

Grasping at Illusions: Stimulating the skin to investigate the cutaneous contribution to  
kinesthesia in the human hand

by

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## **Abstract**

How do you know your hand is moving without looking at it? This “movement sense”, known as kinesthesia, is thought to be primarily informed by receptors in muscles; specifically, the muscle spindles. As we move, muscle spindles discharge when muscles lengthen and, thus, most research has focussed on these receptors. However, receptors in the skin, known as cutaneous receptors, also discharge when we move, although their role in kinesthesia remains less clear. This thesis project was designed to investigate the role of cutaneous receptors in kinesthesia by using electrical stimulation to create illusory hand movements; namely, flexion of the index finger. The frequency and intensity of the stimulation were modulated, separately and simultaneously, to test hypotheses regarding how the central nervous system may use frequency coding and population coding from cutaneous receptors in kinesthesia. Thirty-four healthy participants (22 females, 12 males; aged 18-33) with no neurological or musculoskeletal impairments that affect the movement or sensation in the hands were recruited. Stimulation was applied to the superficial branch of the radial nerve on the dorsum of the right hand. A total of 10 trials were delivered in a random order. Each trial consisted of one of four stimulation patterns: 1) frequency-modulated: the frequency of the stimulation was sinusoidally increased and decreased with intensity held at perceptual threshold; 2) intensity-modulated: stimulation intensity was sinusoidally increased and decreased with frequency held at 55 Hz; 3) combined-modulation: stimulation frequency and intensity were synchronously increased and decreased; 4) sham: stimulation frequency was held at 55 Hz and intensity was held at perceptual threshold throughout the trial. If participants perceived movement, they were instructed to keep their right (stimulated) hand relaxed and to mimic the movements with their left (unstimulated) hand. Prevalence of illusory movements and movement amplitudes of the index finger were quantified using passive motion capture cameras. In total 25/34 (74%) of participants perceived illusory movements, with the mean amplitude of movement ranging from 1-25°. There were no

significant differences between the amplitudes of the frequency-modulated, intensity-modulated, or combined-modulation trials. However, the amplitudes of all three modulated trials were significantly larger than the sham trial. These results suggest that cutaneous receptors play a role in kinesthesia, and that the CNS uses frequency coding and population coding from cutaneous receptors to inform kinesthesia. The simple method used in this project may have applications for the investigation of other basic research questions, or integration with other sensory stimuli such as virtual reality.

## **Preface**

This thesis is an original work by Jessica Leverett. The research project, of which this thesis is a part, received ethics approval from the University of Alberta Research Ethics Board – Health Panel, Project Name “Perception of sensory information from the human hand”, No. Pro00118263, August 1, 2023. No part of this work has been previously published. This work was supported by a Canada Graduate Scholarship – Master’s (CGS-M) from the Natural Sciences and Engineering Council of Canada (NSERC).

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## List of Abbreviations

<b>CNS</b>	Central nervous system
<b>DIP</b>	Distal interphalangeal
<b>FAI</b>	Fast-adapting type I
<b>FAII</b>	Fast-adapting type II
<b>LTMR</b>	Low-threshold mechanoreceptor
<b>MCP</b>	Metacarpophalangeal
<b>PIP</b>	Proximal interphalangeal
<b>PT</b>	Perceptual threshold
<b>SAI</b>	Slowly adapting type I
<b>SAII</b>	Slowly adapting type II

## Chapter 1: General Introduction

### 1.1 Preface

How do you know what your hand is doing without looking at it? The ability to know the movement and position of the body and its limbs is known as kinesthesia (Proske & Gandevia, 2018). Kinesthesia is more mysterious than the senses of hearing or taste, in that we are largely unaware of it throughout our daily lives, yet we know where our limbs are without any defined sensation or visual input. Current views of kinesthesia generally accept that it is due to the integration of signals originating from the central nervous system (CNS) and signals from receptors in joints, muscle, and skin. Of the receptors in the periphery, muscle spindles are widely accepted as the most important for kinesthesia. The relative importance of signals from receptors in the skin, the cutaneous receptors, however, is still to be determined.

The primary goal of this thesis was to investigate the role of cutaneous receptors in kinesthesia. The experiment was designed to test hypotheses regarding the extent to which the CNS uses frequency coding and population coding of feedback from cutaneous receptors by manipulating the frequency and intensity of the stimulation, respectively. The simple method used to apply electrical stimulation to the skin to create these kinesthetic illusions may have applications for virtual reality, rehabilitation settings, or other basic science research questions such as those addressed in this thesis.

This thesis consists of a General Introduction (Chapter 1), a research chapter formatted for submission to the Journal of Physiology (Chapter 2), and a General Discussion (Chapter 3). Chapter 1 briefly outlines the history of kinesthesia, introduces the kinesthetic senses of movement and position, describes the main methods used to investigate kinesthesia, and summarises the roles of the signals from the CNS and periphery in kinesthesia. The second chapter comprises the main project of this thesis, and the third chapter brings together the main findings and puts them in context of the body of work outlined in Chapter 1, and outlines limitations and future directions for this work.

### 1.1 History of Kinesthesia

In 1826, Charles Bell noted that there must be a sixth sense, a 'muscular sense', as humans are aware of the position of the body and their limbs, which are "directed by a sense of the condition of the muscles" (p. 167). While Bell did not use the phrase "muscle sense" in his work, the phrase has been attributed to him (Proske & Gandevia, 2012). The term *kinæsthesis* (from the Greek 'kinein' meaning 'to move', and 'aisthēsis' meaning 'sensation') was first termed by Bastian (1887) and was believed to be a single sense comprising information about both

position and movement. Echoing Bell's views, this sixth sense was called the 'muscular sense' by both Bastian and Sherrington (1907), as early discussions revolved around what signals muscles may produce to provide this information about movement and position of the body. Sherrington (1907) described this 'muscular sense' in depth and coined the term *proprio-ception* to describe 'one's own' receptors, those that encode information regarding what the body, itself, is doing. It was clear that Sherrington believed that receptors in muscles were important providers of this information—a topic that was hotly debated in his time (McCloskey, 1984). Currently, the definition of proprioception includes the senses of position and movement, effort or force, and balance (Proske & Gandevia, 2018).

The current definition of kinesthesia, however, is more controversial. While it seems to be relatively accepted that the senses of position and movement are now considered separated (see Section 1.3, The Kinesthetic Senses), as they utilise different peripheral receptors and are encoded differently within the CNS (for reviews, see Proske & Gandevia, 2009, 2012, 2018; Taylor, 2022), whether or not both of these senses should be deemed as kinesthetic senses is still up for debate. Some authors take the literal definition, that kinesthesia is strictly a 'movement sense' and, therefore, should not include the sense of position (Macefield, 2021; Macefield & Knellwolf, 2018; McCloskey, 1973). It has been suggested that the term *stathesthesia* should be used to refer to the sense of position (Kavounoudias, 2018), though this has not been the trend for the majority of the literature. Others use the terms kinesthesia and proprioception interchangeably, likely due to the fact that the senses of movement and position fall under the proprioceptive umbrella, as mentioned above (Bent & Lowrey, 2013; Héroux et al., 2022, 2024; Mildren et al., 2017; Mildren & Bent, 2016; Taylor, 2022). Some others define kinesthesia as both the senses of movement and position (Goodwin et al., 1972; Lowrey et al., 2010; Proske & Gandevia, 2018). For the purposes of this thesis, the term *kinesthesia* will be used to refer to both the senses of movement and position of the limbs (whether passively imposed or actively generated) without vision, and these will be referred to as the "kinesthetic senses".

