis, software programming, and generation of images and graphical data.

The data analyzed in Chapter 2 was collected as part of a first-in-human device trial conducted by NeuroVista Corporation (Seattle, USA) and the Melbourne University Epilepsy Group. This study is presented in Cook et al. (2013)

Due to the multidisciplinary nature of clinical neurosciences, it would not have been possible to collect the data, described in Chapter 3 and analyzed in Chapters 4 and 5, if it were not for the contributions detailed below.

- Dr. Dean Freestone, Dr. Alan Lai and Mr. Simon Vogrin assisted with center-out task data collection.
- A. Prof. Wendyl D’Souza conducted the clinical functional electrical stimulation
- Mr. Simon Vogrin supervised the acquisition of all structural imaging and performed the CT-MRI co-registration.
The following chapters contain published works that have resulted from the research presented in this thesis.

- Chapter 2 is a modified version of the peer-reviewed published article:


  This work is also related to the peer-reviewed published article:


- Chapter 4 is modified version of the peer-reviewed published article:


- Chapter 5 has been influenced by the following peer-reviewed published articles:


- A number of conference abstracts have also been published:


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List of Abbreviations

ANN .......... Artificial neural network
BCI .......... Brain-computer interface
CNN .......... Convolutional neural network
CNS .......... Central nervous system
CPU .......... Central processing unit
ECoG .......... Electrocorticography
EEG .......... Electroencephalography
EMG .......... Electromyography
FC .......... Fully connected
GPU .......... Graphics processing unit
LFP .......... Local field potential
LME .......... Linear mixed-effects
M1 .......... Primary motor cortex
PCA .......... Principle components analysis
SE .......... Standard error
SNR .......... Signal-to-noise ratio
SUA .......... Single-unit activity
SVM .......... Support vector machine
Chapter 1

Introduction

1.1 Introduction

A brain-computer interface (BCI) is an artificial communication system that uses neural activity to control an external device. The primary goals of BCI systems are to increase the communication and mobility capabilities of individuals with severe physical disabilities (Wolpaw et al., 2002).

BCIs have seen a surge in scientific, clinical and commercial interest in the last 25 years. This is largely due to three factors. One is the increasing availability of relatively inexpensive, powerful computational hardware and software that allows for real-time processing of brain activity. Another is an expanded understanding of the central nervous system (CNS) in both humans and animals; a particularly significant discovery is increased understanding of neural plasticity in healthy brains, as well as in response to trauma and disease. The last factor is the growing recognition of the abilities and needs of individuals physically disabled by disorders such as cerebral palsy, spinal cord injury, stroke and amyotrophic lateral sclerosis.

There is a strong need for a clinical BCI system. Individuals with severe motor disabilities can lose all voluntary muscle control and are sometimes unable to communicate in any way. This can be caused by disease, neuromuscular disorders or physical injury. Neurological impairment of motor function affects an individual’s capacity to live independently and participate in the workforce, leading to significant social and economic burden of disability. The predominant financial costs involved are due to ongoing care. Spinal cord injuries
cause hemi- or paraplegia are estimated to cost the Australian economy $2.0B annually (Collie, 2009) and stroke approximately $2.14B annually (Cadilhac, 2013). BCIs have the potential to restore mobility and independence to individuals with severe motor disabilities, significantly increasing quality of life and decreasing financial burden.

The following section will describe the structure of the human motor system and how motor-related signals are generated in the brain.

1.2 Motor Physiology

1.2.1 Central Nervous System

A key function of the CNS is to actuate muscles, allowing individuals to interact with their environment. Sensorimotor cortical areas interact with spinal and sub-cortical brain structures to control muscles, as illustrated in Figure 1.1.a. The task of producing natural muscle activity is distributed throughout the CNS, with no single area wholly responsible for planning, initiating or controlling movement. For example, while it is understood that cortical areas primarily initiate walking, the ongoing signalling used to maintain a consistent gait is primarily controlled by the spinal cord (Guertin and Steuer, 2009).

Normal CNS outputs are maintained by continuing, adaptive adjustments throughout the system. These outputs can be activities such as walking across a room, speaking particular words or highly complex tasks like playing a piece of music on a piano (Saneyoshi et al., 2010). In normal motor behaviour, cortical activity is one of the many contributors to CNS output. BCI systems often rely on cortical signals for control, effectively replacing the role of motor neurons, and becoming the CNS output. This requires higher level control and plasticity throughout the CNS, allowing the cortical signal to become an ‘output’ of the motor system. This is illustrated in Figure 1.1.b. The cortex is used as the recording site for the majority of BCI systems due to its spatial organization being well understood and it being relatively safe to record from compared to sub-cortical structures.
1.2. MOTOR PHYSIOLOGY

Figure 1.1: Highly simplified model of CNS production of muscle activity compared to CNS production of BCI activity. a) Production of normal motor activation by CNS areas that interact to activate muscles. The CNS is optimized for muscle control. b) Production of activity via BCI. Although the same CNS areas are interacting, the CNS now produces action through cortical control of the BCI system. The BCI uses the cortex as the output of the CNS, as opposed to the spinal motor neurons. The CNS is now optimized for BCI control.

1.2.2 Primary Motor Cortex

The cortex is the outer-most structure of the mammalian brain. It has a varying thickness of 1.5 - 4 mm in humans (Fischl and Dale, 2000). Beneath the cortex are several subcortical areas including the cerebellum, brainstem, thalamus and basal ganglia. The cortex is divided into functionally distinct areas, with the primary motor cortex (M1) located anterior to the central sulcus, between the insular cortex and the dorsal peak of the hemisphere.

The cortex is structured into six laminae (referred to as layers I - VI), discernible by the types of cells they comprise. Each layer is arranged parallel to the cortical surface. Pyramidal cells project their axons to other cortical areas as well as to subcortical regions of the brain. The cortex is also organized into columns often perpendicular to the cortical surface (Mountcastle, 1997). Each column contains tens of thousands of interconnected neurons across each of the six layers. Hence, the cortex has structure not only on the plane parallel to its surface, but also perpendicular to the surface.
Regions of cortex are interconnected by nerve fibres, which also connect the cortex to subcortical areas. In particular, the primary visual cortex and supplementary motor areas are highly functionally integrated with M1.

The fundamental unit of computation in the brain is understood to be the neuron. There is estimated to be on the order of $10^7$ neurons in the human brain, with about 20% of these located in the cerebral cortex (Azevedo et al., 2009). Neurons form extensive networks, through which they communicate by signals known as action potentials or spikes. Spikes are highly stereotyped changes in the potential of the neuronal membrane that occur when excitatory synaptic inputs cause specific ions to flow across the membrane. The action potential then provides synaptic input to other neurons, influencing further action potentials. It is the measurement of action potentials and larger scale potentials that underpins the ability of a BCI to discern movement intention.

Ensembles of neurons produce oscillatory activity through changes in neural firing synchrony (Buzsáki and Draguhn, 2004). Broadly, neural oscillations refer to periodic variations in brain activity. These oscillations are believed to be involved in many neural processes and behaviors, including memory, sleep and perception, as well as movement (Varela et al., 2001; Gray et al., 1989; Engel et al., 2001; Schnitzler and Gross, 2005). Oscillatory networks in the motor system are generated by long-range synchronization across between cortical and sub-cortical brain regions and the spinal cord. An intricate balance of neural synchronization and desynchronization across many brain regions is required for precise motor functionality (Schnitzler and Gross, 2005). By detecting these changes, fine aspects of movement can be decoded from brain activity.

The motor cortex is arranged into the the motor homunculus, a spatial mapping of areas of the cortex associated with distinct motor functions. It is a spatially distorted mapping of the body in which areas requiring fine control, such as the lips or fingers, have a disproportionately high spatial representation on the cortex (Penfield and Boldrey, 1937; Penfield, 1958). The somatotopic representation largely corresponds to the contralateral side of the body. This mapping has some inter-individual variation, and can involve multiple wide spread sites for certain body parts and overlapping areas of representation. M1 is an area of particular interest for motor BCIs.


1.2. MOTOR PHYSIOLOGY

1.2.3 Single-Unit Activity

Neuronal tuning is a property of neurons in which they selectively represent particular cognitive, associative, motor or sensory information (Zhang and Sejnowski, 1999). Georgopoulos et al. (1982) demonstrated that individual motor neurons during both preparation and execution of arm movements fire as a function of arm movement direction. That is, for an individual motor neuron, firing rates peak before and during motion in a preferred direction and are reduced when movements are in directions away from the preferred one. Georgopoulos et al. (1982) modelled firing rate as a function of movement direction using a cosine function,

\[ z_k = h_0 + h_p \cos(\theta_k - \theta_p). \]  

(1.1)

The firing rate, \( z \) of a given neuron \( k \) was modelled as a resting firing rate, \( h_0 \), plus a cosine function of the difference between movement direction, \( \theta_k \), and preferred direction, \( \theta_p \), of the neuron, with a gain of \( h_p \). Georgopoulos further proposed the population-vector algorithm (Georgopoulos et al., 1986), defined as the sum of the vectors decoded from a population of neurons, which is then used to predict the angle and magnitude of intended arm movement. This concept underpins the mapping from motor neuron activity to system output of many BCIs, inferring a user’s movement intent from the fusion of an overdetermined set of measurements (overdetermined in this context refers to more neurons being recorded from than there are system outputs).

Further work by Georgopoulos et al. (1988) generalized directional tuning to three-dimensional arm movements and explored other functions to fit tuning curves. They found that a circular distribution, the von Mises function, better fit the observed firing rates (Amirikian and Georgopulos, 2000; Mahan and Georgopoulos, 2013). It has also been shown that directional tuning is largely consistent within cortical columns, with neurons of similar preferred directional tuning organized into vertically oriented ‘mini-columns’ of at least 500 \( \mu \)m depth (Amirikian and Georgopulos, 2003). It has been proposed that the phenomenon of directional tuning is produced by strong excitatory thalamic input to a cortical column, followed by both excitatory and inhibitory inputs mediated by interneurons parallel to the plane of the cortex (Georgopoulos
et al., 2007). Directional tuning, found throughout cortical and deep brain structures involved in motor activity, is fundamental to decoding movement activity.

The next section will outline the components that comprise a BCI system.

### 1.3 Overview of Brain-Computer Interfaces

BCIs are typically described by three sub-systems. The first is signal acquisition, which transduces neural activity into a recorded signal. The second is signal processing, which removes artifacts, extracts features from the recorded signal and translates them into device commands. The third system is an output device, which actuates the device commands and, in doing so, effects the user’s intent. The interaction between these systems is illustrated in Figure 1.2.

![Figure 1.2: Basic schematic of a BCI system.](image)

Signal acquisition most often involves recording electrical activity from the brain. A range of recording modalities are used to transduce neural activity. Electric potentials can be recorded at the scalp, above or beneath the dura on the cortical surface, or within the cortical tissue. These will be further discussed in Section 1.4. Other methods used to measure neural activity include magnetic field-based methods (magnetoencephalography) and blood oxygenation-based methods (near-infra-red spectroscopy and functional magnetic resonance imaging). Signal acquisition also requires the amplification
and digitization of the input signal, such that further computation can be performed on the signal.

Signal processing is typically defined by two stages: feature extraction and translation. During feature extraction, the signal undergoes processing to reveal features that are correlated to the behaviour of the user. Signal features are influenced by the temporal and spatial scales of the recording, as a given transducer may be recording the activity of one to perhaps millions of neurons. The translation step maps the signal features to the outputs of the BCI. It should also be noted that, during use, neural plasticity allows the user to adapt to the translation algorithm, and hence successful BCI operation depends on effective interaction between the adaptation of the algorithm and the adaptation of the user (Shenoy and Carmena, 2014).

The third component of a BCI is the system output. The output device in many BCIs is a computer screen, displaying information such as selected icons, cursor positions or letters (Simeral et al., 2011). Other applications include controlling a wheelchair or robotic limb (Pires et al., 2008; Hochberg et al., 2012). The output not only allows the user to interact with their environment, but also provides feedback to the user, allowing for correction and learning.

The following section will outline the most common methods of recording neural activity for BCI applications.

1.4 Recording Modalities

Most BCI systems are driven by electrical potentials recorded from the cortex (Wolpaw et al., 2002). Electrical recordings can be taken both invasively and non-invasively. Recording sites for electrophysiological signals commonly used in BCIs are shown in Figure 1.3. A summary of their properties is shown in Table 1.1.

1.4.1 Electroencephalography

Electroencephalography (EEG) is the recording of electric potentials from the scalp. It is a commonly used, relatively inexpensive and safe method of record-
Table 1.1: Summary of typical recording properties of common BCI signals - Single-unit activity (SUA), electrocorticography (ECoG) and electroencephalography (EEG)

<table>
<thead>
<tr>
<th>Property</th>
<th>SUA</th>
<th>ECoG</th>
<th>EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bandwidth</td>
<td>250 – 10k Hz</td>
<td>&lt; 500 Hz</td>
<td>&lt; 40 Hz</td>
</tr>
<tr>
<td>Spatial Resolution</td>
<td>≈ 0.1 mm</td>
<td>≈ 1 mm</td>
<td>≈ 1 cm</td>
</tr>
<tr>
<td>Invasive</td>
<td>Craniotomy, tissue damage</td>
<td>Craniotomy, minimal tissue damage</td>
<td>No</td>
</tr>
<tr>
<td>Stability</td>
<td>Months</td>
<td>Years</td>
<td>Weeks</td>
</tr>
<tr>
<td>Area Coverage</td>
<td>10 mm(^2)</td>
<td>10 – 100 cm(^2)</td>
<td>Whole brain</td>
</tr>
</tbody>
</table>

Although EEG has had many encouraging applications in BCIs (Pfurtscheller et al., 2003b; Nicolas-Alonso and Gomez-Gil, 2012), it has many known limitations compared to invasive recording modalities. EEG has a low spatial resolution restricted to the order of centimeters, compared to the millimeter scale of subdural recordings (Leuthardt et al., 2009) and micrometer scale of intercortical recordings (Moran, 2010). EEG is also far more susceptible to artifacts caused by other physiological electrical activity, such as electromyographic, electrocardiographic or electrooculargraphic potentials. Due to the limitations of spatial scale, the low-pass filtering effect of tissues on the neural signal and artifacts due to non-brain electrical signals, EEG is typically limited to an effective bandwidth of 0 - 40 Hz in BCI applications (Ball et al., 2009a). Various non-medical grade EEG systems exist (typically in the form of wireless headsets) that perform poorly compared to medical grade electrodes and amplifiers, and have yet to demonstrate suitably high accuracy in BCI control to be applied clinically. Consumer BCIs typically suffer considerably from artifact due to poorly shielded electronics and inadequate contact between the skin and electrodes (Ries et al., 2014; Hairston et al., 2014).

High degree-of-freedom BCIs rely on the high amount of information that can be extracted from invasive recordings. Although invasive recordings are of greater risk to the user, non-invasive measurements are yet to provide useful, long-term recordings for BCI. The remainder of this section discusses the
1.4. RECORDING MODALITIES

Figure 1.3: Illustration of recording locations and approximate spatial scales of common modalities. Electroencephalography (EEG) is a non-invasive measurement recorded from the surface of the scalp, with centimeter scale electrodes. Electrocorticography (ECoG) is recorded either above or below the dura using millimeter scale electrodes. Single-unit activity (SUA) and local field potentials (LFP) are recorded from electrodes that penetrate the cortex.

two most prevalent invasive recording modalities in BCIs: microelectrodes and electrocorticography.

1.4.2 Microelectrode Recordings

Microelectrodes record from individual or small populations of neurons. The most common design used in BCIs is the Utah array (Blackrock Micsystems, Salt Lake City, USA), a grid of millimeter-long platinum electrodes, typically spaced hundreds of microns apart (Donoghue, 2008). When recording from M1, electrodes are usually inserted in layer V (Simeral et al., 2011; Buzsáki, 2004), although precise placement into a specific layer can be difficult in practice.

Signals recorded by microelectrodes can be separated into low and high frequency components via digital filtering (often at approximately 300 Hz) to produce two distinctive signals. The low frequency component is known as the local field potential (LFP). The high-frequency component contains the action potentials. Each electrode records spiking activity from multiple neurons. Therefore, spike-sorting algorithms are used to isolate the activity of individual neurons (Lewicki, 1998). The spiking rate has been the basis of many microelectrode-based BCI devices.
1.4. RECORDING MODALITIES

The LFP is an electric field signal that results from the composite neural activity near the electrode tip (Buzsáki et al., 2012). Increased spike frequency and firing synchrony increase the spectral power of the LFP, particularly in higher frequency ranges (>100 Hz) (Buzsáki et al., 2012). Hence, the LFP is correlated to the average firing rate of neurons in local proximity to the electrode tip (Miller et al., 2014).

1.4.3 Examples of Microelectrode-Based BCIs

One of the first invasive BCIs to be used by a motor-impaired individual was achieved using penetrating microelectrodes implanted in the primary motor cortex (Hochberg et al., 2006). The firing rate of neurons in M1 recorded by a 100-channel microelectrode array were decoding using a linear least-mean-squares filter. A user could control a two degree of freedom cursor (i.e. control cursor movement in up-down and left-right directions) to write emails and operate a television using imagined movements.

The second iteration of this system allowed a paralyzed stroke patient to control a seven degree of freedom robotic limb to perform reaching and grasping tasks, including picking up a cup and drinking from it without assistance (Hochberg et al., 2012). The position and angle of the arm’s hand was controlled with six degrees of freedom (three degrees defining position in 3D space, and three defining the pitch, roll and yaw angles of the wrist), and the hand was operated by a single degree of freedom (hand open/close). Each of these trials were highly innovative, demonstrating never-before seen levels of BCI control.

Collinger et al. (2013) conducted a similar study, allowing an individual with severe spinocerebellar degeneration to control a seven degree of freedom arm. The individual was implanted with two 100-channel microelectrode arrays (both in M1), and decoded spiking rates using least-mean-squares and ridge regression (a method that minimizes the variance of the estimate when input channels are highly correlated) (Wang et al., 2007).

A follow-up study presented ten degree of freedom control, adding three
hand-grasp postures (Wodlinger et al., 2015). It was found that most recorded neurons demonstrated significant tuning to all ten dimensions and were not restricted by dimension type (translation, rotation or hand shape). Affalo et al. (2015) showed that by recording only from posterior parietal cortex, comparable decoding accuracies can be achieved to similar studies that have targeted M1.

Despite the successes of microelectrodes in acute BCI performance, they have been shown to have severely limited long-term performance. The functional ability of the electrodes to record spikes deteriorates significantly within months of implantation (Chestek et al., 2011). This is due to a variety of reasons, including direct mechanical damage to the electrode, corrosion of the electrode surface and inflammatory response (McConnell et al., 2009; Potter et al., 2012; Jorfi et al., 2015). This compromised long-term signal quality has been a restriction on long-term human BCI trials, particularly due to the risks involved with the craniotomy and destruction of neural tissue required for implantation. Although the BCI performance presented by Wodlinger et al. (2015) is reported as consistent across the 280 day experiment period, the median spike amplitude decreased significantly from 75 \( \mu \text{V} \) to 50 \( \mu \text{V} \). Due to the low reliability of microelectrodes over extended periods of time, clinical translation of microelectrode BCIs is currently unattainable (Durand et al., 2014; Miranda et al., 2014).

The following section will describe ECoG recordings and device trials that have investigated the use of ECoG in BCI systems.

1.4.4 Electrocorticography

Electrocorticography (ECoG) is the measurement of electrical recordings from the surface of the brain (Schalk and Leuthardt, 2011). ECoG is recorded by placing electrodes underneath the skull, either above or below the dura mater. The electrodes are often made of platinum or stainless steel discs that are embedded in a silicone-plastic base (Wolpaw and Wolpaw, 2011). Standard ECoG grids comprise 2 mm radius disc (exposed size) electrodes with 10 mm pitch placed on the surface of the cortical gyri. Yanagisawa et al. (2009) demonstrated that electrode placement in sulci can provide greater information than the typical gyral positioning. ECoG has a higher recording bandwidth than
scalp EEG, with reported signal features using spectral content up to 600 Hz (Staba et al., 2002; Chao et al., 2010; Miller et al., 2009). Example resting-state ECoG data is shown in Figure 1.4.

