Electrophysiological recording of the brain, visualization, prediction, and interconnectivity

by

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A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
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University of Toronto

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Abstract

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2014

The human brain is a complex network of interconnected neurons. The aim of neuroscience and neuroengineering is to decode the neural activity, visualize it and try to better understand how neurons communicate with each other. This dissertation comprises four contributions to the area. These four topics are discussing how functional relationship between brain activity and movement can be found and whether common features found in different regions are correlated (phase-locked). First, the method of chirplet decomposition offers a new way to visualize the time-frequency content of non-stationary signals with higher resolution than previously possible. The use of Wigner-Ville distribution together with chirplet decomposition allows a clearer visualization in terms of both the temporal and frequency details with detail higher than previously achieved using other methods including Choi-Williams and spectrogram. Second, an improved method of averaging of neural signals over repeated trials is introduced whereby slight variations in the alignment of the neural signal over time is corrected through the use of nonlinear shifts. In earlier studies, time alignment has been performed using linear shift (e.g. alignment with movement onset), but this process alone is not sufficient when the signal timing changes differently over time. To overcome this issue, nonlinear transformations were found to remove any temporal variabilities in the way the task was performed. Third, a multilinear model is demonstrated showing how limb velocity in a reach task can be
predicted from neuroelectrical activity. The model, after fitting, suggested that high frequency oscillations have sufficient information for both detection of movement onset and reconstruction of its movement. The use of a linear model reduces the overall computational requirements and simplifies the reconstruction of movement kinematics. Finally, a fourth method involving the measurement of coherence over time reveals how circuits in the basal ganglia communicate with the cortical layers during voluntary movements. This allows investigating the inter-coupling between the sensorimotor cortex and basal ganglia and how cortico-basal ganglia coupling changes with respect to the movement. The association of coherence with power suggests that a coupling in neural activity between the basal ganglia and the cortical region of the brain is required for the execution of voluntary movements. The coherent activity suggests that similar information can be found in two brain regions.
Acknowledgements

I wish to express my gratitude to my supervisor, Professor Willy Wong, who provided me with constructive guidance, and the tools to conduct my work. I am fortunate to have had this opportunity of working by his side. I would also like to thank my Committee Members, Professor Milos R. Popovic and Professor Robert Chen, for always providing advice and criticism. They have inspired me and I am honoured to have had their guidance during this process.

I wish to thank Professor Milos R Popovic, Robert Chen, Clement Hamani, and Erich T Fonoff for providing the opportunity to conduct this work. It was only through access to their facilities and the populations they serve, that this work could ever have materialized. All are exemplary individuals and working with them has been a most enriching experience for me.
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Chapter 1

Introduction

1.1 Motivation

Many neurological disorders (e.g. amyotrophic lateral sclerosis [186] and Parkinson’s disease [32]), high level spinal cord injury [172], and stroke [34, 56, 132, 230] can disrupt the channels through which the brain commands and controls muscles. These disorders impair the neural pathways that control muscles or impair the muscles themselves [60]. In the absence of methods for repairing the damages done by these disorders, brain-activated neuroprostheses can be used to restore movement to those with motor impairments by providing the brain with a new non-muscular communication channel [211, 227, 230, 234]. Brain machine interface (BMI) is a mean to decode and convey the brain messages to an external device [8, 41, 43, 81, 115, 117, 135, 138, 174, 174, 190, 211, 233, 240]. The messages are not carried by peripheral nerves and muscles, thus activity in these pathways is not needed. Potentially, BMI replaces nerves and muscles by translating the brain signals into actions. BMI has three components: acquisition of signal(s) from the brain, translating the brain signal to actions, and generating the actions.

Brain activity can be recorded using various modalities which can be broadly categorized into two groups, electrophysiological and metabolic recordings [7]. It is under
debate which recording method is best suited for BMI. The acquisition methods include electroencephalography (EEG), electrocorticography (ECoG), local-field potential (LFP), recordings from individual neurons within the brain, magnetoencephalography (MEG), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and optical imaging (i.e., functional Near InfraRed (fNIR)) [7, 11, 29, 34, 34, 52, 53, 81, 83, 116, 117, 138, 174, 176, 190, 193, 224]. However, MEG and imaging techniques (i.e., PET, and fMRI) are still expensive in comparison to other techniques such as EEG [7]. Moreover, most imaging techniques (e.g., PET and fMRI) depend on metabolic processes (e.g., neuron’s glucose consumption); hence, they lack the temporal resolution and are less suitable for rapid communication (>5 bits/min) [7, 156]. On the other hand, non-invasive and invasive electrophysiological methods (i.e., EEG, ECoG, LFP, and single-neuron recordings) are relatively inexpensive, have high temporal resolution, and provide higher information transfer rates (<25 bits/min) [156, 232].

Brain activity changes during planning and execution of voluntary limb movements [5, 43, 157, 169, 216]. Several studies have investigated the relationship between kinematics of voluntary movement and cortical activity [43, 89, 174, 190]. Extent [214] and direction [117, 214] of movement are some of the parameters that can be determined through the analysis of brain activity. Cortical activities have been used for the implementation of BMI systems [66, 84–86, 117–119, 170, 200], including devices capable of predicting and reconstructing voluntary limb movements in space. Despite all advances in decoding the brain activity, the benefits of having BMI does not justify risks associated with invasive implantation of electrodes. Currently, the only way to study benefits and feasibility of implanted BMI is to test the system on patient populations that are implanted with electrodes as part of their clinical treatment. Examples of these populations are individuals with Parkinson’s disease, dystonia, chronic pain, depression, and epilepsy [32, 43, 60, 125, 174, 190, 202, 203, 214]. The electrodes are implanted in different brain regions based on the clinical requirements and are ranged from epidural elec-
trodes, which are implanted over the dura, to deep brain electrodes that are implanted in subcortical structures. To date, it is not clear where the optimal implantation site is for development of BMI. Limb kinematics have been reconstructed from cortical activity [8, 41, 86, 117–119, 135, 138, 174, 190, 191], but limb kinematics has not been related to subcortical structures of the motor system (e.g. basal ganglia). There are many ways to study the relationship between subcortical activity and limb kinematics. A simple way to this relationship is to relate the subcortical activity back to the cortical responses. If such a relationship is found, one can relate the subcortical activity to limb kinematics using the links established between cortical activity and kinematics.

Given the above, there are a number of issues that require further investigation. If one were to develop a BMI with application to complex limb movements, not only should we be able to visualize properly the neural signals to develop an understand of the recordings, but we will need to find a method to deal with variability in the generation of complex arm movements. Second, while a number of studies have already shown it is possible to map cortical brain activity to kinematic, there have not been many studies examining the connection between brain activity and complex arm movements. Finally, to extend the BMI system further to activity from subcortical regions, this would require that more be learned about the relationship between subcortical structures with the cortical responses during movement of the limb.

\section*{1.2 Objectives}

The objectives of the work presented in this document were:

1. To visualize and identify the movement-related changes in spectral density of local field recordings.

2. To explore feasibility of using ECoG activity from epidural electrodes placed over the motor cortex to decode the movement speed performed by a human subject.
3. To study the coherent activity between motor cortex and basal ganglia as well as to explore possibility of extracting similar features from both regions.

1.3 Organization of the document

This dissertation addresses four areas associated with the measurement, processing and interpretation of electrical brain activity:
- Visualization of neural activity
- Time alignment of responses over repeated trials
- Reconstruction of movement kinematics from invasive recordings
- Coherent brain activity

1.3.1 Visualization of neural activity

Time-frequency analysis helps to uncover the components which make up the neural response [55, 169]. The time-frequency representation, if done correctly, also allows for the identification of features which are useful in decoding a person’s intention for use in classification problems. Extensive work has been conducted in visualization of biological signals [55]. The neural activities are typically represented in time domain or time-frequency domain [43, 227]. Visualizing the activity in time domain is often simple but it fails to show the spectral density of the signal. By contrast, spectral analysis show spectral density of neural recordings but does not show how spectral content of the signal changes in time. The time-frequency representations show both temporal changes and spectral density of the neural activity. However, their resolution is limited by how the signal is transformed and represented in time-frequency domain [129]. A visualization technique was developed to estimate distribution of signal energy over the time-frequency space as sum of two-dimensional Gaussian functions (chirplets). Chirplet transformation was introduced by Mann and Haykin [130]. The initial application of chirplet transfo-
Chirplet decomposition results in a compact visualization with higher signal-to-noise-ratio than many conventional visualization methods including spectrogram, Choi-William distribution and smoothed Wigner-Ville distribution [55,209].

### 1.3.2 Time alignment of responses over repeated trials

Single trial neural recordings are noisy and the salient signal properties cannot be discriminated in the noise [103]. Pattern recognition techniques, such as matched filters that are designed to identify the salient signal in noise rely on having a prior knowledge on salient signal’s characteristics or its profile [110,218]. Visualization of the underlying signal is necessary to characterize the signal and to realize what recognition technique can be used. The underlying neural activity is typically found by averaging neural responses over a large number of trials, however one must assume that the neural activity is time-locked to specific events like movement onset or onset of an external stimulus [220].

While the evoked brain activity from external stimuli or highly constrained motor tasks can be thought of as being identical on a trial-by-trial basis, complex movement tasks such as reaching are variable across trials. This variability results in loss or distortion of neural responses. The neural responses should be realigned across the trials due to the difficulty in constraining the limb movement in order to reduce the variability in the way that the movements are performed. We hypothesize that neural events can be better aligned if the kinematic profiles are identical on each trial. Kinematic signals are used to find a transformation serve to remove any temporal variabilities in the way the task are performed. After the alignment of kinematics, the neural activities are expected to occur at near identical times. Consequently, the related neural activities can now be more effectively brought into salience through averaging. This theme (alignment of
neural activities) is discussed in Chapter 4.

1.3.3 Reconstruction of movement kinematics from ECoG activity

An application of reconstructing the limb kinematics from the brain activity is brain machine interface (BMI) where brain commands are transformed to commands for an external machine to move the limb or a robotic arm. BMI provides an alternative mean for the brain to communicate or control the environment [115]. This technology offers an artificial efferent pathway that the brain can use to interact with an external device. The conventional view in developing a BMI system has been to have the device to learn the language of the brain rather than brain learning how to use the device [8, 41, 43, 81, 115, 117, 135, 138, 174, 190, 211, 233, 240]. In this theme, BMI decodes its user’s commands directly from his/her brain activity. The learning process consists of essential steps which results in a mapping function between the brain activity and computer commands. The mapping function is expressed mathematically in terms of a mapping between signal features (e.g., slow potentials or spectral changes) and some corresponding output or command [81, 117, 174]. It is a functional relationship between the associated brain activity and desired outcome (e.g. movement kinematics) [8, 41, 43, 115, 135, 138, 174, 190, 211, 233, 240]. In Chapter 5, I proposed a method which allows reconstruction of arm speed (i.e. speed of the end effector, finger tip or wrist in 3D space) during reaching tasks from the spectral activity of ECoG activity at motor cortex. Using this method, the arm speed of a reaching task can be reconstructed from as few as eight electrocortiographical contacts. The simplicity of this system offers significant advantages over BMIs which require many electrodes.
1.3.4 Coherence of activity between cortex and deep brain regions during arm movements

In Chapter 6, a study is describing the interaction between the activity in the basal ganglia with the sensorimotor cortex during voluntary movements. The basal ganglia are parts of the motor system which are involved in the planning and selection of desired movements [141, 142]. They are closely connected to the motor cortex and thalamus. Coherence\(^1\) was calculated between the sensorimotor cortex and basal ganglia while participants were preforming wrist extension. During movement, the activities of the two regions were found to be coherent. This is likely an indication that two regions are in communication with each other during the performance of a motor task. I explored the time-course of the coherence and related it to other important parameters including the power in the activity. The synchronous activity suggests that activity of one neural ensemble is linearly related to activity of another one neural ensemble due to the correlation between spectral density of neural activities [16]. If such relationship is found between activities of motor cortex and basal ganglia, it is likely that the movement kinematics can be predicted from basal ganglia activity with similar accuracy as motor cortex. This shows the importance of studying the coherent activity between two distant regions of the brain.

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\(^1\)Coherence is cross-correlation between spectral density of two signals. Coherence is described in details in Section (6.3.4).
Chapter 2

Background

2.1 Nervous system

The human nervous system is consists of two divisions, central nervous system and peripheral nervous system [205]. Figure (2.1) illustrates these systems. The central nervous system is constituted by brain and the spinal cord. The peripheral nervous system transmits the signals between the central system on one side and receptors and body effectors on the other side. The basic electrical functional element of the central nervous system is the nerve cell or neuron. Neurons receive information from other neurons, process it, and transmit to other neurons. It is estimated that the human brain has 100 billion ($10^{11}$) neurons and 100 trillion ($10^{14}$) synapses, which are functional connections whereby exuberance potential of a neuron (presynaptic) can cause changes in the membrane potential of another (postsynaptic) neuron [15,104,201]. The communication across synapse is result of electrical and chemical coupling. In chemical interactions, the presynaptic neuron releases neurotransmitter across the synaptic gap which binds to the membrane of the postsynaptic neuron. Electrical synapse is a conductive link between neurons that is formed at a narrow gap (shorter than gaps of chemical synapses) [49]. Due to superposition property of electrical fields (the electrical fields being vectorial additive), it
is thought that mean-field activity, also known as local-field potentials, is reflection of synaptic activities as well as membrane potentials of a large population of neurons. The local-field activity is significantly stronger than a single unit activity, hence it is possible to record the local-field activity of a group of neurons in a greater distance.

2.2 Motor system

The motor system is part of the central nervous system that is involved in movement planning and execution [205]. The major divisions of the motor system are the spinal cord, brainstem, cerebellum, basal ganglia, thalamus and motor cortex (i.e., primary motor cortex, premotor cortex, supplementary motor area, primary somatosensory cortex, and posterior parietal cortex) [205]. The spinal cord is the gateway between the brain and periphery. Spinal motor neuron activity is controlled by neural circuits intrinsic to
the spinal cord and by efferent brain activities. Intrinsic spinal cord circuits are responsible for many reflexes \cite{205}. The descending pathways in the spinal cord carry motor information from higher levels of the central nervous system to the motor nerves that connect to the periphery (e.g., skeletal muscles) \cite{51}. The basal ganglia receive input from the cerebral cortex and have projections, via thalamus, to the frontal cortex to assist in regulating movements \cite{51,141,142,164,205}. Voluntary movements are planned by multiple areas of the cerebral cortex and then transmitted to the supplementary motor and premotor cortices. The plan then is transferred to the primary motor cortex for execution, which send it to lower motoneurons to produce coordinated contraction of the muscles \cite{51}. The motor cortex is somatotopically organized, that is, the body parts (e.g., arm, leg, face) are represented along the cortex \cite{165}. The existence of such a cortical organization was demonstrated by Fritsch and Hitzig using electrical stimulation of the cortex \cite{75}. As techniques of electrical stimulation improved, detailed maps of the motor cortex became available, e.g. Penfield’s homunculus \cite{165}. Penfield’s homunculus illustrates the mediolateral ribbon of the primary motor and sensory cortices broken into sequential representations of different body parts. A summary diagrams of Penfield’s homunculus is shown in Figure (2.2). In the past few decades, experimental evidence has emerged that the representation of body parts are indeed distributed such that the regions controlling a body part overlaps with the regions controlling adjacent body parts \cite{136,189}. This view does not contradict somatotopic organization of the motor cortex, for instance the territory controlling the upper limb is mainly concentrated in one region. As such, significant changes in neural activity at a particular region of the motor cortex have been associated with the attempts to move that body part. Somatotopic organizations are seen in other cortical and subcortical structures (e.g., motor cortex, basal ganglia, and thalamus) of the motor system.
2.3 Basal ganglia

Basal ganglia (BG) are a collection of subcortical structures derived mostly but not exclusively from the telencephalon [164]. The anatomical structures implicated in motor behavior include striatum, globus pallidus or pallidum, subthalamic nucleus and substantia nigra [77,164]. The cerebral cortex is connected to the basal ganglia through various neural pathways [164]. There are cortical-BG motor loops connecting the frontal cortex, basal ganglia and thalamus [77]. Figure (2.3) illustrates anatomical locations of the human basal ganglia and its main motor system connections. The subthalamic nucleus (STN) and the striatum are the main input structures of the basal ganglia and receive excitatory projections from the motor cortex [164]. The internal globus pallidus (GPi), substantia nigra pars reticulata are output nuclei of the basal ganglia with inhibitory projections to motor thalamic nuclei [164]. The basal ganglia output projects to the sensorimotor area via ventrolateral thalamus and is consecutively thought to modify activity of the motor
Figure 2.3: a) Coronal view of the brain, showing the main basal ganglia nuclei. The section is angled rostrocaudally to encounter most of the BG nuclei in a single section. C, cortex; STR, striatum; GPe, globus pallidus pars externa; GPi, globus pallidus pars interna; Th, thalamus; STN, subthalamic nucleus; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata. This figure is modified from [158]. b) The basal ganglia-thalamocortical motor circuit. Black arrows indicate inhibitory connections and gray arrows indicate excitatory connections. The thickness of the arrows corresponds to their presumed activity. Abbreviations: CM, centromedian nucleus of thalamus; CMA, cingulate motor area; Dir., direct pathway; D1 and D2, dopamine receptor subtypes; GPe, external segment of the globus pallidus; GPi, internal segment of the globus pallidus; Indir., indirect pathway; M1, primary motor cortex; Pf, parafascicular nucleus of the thalamus; PMC, premotor cortex; PPN, pedunculopontine nucleus; SMA, supplementary motor area; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; STN, subthalamic nucleus; VA, ventral anterior nucleus of thalamus; VL, ventrolateral nucleus of thalamus. This figure is modified from [77].
cortex [77]. Cortico-BG loop is formed by a number of pathways including the direct, indirect and hyperdirect pathways [98]. The direct pathway is mediated by the cortico-striato-pallido-nigral network and is hypothesized to be responsible for initiating goal-directed behaviour such as the execution of voluntary movements [141,142]. The indirect pathway is involved in movement termination [5,11,141,181]. The STN is believed to play a role in the indirect pathway [164]. Finally, the cortico-subthalamic hyperdirect pathway inhibits competing motor commands. The hyperdirect pathway is mediated by the cortico-subthalamic network [142,155,164]. Electrophysiological and functional imaging studies have not only shown activation of cortico-BG loops during movement processing [4,5,10,11,33,38,58,101,113,216] but also have found abnormal activities in the loop with movement disorders such as PD and dystonia [32,38,70,94,121,122,202,203,229].

### 2.4 Movement disorders and motor system activity

The motor system plans and executes the movements. Local-field potential (LFP) has been recorded from human motor system during movement execution and shown that LFP activities are changing with respect to the movement [4,5,8,10,11,33,38,41,43,58,69,81,101,113,115,117,135,138,155,174,190,211,216,233,240]. LFP activity has been recorded from patient populations because these recordings require surgery and implanting electrodes. In this thesis, patient with Parkinson’s disease and dystonia were studied. Parkinson’s disease is a neurodegenerative disorder causing tremor, rigidity, bradykinesia, and postural instability [80]. Dystonia is a movement disorder that causes sustained muscle contractions [60,158]. Both Parkinson’s disease and dystonia are related to abnormal activities observed in cortico-basal ganglia loop [32,202]. For example, alpha oscillations are correlated with the rest tremor observed in patients with Parkinson’s disease [32]. DBS recordings in dystonic patients revealed increased spectral power in the 4-10Hz band, particularly in recordings from GPe [202]. Currently, it is believed that
dystonia resembles Parkinsonism in features such as the presence of excessive neuronal synchrony throughout the basal ganglia and related areas of thalamus and cortex and in the reduction of activity in GPe [79, 223].

2.4.1 Diagnosis, motor symptoms, and treatment of Parkinson’s Disease

Although quantifying the loss of dopaminergic neurons in the post-mortem examination of the substantia nigra is the gold standard for confirmation of Parkinson’s disease (PD), no definitive lifetime test for diagnosis of PD exists [93]. Diagnosis is usually done based on the medical history and neurological examinations looking for tremor, rigidity, bradykinesia, and postural instability [80]. Tremor is the most noticeable sign of PD and typically observed in rest state (no voluntary movement) [32]. Rigidity is resistance to movement of a body part and usually reduces range of motion [80]. Bradykinesia is slowness of movement and associated with difficulties in movement planning, initiation, and execution [23]. Postural instability manifests itself during the late stages of PD as impaired balance and freezing of gait [93].

Medications used to relieve the Parkinsonian symptoms include levodopa, dopamine agonists, monoamine oxidase B (MAO-B) inhibitors, amantadine and anticholinergics [50]. Levodopa, also known as L-dopa, has been the standard medication for treatment of PD and acts as a dopaminergic agent, that is, levodopa is transformed into dopamine by dopaminergic neurons and recovers the dopamine level and its transmission in nigrostriatal pathway [50]. The effects of dopaminergic medications decrease in more advanced stages of PD and control of PD symptoms becomes more difficult with medication [93].

Deep brain stimulation (DBS) is a surgical treatment for PD patients [32, 38, 125, 229]. The surgical procedure is divided into two stages, implanting the DBS electrodes and the pacemaker (stimulator). First, DBS electrodes are implanted in STN or GPi – STN is the most common target for treatment of Parkinson’s disease [207]. Then, the stim-
ulator is placed in the chest cavity and connected to the DBS electrodes via shielded wires \[125\]. The stimulation parameters (i.e. frequency, amplitude, electrode polarity and pulse width) are tuned after the second surgery \[22\]. Although there are large number of possible parameter combination for DBS stimulation, only a narrow range of parameters has proven to have clinical benefits and the optimal stimulation parameters may often be found during a single programming session which is scheduled after the surgery \[125\]. The stimulation parameters are adjusted by the neurologists to obtain the most induced-stimulation adverse effects \[125\]. The default stimulation setting of stimulation is 130Hz rectangular with 60µs pulse width. After programming the stimulator, the patient (user) can turn the stimulator ON and OFF as desired using a wireless remote controller.

### 2.4.2 Motor symptoms, and treatment of dystonia

Dystonia is a movement disorder causing sustained muscle contractions \[60,158\]. Dystonia is classified according to the part(s) of the body affected by this condition \[202\]. For example, generalized dystonia affects most or all the body parts. Another type of dystonia is focal dystonia which is localized to a specific part \[60\]. The most common focal dystonia is cervical dystonia which is involuntary muscle contractions of neck causing it to turn in a specific direction (e.g., left, right, upward, or downward) \[146\].

A treatment for dystonia is botulinum toxin (BTX) injections in the affected muscle \[97,108\]. Other treatments include oral medications, selective peripheral surgical denervation (cutting the nerves to the muscles with abnormal contractions) and deep brain stimulation \[24,150\]. DBS is a treatment for patients who do not respond to medications and BTX \[18\].
### 2.5 Neural oscillations

Rhythmic activities of the brain are typically divided into frequency bands [35]. These frequency bands are described in Table (2.1). The band activities may change with respect to an event such as movements [28, 163, 169, 216, 227]. For example, beta activity is suppressed while the gamma activity is elevated during movement execution in the motor system [5, 163, 169, 216].

### 2.6 Neural responses to an event

Brain activity changes in response to an external (e.g. sound) or internal stimulus (e.g. motor planning). Evoked potentials are brain responses to internal and external events such as an auditory or visual stimulus, sensory and movement processing [55, 173]. Amplitude and latency of the evoked potential depends on amplitude and profile of the stimulus [12, 160, 184, 190, 214] as well as the brain state (attention, motivation, movement parameters, etc) [88, 194, 221]. The EPs are widely accepted and used in clinical neurology to characterize the neural processes as well as for diagnostic purposes due to simplicity of calculating these potentials [21, 204, 212, 222]. However, one of the challenges in uncovering the salient neural activity is the low signal-to-noise ratio that is common.