Over almost 200 years, there has been debate amongst scholars as to how kinesthetic signals become conscious perceptions. Both Bastian (1887) and Sherrington (1907) suggest that kinesthetic sensations are different from other sensations in that they arise neither solely from the external environment (i.e., the senses of hearing or taste rely on stimuli external to the body) nor the internal environment (i.e., chemoreceptors and baroreceptors in the blood rely on internal stimuli such as oxygen concentrations and blood pressure, respectively), but from a mixture of both. Sherrington (1907) made the distinction that *proprio-ceptors* required stimuli

from both the organism itself (i.e., the volition or reflex response to move) and the receptors on the surface of the organism, which respond to environmental stimuli (i.e., the force or tension within the muscles, tendons, and joints) as the organism moves. The extent to which kinesthesia relies on signals generated within the CNS versus signals from receptors in the periphery is still a topic of debate, although it is generally accepted there is an integration of the two (Proske & Gandevia, 2018; see Section 1.5 The Kinesthetic Signals).

Early debates regarding this ‘muscular sense’ revolved around whether central signals, termed “senses of innervation” by Helmholtz in 1867, were the only signals involved. As summarized by Proske & Gandevia (2012), the main idea behind the senses of innervation argument was that the will or volition to move, through the motor command, was what created sensations of movement and muscular activity. A counterargument, provided by Sherrington (1907), was that when someone moves our limbs passively, we still know we are moving, even without the intent to move. In the 1950s and 1960s, attention turned to sensory receptors in the periphery—including those in muscles, joints, and skin. As described in more detail in Section 1.3 Investigating Kinesthesia, techniques such as microneurography, which enables recordings from single afferents (Vallbo & Hagbarth, 1968), and microstimulation, which enabled stimulation of single afferents, enabled these investigations of the contributions of peripheral receptors to kinesthesia. Each of these signals, and the roles they play in kinesthesia, are addressed in separate sections below.

### **1.3 Investigating Kinesthesia**

The investigation of kinesthesia, particularly with the goal of understanding which signals from the periphery play the largest role, has utilized three main methods: 1) recording from an afferent or group of afferents, 2) stimulating an afferent or group of afferents, or 3) blocking an afferent or group of afferents. The following sections provide a brief overview of these approaches and focuses mainly on methods used in the thesis project—stimulating a group of afferents with electrical stimulation.

#### **1.3.1 Recording from afferents**

In the mid-1960s, Hagbarth and Vallbo developed a technique that enabled the recording of action potentials *in vivo* in humans: microneurography (Vallbo, 2018). To perform this technique, a thin tungsten electrode (shaft diameter 200-250  $\mu\text{m}$  tapered to 5  $\mu\text{m}$  at the tip) is percutaneously inserted into a nerve fascicle (Gandevia & Hales, 1997). Microneurography is demanding, as it requires that the fascicle of the nerve is penetrated by the electrode, which must be stiff enough to pierce the skin and the axon, but flexible enough to withstand

movements of the tissue and still stably record the firing of action potentials along a single axon (Vallbo, 2018). It also requires skilled manipulation of the electrode by the microneurographer to ensure that recordings are from the desired fascicle (Gandevia & Hales, 1997; Vallbo et al., 2004). Prior to this technique, recordings from afferents were performed in decerebrated or anesthetized animals, which shed some light on what was occurring in the neurological system, but for obvious ethical reasons, could not be used to explore these afferents in humans (Vallbo et al., 2004).

Microneurography enabled the exploration of the kinesthetic senses by recording from afferents in the periphery and, because the technique could be performed on awake and responding humans, participants are able to describe their perceptions and perform voluntary activities, which could then be related to the neural activity in real time (Vallbo et al., 2004). Within the field of kinesthesia, microneurography has enabled the categorization, rise and, in the case of joint receptors, fall of the ideas regarding the importance of each receptors' input to kinesthesia. Interestingly, it was the idea of recording from muscle spindles, specifically, which spurred the development of the technique as the researchers were particularly interested in investigating the fusimotor system (Vallbo et al., 2004; Vallbo, 2018). It has been this technique, especially, which has helped to create the arguments for the kinesthetic roles for both muscle spindles and cutaneous receptors. For example, recording from putative Ruffini endings (SAII receptors) has demonstrated their ability to reliably discharge in response to skin stretch during movements (Aimonetti et al., 2007; Edin & Abbs, 1991; Grill & Hallett, 1995). More information on the receptors in the periphery will be provided in their respective sections below.

### 1.3.2 Stimulating afferents or receptors

As noted by Proske & Gandevia (2012), the kinesthetic senses can be difficult to study, as they tend to operate on an unconscious level. One way to bring these sensations into conscious perception is to stimulate specific receptors or their afferents and create kinesthetic illusions. These illusions alter sensations of movement or position and, as a result, participants believe that their limb or body part is moving when it is not or is in a position that is different from its true position. Two of the main techniques used to create these illusions, electrical stimulation and vibration, will be discussed in this section. It is important to note that skin stretch has also been used to create illusions of movement, though this technique is not as commonly used as the others (Blanchard et al., 2011, 2013; Collins et al., 2000, 2005).

Electrical stimulation may be applied percutaneously or transcutaneously. Percutaneous stimulation, also known as microstimulation, utilises thin tungsten electrodes, which are pierced

through the skin into the axon bundles of a nerve. Transcutaneous stimulation utilises electrodes placed on the surface of the skin. Regardless of the method, artificially stimulating an axon or axons (through depolarization of the axonal membrane) can cause action potentials to propagate along the axonal membrane (Grill, 2004). At rest, the inside of the axonal membrane has a negative charge compared to the outside of the membrane. When the stimulation is turned on, negative ions (anions) move toward the positive electrode (anode) and positive ions (cations) toward the negative electrode (cathode). For depolarization to occur, enough positive current must be injected across the membrane to reach threshold and generate action potentials. Under the cathode, anions are repelled away from the negatively charged electrode towards the axonal membrane and cations are attracted towards it. If the current is large enough, the extracellular space around the axonal membrane may become negative enough that the positive ions within the axon begin to move across the membrane and depolarization occurs (Grill, 2004). In the work described in Chapter 2, we use transcutaneous electrical stimulation. The frequency in which the pulses are delivered through this method is intended to mimic the frequency at which the receptors discharge when movement occurs and, thus, creates the kinesthetic illusions of movement.