![Figure 1.4: Example resting-state ECoG data from 10 electrodes.](image)

As placement of ECoG arrays requires intracranial surgery, research into BCIs using ECoG in humans is limited. Most human studies occur with patients with drug-resistant epilepsy who are undergoing invasive monitoring to localize seizure foci and establish eloquent cortex (Van Gompel et al., 2008; Schalk and Leuthardt, 2011; Palmini, 2006). Complications related to electrode implantation occur in about 10% of patients, with permanent deficit in less than 5% of patients and with very rare mortality (Wong et al., 2009). A photograph of the surgical placement of an ECoG grid is shown in Figure 1.5.

During the typical one to three week monitoring period, patients are recruited to participate in experiments. Such participation is limited by the individual’s medical condition, medication, baseline neurological function and willingness to participate. The use of epilepsy patients in experiments also raises the concern that neural activity recorded from able-bodied individuals does not reflect the activity elicited in patients with motor impairments. Despite this concern, epilepsy patients undergoing ECoG monitoring provide a unique potential to investigate ECoG for brain-computer interfacing.

Many designs have sought to improve on the standard clinical ECoG monitoring electrodes, increasing the spatial and temporal resolution of the recorded
signal, as well as improving signal quality and transmitting data wirelessly (Viventi et al., 2011; Thongpang et al., 2011; Muller et al., 2015; Watanabe et al., 2012). Despite this, the vast majority of human studies are still undertaken with recording arrays that have remained largely unchanged for decades due to the demands of clinical epilepsy monitoring (Schramm and Clusmann, 2008).

1.4.5 Examples of ECoG-Based BCIs

Few studies to date have demonstrated BCI control from ECoG in tetraplegic individuals. Wang et al. (2013a) implanted a 32 electrode ECoG grid for a duration of 28 days over the motor cortex of an individual with a C4 level spinal injury. The participant could control a three-dimensional cursor by voluntarily activating sensorimotor cortex. The duration of this study was limited to 28 days due to the risk of infection associated with the ECoG grid implantation, although no adverse events were reported in this study. This work is of great significance, as it demonstrated that a paralyzed individual could achieve high accuracy, three-dimensional control using non-penetrating cortical electrodes.

Vansteensel et al. (2016) used a fully implanted ECoG system (Medtronic, Fridley, USA) to record from an individual with late-stage amyotrophic lateral sclerosis. Sixteen electrodes were implanted over motor and dorsal-frontal
areas, and she could operate typing software enabling independent communication. Most importantly, she could operate the BCI with the assistance of only her carer in her own household, with the entire system either mounted on her wheelchair or implanted. This is a major step forward in the clinical translation of BCI systems, as it removes several of the impracticalities (necessary set-up by researchers, use of stationary desktop computers, infection risk of leads, head-stages or percutaneous connectors) that have encumbered previous systems. This study was a profound step forward for the clinical translation of BCI devices in its demonstration of an invasive BCI in the everyday home environment.

ECoG has been demonstrated as a stable recording modality for BCIs. As ECoG measures the activity of large populations of neurons spanning multiple neural columns, the signal quality is understood to be more robust to changes in the electrode-tissue interface compared to single- or multi-unit activity recordings, which rely on their interface with individual cells (Chao et al., 2010). Long-term studies have demonstrated that ECoG can have stable signal-to-noise ratio over approximately a year (Chao et al., 2010).

Chronic implanted devices for monitoring and neurostimulation of the cortex for the treatment of epilepsy have greatly contributed to the body of knowledge of long-term ECoG recordings. Trials of a seizure prediction device (NeuroVista, Seattle, USA) demonstrated that a recording system can be implanted and remain safely in an ambulatory patient for up to two years (Cook et al., 2013, 2014). A trial of a recording and stimulating device, the RNS device (NeuroPace, Mountain View, USA) demonstrated that electrodes can have stable long-term impedances over two years. However, results for electrodes undergoing recording only (no therapeutic stimulation) are presented only for a duration of five months (Sillay et al., 2013). It is known that stimulation significantly decreases the impedance of electrodes (Newbold et al., 2011; Chen et al., 2014); hence, it is not possible to draw conclusions about the stability of recording-only electrodes from these results. Ryapolova-Webb et al. (2014) demonstrated that signal power measured weekly is steady in the 13-30 Hz and 54-86 Hz power bands over a duration of 700 days, although these results are only presented from two recording electrodes from a single non-human primate subject.
There is a need to further understand how ECoG signals change over the duration of several years, such that it can be assessed for suitability as a long-term neural interface for a BCI. Although previous works have demonstrated that specific features of ECoG recordings and electrode impedance are steady over time, there is a need to better understand how ECoG changes in humans across years. Long-term stability, particularly of gamma signals, is essential for ensuring device utility and progress towards clinical translation of BCIs.

ECoG shows promise as a recording modality due to the stability of the recorded cortical potential and information able to be decoded. BCI systems that rely on the ability to recording spiking activity have shown considerable promise; however, this has not shown to be viable for long-term applications.

The following section will outline various neural signals and how their properties are utilized by BCIs.

1.5 Motor Related Activity

The following section outlines properties of motor activity commonly measured for use in BCIs. It should be noted that although the following features have been observed in recordings from the cortex, this does not imply that the sensorimotor system or individual neurons explicitly use these observed properties to encode movement. However, they have been shown to be useful as the basis for a BCI; i.e., observed activity of individual motor neurons or cortical activity are by-products or epiphenomena of a highly interconnected, dynamic system, the purpose of which is to produce movement, not necessarily to describe it (Schi, 2012; Shenoy et al., 2013; Harrison and Murphy, 2012).

1.5.1 Cortical Potentials

Motor activity at larger spatial scales is measured by cortical potentials recorded by ECoG and EEG. Spectral differences in cortical potentials between idle and movement states are typically reflected in two distinct frequency bands (Miller et al., 2010; Pfurtscheller et al., 2003a; Pfurtscheller and Lopes da Silva, 1999; Miller et al., 2007; Wolpaw and Wolpaw, 2011). The first is a decrease in low frequency power (typically 10 - 30 Hz in ECoG, called the beta band).
This is known as event-related desynchronization, believed to be due to a lack of firing synchrony in the underlying neural population. The second is an increase in higher frequency band power (typically above 40 Hz in ECoG, called the gamma band), described as event related synchronization, due to the expected increase in firing synchrony of motor neurons. The first real-time ECoG BCI used these spectral features to detect imagined and actual movement and speech tasks, and demonstrated that high-accuracy control of a one-dimensional cursor could be achieved with under 30 minutes of training (Leuthardt et al., 2004). Robust two-dimensional control has since been shown to be achievable in a similar training period (Schalk et al., 2008).

Another common feature of the cortical potential often observed is the Bereitschaftspotential (English, ‘readiness potential’) (Kornhuber and Deecke, 1965). This is an increase in the amplitude of the recorded potential over M1 preceding motor activity, most evident approximately 250 ms before the onset of actual movement. It has been shown that this potential tends to increase in peak amplitude with the force used and complexity of motor task (Shibasaki and Hallett, 2006).

The phenomenon of motor-related directional tuning, first observed in M1 neurons, has also been demonstrated at the cortical potential scale. Schalk et al. (2007) were the first to demonstrate directional tuning in ECoG during motor activity in humans. Although previous studies have shown that directional tuning could be observed using single-unit recordings in non-human primate models (Rickert et al., 2005; Waldert et al., 2009), this was the first work to show this in humans using recordings from the cortical surface. Participants in this study tracked a target with a cursor controlled by a joystick with the hand contralateral to the implanted grid. Directional tuning was reported in the study for various frequency bands in the 18 - 190 Hz range, predominately over the primary motor cortex and pre-motor areas. The time-domain ECoG amplitude also demonstrated directional tuning, but more diffusely across M1 than the frequency features, as well as on the frontal lobe. Hence, it was shown that tuning curves could be measured cortically from both spectral and temporal features. A key feature of this work was that the motor task was heavily reliant on coordinated visual and motor activity compared to the use of a center-out task. Hence, it is uncertain from these results how well the models would translate to asynchronous BCI control when no such continuous
stimulus would be present.

Ball et al. (2009b) similarly demonstrated that ECoG signals recorded from primary motor cortex in humans show directional tuning in the time domain. A notable difference in this work from Schalk et al. (2007) was that a center-out task using the arm contralateral to the implant was recorded without using a visual stimulus to continuously prompt the participant. An advantage of the center-out task was that it involved the recruitment of several muscle groups throughout the arm, potentially recruiting more neural activity compared to a wrist-focused joystick task.

Directional tuning has also been demonstrated in the spectral power of cortical potentials recorded ipsilateral to the arm used for a joystick task in a single human patient (Zanos et al., 2008). This study also explicitly demonstrated that individual recording sites can demonstrate directional tuning for different directions when considering the power of different spectral bands.

In summary, directional tuning has been observed in various signal features at multiple recording scales, from microelectrode single-unit activity through to cortical local field potentials. Although directional tuning is poorly understood at the scale of mesoscopic cortical potentials, this scale of recording has demonstrated the greatest capacity for safe and stable long-term recordings. While it is possible to record motor activity non-invasively from the scalp, this has been shown to give insufficient information for accurate BCI control. Similarly, although it is possible to identify motor activity at a single-neuron scale, this is experimentally difficult and does not provide a stable recording over several months. Hence, recordings from the cortical surface have been shown to give a suitable trade-off between safety, long-term recording capability and ability to discern directional motor activity. It is unclear from the aforementioned works how well ECoG directional tuning encoding models can be used to decode movement. Although the existence of tuning curves has been establishing in ECoG signals during motor tasks, how well these curves predict movement has not been thoroughly established.

The next section will describe how properties of recorded neural signs are translated into device outputs.
1.6 Decoding Motor Activity

Regression and classification are methods used in decoders. Regression defines movement as function of the neural feature space. Alternatively, classification seeks to define neural signals into discrete classes of movement activity, creating boundaries in the feature space.

This section focuses on the groups of decoding algorithms most commonly used in BCI.

1.6.1 Regression Methods

Least-mean-squares is a method of deriving an optimal filter from observed data (Kailath et al., 2000). In linear systems, the output parameters $y \in \mathbb{R}^m$, where $m$ is the number of output parameters, can be represented as a linear combination of the recorded neural features $X \in \mathbb{R}^{m \times n}$, where $n$ is the number of recorded data-points:

$$X\beta = y,$$  \hspace{1cm} (1.2)

where $\beta$ is the derived filter and

$$X = \begin{bmatrix} X_{11} & X_{12} & \cdots & X_{1n} \\ X_{21} & X_{22} & \cdots & X_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ X_{m1} & X_{m2} & \cdots & X_{mn} \end{bmatrix}, \beta = \begin{bmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_m \end{bmatrix}, y = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_m \end{bmatrix}. \hspace{1cm} (1.3)$$

Hence an output $y_i (i = 1, 2, ..., n)$ can be described as a linear combination of the inputs to the system:

$$y_i = \beta_1 X_{i1} + \beta_2 X_{i2} + ... + \beta_n X_{in}.$$ \hspace{1cm} (1.4)

As such a system usually has no exact solution, $\beta$ must be derived in a way which ‘best’ fits Equation 1.2. The least-mean-squares optimal filter is given by

$$\hat{\beta} = (X^TX)^{-1}X^Ty.$$ \hspace{1cm} (1.5)
This is often referred to as the optimal linear estimator in neuroscience (Salinas and Abbott, 1994), especially when applied to filtering spike rates. This estimate is optimal assuming the regression errors have zero mean, are uncorrelated, and have equal variance (Kailath et al., 2000). Although this model is relatively simple, it has the advantage of being computationally fast to train and implement in real time. Many variations of this algorithm have been implemented in BCI systems. Regularized least-squares adds additional constraints to the cost function to prevent over-fitting of data and minimize computational costs (Williams et al., 2013). Weighted least-squares assumes measurements have different uncertainties, and hence weights measurements with low noise highly and vice-versa.

The aforementioned trial by Hochberg et al. (2006) used a least-squares derived filter to decode the desired movement direction of a two-dimensional cursor. Even with this relatively simple decoding system, a user could operate a two-dimensional cursor even while talking. A disadvantage of this filter its linear formulation. Although neural features are often modelled more accurately by non-linear methods, the often increased speed of training and implementation and ease of analysis of linear models makes them popular for real-time BCI implementation (Muller et al., 2003).

The important work of Wang et al. (2013a), introduced in Section 1.4.4, utilized a linear least-squares model to control the velocity of a robotic arm in three-dimensional space from ECoG derived features. A feature vector was constructed from the log-transformed power of normalized frequency bands. The output was a three-dimensional velocity vector, determining the wrist position of a robotic arm. Despite the simplicity of the decoding model used, this work demonstrated that ECoG can be used to control a three-dimensional arm.

Overall, relatively simple linear least-squares derived regression models have shown to be effective in real-time BCI application. Despite the limitations of the linear formulation of such filters, they are efficient to compute and implement in real time. Near-instantaneous device response is necessary for BCI use, such that the user is directly able to relate their intention to the device output.
1.6.2 Classification

Classification algorithms sort data into discrete classes. Classification is achieved by deriving a separatrix that divides a feature space into distinct regions. This provides a discrete output of what predicted class input data belongs to. The simplest classifiers operate by creating an $N - 1$ dimension hyperplane in an $N$ dimensional vector space, with the hyperplane forming the decision boundary between two classes. More complex methods use multiple boundaries and non-linear partitions to separate multiple classes of data. A typical classification method is the support vector machine (SVM), which creates a decision boundary by forming a hyperplane that maximally separates the marginal data points from each class (the so-called support vectors).

Artificial neural network models can learn complex features from input data and, as such, require minimal a-priori assumptions about how different features relate to different classes (LeCun et al., 2015). Recently, convolutional neural networks (CNNs) have generated great interest due to their capacity to learn highly non-linear mappings from high-dimensional spaces to output classification, and their ability to learn translation invariant features (Krizhevsky et al., 2012).

To date, a limited number of studies have explored the use of CNNs to decode motor activity from cortex. Khurana et al. (2016) used CNN models to improve upon previous classification performance on open-source scalp EEG motor imagery data. Trakoolwilaiwan et al. (2017) used CNNs to decode similar data from the wavelet transform of functional near-infrared spectroscopy data, significantly outperforming baseline SVM models. Schirrmeister et al. (2017) demonstrated that CNN models can robustly decode imagined hand, foot or no movement (rest) states from time-domain scalp EEG data. Importantly, they showed that CNN models can outperform prescriptive methods such as filter bank common spatial patterns, but without prior programming of features. Wang et al. (2013b) showed that finger flexion can be decoded from continuous ECoG data using a convolutional auto-encoder model. More complex varieties of CNNs such as long short-term memory (LSTM) and recurrent CNNs have also been investigated for ECoG decoding (Xie et al., 2017; Binz et al., 2015; Fathi and Erfanian, 2017); however, these typically require large amounts of data to train. Overall, CNN models have been used for a range of
neural decoding tasks. Their ability to construct high-dimensional, non-linear decision boundaries makes them ideal for processing EEG and ECoG signals that are highly abstracted from the underlying intention of movement and the kinematic and dynamic measurements of movement.

Decoding movement-related information from ECoG using ANN models is still in its infancy compared to other classification methods such as SVMs. Further investigation into how CNNs can be used to decode information such as movement direction is worthwhile as it has the capacity to produce high-accuracy and high degree-of-freedom decoding.

1.7 Conclusions

In this chapter, previous research has been presented that seek to both describe and decode invasive neural signals related to motor activity. Signal features correlating to motor movement (or intended movement) from spatial scales of inter-cortical single-unit activity through to macroscopic cortical recordings have been presented. Neural signal properties used in motor BCI decoding are based on the use of directional tuning models to discern intended movement direction. Regression models for decoding are commonly linear, although may use non-linearities to improve estimation accuracy or improve robustness. Although the mapping from neural feature activity to motor output is demonstrably not linear, these methods have produced great successes. Classification methods are also used to discretely decode motor intention.

To date, several published trials have demonstrated control of external devices using implanted devices in tetraplegic participants using recordings taken intercortically and on the cortical surface. Although microelectrodes have shown good short-term performance, the recording of action potentials is not robust in the long-term. However, disc electrodes have been demonstrated to be more robust in the long-term. The decoding used in these BCI systems has relied on largely black-box models using limited understanding of the spatial and temporal dynamics of the motor related potentials.
1.8 Overview of Thesis

1.8.1 Motivation

Brain-computer interfaces (BCIs) have made significant technological progress in the last few decades. However, clinical translation of BCI devices remains elusive. The absence of a long-term interface for recording action potentials indicates that an alternative method is required. Electrocorticography (ECoG) signals recorded from mesoscopic electrodes on the cortex may provide the necessary long-term robustness, while still providing sufficient information for high-accuracy, high degree-of-freedom decoding.

1.8.2 Thesis Structure

This thesis advocates for ECoG to be recording modality of choice for a clinically relevant BCI system. This will be done by first establishing the longevity of an electrocorticography (ECoG) recording system over a scale of several years. Experimental ECoG data is then presented that is shown to encode directional tuning information in the gamma range. Furthermore, movement direction can be decoded using artificial neural network models for an eight-class BCI. This is summarized in Figure 1.6.

Figure 1.6: Overview of thesis topics, leading towards clinical translation of an ECoG BCI.

This thesis will examine the following hypotheses:
Hypothesis 1: ECoG signals can be recorded for multiple years with a signal quality sufficient to detect motor-related potentials.

Aims:
- Characterize the change in mean power of ECoG in multiple frequency bands across a duration of multiple years
- Characterize the change in the variance of power of ECoG in multiple frequency bands across a duration of multiple years
- Calculate the maximum bandwidth of the ECoG signal across a duration of multiple years

Hypothesis 2: Population vector classification methods using direction tuning of ECoG can predict directions of human arm movements.

Aims:
- Characterize directional tuning curves in high-frequency power of human ECoG during a two-dimensional center-out task
- Demonstrate above-chance decoding with a variety of tuning models and channel selection and weighting methods

Hypothesis 3a: Convolutional neural network (CNN) models can decode movement direction from ECoG.

Hypothesis 3b: CNN decoding accuracy can be improved by aggregating data from multiple time-points and pre-training networks on multiple patients’ data.

Aims:
- Demonstrate above-chance decoding of convolutional neural network models for a finger-tap and center-out task
- Characterize the cross-patient utility of decoder model trained on both individual patient data and multiple patients’ data
- Characterize the utility of training decoder models on multiple time-points of ECoG data
Chapter 2 presents data from a previous first-in-human device trial for a subdural ECoG-based seizure prediction system, and demonstrates that the recorded signal is steady over the recorded duration. Specifically, measures of the signal quality including change in mean ECoG power, signal-to-noise ratio, ECoG power variance and estimated bandwidth remain steady at a group level across the duration of the study. The chapter concludes that subdural ECoG signal quality in humans is stable across a number of years, and hence can form a viable basis for a long-term, implantable BCI system.

Chapter 3 describes the experimental methodology for a two-dimensional center-out task and a finger-drumming task. This data was recorded from patients undergoing subdural ECoG monitoring for epilepsy surgical planning. Data is presented from four adult patients, who each completed at least 150 trials of the center-out task. Recording was undertaken using clinical electrode grids, with exposed electrode surface diameters on the order of millimeters. Recordings were taken broadly across cortex, with coverage across the cohort including frontal, temporal, parietal and occipital lobes. This data is then further analyzed in Chapters 4 and 5.

Chapter 4 presents encoder-decoder models of directional tuning of upper-limb movement intention from ECoG. Directional tuning models are presented that are formed by cosine and von Mises functions. Directionally tuned electrodes are found across the cortex in all patients. Decoder models are then formed by inverting the encoder models and computing population-vectors from the ECoG channels. A population-vector weighted by each channel’s tuning signal-to-noise ratio is also presented. Movement angle could be decoded from three of the four patients’ data at well above chance accuracy, with enhanced accuracy when weighted by the tuning signal-to-noise ratio. This chapter demonstrates that directional tuning exists in high-frequency human ECoG signals during a 2D center-out task, and that movement angle can be decoded using modified population vector methods, warranting further investigation by more complex classification tools.