<table>
<thead>
<tr>
<th>Designation</th>
<th>Frequency range</th>
</tr>
</thead>
<tbody>
<tr>
<td>δ</td>
<td>&lt;4Hz</td>
</tr>
<tr>
<td>θ</td>
<td>4Hz-8Hz</td>
</tr>
<tr>
<td>α</td>
<td>8Hz-12Hz</td>
</tr>
<tr>
<td>β</td>
<td>12Hz-30Hz</td>
</tr>
<tr>
<td>γ</td>
<td>&gt;30Hz</td>
</tr>
</tbody>
</table>

Table 2.1: The frequencies seen in the local-field activity are classified into frequency ranges [35].
in neural recordings. Typically, noise is dealt with by averaging a large number of repeated trials under the assumption that the salient neural responses are time-locked to motor-specific events like movement onset or onset of an external stimulus. Averaging over a large number of trials in time-domain mostly preserves the components that are perfectly time-locked to the event and cancels out the components that are off-phase from trial-to-trial. An alternative to averaging in the time-domain is to average their time-frequency representations. The time-frequency representation of a signal (e.g. a spectrogram) details the spectral content of the signal as a function of time. Similar to averaging over time, averaging over time-frequency space can aid in highlighting the time-dependent spectral changes in neural activity. Time-frequency representations have benefits and drawbacks [129]. Some time-frequency representations do not carry any information regarding phase of the signal. These representations tend to preserve the noise power and visualize it after averaging. Spectrogram is an example of these representations [6, 76]. It is one of the earliest proposed time-frequency representations yet is still commonly used to this day. It is Fourier transform of windowed signal under the assumption that the signal is stationary over each time window. Satisfying the stationarity assumption determines the upper bound for the window length. Moreover, the spectrogram has severe additional drawbacks, both theoretically since it provides biased estimators of the signal instantaneous frequency and group delay [133], and practically since the Gabor-Heisenberg inequality [76] makes tradeoffs between temporal and spectral resolution unavoidable. Some time-frequency representations, e.g. Wigner-Ville distribution (WVD) [228], do not have these drawbacks [129]. In next chapter, I am developing a visualization technique using WVD.
Chapter 3

Visualization of neural activity

Biological signals are often combination of different spectral components which may vary over time \([55, 209]\). It is desirable to transform these signals into the time-frequency domain where a 1D signal is represented in two-dimensional plane of time and frequency. Time-frequency representation shows spectral content of the signal as function of time. This representation is advantageous over spectral analysis methods (e.g. Fourier transform) that show overall spectrum of a signal over the entire trial. Visualization of neural activity in the time-frequency domain results in identification of salient neural activity and accurate picture of how the neural activity changes with respect to an event such as movement \([55, 169]\). Neural activity are often visualized in time-frequency domain through a joint time-frequency transformation which maps a one-dimensional signal into a two dimensional space of time and frequency. This results in a representation that describes how spectral content of the signal evolves over time. Various methods have been developed to visualize the spectral content of signals in time. Examples of these transformations are wavelet transform \([129]\), Gabor transform \([76]\), scalogram \([129]\), and Choi-William transform \([45]\). These methods have been applied to various biological signals and proven their ability in visualizing the signals \([129, 209]\).

Time-frequency transformations can be generally divided into linear and quadratic
A linear time-frequency transformation projects the signal on a set of basis waveforms which are concentrated in both time and frequency [129]. Because the waveforms are localized on the time-frequency plane, one can determine distribution of the signal energy over the time-frequency space by summing up the individual contributions from each projection. Consequently, resolution of these transformations are limited by time-frequency resolution of their basis waveforms [129]. By contrast, quadratic transformations are not projecting the signal into a set of basis waveforms. Wigner-Ville distribution (WVD) is a quadratic transformation [228]. Other quadratic transformations (e.g. spectrogram and Chio-William) can be derived from WVD [47,129]. WVD is calculated by correlating the signal with its translation in time and frequency (i.e. time lag and modulation) [228]. Wigner-Ville distribution of $x(t)$ is defined as

$$ W_x(t, w) = \int_{-\infty}^{+\infty} x(t + \tau/2)x^*(t - \tau/2)e^{-jw\tau}d\tau $$ (3.1)

WVD is composed of auto-terms and cross-terms. The auto-terms are WVD of signal components and cross-terms are produced as result of correlation between signal components. The cross-terms are also known as interference terms and are unwanted components of WVD [129]. These terms are oscillatory in nature (please see section (A.5) for more details) and can be eliminated by low-pass filtering (smoothing) the WVD [48]. However, the smoothing process also affects the auto-terms and lowers the localization of these components. There is a tradeoff between removing the interferences and smoothing the true signal components. Cohen introduced a general class of quadratic time-frequency distributions which are weighted average of WVD [47]. Cohen class is invariant to time translation and frequency modulation, i.e. if signal is translated in time or frequency, its corresponding energy distribution translates in time or frequency by the same amount.

A different approach for representing the signals in time-frequency domain is to reconstruct the signal as a sum of specific functions. If a signal can be systematically decomposed into a sum of sub-components, a time-frequency representation can be obtained from the decomposition simply by summing up the individual contributions from each
component without the interference terms. Thus, this technique provides, in principle, a method for excellent time-frequency visualization. However, if the signal sub-components are not orthogonal\(^1\), there is no systematic way to do the decomposition [55, 129]. One method is to decompose the signal to a set of predefined elements contained in a “dictionary”. The process is typically performed iteratively by choosing a component from the dictionary, projecting the signal on this component, and subtracting the projection from the signal [55, 128]. This process is repeated until the residual energy (error) is lower than a specified value. The residual energy monotonically declines after each iteration. This can be proven as follows. Suppose \(s(t)\) is signal of interest to be constructed in terms of a class of localized elementary functions \(h_p(t)\):

\[
s(t) = \sum_{p=1}^{a} A_p h_p(t) + R(t) \tag{3.2}
\]

where \(R(t)\) is the residual error after the decomposition and \(A_p\)’s are the weights associated with each element. The coefficient can be found using a greedy algorithm. Let \(s_p(t)\) be the remainder after decomposition of \(s(t)\) into \(p - 1\) elements, \(s_p(t) = s(t) - \sum_{i=0}^{p-1} A_i h_i(t)\). If \(h_i(t)\) are normalized (\(||h_i(t)|| = 1\)),

\[
||s_p(t)||^2 = ||s(t)||^2 - \sum_{i=0}^{p-1} |A_i|^2 \tag{3.3}
\]

where \(||.||\) denotes Euclidean norm. The norm of the residual \(s_p(t)\) monotonically decreases after each iteration. Let \(\theta_p\) be the angle between \(s_p(t)\) and \(h_p(t)\); then

\[
\cos \theta_p = \frac{\int s_p(t) h_p^*(t) dt}{||s_p(t)||} = \frac{|A_p|}{||s_p(t)||} \tag{3.4}
\]

Substituting Eq.(3.4) to Eq.(3.3) yields to

\[
||s_p(t)||^2 = (\sin \theta_{p-1})^2 ||s_{p-1}(t)||^2 = ||s(t)||^2 \prod_{i=0}^{p-1} (\sin \theta_i)^2 \tag{3.5}
\]

\(^1\)Two signals are orthogonal if the inner product between them is zero.
Since \((\sin \theta_i)\) is less than one, the sequence \(|s(t)_i|\) monotonically decreases. This suggests that the residual error falls at each iteration and converges to zero if the elements of the dictionary do in fact cover the time-frequency space. However, the decomposition can always be terminated after a specific threshold involving the residue signal energy. It should be noted that the selection of coefficients are unique only if the elementary functions, \(h_p(t)\), are orthogonal.

Matching pursuit is a greedy algorithm to decompose the signal faster than an exhaustive search. Matching pursuit however has a number of drawbacks [128, 129]. It requires that a large dictionary of elementary functions be generated in advance. Maintaining a large dictionary for good resolution and for long-enough signal lengths involves steep storage requirements [128]. Finally, finding the best projection at each iterative step requires intensive computational processing.

I developed a parametric decomposition method that uses the WVD of the signal. This method does not rely on a dictionary, requires far fewer computational steps, and provides results comparable with results generated using matching pursuit or other Cohen classes. This method was developed to decompose the biological signals as summation of Gaussian chirplets [209]. A Gaussian chirplet is a component whereby its instantaneous frequency changes linearly over time and is localized in time by a Gaussian envelop [130]. Chirplets were selected for two reasons. First, chirping phenomenon, i.e. a time-varying and swept frequency wave, exists in many natural signals, e.g., bird whistles [130], in bat echo-location signals [55], and in EEG signals [55]. The instantaneous frequency of these signals increases/decreases linearly with time. Any nonlinear change in instantaneous frequency can be, by Taylor’s theorem, approximated as a first order change. Second, time spread of Gaussian chirplets is variable, thus chirplets are much more capable of describing the signals with time-varying components in compare to time-frequency transformations that project the signal in basis with identical time-spread (e.g. spectrogram and Gabor transform) [3,143,154]. There is no systematic way to decompose
a signal into sum of chirplets because they are not orthogonal [55, 129]. Therefore, it is desirable to have a method to approximate the signals in terms of a weighted sum of chirplet functions.

### 3.1 Organization of this chapter

This chapter is divided into two main sections. First, I describe how a signal can be approximated as sum of chirplets. This section only details how a signal can be decomposed to chirplet and detailed derivations of the equations are later described in Appendix A. In section 3.3, this decomposition method was applied to Electrocorticography recordings from primary cortex of an individual while the participant was performing reaching tasks.

### 3.2 Approximating the Time-Frequency Representation of Biosignals with Chirplets


#### 3.2.1 Abstract

A new member of the Cohen’s class time-frequency distribution is proposed. The kernel function is determined adaptively based on the signal of interest (e.g. neural responses). The kernel preserves the chirp-like components while removing interference terms generated due to the quadratic characteristic of Wigner-Ville distribution. This approach is based on the chirplet as an underlying model of biomedical signals. We illustrate
the method using a number of common biological signals including echo-location and evoked potential signals. Finally, the results are compared with other techniques including chirplet decomposition via matching pursuit and the Choi-Williams distribution function.

3.2.2 Introduction

Many signals of biological origin are non-stationary in nature. Examples include speech signals, bat calls as well as neuroelectric signals like electroencephalography (EEG) [145, 226], heart rate Variability [14] or event-related potentials (ERP) [177]. Time-frequency or time-scale representations, in recent years, have found significant application in non-stationary analysis of a wide-range of signals including biomedical signals [25, 39, 57, 59, 124, 137, 147, 180, 239]. Constructing a time-frequency representation involves mapping a one-dimensional time-domain signal $x(t)$ into a two-dimensional function of time and frequency or time and scale [199]. Time-frequency representations are some of the main tools for nonparametric instantaneous frequency estimation [199]. The position of peaks in the time-frequency representation reveal the main components or structures of the signal.

Among the most commonly used time-frequency distributions are the so-called quadratic distributions. The spectrogram [76], [6] is one of the earliest proposed distributions yet is still commonly used to this day. Nevertheless, the spectrogram has severe drawbacks, both theoretically since it provides biased estimators of the signal instantaneous frequency and group delay [133], and practically since the Gabor-Heisenberg inequality [76] makes tradeoffs between temporal and spectral resolution unavoidable. To overcome these shortcomings, other nonstationary representations have been proposed. Among these include the Cohen’s class [47] of bilinear time-frequency energy distributions. The Wigner-Ville distribution [228], the Margenau-Hill distribution [131], their smoothed versions [46, 67, 91], and others with reduced cross-terms [27, 45, 99, 162] are all mem-
bers of this class. Although Cohen’s class distributions tend to reduce the interference between the various signal sub-components, this reduction can affect the precision by which the instantaneous frequency is estimated. This is mainly due to the pre-defined smoothing kernel functions which do not distinguish between the signal components and the interference terms. Hence, in the process of reducing or removing cross-terms, the kernel also removes signal components. On the contrary, signal-dependent kernels can provide improved time-frequency representation and have been proposed for various applications [9, 48, 100, 102]. An extensive review of the methods proposed for improving time-frequency resolution can be found in [199].

The non-parametric methods of time-frequency analysis described thus far can be contrasted with parametric approaches which attempt to model the underlying signal [61,96]. There has been much debate as to the ideal choice of basis functions to use. Generally speaking, the more similar the basis function is to the signal, the more compact the decomposition. Many biological signals can be thought of as a sum of more elementary components each of which are relatively narrowband in nature. Common examples include speech which consists of a number of formant frequencies illustrating the resonance of the vocal tract. In such a case, chirplets (or chirp signals of limited time extent) can be thought of as a good model of the underlying signal – any narrowband changes in instantaneous frequency can be described mathematically to first order by linear changes in the time-frequency plane [3,143,154]. We have been working on ways to decompose biological signals into a sum of chirplets [55]. A time-frequency representation can be obtained from the decomposition by summing up the individual contributions from each chirplet. This provides a clear time-frequency picture of the signal without the cross-term interference. While we have found that this method yields excellent visualization of biomedical signals, there are some significant challenges to overcome because chirplets do not form an orthogonal basis set. In some earlier work, we used matching pursuit to carry out the decomposition process which we found to be prohibitive in terms of
computational cost. There is a need to find improved ways to carry out this analysis.

This paper proposes a new class of time-frequency distributions for which the kernel function is determined adaptively based on the signal of interest. This approach can be best characterized as a hybrid approach combining both non-parametric and parametric methods using the chirplet as an underlying model of the biomedical signal. The kernel function preserves the chirping components in the signal while eliminating the interference terms generated by the quadratic characteristic of the time-frequency representation. The proposed method filters out the oscillatory cross-terms and instead preserves the "true" signal components which are of low spatial frequency.

### 3.2.3 Proposed Method

**Wigner-Ville distribution and multicomponent signals**

Time-frequency representations via the wavelet [90], windowed Fourier transforms and chirplet transform [130] are computed by correlating the signal with a family of time-frequency atoms. The time-frequency resolution of the distributions is therefore limited by the resolution of these atoms. In contrast, the Wigner-Ville Distribution (WVD) defines signal energy density in time-frequency plane with no restriction on resolution beyond the uncertainty principle. The WVD is computed by correlating the signal with a time and frequency translation of itself [129].

\[
WV_f(t, \omega) = \int_{-\infty}^{\infty} f(t + \frac{\tau}{2}) f^*(t - \frac{\tau}{2}) e^{-i\omega \tau} d\tau
\]  

Due to the quadratic nature of the distribution, the application of the Wigner-Ville distribution is limited by the existence of interference terms. The interference can be best illustrated by considering multicomponent signals. We can think of a multicomponent signal \(f(t)\) as a sum of more elementary monocomponents, \(f(t) = \sum f_k(t)\). In section 3.2.3, we will explore the specific case where the monocomponents are Gaussian chirplet functions. The WVD of a multicomponent signal consists of the summation of auto and
interference terms (cross-terms) due to pair-wise interaction of components.

\[ WV_f(t, \omega) = \sum_k W_{V,f,k} + \sum_{n \neq m} \int_{-\infty}^{\infty} f_n(t + \frac{\tau}{2}) f^*_m(t - \frac{\tau}{2}) e^{-i\omega \tau} d\tau \]  \hspace{1cm} (3.7)

where \( W_{V,f,k} \) is WVD of \( k \)th monocomponent auto-term. Cross-terms may lead to an erroneous visual interpretation of the time-frequency representation, and are also a hindrance to pattern detection, since the interference can overlap with the signal. Due to the marginal properties of the WVD, which states that \( \int WV_f(t, \omega) dt = |F(\omega)|^2 \) and \( \int WV_f(t, \omega) d\omega = 2\pi |f(t)|^2 \), the interference terms are oscillatory and zero-mean if the individual components do not overlap at any point in time and frequency [129]. The spatial frequency of the oscillations depends on the distance between the monocomponents in time-frequency plane, i.e. the farther apart the components, the higher the oscillation frequency. Although these interferences can be attenuated by time-frequency averaging, this will result in the loss of energy localization.

The Cohen’s class distribution extends the Wigner-Ville distribution by introducing a smoothing kernel [47].

\[ WV_{f,\theta} = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} WV_f(\tau, \zeta) \theta(t - \tau, \omega - \zeta) d\tau d\zeta \]  \hspace{1cm} (3.8)

Since convolutions can be more easily manipulated in the transformed space, a two-dimensional Fourier transform of \( WV_f(t, \omega) \) with respect to \( t \) and \( \omega \) yields what is known as the ambiguity function. Based on equation (3.7), the ambiguity function of a multicomponent signal can be expressed in terms of summation of two dimensional Fourier transformation of monocomponents and cross-terms.

\[ A_s(\Omega_1, \Omega_2) = \sum_{k=1}^{N} A_c^k(\Omega_1, \Omega_2) + I(\Omega_1, \Omega_2) \]  \hspace{1cm} (3.9)

where \( A_c^k(\Omega_1, \Omega_2) \) is the ambiguity function of \( k \)th monocomponent and \( I(\Omega_1, \Omega_2) \) the ambiguity function of the interference terms. While it is not always possible to express \( I(\Omega_1, \Omega_2) \) in closed form, one can always work with the expression numerically. The transform of equation (3.8) gives the multiplication of the signal’s ambiguity function
Chapter 3. Visualization of neural activity

![Figure 3.1: Example of an upward chirp is shown in (a) time domain and (b) in time-frequency domain by spectrogram.](image)

with the transform of the kernel. That is, $A_{s,\theta}(\Omega_1, \Omega_2) = A_s(\Omega_1, \Omega_2).A_{\theta}(\Omega_1, \Omega_2)$. An ideal kernel should preserve each individual component and its localization in time-frequency domain while removing the cross-terms, i.e. $A_{\theta}(\Omega_1, \Omega_2).A_s(\Omega_1, \Omega_2) = \sum_{k=1}^{N} A_k(\Omega_1, \Omega_2)$.

The Wigner-Ville and ambiguity representation with Gaussian chirplets

Next we consider the specific case where the monocomponents of a multicomponent function are approximated by Gaussian chirplets.

The chirp is one of the most fundamental signals in nature. Figure 3.1 shows a chirp and its spectrogram as an example. Biological signals are also shown later in this chapter. Many natural and man-made signals can be well approximated using chirps, i.e. seismological signals, radar systems, evoke potentials [55], ultrasound signals [126, 127], and marine-mammal signals [95, 210]. A Gaussian chirplet is a component whereby its instantaneous frequency changes linearly over time and is localized in time by a Gaussian envelop. A normalized Gaussian chirplet is defined in the time domain as

$$c(t) = \left(\frac{\alpha}{\pi}\right)^{\frac{1}{4}} \exp \left\{ -\frac{\alpha(t - t_0)^2}{2} \right\} \exp \left\{ j[\omega_0 + \frac{\beta}{2}(t - t_0)](t - t_0) \right\}$$  \hspace{1cm} (3.10)

where $\alpha > 0$ is time spread of the signal, $t_0$ is center of time, $\omega_0$ is center of frequency,
and $\beta$ is the chirp rate [130]. $f(t)$ is normalized to have unit energy. The Wigner-Ville distribution of $f(t)$ can be expressed as

$$WV_c(t, \omega) = 2\exp\{-\alpha(t - t_0)^2\} \exp\{-\frac{1}{\alpha}[(t - t_0)\beta - (\omega - \omega_0)]^2\}$$  \hspace{1cm} (3.11)

Furthermore, it is notable that when $\alpha \to 0$ the chirplet becomes a chirp, $e^{i[\omega_0 + \frac{\beta}{2}(t-t_0)](t-t_0)}$. Hence the WVD of a chirp becomes

$$\lim_{\alpha \to 0} WV_c(t, \omega) = 2\pi\delta[(t - t_0)\beta - (\omega - \omega_0)]$$  \hspace{1cm} (3.12)

which shows a precise localization of instantaneous frequency and energy. Note however that this is not the case if the changes in instantaneous frequency are not linear [198, 199].

The ambiguity function of a Gaussian chirplet is expressed as

$$A_c(\Omega_1, \Omega_2) = 2\pi\exp\{-\frac{(\Omega_1 - \beta\Omega_2)^2}{4\alpha}\} \exp\{-\frac{\alpha(\Omega_2)^2}{4}\} \exp\{-j(\Omega_1 t_0 + \Omega_2 \omega_0)\}$$  \hspace{1cm} (3.13)

It should be noted that ambiguity function of a Gaussian chirplet is a zero-mean bivariate Gaussian density with covariance matrix determined by the time spread ($\alpha$) and the chirp rate ($\beta$). Due to the oscillatory nature of the cross-terms, the interference is located away from the origin [45, 96]. For instance, consider the signal $g(t)$ which is equal to the sum of two chirplets, $g(t) = A_1 c_1(t, \alpha, \beta, t_1, w_1) + A_2 c_2(t, \alpha, \beta, t_2, w_2)$. The WVD of $g(t)$ is expressed as

$$WV_g(t, w) = |A_1|^2 WV_c(t, w, \alpha, \beta, t_1, w_1) + |A_2|^2 WV_c(t, w, \alpha, \beta, t_2, w_2)$$
$$+ 2\Re \left\{ A_1 A_2^* WV_c(t, w, \alpha, \beta, \frac{t_1 + t_2}{2}, \frac{w_1 + w_2}{2}) e^{j(t(w_1-w_2)-(\omega_1-\omega_2)(t_1-t_2))} \right\}$$  \hspace{1cm} (3.14)

where $WV_c(t, w)$ is defined in equation 3.11. The ambiguity function is

$$I(\Omega_1, \Omega_2) = \left(4\pi e^{-\frac{\Omega_1^2}{4\alpha}} e^{-\frac{\alpha(\Omega_2)^2}{4}} e^{-j[\Omega_1 \frac{t_1 + t_2}{2} + \Omega_2 \frac{w_1 + w_2}{2}]} \right)$$
$$* \left( \delta(t_1 - t_2, \omega_1 - \omega_2) + \delta(t_2 - t_1, \omega_2 - \omega_1) \right)$$  \hspace{1cm} (3.15)
Figure 3.2: (a) WVD of two chirplets (b) Representation of chirplets in ambiguity space. Cross-terms are located between the chirplets in the WVD, while in ambiguity space they are located away from the origin. (c) Radon transformation in the neighborhood of the origin ($\rho = 0$). (d) Optimal kernel in the ambiguity space. (e) Resulting time-frequency representation. (f) Smoothed pseudo Wigner-Ville distribution of the signal. Reduction in energy localization is noticeable in this representation.
where $\delta(t, \omega)$ is a two-dimensional Dirac delta function and ‘∗’ is the two-dimensional convolution operator. The above equation shows that the interferences are concentrated at $(t_1 - t_2, \omega_1 - \omega_2)$ and $(t_2 - t_1, \omega_2 - \omega_1)$ with the auto-terms near the origin. Please see Figure (3.2). This example can be generalized to a sum of any number of chirplets with arbitrary parameters and proves for the general case that the interference terms are located away from the origin [26]. This observation holds important application for the determination of the adaptive kernel to be discussed in the next section.

**Optimal kernel determination**

Equal density contours for the auto-terms of chirplets are defined mathematically by ellipsoids. The direction and length of the principle axes are functions of the chirp rate and the time spread. These axes can be identified with a Radon transform [179]. Analysis of the Radon transform reveals information regarding the monocomponent chirp rates ($\beta$) and time spreads ($\alpha$). Recall that the chirplet components lie at the origin of the ambiguity space while the interference terms are located away from the origin. The Radon transform of ambiguity function of a normalized chirplet can be expressed as

$$R_c(\rho = 0, \theta) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} A_c(\Omega_1, \Omega_2) \delta(\rho - \Omega_1 \cos \theta - \Omega_2 \sin \theta) d\Omega_1 d\Omega_2$$

$$= 2\pi \sqrt{\frac{\pi}{\lambda(\theta)}} \exp\left\{-\frac{[\omega_0 - t_0 \tan \theta]^2}{4\lambda(\theta)}\right\}$$

where $\lambda(\theta) = \frac{\beta^2 + \tan^2 \theta}{4\alpha} + \frac{\alpha}{4}$. Based on the superposition property, the Radon transform will show peaks at values of $\theta$ corresponding to the axes orientations of each of the ellipsoids. In order to exclude the effect of the interference terms in the calculation, the Radon transform is carried out only in neighborhood of the origin. This neighborhood is defined as the circular region around the origin which includes 50% of the signal energy.

To eliminate artifacts due to sharp cut-offs from kernel filtering (e.g. ringing), the edges of the kernel were smoothed. The smoothing process can be carried out by employing a tapering function like a Hanning or Gaussian function. In Figure (3.2d) we show
the example of the use of a two-dimensional Gaussian function. A “cleaned” ambiguity representation is then obtained by multiplying the original ambiguity function with the corresponding mask. Finally, the time-frequency representation of the signal is generated by calculating the inverse Fourier transform of the ambiguity function.

If the signal of interest is not a sum of chirplets, the steps outlined above will result in a representation where the signal’s energy in the time-frequency plane is approximated by a number of localized straight line segments. It should be noted that for such signals, additional non-chirplet-like interference terms will also appear. These interference terms are often low frequency oscillations that overlap with the signal in ambiguity space. For example, a frequency modulated signal and its Wigner Ville representation are illustrated in Figure (3.3). Despite the nature of the signal, the method proposed here can represent the signal in time-frequency space with a high degree of localization. It can be shown that the representation conserved 99% of the original signal’s energy.

The Expectation-Maximization (EM) algorithm was used for finding maximum likelihood estimation of chirplet parameters in the time-frequency plane. All optimization algorithms suffer from difficulties in parameter initialization and in the selection of the number of parameters or components. However, in this case we make use of the parameters estimated from the Radon transformation in ambiguity space. This significantly reduces the time required for optimization as well as improves the robustness of the estimation. The number of components can also be set equal to the number of peaks found in the Radon transformation, and then adjusting the number of components from there to minimize the total error.