Vibration was first used to create illusions of movement about the elbow (Goodwin et al., 1972). The authors proposed that it was primary endings of the muscle spindles responding to this vibratory stimulus and sending a signal to the brain that the muscle was lengthening and creating the illusion of movement (Goodwin et al., 1972). As the frequency of the vibration increased, the velocity of the illusory movement also increased (Goodwin et al., 1972; Roll et al., 1989; Roll & Vedel, 1982). This suggests that the physiological mechanism for this illusion is that the frequency of the vibration mimics the discharge of these receptors during movement. It should be noted, however, that vibration does not only activate muscle afferents. Studies have demonstrated that high-frequency vibration (i.e., 300 Hz) can also affect the cutaneous receptors under the stimulus, which have their own (usually detrimental) effects in kinesthetic acuity (Weerakkody et al., 2007, 2009).

### 1.3.3 Blocking or eliminating receptor feedback

To discern whether a receptor population contributes to kinesthesia, Matthews (1982) suggests there are two main methods of experimentation: 1) eliminate the feedback from that receptor population, leaving others intact, and 2) preserve the feedback from one type of receptor, while eliminating all others. Most studies have opted to remove the feedback from a group of

receptors, passively moved the joint and asked participants to either identify the direction the joint moved or match the position of the joint with the contralateral limb.

During their seminal study investigating the role of muscle receptors, Goodwin et al. (1972) used an ingenious 'anatomical peculiarity' to remove their feedback. When digits II, IV, and V are extended, and the proximal interphalangeal (PIP) joint of digit III is flexed, the distal interphalangeal (DIP) joint cannot be voluntarily moved by the participant. Effectively, the muscles are disengaged from the DIP joint and, as such, any passive movement applied to the joint is not transferred to the muscles or the muscle spindles. When participants had their entire hand anesthetised, and the middle finger was placed in this position, they were unable to detect movements at this joint. They were, however, able to detect movement when the finger was extended, and the muscles re-engaged. Interestingly, Gandevia & McCloskey (1976) used this same peculiarity to try and isolate the input from muscle and other receptors, with and without the muscles engaged. To isolate feedback from muscle receptors, some trials included anesthetization of the finger to remove cutaneous and joint feedback. The findings, however, varied widely amongst participants. Some participants were more accurate when the feedback from joints and skin were available, regardless of muscular input, others were not. Tensing of the muscles, however, always seemed to improve participants' ability to detect movements, though the amount of improvement varied as well.

Other studies have simply used anesthesia to temporarily remove feedback from cutaneous and joint receptors in multiple joints of the hand and the dorsum of the ankle (Clark et al., 1985; Ferrell & Smith, 1988; Lowrey et al., 2010). These studies have produced mixed results, leading to the continued controversy of cutaneous input to kinesthesia. Authors tend to agree, however, that the decrement of a participant's ability to match the position of a joint suggests the importance of the feedback from that missing receptor, and the lack of a decrement implies its opposite. It is important to note that the movements in these studies are generally passive, as active movements may confound the results due to the signals from the CNS, in the form of motor commands (see Section 1.5 Kinesthetic Signals for more information).

#### 1.3.4 Combining methods

Multiple researchers have combined the methods of recording and stimulating from receptors and their afferents to isolate what information the CNS uses to encode kinesthesia. By combining microneurography with tendon vibration, Roll & Vedel (1982) demonstrated that primary endings of the muscle spindle will increase their discharge rate with an increase in the

frequency of the applied vibration from 10-100 Hz. Interestingly, all participants reported an increase in the velocity of the evoked illusory movement, with the highest velocities of the perceived movements reported between 60-80 Hz. When the vibration was increased beyond 80 Hz, however, the velocity of the illusory movement decreased (Roll & Vedel, 1982). In a later study, Roll et al. (1989) reported that vibration frequencies between 80-100 Hz activate the highest number of primary endings, and they will discharge at a 1:1 ratio with the vibrational frequency. When the vibration frequency was increased, however, subharmonic or random discharges were recorded in primary endings, which may explain the decrease in perceived velocity at higher vibrational frequencies. Taken together, these findings suggest that the CNS uses frequency coding from the primary endings to encode the kinesthetic movement sense.

The ideal frequency ranges for muscle spindle primary endings also relies on the position of the joint when the vibration was applied. Roll & Vedel (1982) noted that placing the ankle at 90-95° ensured the best responses from the muscle spindles in the tibialis anterior muscle. This corroborates findings from Cordo et al. (2002), where individual primary endings responded most effectively to an “ideal range” of about 15° within the joint’s range of motion, which varied from receptor to receptor. As the primary endings were recruited at differing ranges within the joint’s movement, their ideal ranges overlapped and, thus, the authors concluded that encoding position sense requires a population of receptors (Cordo et al., 2002).

#### **1.4 The Kinesthetic Senses**

As mentioned previously, it is generally accepted that the kinesthetic senses of movement and position are separate senses. While it could be debated that a movement is simply a change in position, rather than its own separate sense, there is evidence to support the idea that these senses utilise different receptors and are encoded differently within the CNS (Proske, 2006).

In their influential study, Goodwin et al. (1972) used vibration to create illusions of movement about the human elbow joint. As described in the previous section, vibration is a powerful stimulus to muscle spindles and when applied to the biceps brachii, it caused participants to believe their elbow was extending, when it was not. Interestingly, these illusions of movement were also accompanied by sensations of a change in position, which led the authors to suggest that a change in movement and position were two separate, though intertwined, senses (Goodwin et al., 1972). To investigate these findings, McCloskey (1973) used low-frequency vibration (i.e., 20-35 Hz) and high-frequency vibration (i.e., ~100 Hz) and reported that the low-frequency vibration created the illusion of a change in position, whereas the high-frequency vibration created the illusion of movement. These findings have been



attributed to the differences in vibratory stimuli activating different receptors within the muscle. It is believed that the lower-frequency vibration activated the secondary endings in muscle spindles, which encode the length of the muscle, whereas higher-frequency vibration also activated the primary endings, which encode both the change in length of the muscle and the velocity at which this change occurs (Matthews, 1988; Roll et al., 1989). Section 1.5 Kinesthetic Signals expands on the distinction between the types of muscle spindle endings and their respective roles in kinesthesia.

Further evidence that movement and position may be separate senses is provided by experiments in which a change in position can be detected without a conscious perception of movement occurring. Hall & McCloskey (1983) reported that the threshold to detect a movement rises as the velocity of the movement decreases. Thus, if a limb is moved slowly enough participants will not detect that a movement has occurred but will still detect that it has changed position. This holds true for the ankle, knee, and index finger, whereby these joints can be moved at imperceptibly slow speeds (i.e.,  $\sim 1^\circ/\text{min}$ ) yet, when the movement stopped, participants accurately detected the change in position (Clark et al., 1985; Horch et al., 1975; Taylor & McCloskey, 1990).