Chapter 5 shows that artificial neural network models can be used to decode movement from frequency-domain ECoG with relatively high accuracy. Decoding accuracy can be improved by training models with data from multiple time-points before trials, or utilizing data from multiple patients. Fully con-
1.8. OVERVIEW OF THESIS

Connected (FC) and convolutional neural network (CNN) models are presented, with CNNs outperforming the FC models for all patients. It is shown that pooling data across multiple patients for training CNN models significantly increases decoding performance, except for the best performing patient. We explore the use of decoding movement at multiple time-points and show that the CNN tends to have peak decoding accuracy just before movement onset. Finally, we demonstrate that the models do not appear to be learning information regarding how different movement directions are related, as errors in movement angle appear to not have a mean at the correct movement direction. Overall, it is shown that neural network models can decode eight classes of intended movement direction from a two-dimensional center-out task, and that performance is significantly enhanced by training on multiple time-points or patients.

Chapter 6 summarizes the work presented in this thesis, discusses key outcomes and considers future directions for this work and ECoG based BCIs more broadly.
Chapter 2

Consistency of Long-Term Subdural Electrocorticography in Humans

Chapter 2 is a modified version of the published article:

2.1 Introduction

This chapter contributes to knowledge by addressing the following hypothesis, that is untested in the current literature, that ECoG signals can be recorded for multiple years with a signal quality sufficient to detect motor-related potentials. This is an important property of potential implanted brain-computer interface recording systems.

Subdural electrocorticography (ECoG) has the potential to provide a robust control signal for a brain-computer interface (BCI). However, the long-term recording properties of ECoG in humans are poorly understood, as most studies in the BCI field have only used signals recorded for less than 28 days. This chapter will assess human ECoG recordings over durations of many months to investigate changes to recording quality that occur with long-term implantation.
The long-term spectral characteristics of ECoG are of importance to the clinical translation of ECoG-based neural prostheses, especially as high-frequency spectral features are of particular relevance to motor decoding. Understanding long-term reliability of ECoG is critical to the longevity of decoders in BCI devices. A study of the long-term properties of ECoG in terms of spectral characteristics relevant to BCI in humans has not previously been undertaken.

As placement of ECoG electrodes requires a craniotomy or burr hole in the skull, human studies have typically been limited to patients implanted for presurgical evaluation for removal of an epileptic focus or tumor. The majority of reported ECoG studies are of short duration (1-4 weeks) owing to the infection risk inherent in externalizing electrode leads.

This work presents a study of the spectral properties of recorded ECoG on time scales up to 2.1 years from ambulatory, subdural, continuous recordings from 15 humans. This data was recorded for a first-in-human device trial to study device safety and anticipation of epileptic seizures (Cook et al., 2013, 2015). The data totals over 100,000 electrode-hours of predominantly continuous ECoG recordings. This chapter will demonstrate that electrodes showed varying changes in frequency power characteristics over time, both within individual patients and between patients. Group level analyses demonstrated that there were only small changes in effective signal bandwidth and spectral band power across months. Gamma signals were recorded throughout the monitoring period, although there was a decline in signal power for some electrodes.

This work demonstrates that ECoG-based BCI systems can robustly record high-frequency activity over multiple years, albeit with marked inter-subject variability. Group level results demonstrated that ECoG is a promising modality for long-term BCI applications.
2.2 Methods

2.2.1 Signal Recording

Data were recorded continuously by a subdural ECoG seizure prediction system undergoing a first-in-human trial (Cook et al., 2013) (registered clinical trial, number NCT01043406). The study was undertaken across three centers in Melbourne, Australia: Austin Health, Royal Melbourne Hospital, and St. Vincent’s Hospital. Human research ethics approvals were obtained at each of the participating centers. Patients were adults selected primarily on the basis of seizure frequency, with 2-12 identified events per month at time of enrolment.

In summary, 15 patients were implanted with the seizure prediction system, which comprised four major components: (1) implanted lead assemblies, (2) implanted telemetry unit, (3) external advisory device, and (4) external charging device. Each participant was implanted with two silicone lead assemblies each with two electrode arrays that each had four platinum-iridium electrodes (16 electrodes in total). Electrodes had an exposed diameter of 2.3 mm, with a spacing of 10 mm. Leads were placed unilaterally over the area of the cortical surface believed to contain the epileptogenic zone, as determined by prior scalp electroencephalography, structural imaging, and seizure focus studies. Leads were implanted via burr-holes or through prior craniotomy sites where available. The leads were tunneled beneath the neck and terminated at the implanted telemetry unit placed below the collar bone. Duration of implantation varied from 6 months to 2.1 years. Patient demographics and electrode location is shown for each patient in Table 2.1.

The implanted telemetry unit was titanium-encased and hermetically sealed. The unit continuously sampled 16 channels of ECoG at 400 Hz that were wirelessly transmitted to the external personal advisory device. The personal advisory device received the transmitted ECoG for processing and stored it on flash memory. Recordings were referenced in hardware using a common-average method, where each channel was recorded using the average of all 16 channels as a reference and DC offset was removed. Typical responsive alpha rhythms and sleep-related changes were observed during the recordings and verified by neurologists. A radiograph of the system is shown in Figure 2.1.a.
Table 2.1: Patient demographics and electrode placement for each patient. Age is taken from the beginning of the study. * Note that Patient 8 had previous vagal nerve stimulation. Table data reproduced from Cook et al. (2013).

2.2.2 Exclusion of Data

Data were analyzed using 2 minute, non-overlapping windows (epochs). This duration was chosen as it gave an acceptable balance between temporal resolution of analysis and minimizing the influence of random fluctuations in neural activity. Epochs were excluded if there was signal dropout or a seizure event within the window. In these cases, the start of the window was moved to after the event. Signal dropout typically occurred due to flat battery or when the external advisory device was too far away from the implanted telemetry unit,
Figure 2.1: The NeuroVista recording system. (a) Implanted telemetry unit and lead assembly of the seizure prediction system. (b) Example ECoG signal. (c) Mean (± std. dev.) of power-spectral density from Patient 3, electrode 1. Solid black error bar shows 75th and 25th quantiles of the power-spectral density at 190-200 Hz. Dot-dashed black line indicates calculated maximum bandwidth.

which typically occurred during sleep at night-time. Dropouts were characterized by near-zero voltage being recorded from all 16 channels simultaneously. Seizure events were identified by a detection algorithm and verified by neurologists.
2.2. METHODS

2.2.3 Signal Analysis

All signal analyses were conducted in MATLAB (MathWorks, R2015a, USA), on the University of Melbourne MATLAB Distributed Computing Server. Within each 2 minute window, the mean was subtracted, a second-order, zero-phase Butterworth band-pass filter (0.1-195 Hz) was applied, and a second-order, zero-phase Butterworth notch filter at 47-53 Hz was applied to remove line noise (Australian mains power is at 50 Hz). An example of the time-domain ECoG is shown in Figure 2.1b. Preliminary results demonstrated that little effect was found when applying a notch filter at the 100 Hz and 150 Hz harmonics, so they were not applied in this work.

Periodograms were calculated using a modified version of the periodogram function. For each 2 minute (48,000 sample) epoch, the signal was split into non-overlapping segments of 512 samples and a Hamming window was applied to each segment. These segments where then summed and a normalized periodogram was taken. An example periodogram is shown in Figure 2.1c. Spectral power in 10 Hz bands (0-10 Hz, 10-20 Hz, . . . , 190-200 Hz) were then calculated from the mean power in the given bandwidth (approximately 12-13 frequency estimates) of the periodogram. These bands where chosen as they are commonly used in motor-related ECoG studies (Wang et al., 2013a; Schalk and Leuthardt, 2011). The analysis bands around 50 Hz were set to 40-45 Hz and 55-60 Hz to avoid the effects of the notch filter.

The maximum bandwidth, $F_{\text{max}}$, was defined as the highest frequency at which the signal was determined to be significantly different from estimated noise (Bundy et al., 2014; Oxley et al., 2016). It was calculated as the highest frequency with power greater than a threshold,

$$P_t = 1.5 \times (Q_{75}(P_{\text{noise}}) - Q_{25}(P_{\text{noise}})) + Q_{75}(P_{\text{noise}}),$$

where $Q_n(P)$ is the $n^{th}$ quantile of $P$ and $P_{\text{noise}}$ is the mean of the spectrogram in the 190-200 Hz band. Noise was defined in this way as it was the highest spectral band below the Nyquist frequency. Although $P_{\text{noise}}$ will contain signal information, the noise has been approximated in this way as it was not possible to explicitly test the noise properties of the device. This measure estimates the frequency at which the spectral power becomes indistinguishable from the estimated noise. The maximum bandwidth was calculated for each
day of recording for each channel. An example is shown by the black error bars and the dot-dashed lines in Figure 2.1c.

To understand changes in spectral power as a relative measure, the signal-to-noise ratio (SNR) of the band power was calculated as

\[ \epsilon(n) = 10 \times \log_{10} \frac{P_{\text{signal}(n)}}{P_{\text{noise}}}, \]  

(2.2)

where \( P_{\text{signal}(n)} \) is the mean spectrogram power in each frequency band, \( n \), and \( P_{\text{noise}} \) is the mean spectrogram power in the 190 – 200 Hz power band, each calculated daily. To summarize the frequency power results from each patient-electrode, a linear fit was then calculated using a robust least-squares fit for mean power in each frequency band across time, which was repeated for SNR and variance. The gradients of the linear models were then analyzed to assess how each signal measure changed over time.

2.2.4 Statistical Analysis

All statistical analyses were undertaken using the software platform R (version 3.2). For each spectrogram measure, a linear mixed-effects (LME) model was used to determine a linear model of the measure as a function of time (Gelman and Hill, 2006). Each model used the daily calculated ECoG measurement from each channel as input, and produced a linear fit at a group level for the output. The coefficients of the linear fit (intercept and gradient) were then analyzed to determine the rate of signal change. The model assumes that each signal property is a linear function of time and that random effects and model errors have zero mean normal distributions. Normality was verified by visual inspection and by a one-sample Kolmogorov-Smirnov test (using the \texttt{kstest} function in MATLAB) on select samples. Examples of the daily distribution of the SNR and variance are shown in Figure 2.2. Each signal property was set as the response variable, each day as the predictor variable, and each electrode as a grouping variable, producing a random intercept model with a fixed slope. The purpose of this modelling was to understand the average rate of change of each response variable over time. Each signal property was also tested for the effect of electrode position on its strip (i.e., how distal an electrode contact was from the lead) by including day and electrode strip number and their interaction in the fixed model. This was done as the most distal electrodes
2.3 Results

2.3.1 Individual Patient Signal Power

Spectrograms from each patient demonstrated a range of longitudinal behaviors. The mean signal power and SNR calculated daily as functions of time, averaged across the 16 channels for each participant, are shown in Figure 2.3.

As expected for ECoG signals, the raw signal power and SNR decreased as frequency increased (Miller et al., 2009). As can be seen, the mean power...
and SNR are highly congruent for all patients. The variance in signal power calculated daily as a function of time, averaged across the 16 channels for each participant, is shown in Figure 2.4. For several patients, the variance is relatively steady across the duration of the study, but for others changes over time are evident. The variance between frequency bands is similar for most patients.

To summarize the frequency power results from each patient-electrode, a linear fit was then calculated using a least-squares fit for each frequency band. This process was repeated for SNR and variance. The gradient of the linear fit and the corresponding coefficient of determination are presented in Figure 2.5.

![Figure 2.3](image_url)

**Figure 2.3:** Mean daily power (solid line) and SNR (dashed line) for each participant across four frequency bands as a function of time. Each line represents the mean of the 16 channels for each patient, and the mean power within the given bands.

It was found that the daily total variance in signal power had a significantly higher rate of change in all electrodes of Patients 5 and 7 than in the rest of the cohort ($p < 0.001$, one-sided two-sample $t$-test). This is shown in Figure 2.6. Neither patient progressed from the preliminary data acquisition phase
2.3. RESULTS

Figure 2.4: Variance of daily power for each participant, within four frequency bands as a function of time. Each line represents the mean of the 16 channels for each patient, and the mean power within the given bands.

of the device trial due to either an adverse event or poor seizure prediction results (Cook et al., 2013). Hence, the group level signal power and maximum bandwidth results presented herein exclude Patients 5 and 7 and only consider the remaining 13 patients.

2.3.2 Group Level Signal Power

The mean band power model y-intercept, shown in Figure 2.7.a, decreased monotonically as a function of frequency; this was as expected due to the 1/f nature of ECoG spectra. As shown in Figure 2.7.b, the linear model for each frequency band had a positive gradient significantly different from zero ($p < 0.0001$, $t$-test). Model values and statistics are presented in Table 2.2. The lower gradient for 0-10 Hz spectral power compared to the 10-20 Hz band was potentially due to the effects of the hardware band-pass filter and removal of the mean (0 Hz content) for each window. It also demonstrates that changes
2.3. RESULTS

Figure 2.5: (a) Gradient and (b) corresponding $r^2$ value for least-squares linear fit to the mean of 0-10, 10-20, ..., 190-200 Hz bands for each of the 16 electrodes for each patient. Note in the left column that a positive change is indicated in red and negative in blue. Spectral bands around 50 Hz have been adjusted to avoid the effects of the applied notch filter and hence have a narrower bandwidth. (c) & (d) The same measures for mean power SNR. (e) & (f) The same measures for variance.

Across the duration of the study were relatively close to zero, indicating a stable signal recording. No significant effect was found for electrode position on its strip ($p > 0.05$).

Comparable to the absolute measure in Figure 2.7.a, the intercept of the SNR in Figure 2.8.a decreased monotonically as a function of frequency. Model values and statistics are presented in Table 2.3. The gradients of the SNR were
2.3. RESULTS

Figure 2.6: Histogram of gradient of daily variance in total signal power for all patient electrodes. All 32 values in the population that are above $20 \text{V}^4/\text{Hz}^2/\text{year}$ are from the electrodes of Patients 5 and 7.

all relatively close to zero, indicating minimal changes at a group level to the SNR over the duration of the study, although all bands except 60-70 Hz and 150-190 Hz were significantly different from zero ($p < 0.01$, t-test). As demonstrated in Figure 2.8.b, each gradient was at least one order of magnitude less than the intercept for each spectral band, indicating a longitudinally robust SNR in each frequency band. The standard error of the gradient also decreased with increasing frequency. This was expected as the spectrum flattens as frequency increases, and spectral band power become closer to the estimated noise (as illustrated in Figure 2.7).

As shown in Figure 2.9a, similar to the mean daily power measure, the gradient of the power variance decreased almost monotonically with increasing frequency. Model values and statistics are presented in Table 2.4. For each frequency band, the daily variance decreased across the duration of this study ($p < 0.0001$, t-test), as is shown in Figure 2.7b, with lower frequencies decreasing at a greater rate. No significant effect was found for electrode position on the strips ($p > 0.1$).
2.3. RESULTS

Figure 2.7: LME model parameters of mean of spectral bands, calculated for daily average for each patient-electrode, ± standard error. (a) Intercept of LME fit. (b) Gradient of LME fit. * indicates $p < 0.0001$ for the hypothesis that the value is non-zero. Note that spectral bands around 50 Hz have been adjusted to avoid the effects of the applied notch filter and hence have a narrower bandwidth.

2.3.3 Maximum Bandwidth

Figure 2.8 shows the daily maximum bandwidth as a function of time and the linear mixed effects (LME) model. The LME model was calculated across 208 patient-electrodes, providing a general trend across the cohort. Model values and statistics are presented in Table 2.4. The gradient of 0.99 ($\pm$ 0.07) Hz/year ($p < 0.0001$, $t$-test), indicates an overall increase in the maximum bandwidth. Hence, the effective bandwidth of the model was increasing, albeit at a slow rate (1.0% of the y-intercept value per year). No significant effect ($p > 0.1$) was found when comparing electrodes from different positions on the electrode strip (LME model, allowing for interaction between electrode group and time). It should be noted that, as recordings were across many behavior states for each patient, higher frequency activity may be averaged out as high-frequency activity is typically linked to sensory activation and selective attention (Ray et al., 2008b). From these results, it would be expected that this device could record neural oscillations up to at least 98 Hz, with only minor change over
There is generally broad support of the suitability of ECoG for long-term BCI control and, more generally, neural interfacing. Changes in frequency band power are important for BCI applications, which often rely on changes in signal power correlated to movement intentions. For clinical translation of ECoG BCIs, understanding how the high-frequency components of the signal change is of great importance.

Figure 2.3 demonstrated that the mean power and SNR averaged across electrodes for each individual was relatively steady, with low day-to-day variation. However, unlike the analyses in Figures 2.7-2.9, this figure averages years. Therefore, this device could distinguish gamma activity for a BCI system.

### Table 2.2: Linear Mixed Effects model coefficients for mean of spectral bands, calculated for daily average for each patient-electrode. Freq. = Frequency, SE = Standard Error.

<table>
<thead>
<tr>
<th>Freq. (Hz)</th>
<th>Intercept (V²/Hz)</th>
<th>Gradient (V²/Hz/yr)</th>
<th>Intercept SE</th>
<th>Gradient SE</th>
<th>Intercept p-value</th>
<th>Gradient p-value</th>
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</thead>
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<td>0-10</td>
<td>11.13</td>
<td>0.29</td>
<td>0.24</td>
<td>0.01</td>
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<tr>
<td>10-20</td>
<td>4.10</td>
<td>0.33</td>
<td>0.21</td>
<td>0.01</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
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<tr>
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<td>0.25</td>
<td>0.01</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>55-60</td>
<td>-14.29</td>
<td>0.18</td>
<td>0.24</td>
<td>0.01</td>
<td>0.00</td>
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<td>0.01</td>
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<tr>
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<td>0.22</td>
<td>0.01</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>100-110</td>
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<td>0.21</td>
<td>0.01</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>110-120</td>
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<td>0.01</td>
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<td>0.14</td>
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<tr>
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<td>0.00</td>
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across all electrodes and wider spectral bands. Hence, as expected, these group level results are less variable than individual electrode results. Some patients showed far greater changes in average variance across the study; in particular, Patients 6, 10, 12, and 15 showed substantial change in variance in the selected frequency bands. Across the set of 240 electrodes, analyzed in narrower 10 Hz bands, a variety of longitudinal spectral patterns were observed. Linear regression of the mean power demonstrated a range of outcomes: all electrodes and frequency bands increasing (Patient 14), all decreasing (Patient 4), a range of positive and negative gradients associated with particular electrodes (Patient 15), and a range associated with frequency (Patients 10 and 13). Hence, it would be expected in future long-term ECoG devices that a wide range of spectral changes would be observed over time due to differences in behavior and device functionality, and hence decoding systems must be able to account for such subject-specific changes.

That notable variability exists between electrodes from single patients suggests that changes in the power spectrum are potentially influenced by corti-
2.4. DISCUSSION

Table 2.3: Linear Mixed Effects model coefficients for SNR of spectral bands, calculated for daily average for each patient-electrode. Freq. = Frequency, SE = Standard Error.

<table>
<thead>
<tr>
<th>Freq. (Hz)</th>
<th>Intercept</th>
<th>Gradient</th>
<th>Intercept</th>
<th>Gradient</th>
<th>Intercept</th>
<th>Gradient</th>
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<tr>
<td>40-45</td>
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<td>0.01</td>
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<td>0.94</td>
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<td>110-120</td>
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<td>130-140</td>
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<td>0.20</td>
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</table>

Table 2.3 shows the coefficients from a linear mixed-effects model for SNR of spectral bands, calculated for daily average for each patient-electrode. The model assesses the effect of frequency bands on SNR, with coefficients for intercept and gradient values presented. The high variability observed between patients across the signal measures in Figure 2.4 poses a potential difficulty for long-term ECoG recording, as it suggests that individual patient recording outcomes, and hence long-term decoding potential, are difficult to predict. As only Patients 5 and 7 had outlying rates of increase of power variance compared to the rest of the cohort, this suggests that relatively stable long-term recordings were achieved in 13 of the 15 patients.