3.2.4 Results and Discussion

Although biological signals can be found over a wide range of frequencies, they are often narrowband in nature. Chirplets are thus a suitable choice for modeling such signals [55]. The method proposed in this paper uses this property to generate an interference-free
Figure 3.3: (a) Spectrogram of a frequency modulated signal. (b) Wigner-Ville representation of the signal (negative energies discarded). (c) Result of proposed method. (d) Choi-Williams representation of the signal. (e) Decomposition of signal in terms of seven chirplets.
Figure 3.4: Chirplet representations of a bio-acoustical signal. (a) Time-domain representation of the large brown bat echo-location signal (sampled at 0.14 MHz); (b) Spectrum of the signal (calculated with a 0.45 ms Gaussian window); (c) Time-frequency representation of the signal (d) Chirplet decomposition of the signal (represented by five chirplets). (e) Wigner-Ville distribution of the signal (negative energies discarded).
Figure 3.5: (a) Wigner-Ville distribution of a synthetic signal consisting of a sum of elementary signals [55]. (b) Resulting time-frequency representation.

time-frequency representation by approximating the underlying time-frequency structures of the signal by a linear approximation. The result provides not only a clearer picture of the salient signal characteristics but also provides a means for mathematically decomposing signals into chirplets. An example of this is shown in figure (3.4), where a bat echo-location ultrasound signal is represented as combination of four chirplets. We also show results from synthetically generated signals – see figure (3.5) where a signal consisting of a sinusoid, a windowed sinusoid, Gabor logons, sawtooth an impulse and a chirplet is analyzed by the same technique. This signal was adapted from [55]. In both cases, the time-frequency visualization is improved significantly and the main time-frequency structures easily identifiable.

We also provide one example where the time-frequency representation is compared with that obtained from chirplet decomposition with matching pursuit. Certain dynamic brain mechanisms can be investigated through neuroelectrical brain responses called event related potentials (ERP). The visual evoked potential (VEP) is an evoked brain response generated in the visual cortex in response to the presentation of a visual signal. Such signals are noisy and are often averaged before processing. The VEP signal we have
Figure 3.6: (a) Visual evoked response. (b) Wigner-Ville distribution of visual evoked response (negative energies discarded). (c) Resulting signal representation after applying optimal kernel. (d) Result obtained by Cui and Wong through chirplet decomposition via matching pursuit [55] (e) Three chirplet decomposition by the method proposed here. (f) Spectrogram of corresponding signal.
analyzed here is equal to an averaged of 50 trails from a single subject. Three chirplets are estimated for comparison with the results calculated by Cui and Wong [55] using the matching pursuit algorithm. As can be seen through comparison of both figures, the results are quite similar. The time-frequency representation is also verified through a spectrogram.

A main challenge for chirplet decomposition is that Gaussian chirplets do not form an orthogonal basis. One solution is to employ suboptimal schemes like matching pursuit. Figure (3.6) was generated by this particular approach. While the underlying theory of matching pursuit is well established, its numerical implementation in terms of computational speed and accuracy comes at an enormous cost. Matching pursuit requires that a large dictionary of chirplet functions be generated in advance [128]. The signal is decomposed iteratively by finding the best matched dictionary component and then subtracted from the original signal energy. This process continues until the residual energy (error) becomes lower than a specified value. Finding the best projection at each iterative step requires intensive computational processing; maintaining a large dictionary for good resolution and for long-enough signal lengths involves steep storage requirements. In contrast, the method proposed here does not rely on a dictionary and requires far fewer computational steps. More generally, we observe that chirplet decomposition provides significant data compressibility. The VEP signal shown in figure (3.6) consisting of 480 samples can be well-represented by as few as 15 parameters in terms of three Gaussian chirplets.

Earlier it was shown that the cross-term interference arising from a pair of monocomponents is located between the components. Moreover, the interferences are oscillatory in nature and the spatial frequency of these oscillations is a function of the distance between the components in time and frequency, i.e. the closer the two components, the lower the oscillation frequency. In ambiguity space, this would mean that the interference lies closer to the origin. The low frequency interference also appears as a result
of the signal’s instantaneous frequency changing nonlinearly with time. Due to the low frequency nature of these oscillations, the cross-terms may not be completely removed by the kernel due to overlap with signal components in the ambiguity space. Although this interference can be removed at the post-processing stage by (say) least-squares fitting to a Gaussian density, it is important to remember that this interference contributes to the signal’s overall energy distribution.

3.3 Approximating the ECoG activity with Chirplets

Electrocorticography (ECoG) is a method of recording electrical activities of the brain. This technique uses macro-electrodes placed surgically over/under the dura mater and over the surface of the cerebral cortex. The signals obtained using these epidural/subdural electrodes generally have higher signal-to-noise ratio, a wider bandwidth, and higher spatial resolution compared to electroencephalography (EEG) recordings [117, 190]. EEG and other non-invasive recording methods have lower signal-to-noise ratio as well as spatial resolution. Scalp is not transparent to the electrical waves, thus, it scatters and attenuates the waves. Advantage of ECoG electrodes over scalp recordings is that they are implanted under the scalp, thus, the scalp does not have any effect on these recordings. Moreover, ECoG is less invasive than intracortical recordings, as ECoG electrode does not penetrate brain tissue.

In this section, I am processing the ECoG activity recorded from the motor cortex of a 51 years old male participant. The participant was recruited from Functional Neurosurgery Clinic at the Hospital das Clínicas of University of Sao Paulo. The study was approved by the University of Sao Paulo research ethics board, and the participant signed a letter of consent prior to taking part in the experiment. The participant was implanted with two quadripolar epidural electrodes Lamitrode 3240 (St. Jude Medical Inc., U.S.A.). Each strip consists of a single row of four platinum discs that were 4 mm in
diameter and had center-to-center distance of 10 mm. The electrodes were embedded in
a silicone membrane. Contacts of the first strip were labeled 0-3 from distal to proximal
and contacts of the second strip were similarly indexed 4-7. The electrode strips were
placed over the premotor, primary motor, and sensory cortices associated with the upper
extremity representations. The first strip was placed on the cortices such that the second
contact (electrode #1) was over the primary motor cortex. The location of the elec-
trode was confirmed using electrical stimulation and by observing muscle contractions of
the contralateral upper limb. Stimulation parameters were: i) pulse frequency 50 Hz, ii)
pulse duration 100 $\mu$s, iii) monopolar-monophasic pulses, and iv) pulse amplitude 3-10$\mu$A.
Electrode contacts were numbered 0-3 from distal to proximal. Specifically, stimulation
of contact #1 implanted over the motor cortex induced finger or wrist movements. The
second strip was placed dorsal to the first such that contact #5 (the second contact of
the second strip) was positioned over the primary motor cortex and dorsal to contact
#1. Figure (3.7) shows exemplary illustration of the location of implanted electrodes
with respect to the head, on the MRI images, and the cortical area associated with the
upper extremity representations.

The impedance at each ECoG contact was measured to ensure electrode integrity.
In addition to the ECoG measurements, electromyography (EMG) signals from wrist
flexors, wrist extensors, biceps, and triceps were also recorded. ECoG and EMG signals
were all recorded with sampling frequency of 1200 Hz and bandpass filtered between 0.1
to 500Hz.

The participant performed reaching and retrieving tasks after receiving an external
sound cue. The tasks were performed with the contralateral hand to the side where the
electrodes were implanted. The participant sat on a comfortable chair and placed his
hand on his lap (no muscle activity was observed on this state). After hearing an external
cue (i.e. a beep sound), he reached to the target. He was asked to hold her hand on
the target for a few seconds and return to the initial position (i.e. rest). The target was
Figure 3.7: Location of implanted ECoG contacts with respect to the head and on MRI images are shown using BrainLab visualization software. Contacts of the first strip of electrodes are labeled 0-3 from distal to proximal, and contacts of the second strip are similarly indexed 4-7 (please see the upper left corner panel). Primary motor cortex is colored in velvet and primary sensory cortex is colored in amber. The area associated with the hand representation is marked in purple.

placed 40cm from the participant’s chest and where he could comfortably reach.

The recordings were analyzed offline. First, the trials were extracted using the external cue such that movement onset were denoted as time $t = 0s$. Each trial is 12 seconds long (i.e. from 4 second prior to the movement onset until 8 second after it). First, WVD’s were calculated and averaged. Next, the interferences were removed from the
Figure 3.8: (a) Averaged WVD of trials. (b) Averaged smoothed pseudo Wigner-Ville distribution of the trials. Hamming window (0.5 sec) was used to calculate the time-frequency distribution. (c) Averaged spectrogram of trials. The spectrogram was calculated using 0.5 sec Hamming windows with 450 ms overlaps. (d) Time-frequency representation of the signal using the adaptive kernel. (e) Decomposed signal to chirplets. (f) Averaged envelop of biceps activity.
averaged WVD’s by estimating the location of neural components in ambiguity space. This method is described in details in section 3.2.3. Finally, the signal was decomposed to chirplets using an estimation-maximization (EM) algorithm. The result was compared with averaged WVD, pseudo Wigner-Ville distribution, and spectrogram in Figure (3.8). The interferences are observed in averaged WVD (Figure (3.8a)). The interferences are covering the entire space such that the salient components are not easy to spot on the graph. Figures (3.8b and 3.8c) show two representations from Cohen’s class which tend to smooth the WVD to remove the interferences and bring out the salient components. Although Cohen’s class distributions tend to reduce the interference between the various signal sub-components, this reduction can affect the precision by which the signal components are represented. This is mainly due to the pre-defined smoothing kernel functions which do not distinguish between the signal components and the interference terms. Hence, the kernel also removes signal components in the process of reducing or removing cross-terms. It is noted that the components are smoothed in all representations shown in Figures (3.8b and 3.8c). On the contrary, signal-dependent kernels – as introduced in this chapter and shown in Figure (3.8d) – can provide improved time-frequency representation. The result obtained from this method is smoother and sharper in compare to other representations illustrated in Figure (3.8). Finally, the neural activity was decomposed to chirplet components using EM algorithm. The EM algorithm was terminated when time-length of the shortest component was higher than 100 ms. This resulted in decomposing the signal to 10 chirplets. Figure (3.8e) shows result of this decomposition. This figure illustrates the neural activity in details and resolution that was not possible with conventional visualization techniques (Wigner-Ville distribution, Choi-William, and spectrogram) which were discussed earlier in this chapter.

Decomposition of ECoG signal into chirplets shows that the energy of cortical activity is concentrated in three frequency bands, delta, beta and gamma bands. Gamma and delta components are observed during the movement execution while the beta compo-
nents are found in rest state and after the movement termination. These results are consistent with earlier studies that associated beta activity with movement inhibition and termination [5, 42, 101, 171, 181, 208] and gamma activity with movement execution and arousal of motor system [169, 227]. One may use activities at these bands to detect movement onset; i.e. the movement is initiated when beta activity is suppressed and gamma/delta activity is high. Beta and gamma activities have been used to detect the movement onset [86, 227]. Visualization of neural activity suggests that the activity between 18-22Hz (22Hz to be more specific) should be monitored rather than looking at the entire beta (12-30Hz) band. Moreover, it is noted that beta activity is more localized prior to the movement over a period that is considered to be related to movement planning. Although this phenomenon can be observed in all representations, it is more apparent when signal was decomposed into chirplets (Figure (3.8e)). In this section, the trials were averaged without any corrections for cross-trial variability caused by the way that the movements were performed. In the next chapter, a method is introduced to remove these variability and better realignment of neural components across trials.
In Chapter 3, I developed a method to visualize neural activity with higher signal-to-noise-ratio than many conventional visualization methods. Goals of visualization are: (1) illustrating the neural responses and (2) identifying characteristics of the salient neural activity which is a necessary step in recognition of the activities on single trial basis. Pattern recognition techniques, such as matched filters that are designed to identify the salient signal in noise, typically rely on having a prior knowledge on salient signal’s characteristics or its profile [110,218]. Due to contaminating noise that is common in electrophysiological recordings, the neural activity is typically averaged over the repeated trials before the visualization. Under the assumption that neural components occur at identical time instances cross-trials, averaging is expected to suppress the noise. This assumption is not fulfilled in case of complex movements. Controlling the complex movements over the repeated trials is extremely difficult – if not impossible. Thus, the movements are prone to cross-trial variability. In this chapter, I detail a method to remove any temporal variabilities in the way the task was performed. This technique can be used as part of visualizing the salient activity as well as part of a classification system.
Chapter 4. Temporal alignment of ECoG recordings

Alignment of neural activity prior to visualization results in more accurate representation of neural components. More crucially, alignment of neural activity is a necessary part in formulating a movement classification system. This emphasizes on importance of proper temporal alignment of neural activity prior to processing the neural data.

The material presented in this chapter is under review by Journal of Frontiers in Neuroscience.

4.1 Abstract

The classification of neural activity to decode arm movements for brain machine interfaces (BMI) holds enormous potential for neuroprosthetic devices. One difficulty lies in the fact that complex arm movements such as reaching and grasping are prone to cross-trial variability due to the way movements are performed. Typically initiation time, duration of movement and movement speed are variable even as a subject tries to reproduce the same task identically across trials. Therefore, movement-related neural activity will tend to occur at different times across each trial. Due to this mismatch, the averaging of neural activity will not bring into salience movement-related components, a necessary part in formulating a BMI movement classification system. To address this problem, we present a method of alignment that accounts for the variabilities in the way the movements are conducted. In this study, arm speed was used to align neural activity. Four subjects had electrocorticographic (ECoG) electrodes implanted over their primary motor cortex and were asked to perform reaching and retrieving tasks using the upper limb contralateral to the site of electrode implantation. The arm speeds were aligned using a nonlinear transformation of the temporal axes resulting in averaged spectrograms with superior visualization of movement-related neural activity when compared to averaging without alignment.
4.2 Objective and hypotheses

The objective of the work presented in this chapter is to obtain superior visualization of movement-related neural activity by aligning the activities over repeated trials. Self-paced unconstrained voluntary movements are prone to movement variability in initiation time, duration and speed. The movement-related cortical activities would therefore occur at different time instances across different trials. These temporal mismatches add to the difficulty in identifying the salient neural response underlying movement activity. Given that there exists a direct functional relationship between motoneuron activity and arm kinematics, I hypothesize that neural events can be better aligned if the kinematic profiles are identical on each trial. Kinematic signals were used to find a nonlinear transformation of the time axis as calculated by the method of dynamic time-warping. The transformations serve to remove any temporal variabilities in the way the task was performed. The time transformations can then be applied to the spectrogram of the corresponding ECoG signal. This results in well-delineated movement-related components including event-related synchronization/desynchronization which can be used for reconstruction of movement from ECoG activity or movement classification.

4.3 Introduction

The challenge for a brain-machine interface (BMI) is to decode user intent and to transform neural signals into signals which drive an external device like a prosthetic arm. This technology holds enormous potential as an assistive device for individuals with limited ability to perform voluntary movements. Examples of populations that may benefit from this technology include individuals with brain stem stroke, advanced stages of amyotrophic lateral sclerosis [17, 106, 107, 157], severe cerebral palsy [172], and high level cervical spinal cord injury [231]. However, the construction of a BMI platform is predicated first on the ability to identify the salient neural activity associated with upper limb
movement.

A number of studies have explored the relationship between movement-related neural activity and arm movement [17,19,43,69,82,117,139,170,175,175,183,190,219,240]. One of the challenges to uncovering the salient neural activity is the variability of the neural activities as well as the low signal-to-noise ratio that is common in electrophysiological recordings. Typically, noise and variability is dealt with by averaging a large number of repeated trials. To do this, however, one must assume that the neural activity is time-locked to motor-specific events like movement onset. While the evoked brain activity from external stimuli or highly constrained motor tasks can be thought of as being identical on a trial-by-trial basis, this is certainly not true when a subject is performing a complex movement task like reaching. Due to the difficulty in constraining the movement of the arm, it would be unwise to simply take all trials and average them. Instead, we propose a method of realignment through a nonlinear transformation in time. This transformation accounts for differences in movement initiation, arm speeds, and movement durations. After alignment, I expect the neural activities to occur at near identical times and that the related neural activities can now be more effectively brought into salience through averaging.

4.4 Background

Averaging of neural activities is a practice standard in electrophysiology. For example, event-related potentials (ERP) are time-averaged brain responses to a sensory or motor event. They are simple to calculate and are widely used in clinical neurology for diagnostic purposes. The ERPs show mostly low frequency neural activity since the high frequency components tend to be off-phase from trial-to-trial thereby cancelling out through averaging. An alternative to averaging in the time-domain is to average their time-frequency representations. The time-frequency representation of a signal (e.g. a
The electrical activity of the brain can be recorded using a number of different methods including 1) electroencephalography (EEG) where electrodes are placed on the scalp, and 2) single neuron or neuronal ensemble recordings obtained through micro-electrodes placed intra-cortically in proximity of target neurons. Electrocorticography (ECoG) is a method of recording the electrical activities of the brain using macro-electrodes placed surgically over the dura and the surface of the cerebral cortex. The signals obtained using these electrodes generally have higher signal-to-noise ratio, a wider bandwidth and higher spatial resolution when compared to electroencephalography recordings [117,190,192]. In addition, this technology is less invasive than intracortical recordings since the electrodes do not penetrate the brain tissue. In this study, we processed the activity of the motor cortex recorded from two ECoG contacts in a bipolar arrangement.

Typically, during analysis the neuromotor activities are aligned to a ‘go’ signal [20, 182, 219], to movement onset [140,148,183,197] or to movement termination [101]. The alignment strategy is determined in part by the experimental paradigm and by what questions the experimenters would like to answer from their data. For example, activities aligned to the go signal would allow for the study of movement preparation. The problem with event-based alignment is that this does not guarantee that the remainder of the trial is similarly aligned. If we were interested also in, movement termination as an example, the trials would then need to be realigned to the end point of movement cycle. To
eliminate repeated analyses, we instead introduce a new method of alignment involving a nonlinear transformation of time. We believe that this transformation can account for the temporal differences in the way a motor task is conducted.

Temporal alignment of biological signals is not new; for example, such techniques have been employed extensively as part of automatic speech recognition algorithms. Nonlinear time warping has also been used to align physiological signals [151] as well as neural signals [37, 44, 105, 173, 225]. We use it here in the context of aligning movement-related neural activity.

Dynamic time warping [188] is a graph-based approach to calculate the time transform required to align two signals. The time transformation (or time registration path) is calculated by minimizing a cost function which measures the similarities between the time instances of two signals. Dynamic time warping has been used previously to align sensory evoked responses [37, 173, 225]. Picton et al used dynamic time warping to align the brain-stem auditory evoked response showing improvement in the visualization of components over simple averaging [173]. In a similar study, Wang et al showed that the amplitude of the derived visual ERP can be increased by up to 76% after realignment using dynamic time warping. Casarotto et al used dynamic time warping to quantify the latencies between the ERPs obtained from normal and dyslexic children [37]. All of these studies show that a simple shift or linear scaling of time is not sufficient to align evoked components.

Earlier studies of movement-related neural activity rely on simple or constrained movements to avoid problems with averaging of trials. However this is not possible for a study involving complex movements due to the difficulty of constraining the movement of a participant to allow for careful control of arm kinematics. To deal with this issue, we used dynamic time warping to align the neural activities corresponding to the movements. Our method of realignment removes temporal mismatches caused by the way that the tasks are conducted and provides a new way to study complex movement tasks such as
reaching and grasping.

4.5 Material and Methods

4.5.1 Participants

Four male participants were recruited from Functional Neurosurgery Clinic at the Hospital das Clinicas of University of Sao Paulo. The study was approved by the University of Sao Paulo research ethics board, and all participants signed a letter of consent prior to taking part in the experiments. Subject 1 was 51 years old male, subject 2 was 48 years old female, subject 3 was 42 years old male, and subject 4 was 58 years old male. All participants were implanted with unilateral epidural quadripolar electrodes over the motor cortex for the treatment of chronic pain. After the insertion of the electrodes, patients had their systems externalized for 6 days for the selection of optimal stimulation parameters (polarity, amplitude, frequency, duration, etc). Once these were chosen, the electrodes were connected to an implantable pulse generator during a second surgical procedure. The experiment took place over the six days during which the electrode leads were externalized.

4.5.2 Electrodes and postoperative recordings

The placement and choice of number of ECoG contacts were dictated by the clinical requirements unrelated to the purpose and consideration of this study.

The participants were implanted with two quadripolar epidural electrodes Lamitrode 3240 (St. Jude Medical Inc., U.S.A.). Each strip consists of a single row of four platinum discs that were 4 mm in diameter and had center-to-center distance of 10 mm. The electrodes were embedded in a silicon membrane. All participants were implanted with two electrode strips. Contacts of the first strip were labeled 0-3 from distal to proximal and contacts of the second strip were similarly indexed 4-7. The electrode strips were
placed over the premotor, primary motor, and sensory cortices associated with the upper extremity representations. The first strip was placed on the cortices such that the second contact (electrode #1) was over the primary motor cortex. The location of the electrode was confirmed using electrical stimulation and by observing muscle contractions of the contralateral upper limb. Stimulation parameters were: i) pulse frequency 50 Hz, ii) pulse duration 100 µs, iii) monopolar-monophasic pulses, and iv) pulse amplitude 3-10µA. Electrode contacts were numbered 0-3 from distal to proximal. Specifically, stimulation of contact #1 implanted over the motor cortex induced finger or wrist movements. Electrode contacts of the second strip were numbered 4-7 from distal to proximal. The second strip was placed dorsal to the first such that contact #5 (the second contact of the second strip) was positioned over the primary motor cortex and dorsal to contact #1. Figure (3.7) shows exemplary illustration of the location of implanted electrodes with respect to the head, on the MRI images, and the cortical area associated with the upper extremity representations.

In addition to the ECoG measurements, electroencephalography (EEG) signals were recorded at the C3, Cz, Fz, and FP1 locations according to the 10-20 electrode placement system. The EEG signals were recorded for offline processing and to ensure that artifacts such as eye blinks did not affect the ECoG recordings. All EEG signals were referenced to linked earlobes. The electromyography (EMG) signals from wrist flexors, wrist extensors, biceps, and triceps were also recorded. EEG, ECoG and EMG signals were all recorded with sampling frequency of 1200 Hz and bandpass filtered between 0.1 to 500Hz.

4.5.3 Experimental setup

The participants were seated in a comfortable chair. The upper limb movements were recorded using a three dimensional (X, Y, Z) electromagnetic tracker, Fastrack (Polhemus Inc, U.S.A.) and a customized data acquisition software written in C. A motion sensor was placed over the dorsal aspect of the third metacarpal bone of the hand. The three-
dimensional position of the sensor was recorded with sampling frequency of 40 Hz and was time stamped. The upper limb kinematics were recorded using the same computer that captured the ECoG, EEG and EMG data. Thus the kinematic recordings were synchronized with the electrophysiological recordings.

4.5.4 Experimental protocol

ECoG and EMG signals were recorded while the participants performed a reaching task. The task was carried with the arm contralateral to the site of electrode implantation. The task was to reach a target placed 40 cm away from the chest which the participant could do comfortably. At the start of the task the participant had his or her hand in a resting position where the hand was placed on a pillow located on their lap. Under resting conditions EMG muscle activity was not observed. The participants received an auditory cue (“go” signal) to start the reaching task. After completing this, the participants were instructed to wait for few seconds before returning their hand to the initial resting place (retrieving task). The time between the end of the last trial and the cue signal of the next trial was randomized, and in the range of 8-10 seconds. Each participant performed at least 80 reaching tasks.

4.5.5 Analysis

The data were analyzed in the time-frequency domain using a spectrogram. A spectrogram gives the windowed short-time Fourier transform of a signal by describing the frequency content of a signal and how it changes over time. Signals were windowed in segments of 100 ms using a Hamming window. A Fourier transform was then computed for the windowed signal resulting in a spectrum with resolution of 1 Hz. The window was then shifted forward by 10 ms, and the procedure was repeated until the end of the epoch was reached. The resulting spectrogram consists of a matrix where each row represents the power spectrum of a windowed signal. Each column of this matrix represents
the time series of power at a particular frequency ranging between 0-600 Hz. Event-related changes (ERD/ERS) were calculated by normalizing each column (frequency) by the baseline power. The baseline was defined as the average power between 1-2 seconds prior to movement onset. All of the trials were aligned by the movement onset which we designated as t=0. Movement onset itself is defined as the instance where arm speed exceeded a threshold of ‘0.5 cm/s’. A trial is defined as the period beginning 4 second prior to and ending 8 seconds after the onset of the reaching task.

Spectrograms are typically averaged without realignment along the time axis. This is the usual method of finding the spectral density of neural activity and how it changes with respect to movement. We call this method conventional averaging. In the second method, the epochs were warped in time according to the arm kinematics prior to averaging. One trial is chosen as the ‘gold-standard’ or reference trial – all the other trials are then warped to this reference trial using a time-registration path. Given that warping of the signal in the time-domain distorts its spectral content, the time transformations were not applied to the raw ECoG recordings. Instead, warping was performed over the spectral densities such that the neural activity corresponding to the same arm velocity is identical across all trials. In this case, not only will movement onset and offset be aligned, but the neural activity at each time-point will correspond to the same arm speed/position. We call this method time-warped averaging.