There is also evidence that the CNS utilises signals from the periphery to encode the senses of movement and position in different ways. In a complicated study by Sittig et al. (1985), researchers teased apart a main difference between the movement and position senses. Whereas the movement sense was affected by participants' perceptions about the movement, their position sense was not. To briefly summarize, if a participant perceived a movement to be faster than it was, they would proceed to match that movement by moving faster and vice versa (e.g., slower perception meant slower matching), regardless of whether or not vibration was applied to the limb. On the other hand, position sense was only affected when vibration was applied. Participants were accurate at matching the position of a hidden limb and indicating where they thought it was when no vibration was applied.

Recently, Proske & Chen (2021) suggested that there may be two types of position sense, and the difference between them can be elucidated by the methods used to investigate them. The authors propose that tasks which require participants to match the position of one limb to the other measures position sense in "postural space", or the relationship of one body part to another. On the other hand, tasks that require participants to indicate the position of a hidden limb, by means of a pointer or other measurement, measures position sense in "extrapersonal space", or where the limb exists within the external environment. This points to a recent discussion in measurements of kinesthetic or proprioceptive tasks begun by Héroux et al.

(2022), which they describe as *low-level* or *high-level* tasks. *Low-level* tasks require participants to “detect, discriminate, or match” the kinesthetic stimuli (Héroux et al., 2022, p. 811). Examples of these tasks include *detecting* the beginning of a movement, *discriminating* whether that movement is flexion or extension, or *matching* a joint angle or movement between the right and left sides of the body (Héroux et al., 2024). *High-level* tasks, on the other hand, require that the task involve different frames of reference between the movement or change in position and the measurement used to quantify them. Therefore, the first type of position sense described by Proske & Chen (2021), involving “postural space” would be assessed using *low-level* tasks, and the second type of position sense, involving “extrapersonal space”, would be assessed using *high-level* tasks.

## **1.5 Kinesthetic Signals**

Ideas regarding the main sources of kinesthetic information have revolved between central signals, associated with motor commands, and signals from receptors in joints, muscles, and skin. Although some groups include vision as part of kinesthesia, for the purposes of this thesis, kinesthesia is defined as the ability to know the position and movement of the body and its limbs, without visual input. For more information regarding vision and kinesthesia, see Kavounoudias (2018). The following sections provide a brief overview of the different type of signals and the roles they are believed to play in kinesthesia, with a focus on receptors in the skin.

### **1.5.1 Central commands**

Ideas about kinesthesia, particularly the concept that descending central signals create our senses of movement and position are not new. First termed a “sensation of innervation” by Helmholtz in 1867, it was suggested that the effort to move created these sensations and that they were derived from some central mechanism within the CNS (McCloskey, 1978). In the mid-20<sup>th</sup> century, ideas regarding the contribution of motor commands had shifted from being the sole provider of kinesthetic information to a more subsidiary role. Sperry (1950) suggested that a “corollary discharge”, or a copy of the motor command, was relayed to sensory areas of the brain, which then integrated this copy with information from the periphery to inform the kinesthetic senses. Not long after, von Holst (1954) proposed the term “efference copy”, and suggested that the CNS uses this copy of the motor command to determine what is expected to occur. In von Holst’s view, a distinction was made between the afferent signals which arose from the organism’s own actions (reafference) and afferent signals which arose from sources in the organism’s external environment (exafference). For an organism to know the position and

movement of its limbs, the CNS calculates the reafference from this motor command copy. Whether the copy is an exact replica of the motor command or includes predictions based on past experiences is still unknown (Donaldson, 2000).

The modern view is that motor commands contribute to both senses of movement and position. Researchers have demonstrated that asking participants to move a limb that has been temporarily paralysed using an anesthetic and locked into position so that the limb cannot move, created the illusions of movement at the wrist and/or elbow joints (Gandevia et al., 2006; Smith et al., 2009; Walsh et al., 2009, 2010). When the limb is anesthetised and locked into place, the perceived velocity of the illusory movement increased the longer the participant tried to move their limb, and with the amount of force the participant used (Walsh et al., 2010). When the limb is not anesthetised, but still locked into place enabling information from muscle receptors, as the participants performed an isometric contraction, they used the information from the available afferents to bias the direction of the illusory movement (Smith et al., 2009). If the participant tried to flex the joint, for example, the illusory movement would be in the direction of joint flexion. Similarly, participants reported a larger change in position when instructed to increase the amount of force or effort used to try and move the paralysed limb (Gandevia et al., 2006). If the participant performed a contraction prior to locking the limb into position, participants perceived the illusory movement in the same direction as the recent contraction, even though the position of the limb did not change (Walsh et al., 2009). The authors suggested that the recent contractions at the joint were integrated into the motor command as the participant tried to move, thereby biasing the direction of the illusory movement.

### 1.5.2 Receptors in joints

When researchers first began investigating the role of receptors in the periphery, the obvious place to begin was where the movement was occurring: in the joints themselves. As summarized in reviews by McCloskey (1978) and Matthews (1982), the results of numerous studies throughout the 1950s and 1960s, which involved recordings from joint afferents in animals or single afferents dissected from these nerves, demonstrated that joint receptors discharged when the joint was moved, or pressure was applied to it. From these studies, it became widely accepted that the joint receptors were the primary informers of the kinesthetic senses. These studies, however, had two main limitations. First, the recording electrodes were easily dislodged and, as such, many recordings were made during small movements that did not encompass the full range of motion. Second, the single afferents sampled were from the few receptors that were active during the intermediate ranges of movement and, therefore, did not

reflect the majority of the joint receptors. To address these limitations, Burgess & Clark (1969) recorded from dorsal root filaments, rather than within the joint, which enabled recordings from the entire anatomical range of the joint. Burgess & Clark (1969) demonstrated two major differences from previous studies: 1) over half of the afferents discharged during *both* extreme flexion and extension, rendering their input ambiguous for signalling the direction of extreme ranges of motion, and 2) the majority of knee joint afferents were silent throughout the intermediate range of joint motion.

One current view is that joint receptors play a role as *limit detectors* in the kinesthetic senses as their firing rate increases as the anatomical end of range approaches (Macefield, 2021; Proske & Gandevia, 2018). It is thought that joint receptors require the tissue of the joint capsule to tighten—which applies a mechanical force to the receptors and thereby causes them to discharge—and this does not occur until the joint nears its anatomical limit or until torsion is applied to the joint (Hall & McCloskey, 1983). In line with this idea, participants more accurately match position as they approach the anatomical limits of elbow motion, compared to within the mid-range (Proske, 2023). It has been suggested that the joint receptors work in conjunction with muscle spindles to provide a more accurate representation of the limb when nearing its anatomical limit, which may help prevent injury (Proske, 2024).

### 1.5.3 Receptors in muscles

There are two receptors in muscles which may inform kinesthesia, muscle spindles and Golgi tendon organs. It is generally accepted that the main source of kinesthetic signals in the periphery is that from muscle spindles. This section briefly outlines these receptors and their respective roles in kinesthesia.