Due to the different duration of each patient’s recording, a linear mixed effects (LME) model was used to understand the group level statistics of the analyzed features. The maximum bandwidth as determined by the LME model had an intercept value of 98.46 Hz and showed linear increase at a group level with a model gradient of +0.99 Hz/year and with each individual electrode...
2.4. DISCUSSION

Figure 2.9: LME model parameters of variance of spectral band, ± standard error. (a) Intercept of LME fit. (b) Gradient of LME fit. Note that spectral bands around the 50 Hz have been adjusted to avoid the effects of the applied notch filter.

Figure 2.10: Maximum bandwidth calculated for each patient-electrode averaged over each day (red line, ± standard error). Black solid line is LME model with intercept at 98.46 (±0.8) Hz (± standard error) and gradient of +0.99 (±0.07) Hz/year (p < 0.0001, t-test). Black dashed lines represent 95% confidence interval. Black circles indicate when a patient recording stopped. Demonstrating a positive gradient for a linear fit. This is highly encouraging, as it demonstrates that this device can record high-frequency ECoG that is distinguishable from noise. As recordings were taken continually, the ECoG signal included many behavioral states. It is well understood that ECoG gamma
Table 2.4: Linear Mixed Effects model coefficients for power variance of spectral bands, calculated for daily average for each patient-electrode. Freq. = Frequency, SE = Standard Error.

<table>
<thead>
<tr>
<th>Freq. (Hz)</th>
<th>Intercept ((V^4/Hz^2))</th>
<th>Gradient ((V^4/Hz^2/yr))</th>
<th>Intercept SE</th>
<th>Gradient SE</th>
<th>Intercept (p)-value</th>
<th>Gradient (p)-value</th>
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Table 2.5: Linear Mixed Effects model coefficients for maximum bandwidth, calculated for daily average for each patient-electrode. Freq. = Frequency, SE = Standard Error.

<table>
<thead>
<tr>
<th>Intercept (Hz)</th>
<th>Gradient (Hz/yr)</th>
<th>Intercept SE</th>
<th>Gradient SE</th>
<th>Intercept (p)-value</th>
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<td>1.23</td>
<td>0.07</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

power is correlated with selective attention (Ray et al., 2008b). Therefore, it would be expected that the maximum bandwidth would be higher if only using ECoG from epochs containing event-related potentials. Consequently, it is assumed that 98 Hz is a conservative group level measure of the upper frequency bound for this device, and that some signal features above this frequency could be successfully used in neural prostheses.

The maximum bandwidth reported in this study was likely to have been affected by the system Nyquist frequency of 200 Hz. Previous studies investigating characteristics of ECoG signals (Bundy et al., 2014; Miller et al., 2009)
2.4. DISCUSSION

reported noise floor of ECoG recordings with macro electrodes close to 250 Hz when recorded with sampling frequencies on the order of 1 kHz. It should be noted that, as the calculation of maximum bandwidth is dependent on the sampling frequency of the recordings, the maximum bandwidth is strongly affected by the 1/f roll-off nature of the signal when the sampling frequency is not substantially high enough to reach the amplifier noise floor. Hence, the presented maximum bandwidth results are likely to be underestimated. However, these results show that longitudinally over two years there was little change in the estimated maximum bandwidth at a group level, indicating robust group level results.

The results presented in Figures 2.7-2.9 demonstrated that, at a group level, the ECoG signal power varied only slightly across the duration of the recordings. When compared to the estimated noise levels, the spectral power demonstrated gradual decay, with lower frequency spectral bands showing a power increase. It can be seen in Figure 2.8b that the mean daily SNR decreases from 70-150 Hz at a group level. From the results presented in Figure 2.7b, it can be seen that this is due to the signal power in the 190-200 Hz band (noise) increasing on average at a greater rate than the signal in the 70-150 Hz range; hence, the SNR has a lower gradient. However, this increase in noise power is still comparatively small, as reflected by the steady maximum bandwidth.

A drawback of the data used in this study is that, despite the vast duration of ECoG recordings, there was no behavioral information that could be related to the signal. Ideally, motor and cognitive studies would be undertaken periodically over the duration of such long-term recordings to understand how event-related potentials change longitudinally. Factors such as age, cortical locations of electrodes, existence of a prior craniotomy, and medications taken during the trial may have contributed to inter-subject variability and should be further investigated in future trials with greater numbers of participants. Despite not being able to control for these factors, the high number of recording electrodes and long duration of the study has allowed the general trends in the recorded signal to be elucidated.
2.5 Conclusion

This work is unique in the exploration of the effects of long-term implantation on ECoG recordings, primarily in that it used long-term continuous recordings from human patients. This allowed for long-term changes in signal frequencies of common interest in BCI systems to be examined. The results of this chapter demonstrate that the spectral properties of ECoG show minimal change over a duration of multiple years, at a group level. Each electrode for each patient at the conclusion of the study had discernable gamma oscillations, despite some undergoing a decline in signal power. However, individual electrode responses varied markedly, indicating that ECoG-based devices should account for this variability within, and between, patients. Hence, it can be expected that an ECoG BCI system can robustly record motor related gamma signal over a timescale of years, albeit with marked inter-subject variability.
Chapter 3

Movement Experiment Methods

The following chapter describes data collected for further analysis in Chapters 4 and 5.

3.1 Patient Cohort

The patient cohort consisted of adult individuals undergoing sub-dural cortical monitoring for epilepsy surgery planning using electrocorticography (ECoG) grid electrodes from 2014 to 2017. Ethics approval was granted for experimentation at St. Vincents Hospital Melbourne (SVHM) approval number HREC - A006/08. All patients gave informed, written consent prior to grid implantation. Grid placement was determined entirely by clinical need, and was not influenced by this work. Experiments all commenced at least 72 hours after electrode implantation, at least two hours after identified clinical seizures, and 24 hours after functional electrical stimulation for cortical mapping. All patients were also enrolled in other studies; however, all data collected for this study was recorded before the commencement of other experiments. Electrodes were explanted after seven days. Patient 2 had an eight-electrode depth lead that targeted the left hippocampus; however, this was not considered for the purposes of this work. Patient 3 had undergone a previous cortical resection and had previously been implanted with a chronic ECoG recording system (Cook et al., 2013), previously described in Chapter 2.

Patient demographics are provided in Table 3.1. Electrode locations, as determined by co-registered CT-MRI imaging, are shown in Figure 3.1.
3.2. DATA ACQUISITION

Table 3.1: Patient demographics. M = Male, F = Female, L = Left, R = Right.

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Sex</th>
<th>Handedness</th>
<th>Hemisphere of Implant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>R</td>
<td>L</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>R</td>
<td>L</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>R</td>
<td>L</td>
</tr>
</tbody>
</table>

Figure 3.1: Co-registered CT-MRI images showing electrode locations for each patient.

3.2 Data Acquisition

3.2.1 ECoG Data

The ECoG arrays (Ad-Tech Medical Racine, USA) consisted of platinum discs (model CGIE-120-BPN-F1B for Patient 1, FG32C-SP10X-000 for Patient 2,
and FG64C-SP10X-0C6 for Patients 3 and 4). Patient 1’s grid comprised of 2 mm diameter electrodes, with the fifth electrode of each row having a diameter of 4 mm. The electrode pitch was 5 mm horizontally and 10 mm vertically (center-to-center). Patient 2, 3 and 4’s electrodes were 4 mm diameter, with 10 mm spacing horizontally and vertically. The array dimensions were determined entirely by clinical needs. For the purposes of this work, Patient 3’s single electrode not within a grid (the most anterior-inferior electrode in Figure 3.1) was excluded. Signals were sampled at 5 kHz using Neuroscan SynAmps2 EEG amplifiers (24-bit, 64 channels per amplifier) and ProFusion EEG software (version 4.3, 2011) (both Compumedics Ltd., Melbourne, Australia). Video footage of the participant was also captured at 25 frames per second, synchronized to the EEG. Reference electrodes were selected on the basis that they were of low impedance (< 1kΩ) and as spatially distant from epileptic activity as possible. Ground electrodes were placed on the back of the shoulder. All cables were shielded to reduce line noise. Amplifiers were stored in an electrically shielded container during recording. All recordings were undertaken with the patient bed turned off to minimize line noise.

3.2.2 Motion Tracking Data

A Polhemus G4 motion tracking system was used. This system had four sensors, each of which measured 3D position in space and 3 angles of orientation. The system measured positions relative to a hub, which were then zero-mean normalized at the end of recording. Motion tracking was recorded at 120 samples per second. Each sensor was attached to the skin with an adhesive sports bandage. A sensor was attached to the back of the hand, at the midpoint of the wrist and elbow, at the midpoint of the elbow and acromion, and on the acromion. ECoG and motion tracking data were time-locked to the beginning of each trial using a photodiode trigger that activated as the movement target appeared, as well as 25 frame-per-second clinical video that was time-locked to the ECoG.
3.3 Center-Out Task

A center-out task was undertaken with all four patients. This task was selected to produce two-dimensional arm movements at eight equally spaced movement angles. The patient sat upright in bed and had a foam board (size A0, 841 x 1189 mm) placed directly in front of them (resting on an over-bed table) and LCD screen placed at the foot of the bed, as shown in Figure 3.2. All patients confirmed that they could clearly see the screen before commencing. Holding a stylus, participants performed a center-out task by moving from the center point of the board (marked by a red dot) to one of eight targets (marked by a blue dot) spaced evenly by $45^\circ$, 20 cm from the center of the board. Board position was adjusted to ensure the patient could reach every target without needing to lean forwards. Patients used either a pen grip or power grip, depending on comfort. During this time, arm position and ECoG were simultaneously recorded.

A visual cue from the computer monitor was used to show the target and the speed of movement: slow, medium, or fast. This hold cue lasted between one to three seconds. Once the cue disappeared from the screen, the patient commenced their movement. Each trial took a total of ten seconds. Patients were instructed that a ‘slow’ trial should take approximately five seconds, ‘medium’ approximately three seconds, and ‘fast’ as quickly as comfortably possible without loss of accuracy. Trials continued until the participant chose to stop, or for a maximum of 40 minutes. Before the experiment, the experimenter demonstrated several trials, and the patient completed approximately 5-10 practice trials to ensure correct and consistent technique.

Finger-Drumming Task

A finger-drumming task was conducted with Patient 4, as a proof of concept study. The patient reclined in bed and rested their right hand on a table. They were instructed to look at their hand during the experiment (to provide a visual focus); however, they were occasionally distracted by speech and general noise in the room. The patient was supervised during the entire experiment. The first task was to complete 10 separate 30 second blocks of finger-drumming, lifting and dropping the fingers back on the table continuously, interleaved with 30 second periods of rest. Timing were given verbally by the experimenter,
3.3. CENTER-OUT TASK

Figure 3.2: Photograph of experimental setup during center-out task. The patient (face covered by a black square for anonymity) is sitting up in bed, with the foam board immediately in front of their chest. The prompt screen, placed at the end of the bed, displays the current direction with a filled light-blue circle (in this case the top target) and the speed of movement (‘Slow’). The patient has motion tracking sensors attached to their left arm, with a sensor visible on their forearm. The ECoG cabling and copper shielding can be seen clipped to the right shoulder. The photodiode system can be seen attached to the lower-left of the screen, providing a timer signal to the ECoG and motion tracking system at the start of each trial.

saying ‘start’ and ‘stop’ to indicate the beginning of the movement and rest periods, respectively. The second task was identical to the first, but instead the instruction given was to imagine moving their fingers, without performing any overt movement. The patient was asked to fix their gaze on their hand as before, and imagine the sensation of moving their hand, while keeping it as still as possible.
Chapter 4

Encoder-Decoder Models of High-Frequency Directional Tuning in Electrocorticography

Chapter 4 includes work previously published in the following article: Nurse, E.S., Freestone, D.R., Oxley, T.J., Ackland, D.C., Vogrin, S.J., Murphy, M., O’Brien, T.J., Cook, M.J. and Grayden, D.B., 2015, Movement related directional tuning from broadband electrocorticography in humans. In 7th International IEEE/EMBS Conference on Neural Engineering (NER), 22-24 April 2015, (pp. 33-36).

4.1 Introduction

This chapter contributes to knowledge by addressing the following hypothesis, that is untested in the current literature, that population vector classification methods using direction tuning of ECoG can predict directions of human arm movements. A variety of modifications to the standard population vector method will be explored, including methods for weighting and selection of ECoG channels.

Neuronal tuning is a fundamental property of cortical neurons, where individual neurons selectively respond to particular stimuli or cognitive processes. Fine directional tuning of neurons of arm movement direction is a property found throughout the human motor system. Directional tuning is used by brain-computer interface systems to translate movement intention into device
Decoding movement from directional tuning curves is based on the seminal work of Georgopolus et al. (1982, 1986), who showed that Rhesus macaques demonstrate directional tuning in primary motor cortex (M1) neurons during reaching tasks. Neurons had increased firing rates when a macaque moved its arm in specific directions. They used a cosine curve to model accurately the firing rates of individual neurons as a function of movement direction. This is well suited to a linear decoding model, particularly when taking a geometric interpretation of the dot product of two vectors. Consider

$$Z = B \cdot M,$$  \hspace{1cm} (4.1)

where $Z$ is the neural activity matrix in $\mathbb{R}^2$, and is of size $c \times n$, where $c$ is the number of channels and $n$ is the number of recorded trials, $B$ is a $c \times 2$ coefficient matrix, and $M$ is a $2 \times n$ matrix of normalized hand position measurements. Hence, for each trial

$$Z_i = B \cdot M_i = |B||M_i|\cos(\theta_i),$$  \hspace{1cm} (4.2)

where $Z_i$ and $M_i$ are the neural activation and coefficients for the $i_{th}$ channel, respectively. It follows that the neural activity is highest when movement is undertaken in the preferred direction, lowest when movement is in the opposite direction ($\theta_i + 180^\circ$), and intermediate when movement is between these two directions. Equation 4.2 can be solved to determine the preferred movement direction, $\theta_i$, for each channel. The most straightforward solution is an inversion of Equation 4.2, given by

$$\theta_i = \arccos \left( \frac{Z_i}{|B||M_i|} \right).$$  \hspace{1cm} (4.3)

Other methods include the use of regularization or non-linear terms to improve the robustness or precision of model value estimation. The basis of modelling neural encoding-decoding as a linear system, as per Equation 4.1, is the premise for many classifier systems used in BCI devices (Hochberg et al., 2012; Wang et al., 2013a).

This work will use the change in power of high-frequency (62.5 - 200 Hz) ECoG in place of traditional firing rate as a surrogate for neural activity.
Hence, when decoding movement direction by summing multiple ECoG electrodes, the local ensembles as described by Georgopolous are analogous to broad cortical activation. Modelling this relationship is not intended to suggest that the cortical locations being recorded necessarily explicitly processes or organize arm movement direction related information, but rather that we can use this as a heuristic to estimate movement direction from brain activity.

Directional tuning models are often simple to invert to produce decoders. Due to their relative simplicity, they are also fast to compute. In contrast to other decoding methods, directional tuning models provide an explicit relationship between neural activity and movement direction. Unlike classification models that make decisions based on feature position in an abstract, high-dimensional space, directional tuning models represent the relationship by a simple linear system. Directional tuning models also scale well, unlike other families of models that can grow exponentially in computational cost and model dimensionality (Donoho, 2000).

This chapter presents results demonstrating that directional tuning can be observed in ECoG signals during movement preparation while undertaking a two-dimensional center-out task. Furthermore, these models could be used to predict movement direction using a population-vector approach at above chance from three of the four patients tested. Directional tuning was found broadly across cortical areas in all patients. Movement direction prediction by a population-vector is shown to be boosted by weighting channels by a signal-to-noise ratio measure.

4.2 Methods

The following sections describe the method for the generation of directional tuning models for encoding and decoding intended arm movement direction from a two-dimensional center-out task.

4.2.1 ECoG Data

The center-out task data described in Chapter 3 were used to create encoder models and then decode intended movement direction from ECoG. Analysis was undertaken with data from four patients, each selected for having com-
pleted at least 150 trials in a single session. The number of trials for each patient is shown in Table 4.1, which also shows how the trials were divided between training and testing subsets.

Table 4.1: Number of trials for center-out task, showing the total numbers of trials and then numbers of trials used for testing decoder models

<table>
<thead>
<tr>
<th>Patient</th>
<th>Total trials</th>
<th>Test trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>204</td>
<td>41</td>
</tr>
<tr>
<td>2</td>
<td>150</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>207</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>216</td>
<td>43</td>
</tr>
</tbody>
</table>

Signal Processing

Computation was undertaken on a custom-built computer with an Intel Core i7 6850k CPU. All signal processing and analyses were undertaken in MATLAB (version 9.2, R2017a). The 5 kHz ECoG signals were first down-sampled to 500 Hz. A 2nd order notch was applied at 45 Hz to 55 Hz and 145 Hz to 155 Hz to attenuate line noise and the dominant harmonic (Australian mains power is at 50 Hz). Data were taken from 500 ms to 0 ms before the onset of movement at each trial, as determined from the motion tracking device. No channels were discarded for this study.

The magnitude of the discrete Fourier transform was computed and sampled into 64 bins from 62.5 to 200 Hz:

$$X_k = \left\| \sum_{n=0}^{N-1} x(n) \exp^{-i 2\pi k n/N} \right\|,$$

where $x(n)$ is the time-domain data for each channel for each trial, $n$ is the time index, $N$ is the length of $x$ in samples and

$$k = [20, 21, \ldots, 64] \times \frac{200}{64},$$

calculating 45 points from 62.5 to 200 Hz. The lower threshold of 62.5 Hz was chosen because the range of 60-65 Hz is often described as the beginning of the high-gamma band (Ray et al., 2008a; Uhlhaas et al., 2011).
4.2. METHODS

To calculate a single feature per channel per trial, the mean of the log transformed frequency vector was calculated:

\[ y = \text{mean}(\log_{10}(X)), \quad (4.6) \]

where \( X \) is the vector of frequency magnitudes calculated for each channel for each trial. Each trial was normalized relative to resting-state data using a pseudo \( z \)-score; this scales the data such that frequency feature from each trial for each channel has approximately zero mean and each value represents the number of standard deviations a given trial is away from the resting-state mean (assuming values are normally distributed) (Wang et al., 2013a). Thus, the feature is defined as

\[ z = \frac{y - \text{mean}(y_{\text{resting}})}{\text{std}(y_{\text{resting}})}, \quad (4.7) \]

where \( y \) is a scalar representing the magnitude feature for each channel for each trial, \( \text{mean}(y_{\text{resting}}) \) is the mean of the feature calculated over a 10 minute resting period for each channel, and \( \text{std}(y_{\text{resting}}) \) the standard deviation. Note that due to the formulation of Equation 4.7, \( z \) is unitless. Resting state data was recorded during wakefulness, typically immediately prior to experiment setup, and at least three hours before or after an identified seizure event.

Tuning Signal-to-Noise Ratio

To establish if a channel demonstrated one or more peaks in signal power as a function of movement direction, a metric we define as the tuning signal-to-noise ratio (SNR) was calculated, defined as

\[ s = \frac{\sigma^2(Z)}{\frac{1}{8} \sum_{n=1}^{8} \sigma^2(Z_n)}, \quad (4.8) \]

where \( Z \) as the vector of \( z \) values for each of the \( M \) trials, \( Z_n \) are the trials corresponding to direction \( n \) and \( \sigma^2(Z) \) is the variance of all recorded power values for all movement directions for a given channel, defined as

\[ \sigma^2(Z) = \frac{1}{M} \sum_{n=1}^{M} \left( Z - \frac{1}{M} \sum_{n=1}^{M} Z \right)^2. \quad (4.9) \]
This reflects the ratio of the variance of $Z$ in all movement directions to the mean variance of $Z$ in the eight individual different movement directions (Schalk et al., 2007; Rickert et al., 2005; Mehring et al., 2003). Consequently, $\frac{1}{8} \sum_{n=1}^{8} \sigma^2(Z_n)$ is the mean of the variance of the power in each individual direction. Hence, if the variance of the power in each individual direction is low compared to the variance of all recorded power values, the SNR will be greater than one. Conversely, if the variance in each movement direction is high compared to the variance of all movements, the SNR will be close to zero. Note $\sigma^2(Z)$ is unitless as $Z$ is unitless. For each patient, the SNR of each channel was standardized by dividing by the maximum SNR.