4.5.6 Realignment of the trials using dynamic time warping according to arm speed

Time-warping of ECoG signals were carried out over arm velocity such that the velocity profiles would be identical after time-warping is complete. For simplicity, we warped along the X-axis (orthogonal to the chest surface) since it is the largest component over which movement took place. To determine the time registration path, we chose the Euclidean distance as a cost function and found the corresponding time points across the
Figure 4.1: Illustration of nonlinear alignment or time-warping. The time registration path defines how one time point in one trial maps to another time point in a different trial. The difference between two velocities becomes minimal when the time axis is transformed using the time-registration path. The same time-registration path is used to align the cortical activities in time domain or their spectrograms.

two time axes such that the Euclidean distance in arm velocities is minimized. Figure (4.1) show an example of the registration path obtained by time warping two trials. This process aligns the time course of the movements (and therefore the spectral density of the associated neural activity) to a “gold standard”. The gold standard was randomly selected.
Figure 4.2: Superimposed arm velocity along the X-axis for 25 trials when Subject 2 was reaching for a target. The subject’s arm returned to its initial location after a pause of several seconds having reached the target. The trials were aligned to the initial movement onset and are marked as t=0. The variation in the duration of movement is clearly visible.

4.6 Results

4.6.1 Conventional averaging of ECoG signals

Overall, the time-frequency representation of the ECoG response shows a very distinct pattern of activity over the course of the movement. The power in the beta activity (12-30 Hz) is attenuated during the course of movement execution while the power in the gamma activity (65-140 Hz) is increased. These changes in power are statistically significant (p<0.05, Kolmogorov-Smirnov test).

However, the variability in the time course of the velocity profile is significant from trial to trial. Figure (4.2) shows 25 profiles of arm speed along the X-axis for Subject 2. The movement duration deviated from the average by as much as 600 ms across movement durations that last only 2 seconds. Spectral components after averaging are visible, but are either blurred or distorted due to temporal misalignment. To illustrate the effects of averaging without non-linear alignment, we carried out our analysis both by aligning to the movement onset of the reach task (Figures 4.3a and 4.3d, Figures 4.4a and
Figure 4.3: (a,b,c) Data from Subject #1. (a) The average spectrogram and the associated biceps activity as calculated through conventional averaging. Epochs were aligned with respect to onset of the reaching task with no time-warping used. Movement onset is denoted by dash dotted line (‘-.’). The average spectrogram was normalized with respect to the baseline, which is defined as the power between 1 and 2 seconds prior to movement onset. (b) Same as (a) but with data aligned to movement onset of the retrieval task. (c) Same as (a) and (b) but with non-linear warping of the time axis prior to averaging. (d,e,f) Shows the same for Subject #2.

4.4d) as well as aligning to the movement onset of the retrieval task (Figures 4.3b and 4.3e, Figures 4.4b and 4.4e). In each case, gamma activity for example is scattered over the time-course of the movement and localized into multiple components. The breakup of the components is due to temporal misalignment, a result which we also observe with the EMG activities. Also the average of the rectified EMG shows a sharply increasing
signal at the onset of the reaching task (Figures 4.3a and 4.4a), but as the trials become desynchronized over time they do not exhibit the same sharp decrease at the end of the reaching task, nor is the signal as visible at the onset/completion of the retrieval task. Quantitatively, the EMG signals fall in amplitude by as much as 50% after the completion of the reaching task rendering the activity during the retrieval task almost undetectable. Figures 4.3b and 4.3e, 4.4b, and 4.4e show alignment with the onset of the retrieval task but there are similar problems here as well.

4.6.2 Time-warped averaging of ECoG signals

It is clear that a translational shift in time is insufficient to properly align self-paced, voluntary movements. Next we explore the results that can be obtained when a non-
linear alignment is used. Results are shown in Figures 4.3c, 4.3f, 4.4c, and 4.4f, which we compare to the earlier results obtained through conventional averaging of the same trials. The movement-related components (ERD/ERS) are clearly delineated in the warped average spectrograms. Moreover, we see that the time-course of these components matches that of the muscular activity. That is, the gamma ERS and beta ERD appear only when the muscles are activated. Synchronization of the gamma activity is clearly observed for both the reaching and retrieval tasks as single components. Note that gamma ERS is not observed when the subject is holding his/her arm at the target location – this silent period is not found when the trials are averaged solely by onset alignment. The findings for beta ERD are similar. Our observations are consistent across all subjects.

4.7 Discussion

In this chapter, I presented a new method for alignment of neural events over repeated experimental trials. Self-paced unconstrained voluntary movements are prone to movement variability in initiation time, duration and speed. The movement-related cortical activities would therefore occur at different time instances across different trials. These temporal mismatches add to the difficulty in identifying the salient neural response underlying movement activity. Given that there exists a direct functional relationship between motoneuron activity and arm kinematics, I hypothesize that neural events can be better aligned if the kinematic profiles are identical on each trial. Kinematic signals were used to find a nonlinear transformation of the time axis as calculated by the method of dynamic time-warping. The transformations serve to remove any temporal variabilities in the way the task was performed. The time transformations were then applied to the spectrogram of the corresponding ECoG signal. This resulted in well-delineated movement-related components including event-related synchronization/desynchronization. Finally, the spectrograms that are now aligned were averaged. The outcome is a vastly improved
visualization of the neural activity for complex arm movements. When the results are compared to that of conventional averaging with trials aligned only by movement onset, we see instead the movement-related components to be either blurred or absent. The components found through alignment via warping can be traced back to specific events like movement termination and initiation.

Epochs of EEG data are traditionally aligned with respect to an event of interest (e.g. movement onset). However, if the investigator wishes to study another event in the same data set, the data must be realigned to a new marker. Dynamic time-warping eliminates the need for this as an entire trial is aligned on one ‘go’. This has the distinct advantage of allowing for the best possible representation of neural activity across an entire trial. Earlier works have indicated that there is a direct, functional linear relationship between cortical activity and arm velocity [28, 43, 78, 117, 161, 174, 190, 240]. We have made use of this relationship to develop our method. The trials are aligned in accordance with the hypothesis that specific patterns of neural activity (particularly in the beta and gamma activity bands) correspond linearly with movement velocity. Alignment with velocity would therefore result in the alignment of neural activity. However, it is conceivable that our current understanding of the relationship between kinematics and neural activity is not complete and that more future studies may allow for the development of better methods of temporal alignment of neuromotor activity.

With alignment, our findings with ECoG data show a very distinct pattern of activity over the course of the movement. The power in the beta activity (12-30 Hz) was found to be attenuated during the motor tasks whereas power in gamma activity (65-140 Hz) increased correspondingly over the same time period. Beta activity is typically believed to have an inhibitory effect on movement while gamma oscillations are believed to facilitate movement [101, 170]. The coupled changes in beta along with gamma activities illustrate the complexity of the operation of the basal ganglia circuitry. Activity in both bands return to normal levels after cessation of movement although the time-course for recovery
is very different from movement initiation where the neural activity is more abrupt. Similar patterns in neural activity have been found in other recording paradigms: single unit recording, local field, and scalp recordings [85, 86, 134, 170].

The possibility of using ECoG as an activation/control strategy for prosthetic devices requires that a platform be built to identify movement-related ECoG activity. A common approach is to classify the neural activity into a number of “gestures” or tasks. A database of templates each corresponding to a different task is generated and later used to classify online activity. The primary difficulty here is the same as before: it is difficult to expect single trial neural activity to match that of a standardized template. Instead, we can use again non-linear alignment methods to remove temporal variations to better match the signals with the templates. This is a method similar to that which is employed in speech recognition (e.g. [178]). Speech recognition systems quantify words as sequences of short-term spectra (i.e. templates). The sequence of an unknown word can be compared with each of the templates and the closest match is taken to correspond to the input. The performance of such a system depends on the accuracy of the template itself as well as alignment of the template with the signal. Therefore time alignment is an important component in the successful design of such a system. Similarly, we would expect that temporal alignment of neural activity would also improve the performance of a gesture or task-based BMI system. While most modern implementations of automatic speech recognition systems use statistical models like hidden Markov models or neural networks, the basic principles remain the same. Our choice of dynamic time warping was motivated by the ease of implementation as well as its relevance towards the basic scientific question of finding the underlying neural components of upper limb movements.
Chapter 5

Reconstruction of reaching movement trajectories

I described two methods to align the neural activity and to visualize them in Chapters 3 and 4. The movement-related spectral changes are observed in the results presented in these chapters. These observations are made on averaged neural activity. Averaged activity, after alignment, is used to identify the features that can be attributed to the movement. This chapter is aimed to use these features to reconstruct arm movement on single-trial basis. A multilinear model was employed to reconstruct the movement kinematics using ECoG activity recorded from primary motor cortex.

5.1 Abstract

Arm trajectory was reconstructed from recordings made from electrocorticographic (ECoG) contacts placed over the primary motor cortex. Three individuals participated in the study. Participants were implanted with eight ECoG electrodes as part of a clinical intervention for the treatment of chronic pain. ECoG signals and movement kinematics were recorded simultaneously while the participants reached targets placed 40 cm from their chest. The tasks were carried out with the arm contralateral to the site of electrode
implantation. Changes in spectral density of ECoG activity were observed with respect to movement in the low-frequency (<2 Hz), alpha-beta (8-30 Hz), and high-gamma (>65 Hz) bands. An individualized classifier was constructed using ECoG activity bands showing the greatest power change on a per subject basis. Linear discriminant analysis was then used to identify movement onset with almost complete accuracy. Changes in spectral density of ECoG activity were also found to be well-correlated with movement speed. A linear regression model was used to reconstruct movement velocity from ECoG band power. Correlation between predicted and actual arm velocity exceeded 80%. Our results outline the possibility generating arm trajectories using as few as eight ECoG electrodes implanted in a minimally invasive manner.

5.2 Objective and hypotheses

The objective of the work presented in this chapter is to detect arm movements and reconstruct the arm speed from ECoG activity recorded from the primary motor cortex. In Chapter 4, I identified the movement-related changes in spectral density of cortical activity. These changes were statistically significant and were found in multiple frequency bands, namely delta, beta, and gamma bands. In this chapter, I hypothesize that significant changes in amplitudes of gamma and beta activities are indicative of movement onset and there is a functional relationship between the band activities and movement kinematics.

5.3 Introduction

There has been extensive work done trying to extract kinematic parameters from brain activity [8, 41, 81, 135, 138, 174, 190, 211, 233, 240]. Motor activity can be recorded from the brain using both non-invasive methods (e.g. EEG) or more invasive techniques (e.g. deep brain recordings). A number of studies have shown that it is possible to reconstruct
two and three dimensional arm movements [8, 41, 86, 117–119, 135, 138, 174, 190, 191]. In particular, Georgopoulos et al [81] demonstrated that 3D arm movement can be predicted from single-unit activity with high accuracy. Despite these studies, it is still not clear whether less invasive method can be used reliably to extract the upper limb kinematics with the same degree of accuracy. ECoG is a minimally invasive method of recording electrical activities of the brain. This technique uses macroelectrodes placed surgically over or underneath the dura mater, and in contact with the surface of the cerebral cortex. The signals obtained using ECoG electrodes generally have a wider bandwidth and higher spatial resolution compared to EEG recordings [117, 190]. In addition, this recording technology is less invasive than intracortical methods as ECoG electrodes do not penetrate the brain tissue.

The identification of voluntary movements from ECoG recordings is a difficult problem. One area of application for movement identification is in the development assistive devices. In particular, ECoG can be thought of as activation or control strategy for prosthetic devices. This requires building a platform capable of identifying changes in the brain state and translating these changes to control commands. A common approach is to classify the neural activity into a number of "gestures" or tasks. Although it is difficult to expect single trial neural activity to match that of a standardized template, template matching techniques have shown their feasibility in recognition of the movement-related components [84, 86, 118, 119, 227]. In this approach, a database of templates, each corresponding to a different task, is generated and later used to classify online activity. The classification is performed by finding the most similar template to the generated pattern. Thus, the user is required to produce a specific mental state to generate a desired command. Template matching techniques have a number of shortcomings. First, the mental state is not necessarily related with the movement produced. For instance, imagining a leg movement may be mapped to moving forward while imagining a tongue movement is mapped to moving backward. Second, the number of gestures is limited
and the movement parameters are not specified by the user (e.g., all movements are generated with constant speed). In contrast, if the functional relationship between the brain activity and the movement parameters is known, the kinematic parameters can be extracted directly from the brain recordings and used to generate an identical movement with a prosthetic device. As such, the user can conduct any movement with any desired speed and trajectory.

ECoG activity has been shown to be well-correlated to movement and how the movement is conducted [43, 66, 84–86, 89, 117–119, 170, 174, 190, 200]. There have also been attempts to reconstruct arm trajectories in two dimensions using ECoG data using a large number (e.g., 16-96) of ECoG contacts with good electrode coverage of cortical regions [8, 13, 89, 114, 123, 138, 174, 190, 240]. This allows finding the most informative electrode which often varies by participant. Implanting ECoG electrodes over a large area of the brain has a number of disadvantages. First, a large number of sensors increases the computational complexity imposed on the system due to the consumption of bandwidth. Second, implanting a large number of electrodes requires covering a large brain resulting in a more invasive procedure. As such there is a need to explore the possibility of using fewer electrodes. The reconstruction of upper limb kinematics from a small number of electrodes has not been reported yet. To address this gap, we introduce a method to reproduce three-dimensional movements of the arm using activity of the primary motor cortex recorded from eight ECoG contacts. Our results uncover how intended movements are represented by local activity of primary motor cortex and shows plausibility of identifying the movement onset as well as its speed from ECoG activity. This information can be used by prosthetic devices to restore the lost movement for individuals with limited mobility.
5.4 Materials and methods

5.4.1 Participants

Three patients undergoing treatment for chronic pain using cortical electrical stimulation were recruited from the Functional Neurosurgery clinic of Hospital das Clínicas of University of São Paulo, Brazil. Subject 1 was 51 years old male, subject 2 was 48 years old female, and subject 3 was 42 years old male.

The study was approved by the University of São Paulo research ethics board, and all participants signed a letter of consent prior to taking part in the experiments.

5.4.2 Electrodes and postoperative recordings

The participants were implanted with two unilateral epidural quadripolar electrodes over the premotor, primary motor, and sensory cortices for the treatment of chronic pain. Each epidural electrode (Lamitrode 3240; St. Jude Medical Inc., U.S.A.) consisted of a single row of four platinum discs (4 mm in diameter) embedded in a silicone membrane with a center-to-center distance of 10 mm. The placement and number of ECoG contacts were dictated exclusively by clinical requirements and were unrelated to this study.

The first electrode strip was placed with the second contact (electrode #1) on the primary motor cortex over the representation of the upper limb. The location of the electrode was confirmed by observing finger or wrist movements of the contralateral limb in response to electrical stimulation applied during the surgical implantation. Stimulation consisted of amplitude 3–10$\mu$A monopolar pulses of 100 $\mu$s, delivered at 50 Hz. Electrode contacts were numbered 0–3 from distal to proximal. Specifically, stimulation of contact #1 implanted over the motor cortex induced finger or wrist movements. The second electrode strip was placed dorsal to the first such that contact #5 (the second contact of the second strip) was positioned over the primary motor cortex and dorsal to contact #1. Figure (3.7) shows exemplary illustration of the location of implanted electrodes.
with respect to the head, on the MRI images, and the cortical area associated with the upper extremity representations.

After the insertion of the epidural electrodes, the electrode leads were externalized for 6 days to optimize the stimulation parameters (i.e., polarity, amplitude, frequency, and duration). Once these were chosen, the electrodes were internalized and connected to an implantable pulse generator during a second surgery. This experiment took place over the six days during which the electrode leads were externalized.

### 5.4.3 Recordings

In addition to the ECoG measurements, we also recorded electroencephalography (EEG) and electromyographic (EMG) signals. We obtained EEG recordings from four locations (C3, Cz, Fz, and FP1 of the 10-20 electrode placement system; referenced to linked earlobes) to ensure that artifacts (e.g., eye blinks) did not affect the ECoG recordings. We used our EMG recordings to monitor activity of wrist flexors, wrist extensors, biceps, and triceps. EEG, ECoG and EMG signals were all recorded with sampling frequency of 1,200 Hz and bandpass filtered between 0.1 to 500Hz.

The upper limb movements were recorded using a three dimensional (X, Y, Z) electromagnetic tracker (Fastrack, Polhemus Inc, U.S.A.) and a customized data acquisition software written in the C programming language. A motion sensor was placed over the dorsal aspect of the third metacarpal bone of the hand. The three-dimensional position of the sensor was recorded with sampling frequency of 40 Hz and was time stamped. The upper limb kinematics were recorded using the same computer that captured the ECoG, EEG and EMG data.

### 5.4.4 Experimental protocol

The participants were seated in a comfortable chair. The participants performed a reaching task with the arm contralateral to the site of electrode implantation. They were asked
to fixate their gaze to a point located on the midline prior and during the movement. The experimental task started with the participants’ hand resting on a pillow placed on their lap. After 10 seconds, an auditory cue (“go”) signaled to the participants that they had to reach to a target placed 40 cm from their chest and 30 cm to the left or right of the midline. The participants were asked to hold the final position for 2-4 seconds before returning their hand to the resting position. After a resting period of randomized duration (8s–10s) the participants received a new ”go” signal. Task involved the subjects reaching sequentially to the left (RTL) and to the right (RTR) targets. All reaching tasks were repeated at least 40 times.

5.4.5 Processing ECoG recordings

First, we identify changes in the spectral density of the ECoG recordings attributed to the movement. Next, we show that these events are indicative of motor commands and that they can be used to reconstruct the trajectory of the moving arm.

5.4.6 Preprocessing

All of the trials, defined as the period beginning 4 second prior to and ending 8 seconds after the onset of the reaching task, were aligned by the movement onset which we designated as t=0. Movement onset was defined as the instance where arm velocity exceeded a threshold of ’0.5 cm/s’.

The trials were inspected visually and trials with eye blink artifacts were removed. The eye blinks were identified from EEG activity recorded from Fp1 and Fz contacts.
5.4.7 Movement-related changes in spectral density of ECoG activities

Empirically it has been found that band activity changes prior to and during a voluntary movement. A triggered, synchronized decrease in band power is known as event-related desynchronization (ERD) and a corresponding increase is known as an event-related synchronization (ERS) [168]. These events are measured with respect to a chosen baseline in activity. The baseline is typically set to the rest state (in our case, 1-2 sec prior to initiation of movement - when no movement-related activities are expected). This time period was chosen based on our observation that the reaction time of our participants to the 'go' cue was less than 500ms.

The epochs were analyzed in the time-frequency domain using a spectrogram. A spectrogram gives the windowed short-time Fourier transform of a signal by describing the frequency content of a signal and how it changes over time. Signals were windowed in segments of 100 ms (120 samples) using a Hamming window. A Fourier transform was then computed for the windowed signal resulting in a spectrum with resolution of 1 Hz. The window was then shifted forward by 10 ms, and the procedure was repeated until the end of the epoch was reached. The resulting spectrogram consists of a matrix where each row represents the power spectrum of a windowed signal. Each column of this matrix represents the time series of power at a particular frequency. Event-related changes (ERD/ERS) were calculated by normalizing each column (frequency) with the baseline power. The baseline values were compared statistically with the values recorded after the 'go' cue and during the movement phase. Kolmogorov-Smirnov test was used to identify when the band powers are significantly different from the rest period.
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5.4.8 Detecting movement onset

The band powers naturally fluctuate over time, irrespective of movement execution. However, it is expected that the modulations that can be attributed to the movement will be significantly larger than the fluctuations observed in spontaneous (ongoing) activity. In this section, we describe how these changes related to the movement can be identified through background activity. The movement-related modulations are observed in specific frequency bands. For example, it is well-accepted that the beta activity is suppressed during the movement planning and execution [20, 138, 168, 224, 227]. However, both the centre frequency and magnitude of these modulations vary cross-individuals. One may deal with these variations by calculating the power over the entire frequency band rather than measuring the power changes around the peak. This reduces the magnitude of measured ERD’s and ERS’s because the magnitude of these changes falls sharply around their peaks. In particular, bandwidth of gamma ERS may exceed 100Hz while its peak is ranged over a narrow band (see result section (5.5.1), Table (5.1), and Figure (5.1) for more detail). Here, the bandwidth of gamma ERS was defined as the frequency range over which the ERS was above 3dB (100% increase). Similarly, the bandwidth of the peak is defined as the frequency range over which the gamma power is above half its maximum. Despite lack of specificity, the frequency bands are often chosen without consideration of cross-subject variations. In our analysis, the choice of frequency bands was tailored on a per subject basis. We looked for 5Hz bands with maximum ERD/ERS which are the most correlated to movement period. We hypothesized that processing the narrowband around the ERS peak instead of the entire gamma band results in better discrimination between movement and no-movement states. Identified frequency bands were used to develop a movement onset classifier. Linear discriminant analysis was used to determine the optimal set of detection parameters [72]. The classifier was trained using the first 25 trials of the experiment. For each trial, the band powers were calculated over 200 ms windows with 50 ms overlap and windows were labeled as movement and
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no-movement. When the classifier was trained, it was used to detect the movements from the entire ECoG recording. The prediction accuracy of the classifier was evaluated using F1-score. F1-score is a normalized measure suitable to quantify classification accuracy in the case where one outcome (e.g. idling) is more probable than a second outcome (e.g. movement). The F1-score is defined as

$$F1 = \frac{2TP}{2TP + FP + FN}$$

(5.1)

where TP, FP, and FN are true positive, false positive, and false negatives respectively. F1-score has a value between 0 and 1, where 1 denotes perfect classification.

5.4.9 Reconstruction of movement velocity using multi-linear regression

Earlier studies have shown that movement trajectory can be reconstructed from slow cortical potentials [117,135,174,190]. Higher frequency oscillations are generally disregarded as being uninformative although there is no definitive conclusion on this matter. In this section, we will investigate the relative contributions of the various frequency bands in reconstructing movement velocity.

In our prediction model, we assume that arm velocity can be reconstructed from the amplitude of band activities. A multi-linear regression (MLR) model was used to model the relationship between neural recording and kinematic data [89, 123]. Multi-linear regression models have been used to estimate the kinematics from brain activities recorded by EEG [237], MEG [29, 83, 236], and ECoG [123]. The input to our model is the vector consisting of cortical activity measured at each electrode as they change over time. The output is 3D arm velocity. We express the relationship between cortical activity $E(t)$ and motor output $K(t)$ by

$$K(t) = b + E(t)\beta + \eta(t)$$

(5.2)
where both $b$ and the matrix of regression coefficients $\beta$ are constants and are estimated by the method of least-squares from experimental data. The final term in the equation $\eta(t)$ represents the residual errors. Although equation (5.2) describes the process by which hand velocity can be reconstructed from ECoG recordings, it does not take into consideration two important physiological characteristics of the motor system. The first is the delay between the cortical activity and the corresponding motor output. The lag represents a transmission delay between cortical motoneuron spike response and emergence of EMG/kinematic activity, and consists of conduction time in the corticospinal tract, relay in the spinal cord, conduction in motor axons and then the neuromuscular junction \[1, 28, 78, 215\]. We incorporate the delay into the linear model as a fitting parameter. The second physiological characteristic relates to event-related synchronization/desynchronization in the beta and gamma frequency bands. These events are reliable indicators of the starting and stopping of arm movements (see result section for more details). The predicted output $K(t)$ can be “gated” (i.e. turned on or off) by the activity in the gamma band. Specifically, low energy in gamma band is an indicator of the cessation of movement and vice versa. The gating ensures that fluctuations in slow activity do not elicit any movements. The gating function has not, to our knowledge, been used with ECoG recordings. This process is modeled using a threshold function, $h(t)$, and equation (5.2) can now be written as

$$K(t) = b + h(t - u)E(t - u)\beta(u) + \eta(t)$$

(5.3)

where $u$ is the time lag between the cortical activity and the motor output.

The model accuracy was evaluated for each participant through a leave-one-out method. Arm velocity of a single trial was estimated while the remaining trials are used as training set. Training and test data were then permuted until all trials were used as test. At each permutation, Pearson correlation between the estimated velocity and actual limb velocity was calculated.
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5.5 Results

5.5.1 Movement-related activities and movement detection

Movement-related activities were observed in three distinct frequency bands: the very low frequencies (<2Hz), alpha-beta (8-30Hz), and gamma (>30Hz). Power in both the low-frequency and the gamma regions were elevated over the time course of movement execution while power in beta fell over the same period (Figure 5.1). Changes in all three bands were statistically significant for all subjects (p<0.01, Kolmogorov-Smirnov test). The ERD/ERS for each subject are shown in Table (5.1). From the table, we observe that both the centre frequency and the magnitude vary quite a bit between the subjects. Despite these differences, percentile changes in the gamma band was found to be consistently higher than changes in either alpha-beta or the low-frequency band for all subjects. The gamma activity increased by over 100% during movement execution.