Muscle spindles are spindle-shaped, stretch-sensitive mechanoreceptors located in most skeletal muscles (Proske, 1997). Each end of the spindle is attached to muscle fibres via connective tissue, which enables the spindle to deform when the muscle fibre is lengthened. Unlike other mechanoreceptors, muscle spindles have both sensory and motor innervation. Two different sensory endings of the muscle spindle give rise to two separate afferents, which encode different information regarding movement and position sense. The primary endings are innervated by group Ia afferents and the secondary endings are innervated by group II afferents. Primary endings are exquisitely sensitive to low-amplitude vibration and discharge in response to changes in length of the muscle and the velocity at which it occurred. Secondary endings, on the other hand, have a higher mechanical threshold, lower conduction velocity, and are more sensitive to length changes in muscle compared to primary endings (Gandevia, 1996;

Matthews, 1988; McCloskey, 1978). The current view is that primary endings encode information related to both movement and position sense, while the secondary endings encode position sense only.

While these spindles are generally seen as the main kinesthetic receptor (Proske & Gandevia, 2018), they cannot encode all kinesthetic information on their own. As mentioned previously, studies have demonstrated that individual spindles tend to encode specific ranges of movement, enabling them to have a 'preferred sensory direction', but preventing them from responding to the limb's entire range of motion (Aimonetti et al., 2012; Cordo et al., 2002; Jones et al., 2001; Roll et al., 2000, 2004). In addition to this, some muscles cross multiple joints, such as those in the hand or across the wrist and elbow. When participants moved their joints in opposite directions, as is done when the wrist flexes and the elbow extends during reaching and grasping movements, participants were significantly worse at identifying which direction the wrist was moving when the elbow was also moving (Sturnieks et al., 2007). The authors concluded that these decrements in kinesthetic acuity were due to muscle input, rather than joint or skin, because movements were in the intermediate range, reducing the likelihood of joint receptor feedback, and the participant's forearm was resting on a support, which likely reduced the skin stretch that may have occurred during these movements. Finally, as muscle spindles contain both motor and sensory innervation, discharge of muscle spindles may be caused by activity within the receptor, due to intrafusal contractions, or from external sources, such as muscle stretch, rendering their input as potentially ambiguous (Proske, 2005). In summary, while muscle spindles are very sensitive to changes in muscle length, especially stretch, they require multiple receptors to encode kinesthesia.

Golgi tendon organs reside in the musculotendinous junction and the muscle tendons. They are fusiform in shape and, unlike muscle spindles, respond to changes in contractile forces generated within the muscle tendon (Gandevia, 1996). Findings from microneurographic studies demonstrate that Golgi tendon organs are insensitive to the changes in length as they do not discharge in response to vibration or muscle stretch unless the muscle is contracted (Edin & Vallbo, 1990; Roll et al., 1989). Thus, Golgi tendon organs are likely to play a role in proprioception, which includes the perception of force or effort, but have limited, if any, role in kinesthesia.

#### 1.5.4 Receptors in skin

When humans move, skin stretches and deforms, resulting in the discharge of mechanoreceptors in the skin (Aimonetti et al., 2007; Edin, 1992; Edin & Abbs, 1991; Grill &

Hallett, 1995; Knibestöl, 1973, 1975). There are four low-threshold mechanoreceptors (LTMRs) in the skin whose discharge relate to specific movement parameters and, therefore, have potential roles in kinesthesia. The following sections provide an overview of these LTMRs and the roles they play in kinesthesia. Despite the many excellent studies which report on the interesting histology and molecular mechanisms of these receptors, these topics are outside of the scope of this thesis work and will be addressed only when particularly relevant in this review.

The four LTMRs are the Ruffini endings, Pacinian corpuscles, Merkel complexes, and Meissner's corpuscles. These receptors can be distinguished morphologically, as well as by their response properties (Bolanowski et al., 1988; McGlone & Reilly, 2010; Taylor, 2022). In addition to their morphological differences, which will be described in subsequent sections, these receptors can be classified on how they respond to a constant stimulus, and the characteristics of their receptive fields. Fast-adapting (FA) receptors are ideal for signalling changes in a stimulus, as they typically discharge when a stimulus changes (i.e., the beginning or end of a movement). Slow-adapting (SA) receptors, on the other hand discharge continuously while the stimulus is present and their discharge frequencies scale with the stimulus strength or velocity (Edin & Abbs, 1991; McGlone & Reilly, 2010; Taylor, 2022). Type I receptors tend to have small receptive fields, which are circular or ovoid in shape, with distinct borders that encapsulate multiple areas of high sensitivity. Type II receptors tend to have large receptive fields with a single spot of high sensitivity and diffuse borders (Johansson & Vallbo, 1979; Macefield, 2005; Vallbo et al., 1979). Unlike the glabrous skin, which has a high concentration of FAI and FAII receptors (Johansson & Vallbo, 1979), the hairy skin has a higher density of SAI and SAII receptors (Edin, 2001; Edin & Abbs, 1991; Hensel & Boman, 1960; Järvilehto et al., 1981). Within these four LTMRs, the type II receptors are the most responsive to movements (Aimonetti et al., 2007; Hulliger et al., 1979; Knibestöl, 1975) and, therefore, are the receptors most likely to contribute to kinesthesia. The next few subsections introduce the four LTMRs in order of most likely to least likely to contribute to kinesthesia.

#### *1.5.4.1 Ruffini endings*

Ruffini endings are SAII receptors and, of the four LTMRs, they are the most controversial (Fleming & Luo, 2013; Handler & Ginty, 2021). While these receptors have been well categorized in terms of their response properties, there is a relative paucity of them in histological studies, which leads some authors to suggest that there may be other mechanoreceptive tissues that are associated with SAII afferents (Cobo, García-Piqueras, et al.,

2021; Cobo, García-Mesa, et al., 2021; Munger & Ide, 1988; Paré et al., 2003). It is likely that the relative scarcity of this receptor in the histological data is because these receptors are less dense in the glabrous skin, compared to the hairy skin of humans, and most electrophysiological studies of the skin occur in the glabrous skin rather than the hairy skin. Paré et al. (2003) were only able to find one receptor categorized as a Ruffini ending in the glabrous skin of human hands and concluded that there must be some other type of receptor associated with the SAIL afferents reported in microneurographical studies. Recently, another group of researchers set out to find evidence of Ruffini endings in human glabrous skin (Cobo, García-Mesa, et al., 2021). They too, however, were unable to find Ruffini endings in the densities reported in electrophysiological studies and suggest that more studies are performed to investigate these discrepancies. There is little histological information regarding Ruffini endings in the skin, as researchers have not found SAIL-type afferents in the animal models usually used for investigating LTMRs (i.e., mice, rabbits, raccoons, and monkeys) and, therefore, the animals do not have the receptors associated with them and have not been investigated to the depth of the other LTMRs in the skin (Cobo, García-Mesa, et al., 2021; Owens & Lumpkin, 2014; Watkins et al., 2022). For this review, as it is approaching the subject from a physiological standpoint, where there is evidence of SAIL receptors in human skin, Ruffini endings will be associated with SAIL-type receptors and the terms will be used interchangeably.