The calculated SNR for each channel was compared to a null distribution as per Schalk et al. (2007). All values of $Z$ for each channel were assigned to the direction of a randomly chosen trial, and the tuning SNR was recalculated. This was repeated $10^6$ times to generate a null distribution of the tuning SNR for each channel. A channel was considered to have an SNR greater than chance at a significance of $\alpha = 0.05$ if the tuning SNR was greater than 95% of the null distribution.

### 4.2.2 Encoding Models

For each channel, cosine and von Mises functions were fit to the mean of the normalized change in power as a function of movement direction. These models are defined as

$$P_C = a + b \cdot \cos(\theta - \theta_C)$$  \hspace{1cm} (4.10)

and

$$P_{VM} = c + d \cdot \exp^{e \cdot \cos(\theta - \theta_{VM})},$$  \hspace{1cm} (4.11)

where $P_C$, $P_{VM}$, $\theta_C$, and $\theta_{VM}$ are the normalized ECoG power and estimated preferred tuning direction for the cosine and von Mises models, respectively, and $a$, $b$, $c$, $d$, and $e$ are constant, real numbers. Model fits were calculated using the `nlinfit` function in MATLAB, which estimates model parameters using a Levenberg-Marquardt nonlinear least-squares estimate (Seber and Wild, 2005).

Model fits were evaluated by the correlation coefficient ($r^2$) value and the
4.2. METHODS

$p$-value for the cosine function coefficient $b$, calculated from a $t$-test against the null hypothesis that $b$ was equal to zero. Hence, when $p > 0.05$, the data is not suitably represented by a cosine function.

For von Mises encoding-decoding the parameter $e$ allows for narrower or broader tuning curves to be more accurately modelled (Amirikian and Georgopulos, 2000). Non-sinusoidal tuning curves could be expected at the spatial scale of ECoG as it has previously been shown in Georgopoulos et al. (1986) that potentials recorded from neural populations encode narrower tuning curves that individual neurons.

To measure the spread of the tuning curve angles, the circular variance is measured. This was defined as

$$\gamma = 1 - R,$$

(4.12)

where

$$R = \frac{1}{N} \sqrt{\left( \sum_{n=1}^{N} \cos(\theta_n) \right)^2 + \left( \sum_{n=1}^{N} \sin(\theta_n) \right)^2},$$

(4.13)

where $\theta_i$ is the preferred tuning direction of channel $n$ and $N$ is the total number of channels. Hence $\gamma \in [0, 1]$, where $\gamma = 1$ indicates a uniform angular distribution (Fisher, 1995).

4.2.3 Directional Tuning Metrics

Due to the limited number of trials, 50 cross-validations using an $h$-block cross-validation method were used to assess model accuracy. Each cross-validation selected a random 20% of the data for testing. Then, the trial either directly before or after each test-trial was removed from the training set. This block cross-validation of $h = 1$ assumes that the trials immediately neighboring the test trials may contain more information than other trials, and hence give overly-optimistic classification results. Although the model still is not strictly causal in that training examples can be drawn from after a test trial has occurred, the block cross-validation removes the most immediate bias (Lemm et al., 2011; Billinger et al., 2012). Each cross-validation can have a different number of training trials due to this method. The mean number of training trials are 97, 72, 100 and 104 trials, for Patients 1 to 4, respectively. Decoding
models were formed for both cosine and von Mises models. As there could be a broad range of tuning SNR and $r^2$ values, models were generated and tested including one additional channel at a time, in order of decreasing tuning SNR or $r^2$ value. This was done to determine which subset(s) of channels could be used to decode with the highest accuracy.

Test trial movement angles were decoded by summing the $\mathbb{R}^2$ vector from each channel’s model and rounding to the nearest integer multiple of $45^\circ$. The angle of the vector was determined by inverting either the cosine or von Mises model to solve for the angle (Equations 4.11 and 3.5). As neither model is one-to-one, except at $\theta_{VM}$ for the von Mises model and $\theta_C$ and $\theta_C + 180^\circ$ for the cosine model, the angle was randomly selected from the two possible function values. The magnitude of the vector was calculated using three different approaches.

The first approach used unit length for each channel,

$$D = \sum_{n=1}^{N} 1 \cdot \theta_n,$$

where $D$ is the population-vector, $n$ is the number of channels, and $\theta_n$ is the decoded angle from channel $n$. As Equation 4.14 gives equal weight to each channel, it will always be biased towards the direction to which the most channels are tuned, and hence only performs at a chance accuracy for the given distribution of channels. Hence, this was used as a null distribution to compare other decoding methods to.

The second approach used a weighted population-vector as per Georgopoulos et al. (1986), which takes the vector magnitude from tuning curve model outputs:

$$D^w = \sum_{n=1}^{N} w_n \theta_n,$$

where $w_n$ is defined as

$$w_n = |P_n - \frac{1}{N} \sum P_n|$$

and $P$ is the model magnitude as defined in Equation 4.11 for channel $n$. For
the cosine model, this assumes that channel tuning is equivalently strong in both the tuned direction and in the opposite direction.

The third decoding method used the tuning SNR of each channel \( s_n \), defined in Equation 4.8) as an additional weighting to the magnitude,

\[
D^{sw} = \sum_{n=1}^{N} s_n w_n \angle \theta_n.
\]  

(4.17)

Weighting by the SNR allows channels with more distinct tuning to contribute more to the population-vector.

For all three magnitude calculation methods, channels were added in consecutive descending order of both tuning SNR and correlation coefficient values. A one-sided paired-sample \( t \)-test was used to determine if the model-weighted decoding accuracy was significantly greater than the unit vector accuracy. The same test was also used to determine if the tuning SNR weighted decoding was significantly greater than the unweighted model accuracy. Both tests were applied at a significance of \( \alpha = 0.01 \) at each cross-validation.

4.3 Results

4.3.1 Encoding Directional Tuning

For each patient, encoder models were generated using every trial to determine the presence of directional tuning in the data. An example of a tuning curve is shown in Figure 4.1. Note that two cycles of \( \theta \) have been plotted. It can be seen for this representative channel that both models have similar preferred tuning directions, with a phase difference of \( 7^\circ \). The von Mises function had a higher \( r^2 \) value for this channel; however, this is to be expected due to the extra parameter that is used to define the curve. Note that, for this channel, the tuning curve models demonstrate not only an increase in neural activity compared to baseline when moving in the preferred direction, but also a decrease when moving opposite to the preferred direction.

The tuning signal-to-noise ratio (SNR) of each channel that was above chance is shown in Figure 4.2. Non-significantly tuned channels are shown as small black dots. Note that the map of Patient 1 has been flipped in the
Figure 4.1: Example tuning curve from an individual channel. y-axis represents normalized change in power compared to baseline. 0° refers to a movement directly away from the body, with the angle increasing anti-clockwise. Blue bars indicate mean ± standard deviation. Orange and yellow curves show fitted cosine and von Mises distributions, respectively. Note that x-axis repeats for two cycles.

anterior-posterior axis as they had electrodes implanted on the right hemisphere. Patients 1-4 had 19/90 (21%), 9/32 (28%), 10/56 (18%), and 20/56 (36%) significantly tuned channels, respectively. Several significantly tuned channels were not spatially contiguous with other tuned channels, with Patients 1-4 having 3/19 (16%), 3/9 (33%), 5/10 (50%) and 1/20 (5%) non-contiguous channels. Note that the locations of tuned electrodes extended broadly across the recording area for all patients, and was not confined to primary motor areas.

The preferred direction of the cosine model of each significantly tuned channel is shown in Figure 4.3. Channels not significantly tuned are represented by a black dot. As with Figure 4.2, Patient 1’s map has been flipped in the anterior-posterior axis. It can be seen that some neighboring electrodes are tuned to similar angles, implying that these electrodes are recording correlated ECoG signals. The corresponding preferred tuning direction of the von Mises
Figure 4.2: Spatial map of tuning signal-to-noise ratio (SNR) of significantly tuned channels for each of the four participants. Non-tuned channels are represented as small black dots. Note color scale is in arbitrary units. Arrows refer to superior, posterior, inferior and anterior directions. Note that Patient 1’s map is flipped in the anterior-posterior axis as they were the only patient to be implanted on the right hemisphere. Note the brains shown are not patient-specific and are for illustrative purposes only.
models for each channel are within $10^\circ$ difference.

![Brain images showing tuning directions for different patients](image)

**Figure 4.3:** Spatial map of tuning direction of significantly tuned channels for each of the four participants. Non-tuned channels are represented as small black dots. Note that color map is circular, in that $0^\circ$ and $360^\circ$ are represented by the same color. Arrows refer to superior, posterior, inferior and anterior directions. Note that Patient 1’s map is flipped in the anterior-posterior axis as they were the only patient to be implanted on the right hemisphere. Note the brains shown are not patient-specific and are for illustrative purposes only.

Figure 4.4 shows the histogram of tuning angle distribution for each patient, binned into $45^\circ$ arcs centered at each of the eight movement directions. The circular variance (as defined in Equation 4.12) is also shown for each patient. The variance for each patient is greater than 0.5, indicating moderate to high high circular spread of preferred tuning directions. Patient 3 had the lowest variance of 0.63, and Patient 1 had the highest with 0.82. Note that none of the patients had significantly tuned channels in all of the eight movement directions, and Patient 3 only had tuned channels in five of the eight directions.

The spatial maps of the correlation coefficient values for the fits to the cosine model are shown in Figure 4.5. Note that channels where the value of $b$ (the coefficient of the cos term from Equation 4.11) was not significantly different from zero at $\alpha = 0.05$ are not filled. These channels likely had multiple separated peaks or narrow peaks, as they had a significantly high tuning
SNR, but do not fit significantly well to the cosine curve. For Patients 1-4 3/19 (16%), 5/9 (56%), 3/10 (30%), and 7/20 (35%) of the channels with a significant SNR did not have significant cosine tuning.

Histograms of the correlation coefficient values for fits to the cosine model are shown in Figure 4.6. All patients had a median at approximately 0.5, indicating modest goodness of fit to the model.

### 4.3.2 Decoding Movement Direction

After creating models that described how the channels encoded movement, decoding was undertaken by computing the population-vector from inverted encoding models. Decoding was performed using a standard population-vector approach, as well as a tuning SNR-weighted population-vector. For each weighting method, two methods of introducing channels to the model were also explored: ordering by tuning SNR and ordering by model correlation coefficient value (either cosine or von Mises, depending on the encoding model).

Figure 4.7 shows the decoding accuracy of the cosine-based models. For
Figure 4.5: Spatial map of $r^2$ values for the cosine model for significantly tuned channels. Channels with non-significant SNR are represented as small black dots. Channels with non-significant $r^2$ values ($p < 0.05$, $t$-test), but significant tuning SNR are shown as non-filled circles. Arrows refer to superior, posterior, inferior and anterior directions. Note that Patient 1’s map is flipped in the anterior-posterior axis as they were the only patient to be implanted on the right hemisphere. Note the brains shown are not patient-specific and are for illustrative purposes only.
4.3. RESULTS

Figure 4.6: Histogram of $r^2$ values for each of the four patients. The median $r^2$ value for each patient is 0.42, 0.40, 0.38 and 0.44, respectively.

all patients, several combinations of channels for the model-weighted decoder (shown in red) gave significantly higher output than the unit weighting (shown in blue, note chance decoding accuracy is approximately 12.5%), with the exception of Patient 3. Patient 3 had relatively few well-tuned channels, which could explain the poor decoding accuracy. The tuning SNR-weighted model (shown in green) significantly improved the results for Patient 2 for both methods of channel selection where, particularly for the tuning SNR threshold case, the population-vector was not significantly above chance for many combinations of channels. For Patient 4 the mean decoding accuracy fluctuates as more channels are added, which is potentially a result of having a high percentage of significantly tuned channels (36% of total channels), that were all making relatively large contributions to the population-vector.

Figure 4.8 shows the decoding accuracy of the von Mises models. Like the cosine-based models, Patient 3 did no better than chance for any of the presented combination of channels. Patient 1 did significantly better with tuning SNR weighting than the standard population-vector for all channel combinations using 54 -64 channels. Decoding accuracy for all patients increased up
Figure 4.7: Decoding accuracy as a function of number of channels used in cosine model. Plots represent mean ± standard deviation. Blue plot represents unit length vector, red the population-vector and green the tuning SNR-weighted population-vector. Black line represents normalized threshold value (either $r^2$ or tuning SNR). Black dots show when population-vector distribution is significantly higher than the unit vector decoded at $\alpha = 0.01$ for a single-sided paired t-test. Black plus symbols show when tuning SNR weighted population-vector distribution is significantly higher than the standard population-vector at $\alpha = 0.01$ for a single-sided paired t-test. PV: population-vector. SNR: Signal-to-noise ratio.
until approximately 10-20 channels and then remained somewhat consistent. Peak decoding accuracies were not be notably higher than cosine model equivalents.

Table 4.2 shows the peak mean decoding accuracy for each model. Patient 4 had the highest peak decoding accuracy with 48.0%. Although Patient 3’s peak accuracy of 17.7% is above the naive chance accuracy of 12.5%, it was not significantly above the null distribution for any combination of channels.

Table 4.2: Peak mean decoding accuracy for each model combination. Bold indicates highest decoding accuracy for each patient. thr = Threshold, PV = Population vector, SNR-PV = tuning SNR weighed population vector

<table>
<thead>
<tr>
<th>Model</th>
<th>Cosine</th>
<th>von Mises</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r^2$ thr.</td>
<td>SNR thr.</td>
</tr>
<tr>
<td>Vector Length</td>
<td>PV</td>
<td>SNR-PV</td>
</tr>
<tr>
<td>Patient 1</td>
<td>21.2</td>
<td>35.3</td>
</tr>
<tr>
<td>Patient 2</td>
<td>18.45</td>
<td>38.6</td>
</tr>
<tr>
<td>Patient 3</td>
<td>17.7</td>
<td>15.0</td>
</tr>
<tr>
<td>Patient 4</td>
<td>25.6</td>
<td>48.0</td>
</tr>
</tbody>
</table>

4.4 Discussion

The relationship between motor neuron firing rates, cortical potentials and direction of upper-limb movement is well documented (Georgopoulos, 1991). The existence of directional tuning in high-frequency ECoG motivates the use of physiologically-inspired population-vector decoder models for use in BCI systems.

This work showed that all four patients in this study demonstrated directional tuning of high-frequency ECoG across the recording arrays. Relatively poor, although above-chance, decoding using a population-vector approach was achieved for three of four patients.

Figure 4.2 demonstrated that all patients had channels which exhibit above-chance tuning SNR but non-significant fit to a cosine model (at $\alpha = 0.05$). This implies that channels did not necessarily have one individual peak in their activation distribution, or that the peak was overly narrow or broad. The use of the sum of multiple sinusoids, or a polynomial function, could potentially
Figure 4.8: Decoding accuracy as a function of number of channels used in von Mises model. Plots represent mean ± standard deviation. Blue plot represents unit vector length vector, red the population-vector and green the tuning SNR-weighted population-vector. Black line represents normalized threshold value (either $r^2$ or tuning SNR). Black dots show when population-vector distribution is significantly higher than the unit vector decoded at $\alpha = 0.01$ for a single-sided paired $t$-test. Black plus symbols show when the tuning SNR weighted population-vector distribution is significantly higher than the standard population-vector at $\alpha = 0.01$ for a single-sided paired $t$-test.
more accurately encode the response of each channel; however, this would create complications for inversion as these could have > 2 angles corresponding to each neural activation value. Decoding only using channels that demonstrate significant unimodal tuning could improve results, but as shown in the $r^2$ thresholded results in Figures 4.7 and 4.8, decoding using only the highest $r^2$ value channels often performs no significantly better than chance. Decoding results showed that when optimizing the population-vector, a trade-off exists between decoding only with channels that exhibit strong direction tuning, and utilizing as much information as possible from the recorded data.

The use of von Mises functions over cosine functions for modelling the encoding of movement is potentially advantageous, as the additional parameter $e$ in Equation 4.11 means that channels with different widths of tuning can be well represented by the same model. However, from Figures 4.7 and 4.8 it can be seen that the decoding accuracy from von Mises models was not distinctly higher than that from cosine models. Undertaking experiments that allow for movements at more angles, such as a joystick task, would increase the angular resolution of the modelled tuning curves and hence could take better advantage of the additional model parameter.

It can be seen that the tuning angles for several neighboring electrodes are dissimilar (for example the most superior-posterior electrodes of Patient 4). How these discontinuities relate to cortical anatomical and gross functional structure remains unclear from this work. Future work in understanding the spatial distribution of fine motor function across cortex will be important to future ECoG BCI surgical planning, such that potential information being recorded is maximized.

The bias of the distribution of preferred angles for Patient 3 is likely to be the cause of the chance-level decoding results. This may be due to Patient 3’s surgical history, as they were on the only one in the cohort to have had a previous cortical resection, and also had taken part in a medical device trial involving long-term sub-dural ECoG electrode implantation (see Cook et al. (2013) for further detail). These previous surgeries would have disrupted and damaged the organization of the cortex, leading to the inability to successfully decode movement from their ECoG. Their electrode locations were also more dorsal than the other patients. It will be important to explore how directional
4.4. DISCUSSION

For each of the patients with decoding accuracy significantly above chance, the tuning SNR-weighted population-vector had the overall highest mean accuracy. This indicates that the tuning SNR weighting is justified as a method of increasing decoding performance. Non-weighted population-vector decoding relies on the magnitude of the tuning model, and hence channels with ‘shallow’ tuning (i.e. \( w_n \) is close to zero) will make minimal contribution to the population-vector. The weighting by tuning SNR allows channels that demonstrate higher variance across classes to contribute more to the population-vector, and hence more ‘shallow’ tuned channels will make less of a contribution. The significantly improved classification accuracy of the tuning SNR-weighted model justifies its use as an enhancement of the standard population-vector model.

The angular variance of the significantly tuned channel directions was lowest for Patient 3, who also had the lowest decoding performance. It is not clear from the patients with above-chance decoding how angular variance relates to peak decoding accuracy, as Patient 1 has the broadest distribution but the lowest peak decoding accuracy. Data from more patients and with more significantly tuned channels will be required to further elucidate how the angular variance distribution and peak decoding accuracies are related, if at all.

The use of tuning SNR weighting increased the decoding accuracy for all patients with above-chance decoding, for particular combinations of channels. It is unclear from the methods used how including or excluding specific channels can help improve decoding accuracy, other than decoding accuracy improves up until approximately 15 channels have been used. Tuning SNR weighting generally improved both cosine and von Mises decoding results, which is to be expected at it is derived from the data distribution, and therefore is not model specific.

Ideally, more trials for all movement directions could be recorded such that the distributions of each channel can be more precisely determined. Given the relatively limited number of trials in the current data set, it may be that the reliance on the mean value of the feature is biasing the fitting of the encoder...
models. Use of other descriptions of the average such as the median may improve results for both encoding and decoding of the directional tuning models, as the average will be less biased by outlier values.

This work has focused on decoding of movement direction as a discrete classification, as opposed to a continuous decoding of arm kinematics. As such it is difficult to directly quantitatively compare to other studies discussed herein. Similar to other studies, this work has shown that ECoG encodes intended arm movement direction in the high-gamma band, and that movement direction can be decoded from this signal.

It should be noted that this work has only focused on decoding movement direction and not any aspects of the magnitude of movement kinematics or dynamics (i.e. electromyography amplitude, force, speed, acceleration). Further investigation of how ECoG encodes magnitude-related aspects of movement, and how these spatially relate to directional aspects of movement will be important in improved understanding of the motor system and the performance of BCI technologies.

The physical nature of ECoG, and what it is that the recorded signal precisely represents, is still an open area of research. Hence, the existence of tuning curves and above-chance population-vector results in ECoG recordings, and how they relate to directionally tuned neurons, is unclear. Further understanding of how neurons and neuronal populations integrate over time and space to form ECoG potentials may lead to more sophisticated encoder-decoder models that provide higher decoder acuity. Dynamic models such as the neural mass model may prove to provide such decoders (David and Friston, 2003; Bhatt et al., 2016).