From the ERS/ERD activity, we can also make the observation that there is a clear relationship between the length of ERS/ERD with the duration of arm movement. In Figure (5.2), the duration of gamma activity is plotted against duration of EMG activity. A high degree of linear correlation between the two variables is observed as shown by the regression line. The estimated slopes and intercepts along with their confidence interval are listed in Table (5.2). The analysis were also repeated this time forcing the intercept to be equal to zero. The reasons for this will be discussed later. When the intercept was

<table>
<thead>
<tr>
<th>Participant</th>
<th>$\beta$ peak (Hz)</th>
<th>max $\beta$-ERD (%)</th>
<th>$\beta$ bandwidth (Hz)</th>
<th>$\gamma$ peak (Hz)</th>
<th>max $\gamma$-ERS (%)</th>
<th>$\gamma$ bandwidth (Hz)</th>
</tr>
</thead>
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<td>1</td>
<td>22</td>
<td>87</td>
<td>17</td>
<td>155</td>
<td>281</td>
<td>141</td>
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<td>3</td>
<td>22</td>
<td>52</td>
<td>22</td>
<td>77</td>
<td>114</td>
<td>87</td>
</tr>
</tbody>
</table>

Table 5.1: Maximum ERD/ERS observed in gamma and beta bands are shown. We also found the frequency where the maximum changes occurred.
Figure 5.1: Changes in spectral density of ECoG electrode located over primary motor cortex and envelop of the associated biceps activity are shown. The changes are shown in dB. (a) Data of subject 1 showing electrode 2 minus electrode 6. Results clearly show the synchronization of gamma (centered at 158Hz), desynchronization of alpha-beta (10-30Hz), and an increase in energy of slow oscillations (0-2Hz). The time required for the subject to reach the target and return to the initial position was approximately 2 seconds. (b) Same for Subject 2. (c) Same for Subject 3.

forced to be zero, the analysis yielded lines with near unity slopes. Goodness of the fit (R-squared) fell slightly as a result (Table(5.2)). This suggests that, within error, the
Figure 5.2: (a) The duration of gamma activity is plotted versus EMG activity. The estimated slopes and intercepts along with their confidence interval are listed in Table (5.2). (b) Same for beta activity.

duration of gamma activity is equal to the duration of movement. That is, the duration over which gamma activity is elevated provides a means to demarcate movement activity. Similar plots can be made for alpha-beta ERD, and for the low-frequency ERS with overall poorer fit. In particular, the R-squared values for the beta activity were found to be consistently lower than the values for gamma for all subjects. For the low frequency oscillations (<2Hz), the results depart from linearity suggesting that either the reliability of the results are poor or that the underlying relationship is more complex.

The high degree of linear correlation as demonstrated by the regression line fits show that the onset and offset of band-specific ECoG activity can be useful in the detection of movement onset and offset. Detection of movement has important application in the area of brain-activated machine interfaces. In this analysis, we used instead linear discriminate analysis together with the activity in delta, beta and gamma bands. After training and testing with the classifier, results show that gamma activity is the best indicator of movement initiation confirming what we found already with the regression analysis. Specifically, a high level gamma activity provided a reliable indicator of move-
### Table 5.2: Estimated slopes and intercepts of regression lines relating duration of muscle activity with the length of ERS/ERD. The regression lines were recast by constraining the intercepts to zero.

<table>
<thead>
<tr>
<th>Participant</th>
<th>Band</th>
<th>Slope (with 95% confidence bounds)</th>
<th>Intercept (with 95% confidence bounds)</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>γ</td>
<td>0.7595 (0.6553, 0.8638)</td>
<td>0.2194 (0.0818, 0.3569)</td>
<td>0.5604</td>
</tr>
<tr>
<td>2</td>
<td>γ</td>
<td>0.8501 (0.7314, 0.9688)</td>
<td>0.2291 (0.06396, 0.3941)</td>
<td>0.7708</td>
</tr>
<tr>
<td>3</td>
<td>γ</td>
<td>0.9536 (0.7992, 1.108)</td>
<td>0.04843 (-0.08464, 0.1815)</td>
<td>0.6179</td>
</tr>
<tr>
<td>1</td>
<td>γ</td>
<td>0.9716 (0.9491, 0.994)</td>
<td>0</td>
<td>0.4302</td>
</tr>
<tr>
<td>2</td>
<td>γ</td>
<td>1.005 (0.9634, 1.047)</td>
<td>0</td>
<td>0.7419</td>
</tr>
<tr>
<td>3</td>
<td>γ</td>
<td>1.008 (0.9679, 1.048)</td>
<td>0</td>
<td>0.6158</td>
</tr>
<tr>
<td>1</td>
<td>β</td>
<td>0.722 (0.4536, 0.9903)</td>
<td>0.5755 (0.2602, 0.8909)</td>
<td>0.3288</td>
</tr>
<tr>
<td>2</td>
<td>β</td>
<td>0.5813 (0.2784, 0.8841)</td>
<td>0.8627 (0.3937, 1.332)</td>
<td>0.2152</td>
</tr>
<tr>
<td>3</td>
<td>β</td>
<td>0.8643 (0.5604, 1.168)</td>
<td>0.6344 (0.2755, 0.9933)</td>
<td>0.5602</td>
</tr>
<tr>
<td>1</td>
<td>β</td>
<td>1.2 (1.134, 1.265)</td>
<td>0</td>
<td>0.1333</td>
</tr>
<tr>
<td>2</td>
<td>β</td>
<td>1.119 (1.032, 1.207)</td>
<td>0</td>
<td>0.01753</td>
</tr>
<tr>
<td>3</td>
<td>β</td>
<td>1.442 (1.355, 1.529)</td>
<td>0</td>
<td>0.4389</td>
</tr>
</tbody>
</table>
Figure 5.3: Time course of muscle activity and detected movement onsets for Subject 3. Four typical movement cycles are shown. The solid line shows the power of biceps activity. The vertical dash lines represent detected movement onsets by the linear discriminant classifier. Inspection of the classifier coefficients suggest that the movements were detected from gamma activity but not from alpha-beta or very slow oscillations.

Table (5.3) shows F1-scores obtained for all participants. Movements were detected with a near-perfect F1-score. Figure (5.3) shows one example of the EMG activity recorded during the experimental trials for Subject 3 along with the predicted onset times. The figure illustrates the repeated trials under which the subject engaged in a reaching task first, before returning the hand to rest position after performing a retrieving task. Also shown are the predicted movement onsets as shown by the dashed lines.

5.5.2 Effect of choice of frequency bandwidths

Earlier in the paper we made the hypothesis that by customizing or tailoring the frequency band of observation would allow for more accurate detection and prediction of kinematic activity from the underlying ECoG signal. We have already noted that the parameter values for delta, beta and gamma activities differ on a subject-by-subject basis. Next we would like to determine the settings to optimize classifier performance for movement
onset/offset detection. The centre of the frequency window is set to be equal to the peak of the ERS response for the gamma activity. However the bandwidth of the window requires exploration. The accuracy of the movement classifier was calculated as a function of the width of the bandwidth. The bandwidth was changed between 2-60 Hz. Note that the accuracy of declines as bandwidth is increased. We found detection accuracy to be highest when the bandwidth is between 2-10Hz.

5.5.3 Reconstruction of velocity and the delay parameter

In section 5.5.1, we demonstrated that gamma activity can be used to predict movement duration and onset. Next we explore how power in ECoG activity can predict kinematic activity. Equation (5.3) postulates that velocity can be derived from the amplitude of ECoG activity. Since there is a known lag time corresponding to the lag between ECoG and movement which is unknown initially, we need to estimate its value. The transmission delay between cortical motoneuron spike response and emergence of EMG/kinematic activity is reported approximately as 100 ms [1, 28, 78, 215]. Starting with 100 ms delay, we measured accuracy of the multilinear regression model for each subject and the delay value was changed until the best performance was achieved. Leave-one-out method was used to measure the regression model accuracy. Arm velocity of a single trial was estimated while the remaining trials were used as training set. At each permutation, the correlation between the actual arm movement and predicted arm movement was calculated. The average correlation between constructed and actual velocities ranged between 78-95%. Table (5.3) details the prediction accuracy for each participant. Examples of the reconstructed velocity profiles are shown in Figures (5.4 and 5.5). There appears to be good agreement between predicted and actual arm trajectories. Much of the prediction error appears after the arm has reached the target, when the subject is holding his hand in the air at the end of the trial. The residual neural activity after movement termination can thus be attributed to the working of the hand against gravity.
Participant | Detection rate (%) | RTL reconstruction accuracy (%) | RTR reconstruction accuracy (%) | Averaged reconstruction accuracy (%)
--- | --- | --- | --- | ---
1 | 100 | 93 | 97 | 95
2 | 100 | 82 | 93 | 87
3 | 98 | 73 | 82 | 78

Table 5.3: The movement detection rate obtained by LDA and averaged correlation coefficients between the actual and decoded kinematic parameters for reaching to the right (RTR), reaching to the left (RTL), and over all.

Inspection of the model coefficients suggests that the speed is predicted from slow and gamma oscillations but not from alpha-beta oscillations. In particular, the model’s coefficients were larger for gamma in compare to the weights associated with other bands.

We also noted that the magnitude of the speed profiles were very similar for both reaching to the right and reaching to the left ($r=0.84$, $p<0.01$, Pearson correlation). Given this, we also explored the possibility of reconstructing the reaching to the left trials using a model trained on reaching to the right. The following steps were taken. First, the MLR model was trained using all of the reaching to right trials. Next, reaching to the left trials were processed by the MLR model. The averaged correlation between the recorded value of arm speed and the predicted values were 81%. This correlation is close to the accuracy obtained by using left trial only data (83%). That is, predictions of arm velocity were as good using the reaching right data as they were using the reaching left data.

### 5.6 Discussion

In this study, we demonstrated that it is possible to reconstruct arm speed from human ECoG activity recorded from the primary motor cortex during reaching tasks. Participants performed reaching tasks with the hand contralateral to the site of implantation.
Chapter 5. Reconstruction of reaching movement trajectories

Figure 5.4: Subject 1. Arm velocity predicted by described multi-linear regression model from four ECoG electrodes is shown by solid line while actual arm velocity is shown by dashed-lines. (a/d), (b/e), and (c/f) illustrate predicted (solid line) and actual velocity (dotted line) over two different trials of reaching right on x-axis, y-axis, and z-axis, respectively.
Figure 5.5: Subject 2. Arm velocity predicted by described multi-linear regression model from four ECoG electrodes is shown by solid line while actual arm velocity is shown by dashed-lines. (a/d), (b/e), and (c/f) illustrate predicted (solid line) and actual velocity (dotted line) over two different trials of reaching right on x-axis, y-axis, and z-axis, respectively.
We found very slow oscillations, gamma, and beta band activity to be informative for decoding arm kinematics. In our analysis, however, instead of using predefined frequency bands, we adaptively chose frequency bands on a per subject basis. The bands were of size 5Hz, centred at the frequencies where the most significant movement-related were found. We believe that the customized choice of frequency bands increased the accuracy of our model both in terms of movement detection and prediction of movement speeds. A linear discriminate classifier was used to detect movement onset and offset. The classifier detected the movement onset with near-perfect accuracy and is significantly higher than accuracies reported by other methods from earlier studies [86, 119, 227]. Many of these studies used the delta or beta activity to detect movement onset or offset. By contrast, our results showed that gamma activity is the best indicator of movement execution. There are two reasons for this. First, percentile changes in the gamma activity were found to be consistently higher than the change in alpha-beta activity for all subjects. Second, we found that the variance of gamma activity to be smaller than that of beta and slow oscillations. The variance of activity can be attributed to a number of factors including basal or spontaneous activity. Higher levels of spontaneous activity will tend to reduce classifier performance. Using gamma activity, we achieved the highest rate of detection for all of our subjects. The accurate and reliable detection of movement has many applications including the development of movement assistive devices used in rehabilitation settings [34, 56, 152, 230, 234].

We used a multilinear regression model (MLR) to reconstruct the movement speed from ECoG activity. The average correlation between the actual arm velocity and predicted velocity exceeded 80%. The MLR model showed that limb velocity is best predicted from the low frequency and from the gamma band activities. Predictivity was much poorer with the low gamma or alpha-beta bands. Although these results were obtained from reaching to a limited number of directions, we hypothesize that these results can be generalized to reaching to other directions based on directional tuning of
cortical activity [20,117,134,138,183,190,224,227]. In this study, the ECoG activity was recorded from eight contacts with limited coverage over the motor area. Nevertheless, the prediction accuracy achieved in this study exceeds the accuracies obtained by earlier studies with good electrode coverage across the entire motor cortex [8,123,138,174,190]. Schalk et al. [190] investigated circular tracking movements with relatively restricted range. Their study yielded an average correlation of approximately 50% for arm trajectory. Their study had also good electrode coverage across the entire motor cortex. Pistohl et al. [174] extended the investigations of Schlak et al [190] to less restricted, target-directed, full two dimensional joystick movements. They showed that arm trajectory can be predicted from the low frequency component of ECoG with 43% correlation in average. Pistohl et al. also concluded that using the energy of other frequency bands (e.g. 40-80 Hz band) does not significantly improve the prediction of hand position. Moreover, Pistohl et al. found an average delay of 93.7 ms between the movement and both gamma and low-frequency components. This delay is close the delay we found between the cortical activity and movement.

A number of models have been introduced to predict the hand trajectory when it moves between a pair of points. Minimum jerk model is one of these models. Jerk is the second derivative of velocity or the time derivative of acceleration. As such, smoothness of the movement can be quantified by the jerk. That is, the smoother the movement, the less the amplitude of jerk is. Thus, minimum jerk policy reduces the tear on the bio-mechanical system and is inherently simple for the nervous system to implement. It is hypothesized that the central nervous system is moving the arm on a path that results in minimum jerk [68,92,235]. Hogan [92] found a general solution for the minimum jerk path with known initial position, final position and duration as 5th order polynomial. Under the assumption that the initial speed and acceleration are zero, the location of hand through point-point movement is expressed as

$$x_i + (x_f - x_i)(10(t/d)^3 - 15(t/d)^4 + 6(t/d)^5),$$

where $x_i$ is the initial position, $x_f$ is the final position, and $d$ is the movement duration.
Figure 5.6: Example of movement trajectory and its derivatives during a reaching task. (a) Arm position over X, Y and Z axis. (b) Arm velocity over X, Y and Z axis. (c) Acceleration over X, Y and Z axis. (d) Jerk over X, Y and Z axis.

These movements are characterized by straight paths and bell-shaped velocity. The jerk profile is a quadratic function with discontinuity in movement initiation and termination. Although it is possible that the cortical activity is actually encoding jerk rather than velocity, we could not investigate this hypothesis using our kinematic recordings. Minimum jerk predictions are inconsistent with our measurements showing a continuous jerk profile that differs with prediction of minimum jerk model after the movement initiation and at movement termination. Figure (5.6) shows an example of measured velocity, acceleration, and jerk. Despite these differences, jerk was not studied in this study because of the method used to record the kinematics. Only, arm position was recorded using the motion tracker. Consequently, velocity, acceleration and jerk were calculated as consecutive time derivatives of position. Obtained position was contaminated by noise, thus the signal-to-noise ratio is decreased after each derivation. Thus, velocity was preferred over
There are several limitations to the work presented in this study. First, the number of participants of the study here was small. This was due to the fact that only a limited number of individuals undergo implantation of ECoG electrodes over the motor cortex per year. Direct stimulation of motor cortex is not a routine intervention for treatment of pain [71, 166, 217]. This limits further the number of potential participants for this study. Second, not every individual who receives this treatment is able to participate as the studies are conducted a few days after the surgical implantation of the electrodes. Third, the placement and choice of number of ECoG contacts in our study were dictated by clinical requirements unrelated to the purpose and consideration of this study. The electrode placements may not be optimal for this study and our results might be affected by the electrode placement.

The electrodes used here are commercially available and routinely implanted in neurological patients. They have been clinically validated as being stable and reliable. The current configuration has a number of advantages when compared to single neuron or other deep brain recording techniques: 1) the ECoG electrodes do not penetrate the cortical surface thereby reducing the potential risk for brain tissue damage; 2) ECoG measures population activities thus offering a better prospect of long-term recording stability in contrast to single unit recordings; and 3) ECoG requires neither a high sampling rate nor spike detection/sorting capabilities, hence the overall computational requirements are reduced. We reconstructed the arm movement using only 8 ECoG contacts with only two contacts placed on the primary motor cortex. Using a small number of electrodes simplifies the system and results in less computational cost as well as shorter setup time. It is believed that the higher reconstruction accuracy achieved in our study is due to adaptive selection of the frequency bands. The bands were user-specific and were defined around the frequency with the maximum movement-related changes. Moreover, the model used in this study is a simple linear model that requires simple mathematical
operations to estimate the arm velocity. These computations can be carried out by an average-low power processor. We believe that the setup used in this study makes a good choice for applications from a clinical perspective.

5.7 Conclusion

We showed that the movement onset can be detected using ECoG recordings and presented a method for reconstruction of arm velocity from eight ECoG contacts placed over the motor cortex. The results indicate that increase of the gamma activity is the most reliable indicator of the movement onset in compare to changes in activity of the lower-frequencies. The slow and gamma cortical activities were used to develop a linear model which could in turn reconstruct arm velocity from ECoG recordings. Average reconstruction accuracy exceeds 86% for both motions. This method outlines possible reconstruction of arm trajectory using as few as eight ECoG electrodes in a minimally invasive manner.
Chapter 6

Time-course of cortico-basal ganglia coherence

In earlier chapters, I described a new way to visualize the time-frequency content of neural activity with higher resolution than previously possible. The clearer visualization in terms of both temporal and frequency details was achieved using Wigner-Ville distribution together with chirplet decomposition. However, single trial neural recordings are noisy and salient features can not be discriminated from the noise. This issue is typically dealt with by averaging over a large number of trials. The trials should be time-aligned prior to averaging to ensure neural components are occurring at identical time instance on a trial-by-trial basis. A method was detailed for nonlinear transformation of time axis that leads to temporal alignment of neural activity across the trials. After the alignment, the related neural activities could be more effectively brought into salience through averaging. The next step after identification of neural features attributed to the movement, the features were related to arm speed using a multilinear model. In this chapter, I hypothesize that these findings are not specific to motor cortex and it is likely that similar features can be found in activity of basal ganglia. This hypothesis is based on anatomical connections between motor cortex and basal ganglia as well as the coherent activity found between
Motor cortex is anatomically connected to other brain structures through various neural pathways. A number of neural pathways connect motor cortex to basal ganglia and motor cortex interacts with basal ganglia through these pathways to plan and execute movements [5, 11, 38, 63, 101, 111, 181, 216, 238]. These interactions can be quantified using the phase-locked activity between sensorimotor cortex and basal ganglia. Measure of coherence is a mean to quantify the synchronous activity. High coherence implies that the features extracted from basal ganglia and motor cortex are similar such that activity of motor cortex can be estimated using the neural activity recorded from basal ganglia. If activities of motor cortex and basal ganglia are found to be coherent and movement speed can be reconstructed from activity of motor cortex, then it is possible to reconstruct movement speed from basal ganglia activity with similar accuracy as the reconstructions made using the cortical activity.

### 6.1 Abstract

We studied the activity in the globus pallidus internus (GPi) and subthalamic nucleus (STN) as well as their interactions with the sensorimotor cortex during voluntary movements. Seven patients with dystonia and six patients with Parkinson’s disease underwent bilateral deep brain stimulation (DBS). Local field potentials from the DBS electrodes and scalp EEG from sensorimotor cortices were recorded while the patients performed externally triggered and self-initiated wrist movements. Coherence was calculated between the sensorimotor cortex and STN or GPi, and was found to be correlated with changes in power in the beta and gamma bands. Alpha activity was the exception with no significant change in coherence observed between the cortical and sub-cortical levels during movement task. However, a high level of inter-hemispheric coherence was observed in the alpha band which was well correlated with changes in alpha power. The
association of coherence with power suggests that a coupling in neural activity between the basal ganglia and the cortical region of the brain is required for the execution of voluntary movements. Finally, a mathematical model involving coupled neural oscillators was proposed which provides a possible explanation for how inter-cortical coupling takes place.

6.2 Introduction

The primary motor cortex and related cortical structures involved in voluntary movements are closely connected to the basal ganglia (BG) through various neural pathways. There are cortical-BG motor loops connecting the frontal cortex, BG and thalamus [32,164]. The BG-cortical interactions have been difficult to study in humans due to the inaccessibility of the BG activity [229]. Deep brain stimulation (DBS) is an accepted treatment for advanced dystonia or Parkinson disease (PD) and provides a unique opportunity to record electrical activities from the human basal ganglia in relationship to movement and medication state. We recorded the BG activity from patients when the DBS leads have been temporarily externalized in the post-operative period while performing self-paced and externally cued tasks with both ON and OFF medication states. Simultaneous recordings from deep electrodes and from the sensorimotor area allow us to detail interactions between BG and cerebral cortex over time and with respect to medication state.

Changes in cortical and basal ganglia activities, as measured by electroencephalography (EEG) and local field potential (LFP) recordings, have been observed during movement [32,38,171,216,229]. Earlier studies have analyzed these changes in terms of powers measured at frequency bands, e.g. delta (<4Hz), theta (4-8Hz), alpha (8-12Hz), beta (12-30Hz), gamma (>30Hz) [4, 5, 32, 38, 62, 69, 70, 86, 89, 121, 122, 170, 171, 202, 203, 214, 229]. It is well established that beta activity at the cortex and at the BG is suppressed during
movement. By contrast, gamma rhythms increase during the movement phase in both the frontal cortex and BG [38,216]. Moreover, the BG has been implicated in movement execution [38,216] as well as inhibiting unwanted movements [5,11,63,101,111,181,238].

A number of pathways link the BG to the cerebral cortex including the direct, indirect and hyperdirect pathways [98]. The direct pathway is mediated by the cortico-striato-pallido-nigral network and is hypothesized to be responsible for initiating goal-directed behaviour such as the execution of voluntary movements [141,142]. The indirect pathway is involved in movement termination [5,11,141,181]. Finally, the cortico-subthalamic hyperdirect pathway inhibits competing motor commands [5,42,101,171,181,208]. The hyperdirect pathway is mediated by the cortico-subthalamalic network [142,155,164].

Electrophysiological and functional imaging studies have not only shown activation of cortico-BG loops during movement processing [4,5,10,11,33,38,58,101,113,216] but also have found abnormal activities in the loop with movement disorders such as PD and dystonia [32,38,70,121,122,202,203,229]. Symptoms of PD and dystonia have been related to alterations in spectral density and timing of neural activities. The temporal and spectral alterations of neural activities affect the interaction between the brain structures involved in motor planning and execution.

Despite the importance of the temporal relationship in neural activity, the interaction between the BG and cortical regions is often studied only as function of the spectral frequency of the neural activity and not of time [4,10,38,58,113,122,229]. More recently, several studies have looked at time-dependent changes [5,163,181,216] but none have examined it in any great detail with respect to power of neural activities. To address this gap, we present a study here looking at the time-dependent coherence between BG and cortex and tracking the coherence relative to both movement phase and movement power. Our results suggest a complex inter-play between different brains structures.
6.3 Materials and Methods

6.3.1 Patients

We studied seven patients with dystonia who had bilateral DBS electrodes in the GPi and six PD patients with bilateral DBS electrodes in the STN. The participants provided written informed consent and the protocol was approved by the University Health Network (Toronto) Research Ethics Board. Table (6.1) shows their demographic and clinical details. The recordings acquired from the GPi in subjects 1-4 were also used in an earlier study by Tsang et al. [216]. The analysis and aim of this study is to demonstrate correlation between neural activity and coupling between cortex-STN or cortex-GPi. Tsang et al only showed interactions between the cortex and GPi using a more restricted analysis.

The experiments were performed 1-3 days after DBS electrode implantation while the leads were externalized. The participants performed externally triggered and self-initiated brisk wrist extensions while sitting in a comfortable armchair. In the externally triggered paradigm, the participants faced a computer screen with dark background that turned green for 0.5 second at randomized intervals between 6 to 10 seconds. The participant was instructed to perform a brisk wrist extension when the green screen was presented. In self-initiated paradigm, the participants performed self-initiated brisk wrist extensions every 10-15 seconds.

Four of the PD patients were examined while they were withdrawn from the medication for over 12 hours (over night). The experiment was repeated in the following day when the patients were medicated.