Ruffini endings are spindle-shaped receptors which lie in the dermis of the skin (Chambers et al., 1972; Cobo, García-Piqueras, et al., 2021; Cobo, García-Mesa, et al., 2021; Handler & Ginty, 2021). These receptors consist of a thinly lamellated capsule, made up of four or five layers of cells (Chambers et al., 1972; Cobo, García-Mesa, et al., 2021). The structure of these receptors shares many similarities to muscle spindles, including a fluid-filled space within the capsule and collagenous attachment points at opposite ends of the spindle, which enable them to discharge in response to stretching of the skin (Chambers et al., 1972). Ruffini endings have a higher density in hairy skin compared to glabrous skin (Edin & Abbs, 1991). They have large receptive fields with diffuse borders (i.e., > 7 mm or 40 mm<sup>2</sup>; Vallbo & Johansson, 1984; Watkins et al., 2022), which enable them to discharge in response to multiple joint movements or to those that are farther away than type I receptors (Aimonetti et al., 2007; Edin, 1992; Edin & Abbs, 1991).

Ruffini endings have the highest threshold to skin indentation of all four LTMRs, ranging from 5 mN to over 15 mN in some studies (Edin & Abbs, 1991; Schady & Torebjörk, 1983). They are most sensitive to low-frequency vibration (i.e., 8 Hz), but may discharge in response to frequencies as high as 300 Hz (Ochoa & Torebjörk, 1983; Watkins et al., 2022). Until recently, it

was generally believed that stimulation of single Ruffini afferents could not produce conscious percepts, although rare percepts of “movement” or swelling of the skin have been reported (Iggo, 1984; G. Macefield et al., 1990; Ochoa & Torebjörk, 1983; Schady & Torebjörk, 1983; Å. B. Vallbo et al., 1984). Watkins et al. (2022) recently stimulated afferents from Ruffini endings in the glabrous skin of the hand and their participants reported sensations of “pressure, light touch, or squeeze” (p. 2946).

Ruffini endings are most well known for their ability to discharge in response to skin stretch applied parallel to the skin. In the glabrous skin of the hand, Ruffini endings discharge most in response to skin stretch applied in directions parallel to the longitudinal axis of the fingers, although receptors in the palm did not display this same directionality (Johansson, 1978). In the hairy skin, these receptors increase their discharge rate in a unidirectional manner and can respond to movements at multiple joints, responding to movements as far as 8 cm away from the receptor (Aimonetti et al., 2007; Edin, 1992). These receptors have also demonstrated an increase in discharge rate as the velocity of the skin stretch is increased, and in this way can encode the velocity of the movement (Aimonetti et al., 2007; Edin, 1992, 2001). Ruffini endings also continue to fire at a regular discharge rate when a movement is held in a static position and, as such, enables the encoding of the position of the limb (Edin, 2001; Johansson & Vallbo, 1983; Macefield, 2005, 2021). Of all the LTMRs, Ruffini endings are the only one that spontaneously discharges, suggesting that they may constantly encode the position of the limb or joint (Schady & Torebjörk, 1983; Vallbo et al., 1995; Vallbo et al., 1984; Watkins et al., 2022).

#### *1.5.4.2 Pacinian corpuscles*

Pacinian corpuscles are FAII receptors, which are located deep in the dermis and hypodermis of the skin (Cobo, García-Piqueras, et al., 2021). Johannes Gottlieb Lehmann first described them in the 18<sup>th</sup> century, but they retain the name of Fillipo Pacini who rediscovered them in 1841 (Fleming & Luo, 2013). Early psychophysical studies investigating LTMRs of the hand differentiated these receptors first and, as such, named the other receptors “not-Pancinian” (i.e., NPI, NPII, and NPIII for the FAI, SAI, and SAI receptors, respectively) until they, too, were identified (Bolanowski et al., 1988).

Each Pacinian corpuscle is innervated by a single afferent with concentric rings of outer lamellae, giving the receptor the appearance of the cross section of an onion (Johnson et al., 2000). Generally, these receptors will discharge at the beginning and end of a stimulus and fall silent in between. When the outer lamellae are removed, however, this discharge is prolonged throughout the entirety of the stimulus with a large decay in firing rate, which suggests that the



lamellae are responsible for the adaptation rate of the receptor (Handler & Ginty, 2021; Loewenstein & Mendelson, 1965).

Pacinian corpuscles have a higher density in the fingertips compared to the palm of the hand, but are much lower in density compared to type I receptors in both the glabrous and hairy skin (Edin & Abbs, 1991; Johansson & Vallbo, 1979). These receptors have the largest receptive fields with diffuse borders, enabling them to respond to movements from multiple joints, even as far as 25 cm away (Edin & Abbs, 1991; Handler & Ginty, 2021; Macefield, 2005). Pacinian corpuscles have the lowest indentation threshold of all four LTMRs, with thresholds as low as 0.5 mN, enabling them to respond to stimuli as gentle as blowing across the skin (Edin & Abbs, 1991; Johansson & Vallbo, 1983; Knibestöl & Vallbo, 1970; Macefield, 2005; Schady & Torebjörk, 1983). These receptors are well known for their ability to discharge and convey information about high-frequency vibration (Johnson et al., 2000). They can follow vibrational frequencies from 60 to 800 Hz, but respond most effectively to frequency ranges between 200-300 Hz (Bolanowski et al., 1988; Burgess & Perl, 1973; Johansson & Vallbo, 1983; Knibestöl, 1973; Macefield, 2005). There is recent evidence that these receptors may be entrained to fire at lower frequencies (i.e., 20-40 Hz), a range at which was believed to be encoded by FAI receptors only (Birznieks et al., 2019). When their single afferents are stimulated, the most common percept is that of vibration—which scales with the frequency of the stimuli—or buzzing, but other percepts, such as tickling, have also been reported (Ochoa & Torebjörk, 1983; Schady & Torebjörk, 1983; Torebjörk et al., 1987; Vallbo et al., 1984).

It is very likely that Pacinian corpuscles (FAI receptors) contribute to kinesthesia, as most within a sample will respond to movement (Aimonetti et al., 2007; Edin, 1992, 2001; Edin & Abbs, 1991; Vallbo et al., 1979). Pacinian corpuscles demonstrate a unidirectional preference for firing, in that they will increase their discharge rate for a movement in one direction, but will decrease their discharge rate, or not fire at all, for movements in the opposite direction (Aimonetti et al., 2007, 2012). It is likely that Pacinian corpuscles are important for movement sense rather than position sense, however, as although they discharge during a movement, as fast-adapting receptors, they do not signal the sustained position of a joint.