The ability to decode intended movement direction from relatively simple encoder models suggests that the center-out task data recorded in Chapter 3 contains sufficient information to pursue more complex decoding methods. Although the results presented in Figures 4.7 and 4.8 are poor, they suggest that more sophisticated approaches to movement intention prediction will be more accurate. The assumption that all relevant information to movement direction is encoded in a cosine model is of course a highly simplified abstraction of a complex phenomenon, and has resulted in low-accuracy, and likely sub-optimal
decoding in this study. Other signal features such as signal power changes in narrow frequency bands, information theory features, and time domain features of scalp electroencephalography and ECoG have also shown to encode information related to movement direction (Nicolas-Alonso and Gomez-Gil, 2012). Hence, methods such as artificial neural networks are motivated due to their ability to provide high-accuracy classification with minimal prior feature calculation (LeCun et al., 2015). This will be investigated in Chapter 5.

4.5 Conclusion

This chapter has presented directional tuning encoder-decoder models of high-frequency ECoG activity during human arm movements. It was demonstrated that all patients in this study showed evidence of directional tuning across many cortical areas during a 2D center-out task. Cosine and von Mises based models were investigated as the basis for population-vector based decoding, with no discernable difference in decoding accuracy between the two models. Decoding significantly above chance was achieved in three of four patients, however even above chance decoding was poor. It is not clear why one patient had non-significant decoding, but may be due to over-representation of a single movement direction, and previous cortical surgeries. The use of each channel's tuning signal-to-noise ratio was evaluated as a weighting method for population-vector decoding, and increased peak decoding accuracies for all patients. Decoding accuracy appears to peak after approximately 15 channels are used, and plateau after this point. Overall, it was demonstrated that ECoG partially encodes arm movement direction in high-frequency signal features, which can then be used to decode intended movement at above chance accuracy.
Chapter 5

Artificial Neural Networks for Decoding Movement Direction from Electrocorticography

The previous Chapters have demonstrated that electrocorticography (ECoG) is stable and contains important information for directional decoding of arm movements. This Chapter will assess the use of artificial neural network models to decode movement from ECoG in humans.

5.1 Introduction

This chapter contributes to knowledge by addressing the following hypothesis, that is untested in the current literature, that: a) Convolutional neural network (CNN) models can decode movement direction from ECoG, and b) CNN decoding accuracy can be improved by aggregating data from multiple time-points and pre-training networks on multiple patients’ data. CNN models are an appealing option for neural signal decoding, due to their ability to make complex decision boundaries between data classes.

To perform robust classification, different classes of inputs must be separable by a decision boundary. Hence, the data itself must inherently occupy different regions of the domain (such that there is minimal overlap between the distribution of classes), or must be transformed such that it does. A linear classifier can only separate the input space into half-spaces, separated by a hyper-plane (Ro and Pe, 1973). Many pattern recognition problems require
the classification algorithm to be robust to irrelevant input variation but sensitive to particular minor variations. For example, a speech-to-text classifier should be robust to different accents and pitches of voice, but still be able to discern the difference between similar words.

Consider the problem of trying to discriminate whether an image has a cat or a dog in it. This is a task an infant can achieve with high accuracy although it is something that a machine learning has only recently been able to robustly solve. Typically, features that identify individual classes are explicitly defined programmatically. For the problem of differentiating between cats and dogs, many of these features may be common to both classes (i.e. fur, four legs, two eyes). To further complicate the problem, the labels ‘cat’ and ‘dog’ correspond to highly heterogeneous image classes (i.e. the difference between a German shepherd and a pug). To accurately discriminate between these two classes, many abstract, high-level features are required to make the distinction.

Artificial neural network (ANN) models create a decision-making boundary through reinforcement learning. Network weights are learnt via representative data examples, by changing connection strengths between neurons such that the classification error is minimized (further details will be explained in Section 5.2.3). As the input data is propagated through the network, the neurons can be thought to perform dimension reduction that maximally separates classes; then the final layer creates a decision boundary. With each layer, the data becomes more abstracted from the input space and (ideally) more separable. As each layer learns a non-linear input-output mapping, the network becomes more sensitive to class-specific variations and more robust to irrelevant input variation. This minimizes the need for human engineering of features, by allowing for highly abstract features to be learned from high-dimensional, input data, instead of predefined features.

ANN models have achieved previously unprecedented advances in classification accuracy across a range of fields. In 2012 an ANN model made a dramatic improvement on previous results in the ImageNet competition (classifying about one million images into 1000 different classes), half the error of the previous-best algorithm (Krizhevsky et al., 2012). This network was novel in its depth, having eight layers of neurons, and its selection of neuron type and weight initialization to minimize the ‘vanishing weight problem’ (this will
be further discussed in Section 5.2.3. ANNs have also been used for more specific image classification problems, such as face recognition (Taigman et al., 2014) and traffic sign detection (Cireş An et al., 2012). Significant improvements have also been made in other fields, such as speech recognition (Dahl et al., 2012), text translation (Sutskever et al., 2014) and image captioning (Xu et al., 2015). Hence, ANN models are capable of producing solutions to a diverse range of classification problems.

Various disadvantages of ANNs have been overcome since the early 2000’s, which have led to the increasing popularity of ANN models for data classification. Compared to simpler models such as logistic regression, the process of optimizing the weight space of ANNs is very computationally expensive. The training algorithm has been greatly sped-up by parallelizing the process on graphics processing units (GPUs) (Raina et al., 2009). Training processes have also been made faster by the introduction of stochastic gradient descent, where the training set is split into many ‘mini-batches’ that each give a noisy estimate of the optimal weight space over all examples. This produces a weight space of similar optimality to other training techniques, but with far fewer iterations required for the model to converge (Bousquet and Bottou, 2008).

ANN models have many properties that are highly desirable in the analysis of brain signals. Robustness to noise and non-relevant variance in input data demonstrated in other applications is highly desirable as a form of artifact rejection. As there is an incomplete knowledge of the physics underlying the generation of ECoG signals, analyses can benefit from the abstract, ‘black-box’ mapping from the input space to an output decision.

This chapter shows that fully connected (FC) networks and convolutional neural networks (CNNs) can achieve high accuracy in decoding movement from electrocorticography (ECoG) during a finger-tapping task. The CNN achieved a higher accuracy than the FC model for all patients. In this proof-of-concept study, we also demonstrate that CNNs can achieve well above chance classification accuracy during an eight-class center-out task. CNN models significantly out-perform FC models for all patients for the center-out task. Training CNN models on multiple time points for each trial and choosing a movement direction based on the mode of the network outputs boosted performance in three of four patients. This chapter concludes that the high-dimensional, non-linear
transformation learned by the CNN is well-suited to compensate for the low separability inherent in ECoG spectrograms.

5.2 Methods

5.2.1 ECoG Data

Finger-tapping task

The data collected from Patient 4 undertaking a finger-tapping task (described in Chapter 3) was used to construct decoder models to distinguish between movement and resting states, as well as imagined movement and resting states.

Center-out task

The center-out task data described in Chapter 3 were used to construct decoder models of intended movement direction from ECoG. The number of trials used for each patient is shown in Table 5.1.

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Training trials</th>
<th>Test trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>163</td>
<td>41</td>
</tr>
<tr>
<td>2</td>
<td>120</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>166</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>173</td>
<td>43</td>
</tr>
</tbody>
</table>

Due to the relatively limited number of training (80% of total) and testing (20% of total) trials (used to learn model weights and assess model accuracy, respectively), cross-validation is necessary to assess if the proposed models are reliably able to robustly classify the data. As Patient 2 has only 30 test trials, we would expect we will only be able to test 3-4 trials per class for each model, as the center-out task had eight possible movement directions.

Signal Processing

Primary motor cortex location was determined anatomically from the CT images (by identifying the gyrus anterior to the central sulcus) and through clini-
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cal functional stimulation, looking for cortical areas where patients experienced hand or arm muscle contraction of the contralateral limb during stimulation. Stimulation was undertaken using 0.5ms square-wave, charge-balanced pulses of amplitude in the range 1-10 mA. Pulses were delivered in a train of duration 1s containing 50 pulses. Functional stimulation was undertaken by a neurologist, at least three days after implantation, and at least 24 hours prior to experimentation. The $4 \times 4$ electrodes covering hand and arm areas identified by stimulation were selected for further analysis to minimize the size of the input data, and standardize the size between patients. The electrodes used for decoding for each patient are shown in red boxes in Figure 5.1. Due to different electrode sizes and spacing, the electrodes selected for each patient are not necessarily the same. However, a $4 \times 4$ selection of electrodes is still used so that the input size of the network input is uniform between patients.

![Figure 5.1: Co-registered CT-MRI imaging of electrode placement for each patient. $4 \times 4$ grid selected for each patient is outlined in red.](image)

The 5 kHz ECoG signals were first down-sampled to 1 kHz. A 2nd order Butterworth notch filter was applied at 45 to 55 and 145 to 155 Hz to attenuate line noise and the dominant harmonic (Australian mains power is at 50 Hz). Data was taken from 500 ms to 0 ms before the onset of movement at each
5.2. METHODS

trial, as determined from the motion tracking device. The magnitude of the discrete Fourier transform was then computed and log transformed such that

$$X_k = \log_{10} \left( \sum_{n=0}^{N-1} x(n) \exp^{-i \frac{2\pi n}{N}} \right),$$  

(5.1)

where $x(n)$ is the time-domain data for each channel for each trial, $n$ is the time index, $N$ is the length of $x$ in samples and

$$k = [1, 2, ..., 60] \times \frac{200}{60},$$  

(5.2)

calculating 60 points from 3.3 to 200 Hz.

Data from each of the 16 electrodes is represented by 60 frequency features, totaling an input feature space of size 960. Each trial was then normalized using a pseudo $z$-score. This scales the data such that frequency features from each trial have zero mean and values approximately representing the number of standard deviations away from the mean a given feature is (assuming values are normally distributed) (Wang et al., 2013a; LeCun et al., 1998). This is defined as

$$\tilde{X} = \frac{X - \text{mean}(X)}{\text{std}(X)},$$  

(5.3)

where $\text{mean}(X)$ is the mean of the data for each trial, and $\text{std}(X)$ the standard deviation. Each trial was then re-arranged into a three-dimensional representation, separating the 60 frequency features across three $\mathbb{R}^2$ matrices. That is, each trial is now represented by a matrix of size $[16, 20, 3]$, with the first entry of the third dimension representing features in the band 0 - 67 Hz, the second in the band 67 - 133 Hz, and the third in the band 133 - 200 Hz. A sample input is shown in Figure 5.2.

5.2.2 Dimension Reduction Methods

Dimension reduction using principle components analysis (PCA) was undertaken to demonstrate the complexity of the center-out classification problem and visualize how the network is performing. Briefly, PCA transforms data to an uncorrelated, orthogonal basis, such that the variance of the low-dimensional representation is maximized (Abdi and Williams, 2010). To do
5.2. METHODS

Figure 5.2: Example input for a given trial. Each column represents an ECoG channel, raster scanned from left to right. Each row represents a frequency feature. The left image represents features in the band 0-67 Hz, the middle in the band 67 - 133 Hz, and the right in the band 133 - 200 Hz. All images share the same unitless color-scale.

this, the eigenvalues and eigenvectors of the data correlation matrix are computed. Then eigenvectors corresponding to the chosen number of largest eigenvalues are used to reconstruct the data in a space spanned by the selected eigenvalues,

\[
\hat{X} = \tilde{X}VV^T,
\]

where

\[
V = eig_2(\tilde{X}\tilde{X}^T)
\]

and \( \tilde{X} \) is the two-dimensional data matrix of \([\text{trials} \times \text{features}]\) and \( eig_2 \) computes the first two eigenvectors, selected as those corresponding to the eigenvalues with the largest magnitude. Hence, data that becomes clustered and separable after this process are likely to be well classified by linear classification methods. The quality of the dimension reduction is often reported as the percentage of variance explained of the original data by the dimension reduced data (Ringnér, 2008; Nakasatp et al., 1994).

5.2.3 Classification Models

For this work, two ANN classification models were evaluated for each of the two aforementioned tasks. The theory and how they were applied to classifying ECoG data are explained in this section.
5.2. METHODS

Description of Backpropagation

The fully connected (FC) neural network, or multilayer perceptron, is a class of feed-forward ANN consisting of an input, output, and one or more hidden layers neurons (Rumelhart et al., 1986). The hidden layer(s) allow FC networks to approximate any continuous function on a compact subset of \( \mathbb{R}^n \) (Hornik, 1991). Without hidden layers, these networks are limited to only robustly classifying linearly separable data, and cannot, for example, approximate the Boolean XOR function (Minsky and Papert, 1988).

Each neuron, with the exception of those in the input layer, is characterized by weighted inputs, a bias, and a non-linear activation function. Activation functions are typically sigmoid functions, and must necessarily be differentiable at all points for weight training. Two common activation functions are described by:

\[
y(p_i) = \frac{\alpha}{1 + \exp(-\beta v_i)},
\]

(5.6)

and

\[
y(p_i) = \gamma \cdot \tanh(\lambda \cdot v_i) = \gamma \cdot \frac{\exp^{\lambda v_i} - \exp^{-\lambda v_i}}{\exp^{\lambda v_i} + \exp^{-\lambda v_i}}.
\]

(5.7)

Here, \( y_i \) is the output of the neuron, \( \alpha, \beta, \gamma \) and \( \lambda \) are real, non-zero coefficients and \( v_i \) is the weighted sum of the inputs (including the bias) to the neuron:

\[
v_i = \sum_j w_{ij} y_j + b_j;
\]

(5.8)

where weight \( w_{ij} \) connects neuron \( i \) in one layer to neuron \( j \) in the next, and \( b_j \) is the bias of neuron \( j \). The first activation function describes a logistic function that ranges from 0 to \( \alpha \). The second is a hyperbolic tangent, which has a similar shape, but ranges from \(-\gamma\) to \(\gamma\), hence also simulates inhibitory activation. These are illustrated in Figure 5.3.

For this work, only hyperbolic tangent functions will be considered. This is primarily so that the variance of the output of neurons (assuming coefficients are selected appropriately, i.e. \( \gamma = 1.72, \lambda = 0.66 \)) will be close to 1 for input data with variance 1. Particularly, \( y(\pm 1) = \mp 1, y(0) = 0 \), and \( \max(y''(x)) \) occurs at \( x = 1 \). All of these properties are desirable as they minimize the risk that the output will approach \( \pm \infty \) and a zero input corresponds to zero output (LeCun et al., 1998).
Each neuron in each layer connects to the next layer (hence ‘fully connected’) with a weight $w_{ij}$ connecting neuron $i$ in one layer to neuron $j$ in the next. These weights are typically initially generated randomly from a Gaussian distribution, and are learned in a supervised manner through backpropagation. Weights are changed after each input training example is processed, proportional to the amount of error between the generated output and the known result. The error in output neuron $j$ for the $m$th training example is calculated as:

$$
\delta_j(m) = d_j(m) - y_j(w, m),
$$

where $d$ is the target output, and $y$ the output value produced by the network. The weights are adjusted to minimize the mean-squared error,

$$
\argmin_w E(m) = \frac{1}{2} \sum_j \delta_j^2(m).
$$

Most networks adjust weights based on gradient descent methods, which define the change in each weight as

$$
\Delta w_{ij}(m) = -\eta \frac{\partial E(m)}{\partial w_{ij}} = -\eta \frac{\partial E(m)}{\partial v_j(m)} y_i(m),
$$

where $\eta$ is the learning rate of the network. The learning rate is often decreased as the training error decreases. It can be shown that this partial derivative is equivalent to:
\[
- \frac{\partial E(m)}{\partial v_j(m)} = \delta_j(m)\phi'(v_j(m)) = \phi'(v_j(m)) \sum_k \frac{\partial E(m)}{\partial v_k(m)} w_{kj}(m), 
\]  
(5.12)

where \( \phi' \) is the first derivative of the activation function. Hence, the change in error with respect to the input of output neuron \( j \) depends on the change in weights of the \( k \)th neurons, which represent the output layer. So, for the hidden layer weights to change, the output layer weights change according to the derivative of the neural activation function. As such, this algorithm represents a backpropagation of the model error.

Commonly during training dropout is used to increase generalizability of models. All weights leading into a given neuron randomly to zero for a single training example (Srivastava et al., 2014). This is done to minimize the effects of overfitting, as certain neurons will never be exposed to some training examples, as they are ‘switched off’ during training on that example.

**Convolutional Neural Network**

Convolutional neural networks (CNNs) are a variation of FC networks designed to minimize the number of weights required in each layer of a network. Convolutional layers learn sets of filters (or kernels) that are convolved across the input matrix to produce an output activation map of the filter (LeCun et al., 2015). The network learns filters that amplify specific patterns in input data. Due to this convolution process, the learned features are translation (or shift) invariant, transferring information to the next layer regardless of the position of the pattern in the data. For example, a network designed to recognize faces would learn features that would activate when convolved with an image segment of a nose, regardless of if it was in the top left or bottom right of the image. Hence, CNNs typically have less weights than an FC network with the same number of neurons. However, they require more network parameters to be set, such as the size and stride (distance that the filter moves each step during convolution) of the kernels.

Typically, two further steps are undertaken before the activation map is processed by the next layer. First, each feature map output is linearly rectified,

\[
f(x) = \max(0, x). 
\]  
(5.13)
5.2. METHODS

This generally speeds up learning due to many weights being set to zero and increasing the sparsity of the propagation of activation (Glorot et al., 2011). Second, the activations are down-sampled (also called ‘pooled’), typically using a maximum function over an area of the activation, with a stride of greater than one (i.e. under-sampling the activation matrix). For example, a $4 \times 4$ activation function pooled with a $2 \times 2$ filter with a stride of 2 in each dimension will produce a $2 \times 2$ output, reducing the size by a factor of 4, and only propagating the highest, non-negative activations. Hence the output of these post-convolution layer is a non-negative, down-sampled version of the original activation. Pooling also means subsequent layers typically have to learn less weights, decreasing computational requirements and model dimensionality. Other functions such as mean or $\ell^2$ norm have also been used for down-sampling; however, they tend to produce less accurate networks than linear rectification (Scherer et al., 2010).

Generally, multiple layers of convolution and subsequent processing are used to create more complex features, followed by FC layers to map these features non-linearly to output neurons. Typically, the first convolutional layer will learn basic features such as edges (with kernels often resembling Gabor filters), with subsequent layers learning more complex curves and details from images. In the case of the ECoG data, kernels are able to learn increasingly complex features spanning electrodes and frequency features.

The final network layer is typically a softmax (or normalized exponential) function,

$$g(x_m) = \frac{\exp^{y_m}}{\sum_{k=1}^{K} \exp^{y_k}}, \quad m = 1, \ldots, K,$$

(5.14)

where $y_m$ is the activation of the neurons in the output layer, $K$ is the total number of outputs and $g(x)$ has values in the range $[0,1]$ and $\sum g(y_m) = 1$.

Network Training and Parameters

Neural network models were trained in MATLAB (version 9.2, R2017a) using the Neural Network Toolbox. Computation was undertaken on a custom-built machine, using an NVIDIA Titan X Pascal GPU and an Intel Core i7 6850k CPU. Each model was trained on a randomly selected 80% of the $N$ total
trials and performance was assessed using the remaining 20% of trials. This was repeated 50 times per model.

The training data was augmented by adding five replications of the data each with additive noise,

\[ h(\tilde{X}) = \tilde{X} + 0.2 \cdot \epsilon, \]  
\[ \epsilon \sim \mathcal{N}(0, 1), \]

where \( \tilde{X} \) is each value in the original training set (note mean(\( \tilde{X} \)) = 0 and var(\( \tilde{X} \)) = 1), and \( \mathcal{N}(0, 1) \) is the unit normal distribution. Augmenting training data has been shown to improve model generalizability in various image recognition problems (Krizhevsky et al., 2012).

**Finger-drumming task**

FC networks to decode finger-drumming were produced using the hyperparameters shown in Table 5.2.