6.3.2 Data recording and data analysis

The participants were implanted with quadripolar DBS electrodes (Medtronic model 3387). The contacts were used to record GPi or STN local field potentials and are 1.27 mm in diameter and spaced 1.5 mm apart. EEG signals were recorded at Fp1, Fz,
<table>
<thead>
<tr>
<th>Age</th>
<th>Site</th>
<th>Predominant symptoms preoperatively</th>
<th>Medication (dose/day, LED/day in PD)</th>
<th>Therapeutic DBS settings</th>
<th>DBS pair used in the analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>GPi</td>
<td>Cervical Dystonia, pain in neck and rest of body</td>
<td>clonazepam 1.5 mg, gabapentin 1800 mg, nortriptyline 400 mg, lorazepam 3 mg, codeine</td>
<td>RGPI 2.7 V/60s/130 Hz/ (1-, C+), LGPI 2.6V/60s/130 Hz/ (5-, C+)</td>
<td>2-1, 6-5</td>
</tr>
<tr>
<td>58</td>
<td>GPi</td>
<td>Cervical Dystonia, pain in neck</td>
<td>clonazepam 2mg, citalopram 40 mg</td>
<td>RGPI 3.0V/60s/130Hz/ (3-, C+), LGPI 2.9V/90s/130Hz/ (6-, C+)</td>
<td>2-3, 5-6</td>
</tr>
<tr>
<td>52</td>
<td>GPi</td>
<td>Cervical Dystonia with right laterocollis and retrocollis, pain</td>
<td>Lorazepam 12mg</td>
<td>RGPI 3V/60s/130Hz/ (2-, C+), LGPI 1.8V/60s/130Hz/ (6-, C+)</td>
<td>2-1, 5-6</td>
</tr>
<tr>
<td>88</td>
<td>GPi</td>
<td>right hemidystonia</td>
<td>clonazepam 3 mg</td>
<td>LGPI 2.5V/60s/60Hz/ (5-, C+)</td>
<td>2-3, 6-7</td>
</tr>
<tr>
<td>45</td>
<td>GPi</td>
<td>dops-responsive dystonia of the right leg, gait impairment</td>
<td>1090 mg</td>
<td>RGPI 1.4V/60s/130Hz (3-, C+), LGPI 4.0V/60s/130Hz/ (7-, C+)</td>
<td>2-1, 6-7</td>
</tr>
<tr>
<td>44</td>
<td>GPi</td>
<td>Oroficial dystonia/Cranio-cervical dystonia/Meige’s syndrom + pain</td>
<td>Lorazepam 3mg</td>
<td>RGPI 4.3V/60s/130Hz (1-2-, C+) , LGPI 3.3V/120s/130Hz (7-, C+)</td>
<td>2-1, 6-7</td>
</tr>
<tr>
<td>54</td>
<td>STN</td>
<td>longer OFF periods, freezing</td>
<td>1000 mg</td>
<td>RSTN 4.0V/60s/80Hz/ (3-, C+), LSTN 4.4V/60s/80Hz/ (6-, C+)</td>
<td>2-3, 5-6</td>
</tr>
<tr>
<td>65</td>
<td>STN</td>
<td>PD</td>
<td>600 mg</td>
<td>RSTN 3.4V/60s/185Hz/ (2-, C+), LSTN 3.2V/60s/185Hz/ (6-, C+)</td>
<td>2-1, 5-6</td>
</tr>
<tr>
<td>50</td>
<td>STN</td>
<td>Tremor dominant PD</td>
<td>1200 mg</td>
<td>RSTN 3.8V/60s/160 Hz/ (1-, C+), LSTN 2.8V/60s/160 Hz/ (5-, C+)</td>
<td>2-1, 5-6</td>
</tr>
<tr>
<td>50</td>
<td>STN</td>
<td>PD</td>
<td>1100 mg</td>
<td>RSTN 3.0V/60s/130 Hz/ (2-, C+), LSTN 3.4V/60s/130Hz/ (7-, C+)</td>
<td>2-1, 6-7</td>
</tr>
<tr>
<td>56</td>
<td>STN</td>
<td>Tremor dominant PD</td>
<td>1800 mg</td>
<td>RSTN 2.8V/90s/185Hz/ (2-, C+), LSTN 3.8V/90s/185Hz/ (7-, C+)</td>
<td>2-1, 6-7</td>
</tr>
<tr>
<td>44</td>
<td>STN</td>
<td>Tremor dominant PD</td>
<td>850 mg</td>
<td>RSTN 2.1V/60s/130Hz/ (2-, C+), LSTN 2.3V/60s/130Hz/ (5-, 6+)</td>
<td>2-1,6-5</td>
</tr>
</tbody>
</table>

Table 6.1: Clinical details of subjects participated in this study.
Cz, C3 and C4 (according to the 10-20 international system) and referenced to linked ears. These channels were sampled at 2.5 KHz and bandpass filtered between 0.05Hz and 500Hz. EMG was recorded from the extensor carpi radialis and flexor carpi radialis muscles to monitor the wrist muscle activities. EMG signals were sampled at 2.5 KHz and bandpass filtered between 30Hz and 500Hz. SynAmp amplifiers (Neuroscan Laboratories, El Paso, Texas, USA) were used for all recordings.

The data was analyzed using MATLAB. First, monopolar DBS recordings were converted to bipolar recordings using adjacent contacts. This transformation allows us to remove the common activities (including volume conductance and artifacts) while preserving the focal activities. The recordings were then divided into epochs consisting of 4 seconds before and 4 seconds after EMG onset. EMG onset was marked manually. Epochs with eye blink or other artifacts were excluded from the analysis. We obtain over 50 epochs from each participant. The epochs were used to calculate the movement-related spectral changes and coherence.

6.3.3 Movement–related synchronization/desynchronization

Changes in local field activity can be found either as a decrease in band power known as event-related desynchronization (ERD), or an increase in band power known as event-related synchronization (ERS). A spectrogram was used to represent the spectral density of the recordings over time. To obtain the spectrogram of each trial, the signal was divided into overlapping segments of 400 ms by applying a Hamming window. A Fourier transform was computed for the windowed signal resulting in a spectrum with resolution of 1 Hz. Then, the window was shifted by 10 ms, and the procedure was repeated until the end of the epoch was reached. The resulting spectrogram consists of a matrix in which each row represents the power spectrum of a windowed signal. Each column of this matrix shows a time series that represents how the power varies at a given frequency over time. The movement-related spectral changes were then calculated as percentile
changes of the power with respect to a baseline, which we defined as the average power between 3 and 4 seconds prior to onset of muscle activity.

We analyzed the data recorded from the contacts selected for clinical benefit following programming of the stimulator. In some patients, the stimulator case was used as the cathode and a bipolar recording was obtained by subtracting the active contact with an adjacent contacts. The adjacent contact was chosen as the contact with maximum movement-related changes. The clinically-relevant and the pairs chosen for our calculations are listed in Table (6.1).

6.3.4 Coherence between motor cortex and STN/GPi

Coherence was used to quantify the synchronous activity between two recording sites during voluntary movement. Coherence is defined mathematically as

\[
coh(t, f) = \frac{\left| \sum_n F_{in}(t, f) F_{jn}^*(t, f) \right|^2}{\sum_n F_{in}(t, f) F_{in}^*(t, f) \sum_n F_{jn}(t, f) F_{jn}^*(t, f)}
\]

where \( n \) represents the trial number and \( F_{jn}(t, f) \) is the short-time Fourier transformation of channel \( j \) at time \( t \) and frequency \( f \). This measure of coherence quantifies phase-locking and similarity of spectral powers across repeated trials through a cross-correlation of spectral densities. Coherence can range in value from 0 to 1, where 0 indicates that there is no correlation and 1 indicates a perfect correlation; i.e. the phase and amplitude of one recording can be perfectly determined from another recording.

6.4 Results

6.4.1 ERD/ERS in the basal ganglia and in the motor cortex

Changes in spectral density (ERD/ERS) in the basal ganglia and cortical regions are shown in Figure (6.1). The time 0 represents the onset of muscle activity determined from EMG recordings. During the movement phase, which occurs approximately over the
interval 0 and 0.5 second, there is an increase in low-frequency activity (<8Hz) as well as gamma activity (65-80Hz). Alpha-beta activity (8-30Hz) on the other hand decreases during the course of the movement (p<0.001, two-sample Kolmogorov-Smirnov test). The ERD in alpha-beta activity is observed bilaterally in both the sensorimotor cortex as well as in STN and GPi, beginning 2 seconds before the movement onset to about 2 seconds after movement termination. Band-specific activities (α, β, and γ) are shown in Figures 6.2-6.4 (a/b only).

The desynchronization in the beta band was found to be similar in both ON and OFF medication states for self-initiated (r=0.96, p<0.001, Pearson correlation) and externally triggered (r=0.92, p<0.001, Pearson correlation) movements. Post‐movement activity in the beta band shows a rapid rise, exceeding the baseline before gradually returning to baseline level 2 seconds after movement termination. An ERS was found in the gamma band of both STN and GPi recordings for both externally triggered and self-initiated movements (p<0.001, two-sample Kolmogorov-Smirnov test, Figures (6.1) and (6.3)). The gamma ERS was observed in both ON and OFF medication PD participants. However, the gamma activity had larger magnitudes and larger bandwidths in STN than the GPi (Figure (6.1)). Based on these observations, we choose a common bandwidth for gamma between 65-80Hz which would encompass gamma activity for both STN and GPi.

### 6.4.2 Coherence between motor cortex and basal ganglia

Coherence was calculated between the motor cortex and STN, and between the motor cortex and the GPi under a variety of conditions. The cortical activity were recorded using the EEG contacts (C3-Cz or C4-Cz) while the basal ganglia activities were recorded using the DBS contacts. The clinically-relevant and the pairs chosen for our calculations are listed in Table (6.1).

Figure (6.2) shows the time-course of coherence in relation to changes in power for
Figure 6.1: Percentile changes in power at the sensorimotor cortex, GPi, and STN in the side contralateral to the moving wrist with respect to the baseline. Baseline is defined as the averaged power between -4 and -3 seconds. Externally triggered movements are shown in the first column, self-initiated movements in the second column. The trials are aligned such that the EMG onset is indicated at t=0. (a/b) Scalp recording (C3-Cz) from patients with dystonia: EEG’s recorded simultaneously with LFP from GPi. (c/d) Scalp recording (C3-Cz) from PD patients on medication: EEG’s were recorded simultaneously with LFP from STN. (e/f) LFP recordings from GPi of dystonian patients. (g/h) LFP recordings from STN of medicated PD patients.
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Figure 6.2: High beta (20-30Hz) band activity recorded from sensorimotor cortex (Cx), STN and GPi of the side contralateral to the moving wrist. Movement duration indicated by grey background. Left column indicates externally triggered task; right column is self-initiated task. Percentile changes in beta band (20-30Hz) showing (a/b) power (c/d) coherence between cortex (C3-Cz) and either GPi or STN. Grand average of medicated STN patients shown by solid line, non-medicated STN patients shown by dotted line, and GPi is shown by dashed line.

High beta (20-30 Hz) band activity. First, we note that at rest there is a high degree of coherence between cortical activity of STN and cortical activity in the GPi (p<0.001, permutation test, Table (6.2)). Second, we observe that coherence changes over the course of the movement with coherence lowest during movement execution. These changes ap-
Figure 6.3: Gamma band activity recorded from sensorimotor cortex (Cx), STN and GPi of the side contralateral to the moving wrist. Movement duration indicated by grey background. Left column indicates externally triggered task; right column is self-initiated task. Percentile changes in gamma band (65-80Hz) showing (a/b) power (c/d) coherence between cortex (C3-Cz) and either GPi or STN. Grand average of medicated STN patients shown by solid line, non-medicated STN patients shown by dotted line, and GPi is shown by dashed line.

pears to be well-correlated to temporal changes in power (p<0.001, Pearson correlation). That is, coherence is generally higher when beta power is higher. These observations are consistent across self-initiated and externally-triggered trials. For ipsilateral recordings, the results are similar (Figure (6.5)).
Table 6.2: Baseline values of cortico-GPi coherence in dystonia patients and cortico-STN coherencies for ON medication and OFF medication PD patients. The baseline values are detailed for each frequency band. The frequency bands corresponding to those selected for Figures (6.2)-(6.4). Coherence values above 0.05 are statistically significant (permutation test).
Figure 6.4: Alpha band activity recorded from sensorimotor cortex (Cx), STN and GPi of the side contralateral to the moving wrist. Movement duration indicated by grey background. Left column indicates externally triggered task; right column is self-initiated task. Percentile changes in gamma band (8-12Hz) showing (a/b) power (c/d) coherence between cortex (C3-Cz) and either GPi or STN. Grand average of medicated STN patients shown by solid line, non-medicated STN patients shown by dotted line, and GPi is shown by dashed line.
Figure 6.5: Percentile changes in power at the sensorimotor cortex (Cx), GPi, and STN in the side ipsilateral to the moving wrist with respect to the baseline. Baseline is defined as the averaged power between -4 and -3 seconds. Externally triggered movements are shown in the first column, self-initiated movements in the second column. The trials are aligned such that the EMG onset is indicated at t=0. (a/b) Scalp recording from patients with dystonia: EEG’s recorded simultaneously with LFP from GPi. (c/d) Scalp recording from PD patients on medication: EEG’s were recorded simultaneously with LFP from STN. (e/f) LFP recordings from GPi of dystonian patients. (g/h) LFP recordings from STN of medicated PD patients.
Figure 6.6: Gamma band activity recorded from sensorimotor cortex (Cx), STN and GPi of the side ipsilateral to the moving wrist. Movement duration indicated by grey background. Left column indicates externally triggered task; right column is self-initiated task. Percentile changes in gamma band (65-80Hz) showing (a/b) power (c/d) coherence between cortex and either GPi or STN. Grand average of medicated STN patients shown by solid line, non-medicated STN patients shown by dotted line, and GPi is shown by dashed line.
Figure 6.7: Alpha band activity recorded from sensorimotor cortex (Cx), STN and GPi of the side ipsilateral to the moving wrist. Movement duration indicated by grey background. Left column indicates externally triggered task; right column is self-initiated task. Percentile changes in alpha band (8-12Hz) showing (a/b) power (c/d) coherence between cortex and either GPi or STN. Grand average of medicated STN patients shown by solid line, non-medicated STN patients shown by dotted line, and GPi is shown by dashed line.
Figure 6.8: Inter-hemispheric coherence calculated between a) GPi of patients with dystonia, b) STN of PD patients shown in a time-frequency plot.

Coherence calculated in the gamma band shows mixed results. First, we describe the contralateral results. There was a strong increase in cortico-STN coherence that is temporally aligned with the ERS in STN ($r > 0.8$, $p < 0.01$, Spearman correlation). However, there is no clear relationship between the coherence and the gamma power ($r < 0.1$, Spearman correlation). This may be related to the small magnitude of gamma ERS in GPi. For the side ipsilateral to movement, we observed similar trends but they are less significant than that of contralateral results (Figure (6.6)).

### 6.4.3 Inter-hemispheric coherence

In the last section, it was shown that the coherence calculated between the basal ganglia and the cortex is significant in both the beta and the gamma activity bands. Moreover, a change in coherence was observed during the course of movement. Somewhat surprising however was the fact that the results for the alpha band show no such significance despite the fact that a significant alpha ERS is observed in both the ipsilateral and contralateral electrodes. However, the situation is different when we examine the coherence across the left and right brain hemispheres. In Figure (6.8), we show the inter-hemispheric coherence as calculated across the entire EEG frequency spectrum. Despite the fact that
Figure 6.9: Activity from STN and GPi recorded from both the ipsilateral and contralateral side to the moving wrist. Movement duration indicated by grey background. Left column indicates externally triggered task; right column is self-initiated task. Percentile changes in alpha band (8-12Hz) showing (a/b) power (c/d) inter-hemispheric coherence. Grand average of medicated STN patients shown by solid line, non-medicated STN patients shown by dotted line, and GPi is shown by dashed line.
there is significant beta and gamma activity throughout the movement trials, no inter-hemispheric coherence is observed. Around 5-10 Hz, however – and only in that frequency band – we observe a very significant level of coherence during the idling state (i.e. before and after movement execution, $p<0.001$, permutation test) as well as a drop in coherence during the course of arm movement. These results are shown in Figure (6.9) where the coherence in the alpha band is calculated and shown together with changes in alpha power for both the GPi and STN. The coordinated change in both power and coherence is significant ($p<0.001$, Pearson correlation) and is similar to what was observed earlier in the beta and gamma bands between the basal ganglia and the cortex.

6.5 Discussion

A goal of this study was to investigate the functional connectivity between the motor cortical regions and the basal ganglia by showing how cortico-BG synchronization changes over the course of voluntary movements. Our data show a number of interesting results. First we observed similar spectral changes in beta and gamma activity across the different levels of the sensorimotor cortex, GPi and STN. Due to the connections between cortical regions and BG, we expected movement-related changes in power to be accompanied by changes in coherencies across the cortical and basal ganglia regions. Indeed we found significant correlations between cortical-BG coherence and changes in spectral power ($p<0.01$, Pearson correlation). That is, higher levels of coherence are generally associated with higher powers of neural activity. This phenomenon has not, to our knowledge, been reported previously.

There are several reasons why. The first has to do with the relative inaccessibility of deep brain structures. The second is that in many of the earlier studies, the focus has been on quantifying coherence only as a function of frequency over a combined rest and movement periods [4,10,38,58,113,229]. More recent studies examined at temporal
changes in coherence, but do not study the interrelationship between neural activity or power with coherence [163, 216].

Our results show a complex inter-coupling between the sensorimotor cortex and basal ganglia in the high beta (20-30Hz) and gamma (65-80Hz) range for both externally triggered and self-initiated movements. The beta band activity has a high level of coherence during rest, but falls during the movement phase. The opposite was found for gamma where coherence is low in the pre-movement and post-movement phases, but high during movement. In both cases, coherence is essentially time-locked to the neural activity of the neural band. Similar results can be observed for low beta (12-20Hz) but the results are not as dramatic. For lower frequencies (<12 Hz, i.e. alpha band), coherence was not found to be correlated with power changes despite significant movement-related activities in these bands. Similar results have been reported in earlier studies investigating cortico-thalamic, cortico-GPi, and cortico-STN coherencies [159, 163, 216]. These studies further confirm our results that alpha activity is not coherent in the cortico-BG-thalamic loop and that coherence is independent of medication state. By contrast, STN alpha activity was affected by medication such that the ERD was reduced by up to 50% in off medication compared to on medication state in PD. This observation is consistent with other LFP and single unit studies in the STN [32, 120].

Beta band event-related desynchronization has been linked to the processing of movement in the cortico-basal ganglia circuit and has been observed in both the ipsilateral and contralateral sides [4, 5, 58, 181, 216]. Moreover, it has been suggested that abnormalities of these rhythms cause symptoms of movement disorders such as PD [31]. In both self-initiated and externally triggered movements, we found that the beta power and cortico-BG coherences to be highly correlated and independent of the medication state or recording site (p<0.001, Pearson correlation; Figure 6.2). After movement termination, beta activity increases, exceeding baseline activity in both GPi and STN before returning to the base level. Elevated states of beta activity have been associated with
movement inhibition and termination [5, 42, 101, 171, 181, 208]. In the cortex and STN, the time-course of coherence follows a similar trend in both the ipsilateral and contralateral sides with coherence overshooting baseline after movement termination (Figure 6.2). Based on these observations, we hypothesize that beta activity has a crucial role within movement termination and the idling of the motor system. This is compatible with the recent hypothesis that the role of the beta rhythms is to signal the ‘status-quo’ in the brain [64].

Synchronization of gamma activities can be observed bilaterally in the cortex, STN, and GPi during movement execution. We have found gamma ERS to lie predominantly in the 65-80Hz range for both the ON and OFF medication states in PD patients. The coupling or coherence between the cortical and the STN gamma activities increased during the movement phase and was found to be correlated with the gamma ERS in both the STN and the cortex. This correlation was localized in a narrow band around 70Hz. Coupling likely represent communication between the sensorimotor cortex and STN during movement execution [32, 38, 229]. On the other hand, coherence was not significant between GPi and cortex. The difference in coherence between GPi-cortex and STN-cortex may be due to differences in the pathways linking to the cortex. There is a hyperdirect pathway from the cortex to the STN but there is no such pathway from the cortex to the GPi. Differences in the coherence may also be indicative of differences in patient population (dystonia vs PD).

Despite the lack of coherence in the alpha band, a high value of coherence was observed – but in a different measurement paradigm. When coherence is calculated in GPi and in STN across the hemispheres, a very clear component was observed in the 5-12 Hz region (Figure 6.9). This coherence attenuates during arm movement and follows the changes in the ipsilateral and contralateral alpha power. This is a rather surprising result given that inter-hemispheric coherence is observed only in alpha but not in beta or gamma bands despite the high levels of activity in each band. The role of inter-hemispheric alpha in
the rest state is currently not well understood. Inter-hemispheric alpha may have a role in the inhibition of unwanted movements and the maintaining of the idle state [109,170]. However, it is known that there are no direct anatomical connections between the nuclei on each side. Moreover the lack of alpha coherence between BG and cortex suggests that inter-hemispheric coherence is mediated by other subcortical structures like the thalamus. In fact studies have implicated the thalamus as the generator and modulator of alpha activities [193]. The alpha oscillations may in turn govern what messages get passed onto the cortex [167,206]. A drop in alpha coherence during the movement of the arm suggests that there is an opening of the communication channel between BG and cortex. In other words, alpha activity may in fact modulate the beta/gamma coherence found between the BG and cortex. Further studies are required to better elucidate these mechanisms.

Summarized in Figure (6.10) are the results from a single subject (subjectively chosen for the clarity of results) the power and coherence relations as calculated for the alpha, beta and gamma activity bands. Once again, beta and gamma coherence are calculated between cortex and BG, while the alpha coherence is inter-hemispheric. The coordinated changes in both power and coherence across the various structures and levels highlight the intricate interrelation of the various structures of the motor control system.

The main finding of this paper – that neural activity (ERS/ERD) is coupled to changes in coherence between the cortex and BG – implies that coupling occurs when there is a sufficiently high level of neural activity. This is surprising for the simple reason that coupling (or coherence) measures the phase-locking of neural networks, and is not dependent on the overall magnitude of neural activity. Theoretically speaking, coupling can occur even when neural activity is low, something that we do not find in our data. If there is noise in the system, it is entirely possible that the coherence is lost when the signals are weak relative to the noise. Thus coherence only appears when the activity is sufficiently high compared to noise and coherence increases monotonically with respect to the signal powers. This phenomenon has been discovered and known as ‘power
Figure 6.10: Single subject data (subject #10) showing alpha, beta and gamma coherence/power. Movement duration indicated by grey background. Left column indicates coherence; right column is power. (a/b) Coherence in beta band (20-30Hz) between cortex-STN of the contralateral side to the moving wrist as well as beta activity power. (c/d) Same as a-b showing activities in the gamma band (65-80 Hz). Alpha band activity (8-12Hz) showing (e) inter-hemispheric coherence and (f) LFP power of the contralateral side to the moving wrist. Note the coordinated change in alpha, beta and gamma values between BG and cortex, as well as cross-hemisphere. Please see text for more details.
confound’ [65,153]. This phenomenon is identified in recordings with common reference [65]. When the signals are recorded with respect to a common reference, coherence increases/decreases as a consequence of increase/decrease of activity at the reference. However from the inspection of our data we have discounted this possibility for two reasons. First, our recordings were reference-free. Second, there are cases clearly where coherence remains high even when activity is low. Alpha power suppressed during the movement while alpha coherence remained high. Using the same recordings and within the same frequency band, inter-hemispheric coherence was correlated with the activity observed at both contralateral and ipsilateral side to the moving hand. This shows that the changes observed in coherence are not caused by errors in estimating the signal phase or changes in signal-to-noise ratio (i.e. coherence is high when the powers are high and vise versa). A model is required to better understand the implications of our observations.

The “communication through coherence” hypothesis proposes that communication across neural networks can only take place when the oscillatory activities between different brain regions are coherent [73,74]. The rhythmic patterns of excitability across communicating networks provide a temporal window for communication because the input-output channels of the networks are then synchronized and open at the same times. Coherence could thus enable a network to respond selectively to target inputs while ignoring other inputs [2]. Next we show that for reasonable implementations of a coupled network model, the coherence or phase-locking between two networks is dependent on the level of population activity of the network.

A neuron can be thought of as an oscillator with a natural frequency and phase. The frequency maps to the firing rate of the neuron, and the phase to the timing of the spike events. The Kuramoto model [112] is one such model that has been widely studied and adopted (e.g. [30,87,195,213]). Networks of neurons can be modeled in terms of oscillators that are coupled together. One main feature of the model is that the frequency of each oscillator can be changed or modified through pair-wise interactions
with other oscillators. That is, through interaction and coupling, a network of oscillators can achieve phase or firing synchronization. The Kuramoto model has been applied to the study of cortical activities [30,87,195,213], as well as to the neurobiological basis of memory [196].

The classic Kuramoto model assumes all-to-all connections between oscillators. Effectively this means that all the neurons are interconnected. The interaction between the \( n \)th oscillator and others is given by the equation

\[
\frac{d}{dt} \theta_n = \omega_n + \sum_{m=1}^{N} K_{mn} \sin(\theta_m - \theta_n)
\]  

(6.2)

where \( K_{mn} \) is strength of the interaction between the \( m \)th and \( n \)th oscillators or neurons, \( \omega_n \) is the neuron’s natural frequency, and \( \theta_n \) represents its phase. The sinusoidal function modulates the phase interaction between the neurons, limiting the magnitude of this interaction. We modified the traditional Kuramoto model in two ways. First, each cortical/BG neuron is not connected to every other cortical/BG neurons. Our model uses random connections so that each neuron is no longer connected to all of the other neurons. Each neuron is connected to other neurons with probability \( p_i \). This probability controls the interconnectivity of neurons within each network. Higher \( p_i \) results in networks with more synapses and vice versa. For example, probability of 1 represents a network of neurons with all-to-all connections while probability of 0 results in a network with no synapses. Second, since we are interested in studying the inter-relation between different networks (i.e. the cortical vs. subcortical networks), the model was constructed as two separate networks with additional connections linking these networks with probability \( p_c \). This parameter controls the interactions between the two networks. The coherence between the networks increases monotonically with respect to \( p_c \). Please see Figure (6.11) for a schematic representation of the model. This model allows us to study how changes in power of a network affect the coherence between the networks and power of the second network.