#### *1.5.4.3 Merkel complexes*

Merkel complexes, also known as Merkel cells or Merkel discs or Merkel cell-neurites, are SAI-type receptors and are located in the basal epidermis of the skin in mammals (Fleming & Luo, 2013; Munger & Ide, 1988). Merkel complexes were originally termed “touch domes” by Friedrich Merkel in 1875, as it was believed that they mediate mechanosensation (Fleming & Luo, 2013; Zimmerman et al., 2014). Merkel complexes are ovoid in shape, and are the smallest

of the four LTMRs, measuring 10-15  $\mu\text{m}$  in length (Fleming & Luo, 2013). In the hairy skin, these receptors are comprised of a single axon that splits into multiple endings, each of which innervate a Merkel cell, that cluster together to form a “touch dome” (Iggo & Muir, 1969; Macefield, 2005). Iggo & Muir (1969) described these receptors, as being visible as “dome-shaped elevations” on the epidermis of the cat (p.766). These individual Merkel cells may be the areas of highest sensitivity within the Merkel complexes’ receptive fields (Vallbo et al., 1995).

Merkel complexes are more dense in the fingertips of humans, compared to the skin of the palm, although they are not as numerous as Meissner’s corpuscles (Johansson & Vallbo, 1979). In the hairy skin, these receptors are found evenly distributed throughout the dorsum of the hand (Edin & Abbs, 1991). Merkel complexes can have small receptive fields, about 1-2 mm or 5 mm<sup>2</sup> (Johnson et al., 2000), but they may be larger on the dorsum of the hand and forearm, ranging from 3-21 mm<sup>2</sup> (Schady & Torebjörk, 1983; Vallbo et al., 1995). Their threshold to indentation is higher than both FA LTMRs, requiring a median pressure of 5.3 mN to produce excitation (Schady & Torebjörk, 1983), although it is not as high as the previously mentioned Ruffini endings (SAII receptors).

Merkel complexes are believed to encode texture, especially at the fingertips, as they are particularly sensitive to spatial features of stimuli to the sub-millimeter range (Jarocka et al., 2021; Johnson, 2001). These receptors are especially sensitive to the edges of objects when they contact the skin and are believed to encode the texture or roughness of objects (Blake et al., 1997; Handler & Ginty, 2021). Merkel complexes respond to low-frequency vibration (i.e., 3-32 Hz), with their ‘best’ responses found at 8 and 16 Hz (Johansson et al., 1982; Ochoa & Torebjörk, 1983). They will discharge, however, at frequencies as high as 400 Hz (Johansson et al., 1982). When single afferents are stimulated, the percept elicited is described as pressure, squeezing, (Ochoa & Torebjörk, 1983; Schady & Torebjörk, 1983; Torebjörk et al., 1987; Vallbo et al., 1984), or a “sharp pencil indentation, pinching, or internal pulling” (Watkins et al., 2022, p. 2946).

In regards to their ability to encode movement, Merkel complexes increase their discharge rate as the joint flexes and decreases as it extends (Edin & Abbs, 1991). However, these receptors are not as sensitive to changes in force caused by indentation as the Ruffini endings (Vallbo et al., 1995). Some studies have noted a directional component to the changes in discharge rates of Merkel complexes, but mention that they are not as selective as the type II receptors (Ruffini endings and Pacinian corpuscles; Aimonetti et al., 2007; Hulliger et al., 1979; Knibestöl, 1975). Birznieks et al. (2001) suggest that the direction of the forces applied may explain the changes in sensitivity, noting that Merkel complexes tend to be more sensitive to

forces applied perpendicularly to the skin, whereas Ruffini endings are more sensitive to forces applied parallel to the skin. Taken together, these findings suggest that Merkel complexes may have a role in the kinesthetic movement sense, but they are not as selective in reporting direction as the Ruffini endings (SAII receptors) and Pacinian corpuscles (FAII receptors). It is likely that these receptors inform the kinesthetic position sense. When the strain on the skin was increased and held, as is seen with a movement into flexion and then holding that position, there was a marked decline in the discharge rate with an abnormal firing pattern (Edin, 1992, 2001). The receptor can continue to fire for up to 30 minutes, providing information to the CNS regarding the position of the joint for long periods of time (Handler & Ginty, 2021; Iggo & Muir, 1969; Werner & Mountcastle, 1965).

#### 1.5.4.4 Meissner's corpuscles

Meissner's corpuscles, FAI receptors, reside in the conical protrusions of the dermis into the epidermis (Munger & Ide, 1988). Interestingly, although Meissner's corpuscles were first described by Wagner and Meissner in 1852, it was due to a monograph written by Meissner in 1853 that the name Meissner became associated with the receptors (Munger & Ide, 1988). These receptors are more numerous in the glabrous skin of the hand compared to the hairy skin, and are most dense in the fingertips, followed by the fingers, where they cluster around knuckles. Much like the other three LTMRs, Meissner's corpuscles have the lowest density in the skin of the palm of the hand (Johansson & Vallbo, 1979). These LTMRs are ovoid in shape and consist of several spots of sensitivity within their receptive field, which is, on average, 1-2 mm or 5 mm<sup>2</sup> (Johansson, 1978; Johansson & Vallbo, 1983; Johnson et al., 2000; Knibestöl & Vallbo, 1970; Macefield, 2005). Indentation thresholds to excite these receptors are relatively low, requiring a median force of only 1.37 mN of pressure to begin discharging (Schady & Torebjörk, 1983). These receptors respond to light stroking across the skin, shear forces or 'slips', and low-frequency vibration (Johansson et al., 1982; Macefield, 2005).

Although Meissner's corpuscles respond to low-frequency vibration, they are most sensitive to ranges within 8-64 Hz (with their 'best' responses at 32 Hz; Johansson et al., 1982), 20-40 Hz (Talbot et al., 1968), or 40-60 Hz (Johnson et al., 2000), and they can discharge up to frequencies of 100 Hz (Iggo, 1984) or 200 Hz (Hollins & Roy, 1996). Stimulating single afferents produces the percept of "fluttering" or intermittent tapping in the area of the receptive field (Iggo, 1984; Ochoa & Torebjörk, 1983; Torebjörk et al., 1987; Vallbo et al., 1984). While they are quite sensitive to stimuli within the receptive field, they have well-defined borders, and any stimuli delivered outside of them results in markedly diminished responses from the receptor. Due to this stringent selectivity, Meissner's corpuscles are associated with fine discrimination and, at

the fingertips, have a spatial sensitivity within the sub-millimeter range (Jarocka et al., 2021; Johansson & Vallbo, 1979; Knibestöl, 1973). In the glabrous skin, Meissner's corpuscles tend to discharge when a nearby joint moves, regardless of the direction (Hulliger et al., 1979; Knibestöl & Vallbo, 1970). In the hairy skin of the hand and fingers, however, Meissner's corpuscles discharge slightly more during flexion than extension, and will only respond to movements about a single joint (Edin & Abbs, 1991). One idea about Meissner's corpuscles is that they provide information about which joint has moved, rather than the direction, speed, or amplitude of the movement (Edin & Abbs, 1991).