<table>
<thead>
<tr>
<th>Layer Number</th>
<th>Type</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fully connected</td>
<td>128</td>
</tr>
<tr>
<td>2</td>
<td>Fully connected</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>Fully connected</td>
<td>2</td>
</tr>
</tbody>
</table>

CNNs for the finger-drumming task were constructed using the hyperparameters listed in Table 5.3.

For both models, learning was undertaken using stochastic gradient descent, with an initial learning rate of 0.1. Learning occurred for 500 epochs, with the learning rate decreasing by a factor of 10 every 75 epochs. Model training was implemented using MATLAB’s built in `TrainNetwork` function from the Neural Network toolbox. For all models presented in this chapter, a dropout rate of 30% was applied to all convolutional and fully connected layers.
Table 5.3: CNN model parameters for finger-drumming task. Total number of weight and bias parameters was 1554.

<table>
<thead>
<tr>
<th>Layer Number</th>
<th>Type</th>
<th>Size</th>
<th>Stride</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Convolution</td>
<td>10 × [8,4]</td>
<td>[2,2]</td>
</tr>
<tr>
<td>1</td>
<td>Rectified linear unit</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>Maximum pooling</td>
<td>[2,2]</td>
<td>[2,2]</td>
</tr>
<tr>
<td>2</td>
<td>Convolution</td>
<td>10 × [2,2]</td>
<td>[1,1]</td>
</tr>
<tr>
<td>2</td>
<td>Rectified linear unit</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Fully connected</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Fully connected</td>
<td>2</td>
<td>-</td>
</tr>
</tbody>
</table>

Center-out task
FC networks for the center-out task were constructed using the hyperparameters listed in Table 5.4.

Table 5.4: FC model parameters for center-out task. Total number of weight and bias parameters was 31416.

<table>
<thead>
<tr>
<th>Layer Number</th>
<th>Type</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fully connected</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>Fully connected</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>Fully connected</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 5.5: Center-out ask CNN model parameters. Total number of weight and bias parameters was 10888.

<table>
<thead>
<tr>
<th>Layer Number</th>
<th>Type</th>
<th>Size</th>
<th>Stride</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Convolution</td>
<td>16 × [10,1]</td>
<td>[1,1]</td>
</tr>
<tr>
<td>1</td>
<td>Rectified linear unit</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>Maximum pooling</td>
<td>[2,2]</td>
<td>[2,2]</td>
</tr>
<tr>
<td>2</td>
<td>Fully connected</td>
<td>16</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Fully connected</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>

CNNs for the center-out task were constructed using the hyperparameters listed in Table 5.5. For both models, learning was undertaken using stochastic gradient descent, with an initial learning rate of 0.1. Learning occurred for 1000 epochs, with the learning rate decreasing by a factor of 10 every 200 epochs. All network layer, size, and training parameters were selected on a trial-and-error basis.
5.2. METHODS

Transfer Learning

The use of pre-training models on other data, before training on the pertinent data (so-called transfer-learning (Oquab et al., 2014)) was explored for the center-out task. Transfer learning is known to improve accuracy by initializing the weight space such that features are pre-trained on similar data, as opposed to being initialized randomly. The model described in Table 5.5 was used, with learning occurring for 5000 iterations, decreasing by a factor of 10 every 100 epochs. First, the model was trained on data from three patients (the pre-training set), followed by 80% of the remaining patient, with the remaining 20% of the given patient’s data set aside for testing.

Decoding using Multiple Time Windows

In order to explore the decoding potential of CNNs over multiple time windows, ECoG decoding was also performed using spectrograms from multiple time-points before the onset of movement. Four further spectrograms were calculated for each trial using the method described in Section 5.2.1, but with the ECoG data taken from $[-900, -400]$, $[-800, -300]$, $[-700, -200]$ and $[-600, -100]$ ms before the onset of movement. Including the data from $[-500, 0]$ ms, each trial was represented by five spectrograms. CNN models were trained using data from all five time windows for each trial. This was repeated 50 times for different training and testing splits. The network and learning parameters described in Table 5.5 were used. The predicted movement direction for each trial was generated by a voting scheme. The voting scheme was calculated the mean of the five decoded angles (from the five spectrograms per trial) and rounding to the nearest label, or calculating the mode of the decoded angles (or the mean if there is no unique mode). These two options were explored to try and maximize decoding accuracy. Models were assessed not just for overall decoding accuracy, but also decoding accuracy as a function of time.

Model Evaluation

Models were evaluated by two metrics; classification accuracy and Cohen’s kappa. Accuracy is defined as

$$A = \frac{\sum_{\alpha=1}^{\gamma} C_{\alpha\alpha}}{\sum_{\alpha=1}^{\gamma} \sum_{\beta=1}^{\gamma} C_{\alpha\beta}},$$

(5.17)
where \( \gamma \) is the number of classes, \( C \) is the \( \gamma \times \gamma \) confusion matrix and \( \alpha \) and \( \beta \) are counting variables. Due to there being constraints on the size of the data for each patient, a permutation test was used to determine if accuracy was above chance level (Billinger et al., 2012). Briefly, the labels of the true test set were randomly ordered, then a random guess was made for each label. The accuracy was then calculated as the correct number of guesses divided by the total number of guesses. Repeating this process many times generated a null distribution of chance-value accuracies. The one-sided \( p \)-value was defined as the fraction of random classifier outcomes greater than the neural network performance (equivalent to a one-sided \( z \)-test). For this work, the distribution was generated from \( 10^8 \) random classifiers and significance was set at \( p < 0.05 \).

As accuracy only accounts for the ratio of correct classifications to total classifications, it may not reflect biases in classification outcomes. Hence, Cohen’s kappa was also used to evaluate performance. Cohen’s kappa is defined as

\[
\kappa = \frac{A - P}{1 - P},
\]

where

\[
P = \frac{\sum_{\alpha=1}^{\gamma} C_{\alpha C_{\alpha}}}{\left( \sum_{\alpha=1}^{\gamma} \sum_{\beta=1}^{\gamma} C_{\alpha \beta} \right)^2}
\]

and \( C_{\alpha \beta} \) and \( C_{\alpha \alpha} \) are all the elements in column \( \alpha \) and row \( \alpha \) of \( C \), respectively. Cohen’s kappa will equal zero when a classifier is decoding at chance performance for any individual class. A 95% confidence interval can be calculated as (McHugh, 2012)

\[
CI_{95} = \kappa \pm 1.96 \cdot \sqrt{\frac{A(1 - A)}{\sum_{\alpha=1}^{\gamma} \sum_{\beta=1}^{\gamma} C_{\alpha \beta}^2 (1 - P)^2}}.
\]

Hence, when \( CI_{95} > 0 \), classification can be assumed to be above chance at a significance of \( p < 0.05 \).

5.3 Results
5.3. RESULTS

5.3.1 Finger-Drumming Task

Both overt and imagined movement decoding performance were compared for
the fully connected (FC) and convolutional neural network (CNN) models.
Figure 5.4 shows the classification accuracy for each of the two tasks as decoded
by each of the two models.

![Figure 5.4: Model comparison for overt and imagined finger-drumming task. Bars represent mean value over 50-fold cross validation, error bars represent standard deviation. Red dashed line indicates chance outcome (50%). All accuracy values were significantly above chance ($p < 0.01$, permutation test). There was a significant difference ($p < 0.01$, t-test) between imagined movement classification accuracy for the two decoding models. There was also a significant difference ($p < 0.05$, t-test) between overt and imagined movement classification for the both models. FC: Fully connected network. CNN: Convolutional neural network.](image)

Classification performance was significantly above chance for both tasks,
as decoded by FC and CNN networks ($p < 0.01$, permutation test). No sig-
nificant difference in classification accuracy was found between the overt and
imagined datasets as decoded by the FC network ($p < 0.05$, t-test). This im-
plies that the model could extract an equivalent amount of information out of
both conditions, despite known differences in cortical representation of these
tasks (McFarland et al., 2000; Miller et al., 2010). The CNN showed signif-
icantly higher accuracy for overt movement decoding compared to imagined
movements, with a mean improvement of 4.7% ($p < 0.05$, t-test). For both
tasks, CNN demonstrated significantly improved decoding accuracy over the
FC network, with a mean improvement of 10.8% and 6.2% points for the overt
and imagined tasks, respectively ($p < 0.01$, t-test). This demonstrates that
the translation invariance, as well as the lower number of weights inherent in
the CNN model, were able to more robustly detect features from the spatial-
frequency data in both tasks.

5.3.2 Center-Out Task

Data Separability

For the purposes of illustration, the first two components of Patient 4’s data
(originally 960 dimensions) are shown in Figure 5.5 before and after normaliza-
tion and transformation by a CNN model. As can be seen, data from different
classes in the input space overlapped significantly, making classification with
this formulation of the data difficult without greatly overfitting (i.e. poor gen-
eralizability to previously unseen data). Conversely, after processing by the
network, the data was far more clustered by class, and a much higher propor-
tion of the variance was explained in the first two principle components. As
expected by the design of the preceding fully connected layer, most of the data
appears to cluster between [-1, 1] in both dimensions.

Interestingly, the network output space appears to transform the data such
that the spatial relationship between some classes is preserved. For example,
many of the samples from classes four and five seem to be spatially close, as
well as seven and eight.

Classification

A legend for the movement direction labels is shown in Figure 5.6. Normalized
confusion matrices for four patients are shown for the FC model in Figure 5.7
and for the CNN in Figure 5.8, showing mean results over 50-fold cross valida-
tion. Each diagonal value refers to the percentage of trials that were classified
correctly for that direction, and each off diagonal represents the percentage
of trials in the actual movement direction (column) that were incorrectly pre-
dicted to that class (row). Patient 4 had the highest mean classification accu-
cracy using both models, with 57% and 73% overall accuracy for the FC and
CNN models, respectively. Patient 2 had the lowest classification accuracy
using both models, with 25% and 36% overall accuracy for the FC and CNN
models, respectively. All cross validations for all patients performed above
5.3. RESULTS

Figure 5.5: A scatter-plot of the first two principal components of Patient 4’s center-out task data before and after data transformation by the model. Dot color refers to movement direction. Components one and two account for 7.8% and 2.6% of the sum of the eigenvalues for the input data, and 57.3% and 25.3% of the eigenvalues for the transformed data.
chance accuracy (approximately 12.5%), to a significance of $p < 10^{-4}$ (permutation test). As can be seen by horizontal bands in the confusion matrices (e.g. Patient 2, Class 8, Figure 5.7), some models may be poorly optimized and are biased towards particular classes, even over multiple cross-validations.

![Diagram of movement direction labels.](image)

**Figure 5.6:** Diagram of movement direction labels.

Figure 5.9 shows the overall mean accuracy of each cross-validation for each patient for both the FC and CNN models. The mean of the CNN model was significantly greater than the FC model for each patient ($p < 0.001$, $t$-test), with a mean improvement of 17.5%. Patient 4’s FC results show a high range of 39.5% points, although the CNN results are still significantly greater ($p < 0.01$, $t$-test).

For each patient, the mean accuracy of each model is presented as a linear function of the number of training trials in Figure 5.10a. Similarly, in Figure 5.10b, the linear function between FC and CNN mean accuracy is shown. No linear fits were significant at $p < 0.05$; however, as only four observations are used per model, this is not unexpected.

To test the generalizability of each model, the data from each patient was tested on a representative CNN model from each of the other patients. As the first layer of the CNN has kernels that only span the frequency domain, and hence are spatially invariant, the models may learn frequency features common to multiple patients. Decoding accuracies and corresponding $p$ values are shown in Figure 5.11 (no multiple comparison correction applied, however all 0.00 values remain less than $10^{-4}$ when Bonferroni correction is applied). Only
5.3. RESULTS

Figure 5.7: Normalized classification results for 50-fold cross validation of the FC decoder model. Numerical values indicate mean decoding accuracy. Diagonal values indicate percentage of correct classifications for that class. The results for each test training split were found to have above chance classification accuracy ($p < 10^{-6}$). The patients had 14, 39, 17 and 0/50 kappa scores not significantly above zero. Labels refers to movement directions $0^\circ$, $45^\circ$, etc.
5.3. RESULTS

Figure 5.8: Normalized classification results for 50-fold cross validation of the CNN decoder model. Numerical values indicate mean decoding accuracy. Entries in diagonal cells indicate percentage of correct classifications for that class. The results for each test training split were found to have above chance classification accuracy ($p < 10^{-6}$), and Cohen’s kappa ($p < 0.05$), with the exception of Patient 2, where 14/50 had kappa scores not significantly above zero. Labels refers to movement directions $0^\circ$, $45^\circ$, etc.
5.3. RESULTS

Figure 5.9: Comparison of FC and CNN results for each patient. 50 cross-validations were used for both models. For each patient, CNN results are significantly higher ($p < 0.001$, $t$-test).

Figure 5.10: a) Mean decoding accuracy for each patient as a function of number of training trials for FC and CNN models, and corresponding linear fits. FC: $r^2 = 0.421$, $p = 0.351$. CNN: $r^2 = 0.757$, $p = 0.13$. b) Mean CNN decoding accuracy compared to mean FC decoding accuracy, and corresponding linear fit. $r^2 = 0.866$, $p = 0.067$. 
models that were trained and tested on data from the same patient demonstrated decoding accuracy at above chance levels \( (p < 0.05) \), suggesting that the trained models are learning features that are specific to each patient.

![Decoding accuracies and p-values for each patient dataset on a single representative model for each patient.](image)

**Figure 5.11:** Decoding accuracies and \( p \)-values for each patient dataset on a single representative model for each patient. No multiple comparison correction has been applied to the \( p \)-values. Only diagonal entries (corresponding to the model being trained on data from the same patient as the testing set) show significance at \( p < 0.05 \).

Expanding on the previous result, models were trained for each patient using all the available data from all patients, and testing on a withheld 20% portion from each patient. Decoding accuracies for 50 cross-validations are shown in Figure 5.12, comparing the cross-trained CNN to the baseline, patient-specific models. For each patient, the two models have significantly different mean decoding accuracies \( (p < 0.001, t\text{-test}) \), but notably Patient 4’s patient-specific CNN model outperforms the cross-patient CNN model. The four cross-patient CNN models have non-significant differences in mean decoding accuracies \( (t\text{-test}, \text{significance at } p < 0.05, \text{range 0.066 - 0.809}) \).

Cross-patient models were also generated using FC networks. As demonstrated in Figure 5.13, the patient-specific models had significantly higher decoding accuracy \( (p < 0.001, t\text{-test}) \). Cross-patient models for all four patients were not decoding significantly better than chance \( (p < 0.05, t\text{-test}) \), at approximately 12.5%.

CNN models were trained using data from five time points before movement onset. Shown in Figure 5.14, the baseline results refer to raw decoding accuracy from these models at all five time points. Mean and mode refer to the
5.3. RESULTS

Figure 5.12: Comparison between patient-specific CNN models and cross-patient CNN for 50 cross validations for each patient. Each patient showed a significant difference in mean decoding accuracies between the two models ($p < 0.001$, $t$-test). Patient 4 was the only one to demonstrate higher patient-specific model decoding accuracy than cross-patient model. The mean cross-patient CNN model decoding accuracy was not significantly different between each of the four patients ($t$-test, significance at $p < 0.05$).

Figure 5.13: Comparison between patient-specific FC models and cross-patient FC for 50 cross validations for each patient. Each patient showed a significant difference in mean decoding accuracies between the two models ($p < 0.001$, $t$-test). No patients demonstrated higher cross-patient model decoding accuracy than patient-specific model. The mean cross-patient FC model decoding accuracy was not significantly different between any of the four patients ($t$-test, significance at $p < 0.05$).
voting method of outputs from a single trial to make a single decoding decision. Mean voting performed significantly worse for all patients (\(t\)-test, \(p < 0.001\)), indicating that errors were not necessarily ‘close’ to the correct option, but may instead be wrong by a considerable angle. Mode-voting demonstrated a significant improvement in three of four patients, but with limited difference (mean 2.3% point improvement).

Figure 5.14: Comparison between baseline CNN decoding and voting between multiple results for 50 cross validations for each patient. Each patient showed a significant difference in mean decoding accuracies between baseline and mean-voting results (\(p < 0.001\), \(t\)-test), and three of four patients showed a significant improvement with mode-voting results (\(p < 0.001\), \(t\)-test).

A breakdown of the baseline results for each patient at each time window is shown in Figure 5.15. A linear fit to the mean of the results across all patients at each time point yielded \(y = 41.1 + 3.7x\), \(r^2 = 0.802\), \(p = 0.046\), indicating that decoding accuracy mildly improves as spectrograms are calculated closer to the onset of movement.

5.4 Discussion

This work has presented artificial neural network models for the classification of movement from human ECoG data. It was demonstrated that both FC and CNN models can decode the direction of intended movement at above chance
5.4. DISCUSSION

Figure 5.15: Comparison between baseline CNN decoding results by time window and patient (all patients pooled together shown in black). Plots show mean ± standard deviation. A line of best fit (not shown) to the mean gives $y = 41.1 + 3.7x$, $r^2 = 0.802$, $p = 0.046$, indicating an increase in decoding accuracy as the spectrogram is calculated closer to before movement onset.

accuracies. CNN models demonstrated higher mean decoding accuracy for all four patients compared to FC neural networks. CNN models when trained on only a single patient’s data generalized poorly when tested with data from other patients, demonstrating decoding accuracies not significantly different from chance. Training models on data from multiple patients increased performance significantly in the case of the CNN model, but not the FC network. CNN models benefited from training with data from multiple time-windows and pooling results by taking the mode of the outputs for three of four patients. Overall, we demonstrated that ANN models can robustly decode information from human ECoG data for the purpose of brain-computer interfacing.

Improvement in ANN training methods, efficiency in training, increased digitization and merging of data resources has led to a resurgence in the use of ANNs for data classification. This work has demonstrated that properties of ANN models that have made them popular for image and speech recognition tasks are also favorable for ECoG classification. The results suggest that not only can ANN models be used for robust classification of intended movement for individual patients from a limited number of trials, but that pooling data across patients can significantly increase classification accuracy for individual patients.
As demonstrated in Figure 1, both FC and CNN models can robustly decode whether movement was occurring or not from ECoG. This is to be expected, as it is well understood that changes in neural oscillations occur during movement compared to rest, particularly in the gamma and high-gamma bands (Pfurtscheller et al., 1996). The CNN outperformed the decoding accuracy of the FC model for both overt and imagined movement. This is interesting, particularly as the FC network has two orders of magnitude more model parameters than the CNN model ($\approx 10^5$ and $10^3$, respectively). Hence, it can be assumed that the CNN is able to learn more robust features of the spectrograms to distinguish rest from movement, even despite the lower number of parameters. It is unexpected to see that the FC network decoded both intended and overt movement with similar accuracy; however, the CNN model could decode overt movement with significantly higher accuracy. Overall, this analysis demonstrated that ANN models can decode features of movement from ECoG at well above chance level.

The use of principal components analysis (PCA) is a useful tool in visualizing the separability of a given set of data. Figure 5.5 demonstrates that although the input space of the spectrogram data was poorly reproduced with only the first two principal components, and the eight classes were highly overlapping, the CNN could transform the data into a basis that was far more clustered. Interestingly, the most variance was found in data recorded at 0 and $315^\circ$, which would require the greatest reach for this patient (Patient 4), as the patient was using their right arm, and these correspond to the movements furthest away from their body. As all ECoG data were taken before the onset of movement, this may correspond to the perceived increase in effort during movement planning. It is also interesting to see that movements in similar directions appear to be represented in similar regions of this space. From this network transformed space, the final layer of the network was better able to separate the data into different movement classes.

The FC model could decode movement at above chance accuracy for all patients for 50 cross validations. However, Patients 1, 2 and 3 did not consistently perform at above chance level for the Cohen’s kappa score. This implies that although the decoding model was guessing significantly more than $\approx 1/8$ trials correctly, the FC networks were being biased towards specific outputs.
This could potentially be improved by increasing the dropout in the penultimate layer of the network to reduce the likelihood of the model outputs being biased by particular features. Similarly, a greater amount of training data may improve this, as Patient 4 had no kappa scores at the chance level and had the most trials. Although all patients had accuracies at well above chance level, the overall accuracies were still not high enough to dependably decode movement direction, with only Patient 4 reliably decoding the correct movement direction more than half the time, from the average model outcomes. Hence, the FC model is likely to be unsuitable for translation to decoding the movement of an actual device in the presented formulation.