In our simulations we have found the mean field activity of the network (i.e. the local
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Figure 6.11: A schematic illustration of the interaction between two neuronal populations. Each network is separately connected with interactions between the neurons which belong to one network. Typical synchronization models (e.g. the Kuramoto model) describe the phase synchronization that happens in a single network. Our work generalizes the classical models by looking at interactions between networks of neurons. Such a model could describe, for example, the interaction between the cortical and BG regions of the brain.

Field potential) to be coupled to the coherence between the two neuronal populations. Figure (6.12) shows the results from one simulation of the model with two randomly interconnected networks, each of size 800 neurons. Separately, in each network the neurons are interconnected with 80% probability. That is, each neuron is connected on average to 600-800 neurons. For simplicity, we have set the connections to have identical coupling strengths. Finally, the two networks are connected through 160 additional links between Network 1 and Network 2.

In order to mimic the behaviour observed in our experiments, we varied the coupling strength of Network 1 resulting in an increase in the strength of the mean field. For the first simulation, coupling strength was increased linearly from 1.7 to 2.4 between time $t = 0s$ and 0.7s, held constant and then decreased back to 1.7 between $t = 0.8$ and 1.5s. For the other simulation, the order was reversed: the drop in coupling strength came before the increase. We observe that the qualitative behaviour of the figure matches that of the results shown earlier for both beta and gamma band activity between BG
Figure 6.12: Simulated mean field activity (e.g. LFP) for two coupled networks of neurons. Two scenarios are illustrated: (a) coherence and power are high during idle period followed by a drop during movement; (b) coherence and power are lower but rise during movement phase. Note the correlated changes in both power and coherence. Please see text for more detail.

and cortex (see Figure 6.3). That is, the Kuramoto model, crude as it is, provides one possible explanation for why the coherence between networks is coupled to the activity in the networks – neural pathways allow one neural ensemble to control activity of another neural ensemble by synchronizing/desynchronizing the neurons of the second network. We can generalize these results further over a wide range of parameter values by demonstrating that the dynamical activity of the network converges to a limit cycle when the connectivity between the networks exceeds a threshold. Our findings are consistent with an earlier study by Mirollo and Strogatz [144] where it was found that a high level of neural activity leads to an increase in coherence in population activity.

There are several limitations to the current study. Our findings in this paper may be affected by PD or dystonia, and it is not possible to record GPi and STN activities from normal subjects. The number of subjects for this study was limited by the available
pool of patients undergoing DBS treatment. Because of the small sample size, a larger study will be required to further confirm our findings. Moreover, the dataset used in our calculations is not homogenous. One of the PD patients was recorded only in the ON medication state; moreover, the dystonia patients each suffer from differing types of dystonia. Our results may also be affected by the microlesion effect [40,176]. However, since we have observed similar findings in both PD and dystonia patients, our findings are likely to be physiological rather than specific to a particular disease condition.

6.6 Conclusion

Local field potential activity from the STN and GPi was recorded simultaneous with EEG above the motor cortex from Parkinson’s and dystonia subjects during wrist movement. The beta band activity in both nuclei attenuated during the movement task while gamma activity rose over the same interval of time. Moreover, the time-course of coherence between STN-cortex or GPi-cortex was found to be time-locked to the changes in activity whereby coherence was high when the LFP response was high, and vice versa. No such coherence was found for alpha activity. However a high degree of inter-hemispheric coherence was observed for the alpha band. Moreover changes in the inter-hemispheric coherence over time match that of alpha power in a manner similar to how cortical/BG coherence changes over time in the beta and gamma bands. A model involving coupled neural oscillators was proposed to account for the qualitative nature of the findings. Our observations suggest a complex interplay between the cortical and basal ganglia structures during movement execution and highlight possible neural pathways involved in motor coordination.
Chapter 7

General discussion

7.1 From basal ganglia activity to arm kinematics

Inaccessibility of human basal ganglia activity has been the major barrier to learning more about role of basal ganglia in movement planning and execution [229]. Over the past few decades, deep brain stimulation (DBS) has provided a unique opportunity to record electrical activity of human basal ganglia in relationship to movement [5,125,216]. DBS recordings have shown activation/deactivation of cortico-BG loops during movement processing and role of basal ganglia in movement planning, execution, and inhibition [4,5,10,11,38,58,101,113,216]. I showed that the spectral density of basal ganglia changes with respect to the movement and that these changes are coupled with the changes observed in recordings from motor cortex. Changes in spectral density of basal ganglia have been reported but it has not been show that the movement-related changes are correlated with the cortico-BG coherence [5,169,174,216,227]. The main finding of our study was that neural activity (ERS/ERD) is coupled to changes in coherence between the cortex and basal ganglia. This suggests that the cortical responses and basal ganglia activity are phase-locked. Thus, activity of one site can be estimated from activity of other site due to this phase-locking. Despite this close relationship between cortical and basal ganglia
activities, there have been no reports linking basal ganglia activity to limb kinematics (e.g. speed or position). On the contrary, several studies investigated cortical activity with respect to limb movements and drawn functional relationships between cortical activity and limb kinematics [8,41,81,135,138,174,190,211,233,240]. These advances are in part result of accessibility to the cortical activity using non-invasive (e.g. EEG) or minimally invasive (e.g., ECoG) recording methods [8,41,81,86,135,138,174,190,211,233,240]. This thesis has sought to bridge this gap by relating basal ganglia activity to cortical activity as well as limb kinematics. We have shown, perhaps for the very first time, a plausible mathematical and conceptual link that can be drawn, as well as a systematic set of tools which will allow for further investigation on plausible models relating BG activity to arm kinematics.

There is a complex interplay between the motor cortex and basal ganglia structures during movement execution [4,5,10,11,33,38,58,101,113,142,216]. These interactions are mediated by the neural pathways connecting cortex to basal ganglia. These pathways are involved in motor coordination and movement regulation [10,11,33,38,51,58,101,164,205]. Through these pathways, cortex and basal ganglia form a complex network which is difficult to study from mathematical point of view, mainly because activities of all basal ganglia structures are not recorded simultaneously due to surgical and clinical considerations. Basal ganglia activity can be recorded using DBS electrodes implanted in patients as part of their treatments. DBS electrodes are placed at a specific target (e.g., subthalamic nucleus) where electrical stimulation delivers the maximum therapeutic result. Therefore, it is not typically possible to record from all or multiple structures of BG. However, it is recognized that motor cortex and basal ganglia form a functional network where both are indispensable [77], thus the following overall problem is formulated. A way to find out significance of BG activity is to relate it back to cortical responses that are related to the movement kinematics. We draw a relationship between basal ganglia activity and these cortical responses by showing that these cortical responses
Figure 7.1: Schematic illustrates how four parts of this thesis (i.e. visualization, temporal alignment of neural activity, reconstruction of movement speed, and coherence between motor cortex and basal ganglia) are interconnected. These parts show a plausible mathematical and conceptual link to relate BG activity to arm kinematics without knowing the exact relationship between cortical responses and BG activity and cortical responses. Known links are shown with solid arrows while unknown links are dashed.

and basal ganglia activity are coupled. We showed that sensorimotor cortex is coherent with BG and the coherent activity changes during motor processing. Coherence is the cross-correlation between spectral density of cortical and basal ganglia activity. As such, if the cortex and basal ganglia are coherent, cortical activity can be estimated from BG activity and vice versa. However, there are additional problems in reconstructing kinematics from basal ganglia activity, the cortical activity should be related back to kinematics. Although extensive work has been done in relating the cortical activity to kinematics \([7, 8, 41, 81, 135, 138, 174, 190, 211, 211, 230, 233, 234, 240]\), there are issues associated with variability in self-generated movements and also in the ability to visualize these signals. This thesis provides solutions to remove the variability caused by the way
movements were performed over repeated trials, and to visualize the neural signals in time-frequency domain with a resolution higher than previously possible. Epochs of neural data are traditionally aligned with respect to an event of interest (e.g. movement onset). However, if the investigator wishes to study another event in the same data set, the data must be realigned to a new marker. Our alignment method eliminates the need for this as an entire trial is aligned on one 'go’. This has the distinct advantage of allowing for the best possible representation of neural activity across an entire trial.

We could reconstruct limb speed from the cortical activity during reaching tasks with high accuracy – Pearson correlation between reconstructed speed and actual speed exceeded 80%. The accuracy achieved using the linear regression model was higher than the correlations reported by earlier studies [117, 174, 190]. Many of these studies used the delta or beta activity to detect movement onset and reconstruct the limb kinematics. By contrast, our results showed that gamma activity is the best indicator of movement execution and its kinematics. Moreover, the ECoG activity was recorded from eight contacts with limited coverage over the motor area, the prediction accuracy achieved in this study exceeds the accuracies obtained by earlier studies with good electrode coverage across the entire motor cortex [8, 123, 138, 174, 190]. Although cortical activity was processed to generate these results, BG activity can also be processed using these methods. Finally, we linked the cortical activity to basal ganglia activity using measure of coherence. This draws a plausible link between BG activity and limb kinematics.

7.2 Nonlinear transformation of time to classify movements and study relative timing of BG nuclei

Dynamic time warping was used for alignment of neural activity over repeated trials. The cortical responses were warped under the assumption that neural responses are better aligned if the kinematic profiles are identical on trial-by-trial basis. This assumption
is based on both correlation and linear relationship found between the cortical activity and kinematics [43, 117, 135, 174, 190]. Due to coherence observed between BG activity and cortical responses, it is likely that similar assumption can be made for BG activity. Consequently, temporal alignment of BG activity using kinematics is expected to result in well-delineated movement-related components including event-related synchronization/desynchronization which can be used for reconstruction of movement from BG activity or movement classification. It has been challenging to classify movements performed with the same body part based on the brain activity. Undoubtedly, the brain activity is task-dependent and should differ when two movements are performed. However, it is not clear whether ECoG or LFP activity is specific enough to classify different yet similar movement tasks. The movements can be classified using template matching algorithms [110, 218]. A common approach is to match online neural activity with a number of “gestures” or tasks [43, 85, 86, 118, 119]. A database of templates each corresponding to a different task is generated and later used to classify online activity. The primary difficulty is to expect single trial neural activity to match that of a standardized template. Instead, dynamic time warping method can be used to remove temporal variations to better match the signals with the templates. This is a method similar to that which is employed in speech recognition (e.g. [178]). Speech recognition systems quantity words as sequences of short-term spectra (i.e. templates). The sequence of an unknown word can be compared with each of the templates and the closest match is taken to correspond to the input. The performance of such a system depends on the accuracy of the template itself as well as alignment of the template with the signal. Therefore time alignment is an important component in the successful design of such a system. Dynamic time warping is a tool to achieve both. Although dynamic time warping can be used to align the template with the signal, our choice of dynamic time warping was motivated by the ease of implementation as well as its relevance towards the basic scientific question of finding the underlying neural components of upper limb movements. Temporal alignment of neural
activities led to superior visualization of salient neural activity with the resolution that was not possible through conventional alignment techniques. We have shown that these techniques work well for cortical responses. A possible future direction, if we are able to more accessibly record from a number of deep brain structures, is to investigate if similar techniques can work with deep brain activity. This will allow us to better investigate the relative timings between the different nuclei in basal ganglia and to look for differences in basal ganglia activity between different motion tasks. The relative timing between activity of basal ganglia nuclei and cortical activity is significant physiological characteristic of cortico-BG loop such that any abnormality in these timings results in movement disorders such as Parkinson’s disease \[32, 38, 70, 121, 122, 202, 203, 229\]. It is recognized that the symptoms of movement disorders are result of changes in spectral density (firing rate) of neural activity but more importantly due to temporal mismatch between neuron’s activity. These mismatches affect the interaction between the brain structures involved in motor planning and execution. Therefore, studying the timing between neural ensembles can uncover the mechanisms responsible for symptoms observed in movement disorders and consequently manage these symptoms. More recently, several studies have looked at time-dependent changes \[5, 163, 181\]. The “communication through coherence” hypothesis proposes that communication across neural networks can only take place when the oscillatory activities between different brain regions are time-locked and the exact timing between these activities are crucial in communication \[2, 73, 74\]. Dynamic time-warping allows us to measure the timings on trial-by-trial basis. Thus, these timings can be studies in more details than current methods including measure of coherence.
7.3 Detection of movement initiation and termination

Results presented in section 5.5.1 show that gamma activity is the best indicator of movement initiation and duration of gamma component is related to movement duration. Arm movements were detected with near-perfect accuracy which is significantly higher than accuracies reported by other methods from earlier studies [86, 119, 227]. Earlier studies typically used the delta or beta activity to detect movement onset or offset. By contrast, our results showed that gamma activity is the best indicator of movement execution. There are two reasons for this. The percentile changes in the gamma activity were found to be consistently higher than the change in alpha-beta activity and the variance of these activities were lower than other bands. Therefore, gamma activity during movement execution could be discriminated from its baseline value with higher accuracy. Next, it was shown that both BG activity and cortico-BG coherence increase in gamma band during movement execution. Thus, it is likely that movement onset and duration can be identified from BG activity. This has a number of applications where BG activity can be used for activation of external devices. For example, it can be used to change the DBS pattern from continuous to selective stimulation. If it is desired to stimulate BG only during movement, the stimulator can be turned ON automatically only when the patient attempts to move his/her body extremities. Adaptive stimulation paradigms have been shown to be more effective than continuous stimulation which is widely used therapy for advanced Parkinson’s disease [185]. Another example of these devices is movement assistive devices used for movement therapy and motor relearning. Currently, the commands to activate the movement assistive devices are generated through external means (e.g. therapist) or moving a body part unrelated to the actual movement (e.g. contractions of chest muscle is mapped to finger flexion). Detecting the movements from brain activity tremendously changes how these systems are activated and provides an interesting
opportunity to control prosthetic devices for movement restoration with high degree of transparency. This has enormous potential in prosthetics and rehabilitation applications. For example, the switch can be used as a mean to voluntarily initiate movements or neural stimulation as part of a clinical intervention to improve voluntary control of paralyzed muscles. This motor recovery is thought to be result of Hebbian mechanisms [36,149]. In short, the motor relearning is the result of proper efferent sensory feedbacks in response to the afferent cortical commands. If the timing between the feedback and the command resembles its physiological values, the synaptic connections transferring afferent and efferent activities are strengthened by the nervous system. If the cortical commands (person’s intention to move) are identified from the cortical activity, the feedbacks (body movements or functional stimulation of nerves/muscles) can be generated by an external device. Intuitively, the feedback should be similar/identical to the attempted movement, e.g. a functional electrical stimulation unit contracts the finger muscle when the person is attempting to close his hand.

Detection of movement onset and offset uncovers the neural processes involved in movement initiation and inhibition. Activity of basal ganglia is associated with selection of desired movement, inhibition of unwanted movements, and movement termination [5,11,54,63,101,111,141,142,181,187,238]. Movement detection allows us to study how activity of basal ganglia changes during movement phases which further provides an opportunity to find both physiological and pathological processes responsible for movement processing and inabilities to initiate or terminate movements. It is believed that some symptoms of movement disorders (e.g. tremor, rigidity, and bradykinesia) are due to abnormal activity of basal ganglia. For example, rest tremor in individuals suffering from Parkinson’s disease has been correlated with rhythmic activities found in motor cortex and basal ganglia [32]. Detection of movement onset and offset uncovers the neural features that can be attributed to movement initiation or termination. This provides an opportunity to study how these features differs in patients with different symptoms and
how these features can be related back to physiological mechanisms involved in movement execution. This could potentially open a door for diagnosis of movement disorders in their early stages using electrophysiological recordings. It is recognized that motor cortex and basal ganglia form a functional network where basal ganglia activity affects the activity recorded in cortex. Thus, the abnormal electrophysiological activity may be recorded from cortical regions. Moreover, these recordings can be used to manage the symptoms by investigating effect of chemical or electrical stimulations on these abnormal activities. For example, low gamma activity at cortical or basal ganglia regions was associated with low level of dopamine in deep brain regions [38, 229].

7.4 Reconstruction of limb kinematics from brain activity

Past studies have shown that limb movement can be decoded from local field potential recordings [135] or even single-unit activity [211, 233]. In particular Georgopoulos et al [81] have shown success in predicting 3D arm movement from single-unit activity with high accuracy. Our study attempts to do the same with human ECoG activity. We have been using the gamma and low frequency components of ECoG to decode limb velocity – an approach that is similar to some earlier studies [134, 135, 190, 227, 240]. However it is important to be mindful of the possible challenges in using low frequency potentials. For example, there is the possibility that the recorded signals are unrelated to the actual time-course of movement as would be the case if the recorded potentials are simply ‘event-related’. We do not believe that this is an issue with our current study.

Our predictions show a high degree of correlation with arm velocity (exceeding 80%) albeit with only two classes of motion (left and right reaching tasks). To date, very few studies have addressed the issue of predicting complex movement trajectories from human ECoG data. For example, Schalk et al. [190] investigated circular tracking movements
with relatively restricted range. Their study yielded an average correlation of approximately 50% for arm trajectory. Their study had also good electrode coverage across the entire motor cortex. Pistohl et al. [174] extended the investigations of Schalk et al. [190] to less restricted, target-directed, full two dimensional movements. They showed that arm trajectory can be predicted from the low frequency and gamma components of ECoG with average correlation of 43% correlation [174]. Our study continues in this vein and demonstrates good prediction accuracy of 3D kinematic movement over a limited number of tasks. Future studies expanding both the range, the conditions, as well as number of tasks can help further explore the efficacy of the prediction model proposed in this paper for full range 3D movement.
Chapter 8

Conclusions

This thesis comprises a number of technical achievements related to the general problems of measurement, recording and prediction of upper limb kinematics from invasive electrical recordings of human brain. An area where these techniques will have practical applications would be in the development and construction of a brain machine interface platform by which a person can control a computing device using only the brain activity.

Additionally, a critical achievement of the work in the thesis is the recording of brain activity from arm movements from a number of different levels and recordings sites within the brain. The recording sites were ranging from surface recordings using epidural electrodes to deep brain recordings from DBS electrodes. This is an achievement that has rarely ever been accomplished by a single lab. It is in that sense that this thesis can give wide reaching perspective on the neural nature of movement activation and generation.

Much of the thesis was then devoted to developing the tools that would allow for the interpretation and processing of the measurements we recorded.

More specifically, in first part of this dissertation, I developed a method visualize the neural activity in time-frequency domain. At level of neural ensembles, the neural responses are typically measured in terms of changes in the spectral density of the activities. These changes show how collaborative activity of the neurons changes with respect to an
event such as movement or a stimulus. These spectral changes are presented as function of time in time-frequency domain. I showed that the visualization method proposed in this thesis provides a clearer picture of the salient neural activity, simplifies representation of the salient activities, and provides a means for mathematically decomposing signals into chiplets. It was shown that ECoG activity of motor cortex during reaching tasks can be represented using a small number (<10) of chirplets.

Complex arm movements such as reaching are prone to cross-trial variability due to the way movements are performed. Typically, initiation time, duration of movement and movement speed are variable even as a subject tries to reproduce the same task identically across trials. Therefore, movement-related activity will tend to occur at different times across each trial. To solve this issue, a method was proposed for temporal alignment of the recordings through nonlinear transformation of time. This transformation accounts for differences in movement initiation, arm speeds, and movement durations. After the alignment, the neural activities occurred at near identical times and that the related neural activities were more effectively brought into salience through averaging. The results showed that the neural components are preserved and illustrated using this method while these components were blurred or are unnoticeable when the responses were processed using the conventional methods and without any temporal realignment.

In the third part of this dissertation, linear models were used to identify the user intention to move, and to reconstruct the movement trajectory from the cortical activity. These models show high accuracy in both detection and reconstruction of movements. The movement onsets were detected with near perfect rate. The correlation between actual and reconstructed movement speeds was exceeding 80%. Inspection of the models suggests that the speed and movement onsets were predicted mainly from gamma oscillations but not from slower oscillations (e.g. beta and delta activities). It should be noted that the arm movement was reconstructed using only 8 ECoG contacts with only two contacts placed on the primary motor cortex. Using a small number of electrodes
simplifies the system and results in less computational cost as well as shorter setup time. The computation load can be bared by an average-low power processor. It is believed that the setup used in this study makes a good choice for applications from a clinical perspective.

Finally, we draw a link between activities of basal ganglia and motor cortex by showing that these activities are coherent, i.e. spectral content of activities are correlated. The time-course of coherence between STN-cortex or Gpi-cortex was found to be time-locked to the changes in activity whereby coherence was high when the LFP response was high, and vice versa. The time-locking between coherence and powers were observed in beta and gamma bands. No such coherence was found for alpha activity. However, changes in the inter-hemispheric coherence over time match that of alpha power in a manner similar to how cortical/BG coherence changes over time in the beta and gamma bands. A model involving coupled neural oscillators was proposed to account for the qualitative nature of the findings. Our observations suggest a complex interplay between the cortical and basal ganglia structures during movement execution and a plausible link between motor cortex and basal ganglia activities. This highlights possibility of detecting and reconstructing limb kinematics from basal ganglia activity.
Appendix A

Estimation of chirplet parameters

This appendix aims to derive the equations used in sections 3.2 and discuss the methods in more details.

A.1 Averaged Wigner-Ville distribution of signal

Neural recordings are noisy by nature. Averaging a large number of repeated trials is one way to improve signal to noise ratio. In this section, I will show that the expected value of the WVD is unaffected by additive, uncorrelated noise and averaged WVD of an independent additive noise is constant at each time and frequency point. We assume that the additive noise is zero-mean and independent of the signal. Suppose \( x(t) = s(t) + n(t) \), where \( s(t) \) is the signal and \( n(t) \) is the additive noise. The expected value of Wigner-Ville distribution, \( W_x(t, w) \), is

\[
E[W_x(t, w)] = \int_{-\infty}^{+\infty} s(t + \tau/2)s^*(t - \tau/2)e^{-jw\tau}d\tau \\
+ \int_{-\infty}^{+\infty} s^*(t - \tau/2)E[n(t + \tau/2)]e^{-jw\tau}d\tau \\
+ \int_{-\infty}^{+\infty} s(t + \tau/2)E[n^*(t - \tau/2)]e^{-jw\tau}d\tau \\
+ \int_{-\infty}^{+\infty} E[n(t + \tau/2)n^*(t - \tau/2)]e^{-jw\tau}d\tau \tag{A.1}
\]
Because the noise is zero-mean, \( \int s^*(t - \tau/2)E[n(t + \tau/2)]e^{-jw\tau}d\tau = 0 \) and \( \int s(t + \tau/2)E[n^*(t - \tau/2)]e^{-jw\tau}d\tau = 0 \). Thus,

\[
E[W_x(t, w)] = \int_{-\infty}^{+\infty} s(t + \tau/2)s^*(t - \tau/2)e^{-jw\tau}d\tau + \int_{-\infty}^{+\infty} E[n(t + \tau/2)n^*(t - \tau/2)]e^{-jw\tau}d\tau \tag{A.2}
\]

If the noise instants are independent identical variables, \( \int_{-\infty}^{+\infty} E[n(t + \tau/2)n^*(t - \tau/2)]e^{-jw\tau}d\tau = \sigma_n^2 \), where \( \sigma_n^2 \) is the noise variance (power). Therefore, averaged WVD of \( x(t) \) is WVD of the signal plus the noise power.

\[
E[W_x(t, w)] = \int_{-\infty}^{+\infty} s(t + \tau/2)s^*(t - \tau/2)e^{-jw\tau}d\tau + \sigma_n^2 \tag{A.3}
\]

### A.2 Wigner-Ville Distribution of a Gaussian Chirplet

Chirplet is a time-varying and swept frequency wave. A Gaussian chirplet has Gaussian envelop and its instantaneous frequency is a line as function of time. A normalized Gaussian chirplet is expressed in the time domain as

\[
f(t) = \left(\frac{\alpha}{\pi}\right)^{\frac{1}{4}} \exp\left\{-\frac{\alpha(t - t_0)^2}{2}\right\} \exp\left\{j[w_0 + \beta(t - t_0)](t - t_0)\right\} \tag{A.4}
\]

where \( \alpha > 0 \) is inversely related to the time spread of the chirplet, \( t_0 \) is center of time, \( w_0 \) is center of frequency, and \( \beta \) is the chirp rate. \( f(t) \) is normalized to have unity energy. Wigner Ville distribution of \( f(t) \) is

\[
WVF(t, w) = \int_{-\infty}^{+\infty} f(t + \frac{\tau}{2})f^*(t - \frac{\tau}{2})e^{-iw\tau}d\tau
\]

\[
= \int_{-\infty}^{+\infty} \left(\frac{\alpha}{\pi}\right)^{\frac{1}{2}} \exp\left\{-\frac{\alpha(t - t_0 + \frac{\tau}{2})^2}{2}\right\} \exp\left\{j[w_0 + \frac{\beta(t - t_0 + \frac{\tau}{2})]}(t - t_0 + \frac{\tau}{2})\right\} \exp\left\{-\frac{\alpha(t - t_0 - \frac{\tau}{2})^2}{2}\right\} \exp\left\{-j[w_0 + \frac{\beta(t - t_0 - \frac{\tau}{2})]}(t - t_0 - \frac{\tau}{2})\right\}e^{-iw\tau}d\tau
\]

\[
= \int_{-\infty}^{+\infty} \left(\frac{\alpha}{\pi}\right)^{\frac{1}{2}} \exp\left\{-\alpha(0)^2 + \tau^2/4\right\}e^{j(t - t_0)\tau}e^{-j(w - w_0)\tau}d\tau
\]

\[
= \left(\frac{\alpha}{\pi}\right)^{\frac{1}{2}} \exp\left\{-\alpha(0)^2\right\} \int_{-\infty}^{+\infty} \exp\left\{-\frac{\alpha\tau^2}{4}\right\} \exp\left\{-j[(t - t_0)\beta - (w - w_0)]\tau\right\}d\tau
\]

\[
= 2 \exp\left\{-\alpha(0)^2\right\} \exp\left\{-\frac{1}{\alpha}[((t - t_0)\beta - (w - w_0))^2]\right\} \tag{A.5}
\]
Figure A.1: WVD of a chirplet is calculated empirically and theoretically in natural logarithmic scale. The chirplet parameters are $\alpha = 20$, $\beta = 50$, $t_0=1$ s, and $f_0=100$ Hz.