Like to FC model, the CNN decoding performance was above chance accuracy for all cross-validations for all patients. In 14/50 cross validations for Patient 2 Cohen’s kappa was not significantly above zero. Decoding accuracy was significantly higher on average compared to the FC model, with three of four patients having trials correctly classified at least half of the time on average.

For each of the four patients, mean decoding accuracy was significantly higher using the CNN compared to the FC model. For Patient 1, all CNN decoding accuracies were higher than FC model accuracies across 50 cross validations for both models. Although the range of results for Patient 4 FC models were higher than other patients, the CNN model still has higher mean accuracy for these data. The CNN model for this task has almost a third the number of parameters of the FC model, hence the increased mean classification accuracy could be due to less overfitting to the training set for each patient.

As shown in Figure 5.10, the classification accuracy for both models appeared to increase as a function of the number of training trials. However, a linear fit was not significant for either model. This was likely due to a low number of observations (n = 4), so it would be expected that this trend would be further elucidated by including more patients. Similarly, no significant correlation was found between mean decoding results between the FC and CNN models, but the p-value of 0.07 suggests a close, albeit not statistically significant, relationship. Despite the lack of significance for any of these model fits, it is reasonable to assume that an increased number of trials would help boost performance for these decoding models, as this has been observed in
other neural network studies (Zhou et al., 2014).

Figure 5.11 demonstrates that, when trained on a single patient, the CNN models generate features that are specific to the spectrograms of each patient’s dataset, and generalize poorly to data from other patients. None of the models trained on data from patients that were not in the test set were able to classify at an above chance level. This implies that the networks are learning attributes of spectrograms that relate to movement directions that are specific to individual patients. This is somewhat to be expected, as all individuals have features and idiosyncrasies that distinguish their EEG/ECoG, and electrode placement across the four patients is across broad regions of cortex, and is not specific to motor regions. Although the \( p \)-values show a large range in the off-diagonal entries, these must be compared to their corresponding accuracy values, which would only differ by \( < 3 \) correct classifications, and hence it cannot be expected that using models trained on one patient’s data and tested on another will provide robust classification.

Similar to many studies in the field of seizure prediction (Mormann et al., 2007), this data had a limited number of training examples to generate patient-specific models for classification of ECoG events. Hence, models were be created by pooling data across patients, increasing the number of training examples, and potentially the overall performance. Importantly, each patient’s data was normalized in the same way (each input has zero mean and unit variance), such that these basic statistics were consistent between patients. As demonstrated in Figure 5.12, mean classification accuracy was increased for three of four patients using this method with CNN models. Patient 4’s results did not improve using this method; however, they demonstrated the best average performance with the patient-specific CNN. Hence, it may be expected that Patient 4 suffered a performance drop, particularly if features distinct to their data are being ‘washed out’ by training on data from other patients. The CNN cross-patient models performed similarly for all four patients, suggesting that they generalized well across patients. Conversely, the cross-patient FC models performed no better than chance for all patients.

Unlike the CNN model, the FC features are not translation invariant, and hence the spatial or frequency feature differences between patients may lead to features generalizing poorly between patients. The increased cross-CNN
performance suggests that, much like in the field of image classification, pre-training on similar data can allow models to learn features that are highly similar to those required for robust classification. An alternative description of this effect is that the models were being seeded in a region of the weight space that is close to an optimal point, as opposed to the typical random seeding process. This suggests that ECoG features that distinguished the different movement directions were somewhat similar between patients, but not identical; as we have already demonstrated in Figure 5.13 that this leads to chance level classification. Similarly, these features may be location specific, and hence translation invariance of features is necessary to perform robust classification.

The use of multiple spectrograms from a single trial, taken at different time windows, was explored. Training a CNN model on (overlapping) data from five time windows and evaluating outcomes based on the mean and mode of the outputs produced mixed results, as shown in Figure 5.14. The mean-voting results were significantly worse in all four patients, indicating that the errors in the model were not ‘cancelling out’. This is likely due to the CNN model having no explicit understanding of the spatial relationship between the eight outputs. The mode-voting results gave a significant improvement for three of four patients, albeit with a mean improvement of 2.03 \% points. As shown in Figure 5.15, the decoding accuracy for each patient did not necessarily increase monotonically with respect to time; however, when analyzed together there is a significant positive linear trend. This indicates that the model could decode more relevant information from the spectrograms taken closer to the onset of movement.

A key limitation of this study is the relatively small number of trials that form the basis of each model. Even with the augmentation of training trials with noise, the use of multiple time-points per trial, and using data from multiple patients, the number of overall training examples is still relatively low compared to many CNN applications (LeCun et al., 2015). Future work should ideally use as many trials as possible in training models in order to fully understand their potential in ECoG decoding. With relatively few trials and patients in this work, it is not clear how well these results would generalize to other individuals, particularly those without a focal epilepsy. However, the decoding accuracies presented in this work are encouraging, even with a rela-
5.4. DISCUSSION

A relatively small data-set collected from each patient in a limited amount of time.

Although the well above chance decoding accuracies presented are encouraging, these models still require further development for translation into real-time control of an actuator (such as a prosthetic limb or computer cursor). As the model was only trained on the ECoG occurring just before movement onset, there is no capability for ongoing corrections or adjustments of movements. Ongoing adjustments are desirable as it occurs naturally during limb movement. The models presented did not explicitly account for certain classes of movement being more similar than others. Future work will investigate using ANN models for regression of ECoG to movement kinematics, instead of discrete categorization. This will hopefully allow for more natural, continuous decoding, as well as a model that has a better spatial understanding of the relationship between outputs. This could be realized by decoding a vector of kinematic parameters such as hand position or velocity, or angles between joints of the arm and hand.

A general issue with decoding information from EEG or ECoG signals is the abstract nature of the signal itself. Despite approximately 100 years of use of EEG in humans, and approximately 70 years of clinical ECoG, a mapping between neural firing and the EEG signal is not known. Cortical EEG is also only a minor snapshot of the functionality of the mammalian motor system, which involves integration of the visual system, deep brain structures, and the peripheral nervous system. Hence, the use of black-box style modelling is well justified, as our input data is highly abstracted from the underlying system being decoded.

It is unclear what the effects of the patients’ epilepsy are on the results of this study. For the decoding of movement compared to rest in the finger-tapping study, it may be that features such as epileptic spikes are being learned by the model, that may coincide with either, or both of the movement states. For the case of the center-out task, it is likely that any epileptic discharges are simply an artifact in the input spectrograms, and do not particularly coincide with any of the movement classes. Further work decoding movement from non-epileptic sources, such as from non-human primates, or humans with ECoG for non-epilepsy related monitoring, may help elucidate the effects of epilepsy on decoding performance.
5.5. CONCLUSIONS

Most ECoG motor decoding focuses on continuous prediction of arm/hand position (Schalk and Leuthardt, 2011). This work has focused on discrete decoding of movement, producing an eight-class decoder. Instead of directly mapping ECoG to movement, this could allow a user to control movement of a device in 3D space (up-down, left-right, forward-backwards) and two controls for grasping.

This work has applied two common ANN models, FC and CNNs, to decode spectrograms of a time-series signal. Future work in this field should assess the utility of networks, such as the WaveNet, to undertake time-series classification of the raw voltage signal (Ribeiro et al., 2016). This not only would decrease computational requirements of the spectrogram calculation, but would hopefully increase decoding accuracy by learning temporally invariant features of ECoG relating to movement.

The ubiquity of ANN models in data analysis applications has led to an abundance of hardware for time- and energy-efficient deployment of ANNs (Schuman et al., 2017). This is important for real-time, portable applications, where standard CPU/GPU computation may not be sufficient. Early work into EEG decoding with the TrueNorth platform, hardware that replicates stochastic binary weighted CNNs, has shown decoding results commensurate with standard CNN models (Nurse et al., 2016; Mashford et al., 2017). Further advances in hardware will allow for translation of ANN models for real-time ECoG decoding devices.

The rapid advances in the implementation of ANN-based machine learning has revolutionized fields such as computer vision and text analysis. With growing corpora of open-source neural data repositories and advances in signal processing techniques, ANN models have the potential to similarly transform the problem of intention decoding.

5.5 Conclusions

Improvement in training methods, algorithm efficiency, and increased digitization and merging of data resources has led to a resurgence in the use of ANNs for classification. This work has demonstrated that properties of con-
volitional neural network (CNN) models that have made them popular for image and speech recognition tasks are also favorable for ECoG classification. The results suggest that not only can CNN models be used for robust classification of intended movement for individual patients from a limited number of trials, but that pooling data across patients and across different time points can significantly increase classification accuracy for individual patients.
Chapter 6

Conclusion

6.1 Summary

Brain-computer interfaces (BCIs) are becoming accepted as assistive technologies for individuals with motor disabilities (Chaudhary et al., 2016). Invasive BCI systems have demonstrated profound capabilities to control output devices (Hochberg et al., 2006, 2012). However, the degradation of the electrode-tissue interface of intracortical microelectrodes have prevented the widespread clinical translation of such devices (Jorfi et al., 2015; McConnell et al., 2009). Electro-corticography (ECoG) has shown promise as an alternative, invasive recording modality for BCIs (Wang et al., 2013a; Vansteensel et al., 2016; Schalk and Leuthardt, 2011).

The work presented in this thesis has focused on advancing the progress of a clinically viable ECoG-based BCI. Chapter 2 evaluated the stability of ECoG signals over timescales of multiple years. At a group-level the ECoG signal is stable, demonstrating the potential of long-term BCI recording. Chapter 3 presented the methods for a two-dimensional center-out task and finger-drumming task performed by humans undergoing clinical ECoG monitoring. Chapter 4 investigated the use of directional tuning models to describe how movement direction is encoded in high-frequency ECoG. Wide spread encoding was found. Also population-vector methods were investigated to decode movement from inverted directional tuning models. Decoding performance was above change for three of four patients, and motives further investigation of decoding movement from this data. Chapter 5 explained the use of artificial neural networks as decoders. It demonstrated that convolutional neural net-
work models (CNNs) can be used to accurately classify movement direction from frequency-domain ECoG data.

6.1.1 Long-Term Properties of ECoG

Numerous pre-clinical and clinical ECoG device trials, as well as long-term pre-clinical ECoG experiments, have provided a body of knowledge suggesting that ECoG can record motor-related potentials over a duration of multiple years. Yet, exactly how recorded ECoG signals change over such a time-scale in humans had yet to be rigorously quantified.

Despite many years of high-quality research, BCI systems still require a great deal of development before clinical translation will be achievable. Knowing that high-frequency ECoG signals are recordable consistently for multiple years is of great importance to future BCI device development. The evidence shown in Chapter 2 demonstrates that an ECoG electrode system can be implanted with the expectation that the device’s ability to discern motor-related potentials will not be attenuated over years, and hence not require electrode removal or replacement. The dataset presented is highly unique in its duration of continuous ECoG recordings, and provides a unique ability to assess the longevity of ECoG. This is in contrast to current microelectrode systems, which so far have required explantation within a few years. Hence, it can been seen that sub-dural ECoG is a prudent choice of long-term BCI recording compared to microelectrodes due to it’s safety and reliability. Hopefully, the expansion of the study undertaken by Vansteensel et al. (2016), which provided definitive evidence of clinical relevance of an ECoG BCI, can provide a pathway to the translation of BCI-operated assistive technologies.

6.1.2 Encoder-Decoder Models of Directional Tuning

The relationship between motor neural firing rates and direction of arm movement is well documented (Georgopoulos, 1991). It has since been demonstrated that direction-dependent activation can also be measured from ECoG-related signals (Schalk et al., 2007; Ball et al., 2009b). Chapter 4 demonstrated how such models can be used to decode movement direction from ECoG.
The simple, physiologically-inspired nature of directional tuning models provides high-level insights into the cortical representation of upper-limb movement direction. That such a straightforward model can produce above-chance decoding is highly encouraging for the future application of physical models. In particular, how the time-domain development of directional representation and interaction between electrodes can be included into such models may provide insights to how ensembles of cortical neurons encode and ultimately generate movement. This work has further validated directional tuning as a viable model of encoding and decoding of upper-arm movement, and will hopefully encourage the use of physiological models of higher complexity.

6.1.3 Artificial Neural Networks for Decoding Movement

Artificial neural network (ANN) models are rapidly becoming a tool of choice for classification of data (LeCun et al., 2015). This is due to their ability to learn highly non-linear transformations from the input data space to the output domain, and technological and algorithmic advances have made their training much faster. So far, relatively few studies have been undertaken in the BCI field with the commonly used convolutional neural network (CNN). In particular, few studies have focused on decoding movement from ECoG.

Many BCI decoding systems still rely on low complexity models to classify data. Although these can create tortuous decision boundaries between data points, the advent of modifications such as convolutional layers and neuron dropout have made these models highly advantageous for image classification. In particular, the ability of convolutional layers to learn translation invariant features means neural activation occurring in different temporal or spectral locations between different inputs makes these models more robust to variations in input data. Hence, by minimizing the a-priori assumptions on the input data, the testing accuracy or, ideally, accuracy during device deployment can hopefully be maximized. ANN models can be designed to be invariant to particular variations in input data, and hence offer a significant advantage for clinical translation of BCIs. The sparsity that exists in many ANNs (many weights are close to zero) is also a useful attribute, as this means individual (artificial) neurons can be highly sensitive to particular patterns of data. As ECoG can have many patient-specific properties and may be recording over
a range of attentive states, the ability to model these nuances is desirable in decoder models. Although these early results of ECoG analysis by CNNs have been promising, and in some cases highly accurate, a great deal more should be done to optimize how networks and ECoG data can be structured to maximize the benefit of these properties.

6.2 Future Research Directions

6.2.1 Alternative Methods of Recording Electroencephalographic Signals

Since most ECoG BCI studies use electrodes placed for clinical epilepsy monitoring, the types of electrodes used are driven by this clinical purpose. This means that many studies are limited to centimeter scale electrode grid resolution, that have changed minimally since the introduction of ECoG as a clinical tool (Penfield and Jasper, 1954). It has been demonstrated that the use of micrometer scale ECoG can record novel spatial neural dynamics, not recordable from centimeter scale ECoG (Viventi et al., 2011). It is also advantageous from an implantation perspective, requiring only a small burr-hole for implantation. Progress in creating fully-implantable, micrometer scale ECoG systems has been promising (Maharbiz et al., 2017), and may prove to revolutionize how neural activity is recorded for BCIs.

Electrode implantation not requiring a craniotomy may also increase use of BCI systems by avoiding the risks associated with opening the skull. One such technology is sub-scalp electroencephalography (EEG) (Benovitski et al., 2017), which requires only a small incision to subcutaneously place electrodes. Another is recording from within cortical veins using electrodes mounted onto a self-expanding stent (Oxley et al., 2016). This has been shown to have similar signal properties to epidural ECoG in an ovine model and gives consistent recordings for at least 28 weeks.

As more BCI studies investigate ECoG in patients with paralysis, it is hoped that an increase in the spatial and temporal information can improve decoder accuracy and hence device utility for users. Similarly, the advent of minimally invasive, stable neural interfaces may attract more users due to
lower surgical risks.

### 6.2.2 Interpreting Motor Activity from Neural Signals

An underlying hypothesis of many BCI technologies is that sampling from more (if not all) areas of cortex will allow for greater capacity to decode information from the brain (Abbott, 2013). For example, BCI systems using microelectrode arrays commonly record from primary and the supplementary motor area in an effort to sample a broader range of neurons from the motor system. It is approximated that, since 1960, the capacity to simultaneously record individual neurons has doubled every seven years (Stevenson and Kording, 2011). Although methods such as population-vector decoding and linear regression algorithmically scale well with the addition of more signal sources, it is not clear if these methods suitably capture the complexity inherent at the scale of modern motor electrophysiology recordings. Modelling and understanding how neurons or cortical regions interact and influence each other will become more important as electrode arrays incorporate more recording channels. The focus on modelling neural activity as something that describes movement, and not as a ‘snapshot’ of a much larger, complex system, is also a concern of such models. Describing neural activity in terms of state-space models, where the recorded potential is not necessarily assumed to represent actual movement, could be useful for future BCI applications.

With the clinical translation of BCI technologies, it will be important to consider what criteria should be followed to re-train classifiers. As the brain undergoes plasticity and changes occur in neural interfaces, it will be important to understand how often is optimal to re-train decoding algorithms without causing undue frustration for the user.

### 6.2.3 Advances in Artificial Neural Network Models

ANN models have fundamentally changed how a range of data classification problems are being solved. For example, using ANNs, tasks such as speech recognition (Hinton et al., 2012), document sentiment analysis, and question answering (Bordes et al., 2014) are problems that any internet-connected smartphone can now undertake within a few seconds. A major challenge in replicating this success in BCI technologies is generating enough data to train these high-complexity models. Corpora such as the International Epilepsy
Electrophysiology Portal (Wagenaar et al., 2013) provide a practical model for how neuroscience data can be collated and widely disseminated. Access to datasets recorded from a variety of patients, electrode types, and recording conditions allows algorithms to be tested far more robustly than the majority of studies that only present data from a few patients under similar conditions. Opening BCI classification to the broader data science community through platforms such as Kaggle competitions (Kaggle, 2017) may also provide greater advances in decoding methods. Increased commercial interests in BCI technologies from Silicon Valley personalities such as Mark Zuckerberg (through Facebook and the Zuckerberg-Chan Initiative), Brian Johnson (through Kernal) and Elon Musk (through Neuralink) are also likely to effect the course of future BCI research and development (IEEE Spectrum, 2017). For neural network models to advance as a decoder model-of-choice for BCIs, the methods that data is collated and used to train models between patients are likely to become increasingly important.

The use of ANNs could greatly change how real-time neural signals are classified for BCI systems. Unfortunately, due to the unclear relationship between structure and quantity of data, network structure (such as numbers, types and sizes of layers) and network training parameters (such as learning rate, dropout rate and batch size) it is difficult to be sure that an ideal model has been constructed for a given dataset. Hopefully, future work can provide insights and methods into how networks can be most optimally generated.

6.2.4 Ethical Consideration of ECoG BCIs

The use of long-term neural interfaces also requires consideration of the risks and ethical impacts such devices can have. The potential harm craniotomy or burr-hole surgeries can have are immense. This risk may be unacceptable for many, particularly when BCI devices are not explicitly providing therapeutic benefit to the individual’s disease or injury. The perception of self-change that neural interfaces can bring on also requires consideration. A patient from the NeuroVista device trial (outlined in Chapter 2) stated in an interview (Gilbert et al., 2017):

It becomes part of you. Because that’s what it did, it was me, it became me, [...] with this device I found myself.
Although this refers to the experience of a seizure prediction system, it can be seen how wholly the patient has embodied the device, and how it is not spoken about as a piece of medical technology, but rather a part of the self. Understanding this relationship, and avoiding potential self-estrangement will be of key importance to wide-spread translation of BCI devices.

6.3 Final Remarks

This thesis has presented research that furthers the argument for ECoG as the recording modality of choice for long-term BCI systems. This work provides definitive evidence that ECoG recorded from humans can be recorded continuously for multiple years with minimal signal degradation. It has expanded upon previous studies of directional tuning of ECoG by recording activity during a two-dimensional center-out task and exploring population-vector approaches for decoding movement direction. Finally, this thesis demonstrated the utility of ANN models for decoding movement direction from frequency-domain ECoG. All elements that are needed to construct an ECoG-based BCI are in place with modern ECoG recordings, providing a stable neural signal with sufficient information for high-accuracy decoding.

This thesis has shown that ECoG recorded subdurally can form the basis of a clinically-relevant, long-term BCI. While a range of recording technologies have been proposed to record neural activity for a BCI, this thesis has demonstrated that ECoG is the most appropriate technology that has demonstrated suitable robustness and safety for long-term implantation, and sufficient information can be extracted to control assistive technologies.
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