Figure (A.1) shows agreement between analytical and empirical WVDs of a chirplet. WVD of a chirp can be derived from equation (A.5). Chirplet becomes a chirp when $\alpha \to 0^+$. Therefore, WVD of a chirp is

$$\lim_{\alpha \to 0^+} WV_f(t, w) = 2\pi \delta[(t-t_0)\beta - (w-w_0)]$$

### A.3 Radon Transform of WVD of a Gaussian Chirplet

Radon transform is defined as integral of a two dimensional function over straight lines. It has been used in many applications of image processing to find the lines in an image. Radon transform and its inverse transformation has been also used in CAD scan devices to reconstruct the images. CAD scan device identifies the body tissues and their locations using the X-ray interactions with the body tissues. The X-ray is attenuated as it travels through the tissues. Tissues with different molecular structure have different attenuation level. For example bone attenuation level is higher than water. Because X-ray is traveling on a line, inverse Radon transform is used to estimate how much X-ray was attenuated
at each point in space. A 3D image of the internal body organs is reconstructed using the estimated attenuation levels.

The WVD of a chirp is a straight line, while a chirplet is a bivariate Gaussian distribution oriented along a line with same slope as its chirp rate. As such, it is expected that the maximum of the Radon transform to be related to both the chirp rate and the chirplet center.

Radon transform is formulated in two different ways, i.e., line integration and Herman’s formulation. Results of these formulations are interchangeable through variable transformations. Next, I derive Radon transform of WVD of a Gaussian chirplet using these definitions.

A.3.1 Line integration

The Radon transform is defined as integration over a line:

\[ R(r, m)[WV_f] = \int_{-\infty}^{\infty} WV_f(t, r + mt) dt \]

where \( r \) is the line intercept with the frequency axis and \( m \) is its slope.

\[
R(r, m)[WV_f(t, w)] = \int_{-\infty}^{\infty} 2 \exp\{-\alpha(t - t_0)^2\} \exp\{-\frac{1}{\alpha}[(t - t_0)\beta - (r + mt - w_0)]^2\} dt \\
= \int_{-\infty}^{\infty} 2 \exp\{-\alpha(t - t_0)^2\} \exp\left\{-\frac{1}{\alpha}t(m - \beta) + r - w_0 + \beta t_0\right\} dt \\
= 2 \int_{-\infty}^{\infty} e^{-\alpha(t-w)^2} \exp\left\{-\frac{(m - \beta)^2}{\alpha}\left[t + \frac{r - w_0 + \beta t_0}{(m - \beta)}\right]^2\right\} dt \\
= 2 \times 2\pi \sqrt{\frac{1}{2\alpha} \times \frac{\alpha}{2(m-\beta)^2}} \exp\left\{-\frac{1}{2\alpha} + \frac{\alpha}{2(m-\beta)^2}\right\} \\
= \frac{2\sqrt{\alpha\pi}}{(m - \beta)^2 + \alpha^2} \exp\left\{-2\alpha\frac{[mt_0 + r - w_0]^2}{(m - \beta)^2 + \alpha^2}\right\} \tag{A.6}
\]
\[
\frac{\partial}{\partial r} R(r, m)[WV_f(t, w)] = 0 \Rightarrow r_p = w_0 - mt_0 \quad (A.7)
\]
\[
\frac{\partial}{\partial m} R(r_p, m)[WV_f(t, w)] = 0 \Rightarrow m_p = \beta \quad (A.8)
\]
\[
R(r_p, m_p)[WV_f(t, w)] = 2\sqrt{\frac{\pi}{\alpha}} \quad (A.9)
\]

\[m_p\] is equal to \[\beta\] and is not affected by the Gaussian enveloped.

### A.3.2 Herman’s definition

Herman formulated Radon transform of a function, \(f(t)\), as
\[
R(\rho, \theta) = \int_{-\infty}^{\infty} f(\rho \cos \theta - s \sin \theta, \rho \sin \theta + s \cos \theta) \, ds
\]

Similarly, Radon transform of \(WV_f(t, w)\) is
\[
R(\rho, \theta)[WV_f] = \int_{-\infty}^{\infty} WV_f(\rho \cos \theta - s \sin \theta, \rho \sin \theta + s \cos \theta) \, ds
\]
\[
= \int_{-\infty}^{\infty} 2 \exp\left\{-\alpha(\rho \cos \theta - s \sin \theta - t_0)^2\right\}
\]
\[
\exp\left\{-\frac{1}{\alpha}[(\rho \cos \theta - s \sin \theta - t_0)\beta - (\rho \sin \theta + s \cos \theta - w_0)]^2\right\} ds
\]
\[
= 2 \int_{-\infty}^{\infty} \exp\left\{-\frac{(\rho \cos(\theta) - s \sin(\theta) - t_0)^2}{\frac{1}{\alpha}}\right\}
\]
\[
\exp\left\{-\frac{1}{\alpha}(\cos(\theta) + \beta \sin(\theta))^2[s - \frac{\rho(\beta \cos(\theta) - \sin(\theta)) + w_0 - \beta t_0}{\cos(\theta) + \beta \sin(\theta)}]^2\right\} ds
\]
\[
= \frac{2\sqrt{\alpha \pi}}{\sqrt{K_\theta}} \exp\left\{-\alpha \frac{[\rho - t_0 \cos \theta - w_0 \sin \theta]^2}{K_\theta}\right\} \quad (A.10)
\]

where \(K_\theta = (\cos \theta + \beta \sin \theta)^2 + \alpha^2 \sin^2 \theta\). Next, I will find where maxima of this transformation is located at. The maximum is at the point where partial derivatives of \(R(\rho, \theta)[WV_g]\) in respect to \(\rho\) and \(\theta\) are zero.
Appendix A. Estimation of chirplet parameters

\[ \frac{\partial}{\partial \rho} R(\rho, \theta) [W V_g] = 0 \Rightarrow \rho_m = \rho_p(\theta) = t_0 \cos \theta + w_0 \sin \theta \]  
(A.11)

\[ \frac{\partial}{\partial \theta} R(\rho_m, \theta) [W V_g] = 0 \Rightarrow \frac{\partial}{\partial \theta} \frac{1}{\sqrt{K_\theta}} = 0 \]

\[ \Rightarrow 2(- \sin \theta + \beta \cos \theta)(\cos \theta + \beta \sin \theta) + 2\alpha^2 \cos \theta \sin \theta = 0 \]

\[ \Rightarrow 2\beta \cos(2\theta) + (\beta^2 - 1 + 2\alpha^2) \sin(2\theta) = 0 \]

\[ \Rightarrow \tan(2\theta_m) = -\frac{2\beta}{\beta^2 - 1 + 2\alpha^2} \]  
(A.12)

Thus, maxima of the radon transform of a Gaussian chirplet is not just function of the chirp rate, \( \beta \), but also its time spread, \( \alpha \). It should be noted that \( \tan(\theta_m) \) converges to \( \beta \) for a chirp (i.e., when \( \alpha \to 0^+ \)).

A.3.3 Estimation of the Gaussian chirplet parameters from Radon-Wigner distribution

Herman’s definition, equation (A.10), is used here to estimate the parameters of an arbitrary Gaussian chirplet, \( g(t) = A f_N(t) \), where \( A \) represents the total energy of the chirplet.

\[ R(\rho, \theta) [W V_g] = \frac{2|A|^2 \sqrt{\alpha \pi}}{\sqrt{K_\theta}} \exp\left\{-\alpha \frac{[\rho - t_0 \cos \theta - w_0 \sin \theta]^2}{K_\theta}\right\} \]  
(A.13)

Equation (A.13) has interesting properties for constant \( \theta \). \( R(\rho, \theta) [W V_g] \) is a Gaussian function with mean of \( \rho_p(\theta) = t_0 \cos \theta + w_0 \sin \theta \). Thus, the Radon transform is maximum at \( \rho_p(\theta) \) in each slice. The location and value of the maxima allows estimation of the chirplet centres, \( t_0 \) and \( f_0 \), as well as its chirp rate, \( \beta \), and time spread, \( \alpha \).

Estimation of \( t_0 \) and \( f_0 \):

For any two arbitrary angles, \( \theta_1 \) and \( \theta_2 \):

\[
\begin{aligned}
\rho_p(\theta_1) &= t_0 \cos(\theta_1) + w_0 \sin(\theta_1) \\
\rho_p(\theta_2) &= t_0 \cos(\theta_2) + w_0 \sin(\theta_2)
\end{aligned}
\]

\[
\begin{aligned}
t_0 &= \frac{\rho_p(\theta_1) \sin(\theta_2) - \rho_p(\theta_2) \sin(\theta_1)}{\cos(\theta_1) \sin(\theta_2) - \cos(\theta_2) \sin(\theta_1)} \\
w_0 &= \frac{\rho_p(\theta_2) \cos(\theta_1) - \rho_p(\theta_1) \cos(\theta_2)}{\cos(\theta_1) \sin(\theta_2) - \cos(\theta_2) \sin(\theta_1)}
\end{aligned}
\]  
(A.14)
It is noted that $\rho_p(\theta)$ is equal to $t_0$ or $w_0$ at two specific angles.

$$
\begin{cases}
\rho_p(\frac{\pi}{2}) = w_0 \\
\rho_p(0) = t_0
\end{cases}
$$

(A.15)

**Estimation of $\alpha$ and $\beta$:**

The ratio between Radon transforms at any two arbitrary angles, $\theta_1$ and $\theta_2$, is function of $\alpha$ and $\beta$.

$$
\frac{R(\rho_p(\theta_1), \theta_1)[WV_g]}{R(\rho_p(\theta_2), \theta_2)[WV_g]} = \sqrt{\frac{K_{\theta_2}}{K_{\theta_1}}} = \sqrt{\frac{(\cos(\theta_2) + \beta \sin(\theta_2))^2 + \alpha^2 \sin^2(\theta_2)}{(\cos(\theta_1) + \beta \sin(\theta_1))^2 + \alpha^2 \sin^2(\theta_1)}}
$$

(A.16)

The ratio of the maximum values can be used to estimate both $\alpha$ and $\beta$.

$$
\frac{R(\rho_p(0), 0)[WV_g]}{R(\rho_p(\frac{\pi}{2}), \frac{\pi}{2})[WV_g]} = \sqrt{\frac{K_{\frac{\pi}{2}}}{K_0}} = \sqrt{\alpha^2 + \beta^2}
$$

(A.17)

$$
\frac{R(\rho_p(0), 0)[WV_g]}{R(\rho_p(\frac{\pi}{4}), \frac{\pi}{4})[WV_g]} = \sqrt{\frac{K_{\frac{\pi}{4}}}{K_0}} = \sqrt{0.5(\alpha^2 + (1 + \beta^2))}
$$

(A.18)

These ratios are both function of $\alpha$ and $\beta$. $\alpha$ and $\beta$ can be estimated separately using the equations below.

For $\alpha$,

$$
\frac{R(\rho_p(0), 0)[WV_g]}{R(\rho_p(0) + \lambda, 0)[WV_g]} = e^{-\alpha \lambda}
$$

$$
\Rightarrow \alpha = -\frac{1}{\lambda} \ln(R(\rho_p(0), 0)[WV_g]) - \ln(R(\rho_p(0) + \lambda, 0)[WV_g])
$$

$$
\Rightarrow \alpha = -\frac{\partial}{\partial \rho} \ln(R(\rho, 0)[WV_g]) \bigg|_{\rho = \rho_p(\theta)}
$$

(A.19)

For $\beta$,

$$
2\left(\frac{R(\rho_p(0), 0)[WV_g]}{R(\rho_p(\frac{\pi}{2}), \frac{\pi}{2})[WV_g]}\right)^2 - \left(\frac{R(\rho_p(0), 0)[WV_g]}{R(\rho_p(\frac{\pi}{4}), \frac{\pi}{4})[WV_g]}\right)^2 = 2\left(\frac{K_0}{K_{\frac{\pi}{4}}}\right)^2 - \left(\frac{K_0}{K_{\frac{\pi}{2}}}\right)^2 = 2\beta + 1
$$

(A.20)

**A.4 Ambiguity function**

Ambiguity function of a two dimensional function is simply its two dimensional Fourier transform. It is easier to study the Cohen class in the ambiguity space than studying
Appendix A. Estimation of chirplet parameters

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convolution of the kernel with the signals. First, I derive ambiguity function of WVD of a Gaussian chirplet. Let \( g(t, w) \) be WVD of a chirplet that is centered at \( t_0 = 0 \) and \( w_0 = 0 \). Two dimensional Fourier transform of \( g(t, w) \) is

\[
F\{WV_g(t, w)\} = FW_g(\Omega_1, \Omega_2)
\]

\[
= 2 \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \pi e^{-\frac{\lambda_2^2}{4\alpha}} \delta(\lambda_2) e^{-\frac{\alpha(\lambda_2 - \Omega_2)^2}{4}} \delta((\Omega_1 - \lambda_2 - \Omega_2) - (\lambda_1 - \Omega_1)) d\lambda_2 d\lambda_1
\]

\[
= 2 \pi \exp\{-\frac{(\Omega_1 - \beta \Omega_2)^2}{4\alpha}\} \exp\{-\frac{\alpha(\Omega_2)^2}{4}\}
\]

(A.21)

Thus, Fourier transform of WVD of a chirplet centered at \( t_0 \) and \( w_0 \) is

\[
F\{WV_f(t, w)\} = F\{WV_g(t, w)\} \exp\{-j(\Omega_1 t_0 + \Omega_2 w_0)\}
\]

\[
= 2 \pi \exp\{-\frac{(\Omega_1 - \beta \Omega_2)^2}{4\alpha}\} \exp\{-\frac{\alpha(\Omega_2)^2}{4}\} \exp\{-j(\Omega_1 t_0 + \Omega_2 w_0)\}
\]

(A.22)

It is noted that Fourier-WV of a Gaussian chirplet is centered at the origin with orientation related to the chirp rate, \( \beta \).

A.4.1 Marginal transformation of chirplet’s ambiguity function

Marginal transformation is integral of ambiguity in respect to a dimension. Basically, it is projection of the ambiguity function on a single axes.

\[
FW^{1}_{mf}(\Omega_2) = \int_{-\infty}^{\infty} FW_f(\Omega_1, \Omega_2) d\Omega_1
\]

\[
= \int_{-\infty}^{\infty} 2 \pi \exp\{-\frac{(\Omega_1 - \beta \Omega_2)^2}{4\alpha}\} \exp\{-\frac{\alpha(\Omega_2)^2}{4}\} \exp\{-j(\Omega_1 t_0 + \Omega_2 w_0)\} d\Omega_1
\]

\[
= 4\sqrt{\pi\beta} \alpha \exp\{-\frac{\alpha(\Omega_2)^2}{4}\} \exp\{-\alpha t_0^2\} \exp\{-j\Omega_2(w_0 + \beta t_0)\}
\]

(A.23)
\[FW_{mf}^2(\Omega_1) = \int_{-\infty}^{\infty} FW_f(\Omega_1, \Omega_2) d\Omega_2\]
\[= \int_{-\infty}^{\infty} 2\pi \exp\left\{-\frac{(\Omega_1 - \beta_2\Omega_2)^2}{4\alpha}\right\} \exp\left\{-\frac{\alpha(\Omega_2)^2}{4}\right\} \exp\{-j(\Omega_1\tau_0 + \Omega_2\omega_0)\} d\Omega_2\]
\[= 2\pi e^{-j(\Omega_1\tau_0)} \int_{-\infty}^{\infty} \exp\left\{-\frac{(\Omega_1 - \beta_2\Omega_2)^2}{4\alpha}\right\} \exp\left\{-\frac{\alpha(\Omega_2)^2}{4}\right\} \exp\{-j\Omega_2\omega_0\} d\Omega_2\]
\[= 2\pi e^{-j(\Omega_1\tau_0)} \int_{-\infty}^{\infty} \exp\left\{-\frac{\Omega_2^2 + \beta^2\Omega_2^2 - 2\beta\Omega_1\Omega_2 + \alpha^2\Omega_2^2}{4\alpha}\right\} d\Omega_2\]
\[= 2\pi \sqrt{\frac{4\pi\alpha}{\alpha^2 + \beta^2}} \exp\left\{-\frac{\alpha w_0^2}{\alpha^2 + \beta^2}\right\} \exp\left\{-\frac{\Omega_2^2 [1 - \left(\frac{\beta}{\alpha^2 + \beta^2}\right)^2]}{4\alpha}\right\} \times \exp\left\{-j\Omega_1(t_0 + \frac{\beta w_0}{\alpha^2 + \beta^2})\right\}\] (A.24)

### A.5 WVD of cross-term between two chirplets

Assuming \(f_1\) and \(f_2\) are two time-frequency atoms/elements defined as

\[f_i(t) = a_i e^{j\theta_i} g(t - t_i) e^{w_i t}\]

where \(g(t)\) is a time window centered at \(t = 0\). The interferences are result of quadratic definition of WVD.

\[I[f_1, f_2](t, w) = 2 \text{Re}\left\{ \int_{-\infty}^{\infty} f_1(t + \tau/2) f_2^*(t - \tau/2) e^{-j\tau w} d\tau\right\}\]
\[= 2 \text{Re}\left\{ a_1^* a_2 e^{j(\theta_1 - \theta_2)} \int_{-\infty}^{\infty} g(t - t_m + \frac{\phi}{2}) g^*(t - t_m - \frac{\phi}{2}) e^{j(w_1 - w_2)(t - t_m)} e^{j(w_1 + w_2)\phi} e^{-j w \phi} d\phi\right\}\]

Let \(t_m = \frac{t_1 + t_2}{2}, w_m = \frac{w_1 + w_2}{2}, D_t = t_1 - t_2, D_w = w_1 - w_2,\) and \(\phi = \tau - D_t.\)

\[I[f_1, f_2](t, w) = 2 \text{Re}\left\{ a_1^* a_2 e^{j(\theta_1 - \theta_2)} \int_{-\infty}^{\infty} g(t - t_m) \exp\left\{\frac{\phi}{2} (t - t_m - \frac{\phi}{2})\right\} e^{j[w_1 - w_2](t - t_m)} e^{j(w_1 + w_2)\phi} e^{-j w \phi} d\phi\right\}\]
\[= 2 \text{Re}\left\{ a_1^* a_2 e^{j(\theta_1 - \theta_2) + D_w(t - t_m) + D_t w_m) WVD_g(t - t_m, w - w_m)\right\}\]
\[= 2 \text{Re}\left\{ a_1^* a_2 e^{j(\theta_1 - \theta_2) + D_w(t - t_m) - D_t (w - w_m) + D_w t_m) WVD_g(t - t_m, w - w_m)\right\}\] (A.25)
\[= 2 a_1 a_2^* WVD_g(t - t_m, w - w_m)\]

\[\cos\left[ (\theta_1 - \theta_2) + D_w(t - t_m) - D_t (w - w_m) + D_w t_m \right]\] (A.26)
where $WVD_g(t, w)$ is WVD of $g(t)$. Equation (A.26) suggests that the interference term is an oscillatory waveform centered at the midpoint $(t_m, w_m)$ between the two components. The frequency of the oscillations is proportional to the Euclidean distance between the components, $\sqrt{D_w^2 + D_t^2}$. The cross-term is orientated such that its centerline is perpendicular to the line that connects $(t_1, w_1)$ and $(t_2, w_2)$. Figure (A.2) shows WVD of two chirplets and its ambiguity function. It illustrates that the cross-term is oscillatory and located between the two chirplets. Moreover, the cross-term is not at the origin of the ambiguity function and can be distinguished from the components corresponding to the chirplets (components centered at the origin of the ambiguity function with orientations related to the chirp rates).

### A.6 Removing the cross-terms

The cross-terms can be removed from the WVD through smoothing due to their oscillatory behavior. However, smoothing is not specific to the cross-term, it also smooths (blurs) the auto-terms. Smoothing process is a low-pass filter. It can be implemented in the ambiguity space. In ambiguity space, low-pass filter is a spatial filter that suppresses the energy of the points that are distant from the origin. Since cross-terms are high-frequency oscillations, it is expected that smoothing preserves the auto-terms while removing the cross-terms. However, energy of the auto-terms are partially removed by low pass filtering because the filter’s frequency response falls as function of distance from the origin which could in fact suppress a part of signal’s energy. For example, Choi-William kernel falls monotonically as function of distance from the origin. Figure (A.3) shows the kernel for two different values.

$$\Phi (\eta, \tau) = \exp \left[-\alpha (\eta \tau)^2\right]$$ (A.27)

This kernel has equal spread over time and frequency. The kernel’s ambiguity function falls monotonically in all directions. Therefore, the chirplet energy is altered irrespective of the kernel parameter, $\alpha$. The filter parameter is chosen considering a trade-off between smoothing the auto-terms versus removing the cross-terms. That is, the smaller $\alpha$ is, the less auto-terms are affected by the kernel but the less cross-terms are removed. By contrast, I am introducing
Figure A.2: Real part of WVD of a signal consists of two chirplets (top) and its ambiguity function (bottom). The amplitudes are shown in dB. The cross-term is located between the two chirplets in WVD and away from the center of the ambiguity function. The components corresponding to the chirplets are centered at the origin of the ambiguity space with orientations corresponding to the chirp rates.

A suboptimal method to minimize the energy removed from the auto-terms while maximizing the energy removed from the cross-terms. I tailored the choice of kernel such that the kernel was adaptively shaped around the auto-terms. If cross-terms are not overlapping with the
Figure A.3: Ambiguity functions of Choi-Williams kernel are shown for $\alpha=0.5$ and $\alpha=5$.

This method is described in section (3.2) with more details. Next, I calculate how energy of a chirplet distributed in the ambiguity space as function of distance from the origin.

### A.7 Energy distribution of ambiguity function

In previous section, I argued that the interferences observed in WVD can be removed by smoothing the representation. The total energy confined within distance $R$ of the origin of the ambiguity function.

\[
E(R) = \int_0^{2\pi} \int_0^R 2\pi \exp\left(-\frac{(r \cos \theta - \beta r \sin \theta)^2}{4\alpha} \right) \exp\left(-\frac{\alpha (r \sin \theta)^2}{4}\right) r^2 \, dr \, d\theta
\]

\[
= 4\pi^2 \int_0^{2\pi} \int_0^R \exp\left(\frac{-[(\cos \theta - \beta \sin \theta)^2 + (\alpha \sin \theta)^2]}{2\alpha} r^2 \right) dr \, d\theta
\]

\[
= 4\pi^2 \int_0^{2\pi} \frac{\text{erf}(R\phi(\theta))}{\phi(\theta)} d\theta
\]

(A.28)

where $\phi(\theta) = \sqrt{\frac{(\cos \theta - \beta \sin \theta)^2 + (\alpha \sin \theta)^2}{2\alpha}}$ and erf(.) is the error function. The energy at distance $R$ from the origin and at angle $\theta$ is

\[
E(R, \theta) = \frac{4\pi^2}{\phi(\theta)} \text{erf}(R\phi(\theta))
\]

(A.29)
A.8 Signals with multiple components

Thus far, the WVD of a chirplet and the cross-term generated between two chirplets were formulated. These results can be extended to signals that are combination of multiple chirplets such that the cross-terms are created between each two component. As such, WVD of a signal with $n$ components has $\frac{n(n-1)}{2}$ interference terms.
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ganglia give rise, respectively, to poverty and slowness of movement (i.e., Parkinson’s disease) or dyskinesias.