In summary, it is likely that Edin & Abbs (1991) were correct in suggesting that all four LTMRs play a role in kinesthesia. The Ruffini endings (SAII receptors) may be the most important as the change in their frequency can encode reliable information about movement direction, velocity, and position. Due to their large receptive fields, however, they are unlikely to provide high-fidelity information about *which* joint was moving. When their discharge patterns are integrated with those from Pacinian corpuscles (FAII receptors), these two LTMRs are as accurate in informing the direction and velocity of a movement as muscle spindles (Aimonetti et al., 2012). However, as Pacinian corpuscles have the largest receptive fields of all the LTMRs, they are unable to disambiguate which joint may be moving—especially in areas with multiple joints moving, such as the skin of the fingers. The small, distinct receptive fields of the type I receptors (Merkel complexes and Meissner's corpuscles) can inform the location of the movement as they rarely discharge for movements of more than one joint. All in all, this suggests that the integration of all four LTMRs are needed to disambiguate the movements and positions of the joints in the hands, and that the CNS may use this population coding in kinesthesia.

## **1.6 Thesis Overview**

The main goal of the project in this thesis is to contribute to the understanding of the role of cutaneous receptors in kinesthesia of the human hand. Previous studies have suggested the CNS uses both frequency coding (i.e., the changes in the discharge rates of receptors) and population coding (i.e., the changes in the number and type of receptors firing) to encode movements and changes in position from muscle spindles, and it is likely that the CNS uses this information from the skin as well. We predicted that modulating either the frequency or the intensity of the stimulation would create illusory movements in the hand, but modulating both, synchronously, would create illusory movements the majority of participants and that these illusory movements would have the largest amplitude. We also predicted that application of the

electrical stimulation to the back of the hand would create illusory movements in the direction of flexion when the modulation was increased, and extension when the modulation was decreased. To test these predictions, we used three modulated patterns of electrical stimulation: 1) modulation of frequency with the intensity held constant, 2) modulation of intensity with the frequency held constant, and 3) combined modulation of frequency and intensity, synchronized together. The increase in frequency was designed to mimic frequency coding that occurs when the joints of the index finger move into flexion (as demonstrated by Edin & Abbs, 1991), and the increase in intensity was designed to mimic population coding that occurs as a larger number of receptors begin firing as the amplitude of the movement increases.

If the simple technique used to apply electrical stimulation to the dorsum of the hand can create kinesthetic illusions in the index finger, it may be combined with other stimuli (such as vibration) to create larger, more believable illusions. As demonstrated in previous studies, the combined stimuli from different receptor types creates larger illusions of movement than the stimulation of single receptor types (Blanchard et al., 2011, 2013; Collins et al., 2000, 2005; Honda et al., 2022; Takahashi et al., 2019). To be used in this way, however, this technique should be reliable enough to create illusions in the majority of participants, with a consistent direction of the illusory movement reported by participants.

## **Chapter 2: Electrical stimulation of cutaneous afferents to produce kinesthetic illusion in the human hand**

### **2.1 Introduction**

For you to know what your hand is doing without looking at it, signals from peripheral sensory receptors and central signals, associated with motor commands, are integrated to create kinesthesia. Kinesthesia is the ability to sense the movement and position of the body and its limbs without vision (for reviews, see Proske & Gandevia, 2009, 2012, 2018). In the mid-1960s, receptors in the joints were believed to be the main source of kinesthetic information (Matthews, 1982; McCloskey, 1978). Currently, it is generally thought that muscle spindles play the primary role in kinesthesia (Macefield & Knellwolf, 2018; Proske & Gandevia, 2018). Evidence has been accumulating to suggest that cutaneous receptors are also important for kinesthesia (Macefield, 2021; Prochazka, 2021), however, their specific role remains controversial. The present study was designed to explore the role of cutaneous receptors in kinesthesia in the human hand.

Several groups have used microneurography to record from cutaneous afferents during movement (Aimonetti et al., 2007, 2012; Edin, 1992, 2001, 2004; Edin & Abbs, 1991; Edin & Johansson, 1995; Knibestöl, 1975; Knibestöl & Vallbo, 1970; Vallbo et al., 1995; Vallbo & Hagbarth, 1968). Such studies indicated that, of the myriad receptors in the human hairy skin, four low-threshold mechanoreceptors are the ones that are most likely to provide the signals used for kinesthesia (Edin & Abbs, 1991). Of these, the Ruffini endings, which adapt slowly to sustained stimuli and have large receptive fields, may be most important for kinesthesia. Discharge rates of Ruffini endings in the skin of the dorsum of the hand increase when the skin stretches as the fingers flex and decrease as the fingers extend, and frequencies scale with movement velocity (Edin & Abbs, 1991; Edin & Johansson, 1995; Vallbo, 2018). In fact, it has been suggested that Ruffini endings are just as sensitive as muscle spindles in their ability to encode the position or movement of a joint (Aimonetti et al., 2007, 2012).

Despite such insights from microneurographic studies, much of what is known about kinesthesia and peripheral receptors has come from experiments designed to produce illusions of movement by stimulating specific receptor populations or their afferents (Proske & Gandevia, 2018). The reasoning behind such experiments is this: if a receptor is important for kinesthesia, artificially activating the receptor or its afferent to mimic its discharge during movement should produce the illusion that movement is occurring—when it is not. Indeed, vibration of a muscle or its tendon powerfully activates muscle spindles and can produce illusions of movement at various joints that are consistent with lengthening of the vibrated muscle. Such “movement

illusions” have been the key piece of evidence to support the idea that spindles are the preeminent receptors for kinesthesia.

Previous studies investigating muscle spindles have demonstrated that these receptors inform the CNS using both frequency coding and population coding. Primary endings of muscle spindles will increase their discharge rate as the velocity of the movement increases (Roll et al., 1989; Roll & Vedel, 1982). These studies demonstrated that changing the frequency of the applied vibration mimics the frequency coding of muscle spindles, as their participants reported that an increase in vibration frequency increased the velocity of the illusory movement. While they are incredibly sensitive to the changes in length of a muscle, each individual spindle only encodes about 15° of movement at each joint (Cordo et al., 2002). Therefore, multiple muscle spindles are required to encode the entire range of motion at any given joint, especially if that movement occurs in more than one direction. Multiple studies have demonstrated that the CNS uses population coding from muscle spindles to inform the direction, amplitude, and velocity of movement about a joint (Aimonetti et al., 2012; Bergenheim et al., 2000; Cordo et al., 2002; Jones et al., 2001; Roll et al., 2000).

Illusions of movement, however, can also be produced by artificially activating feedback from cutaneous receptors, either by stretching the skin (Bark et al., 2008; Blanchard et al., 2011, 2013; Collins et al., 2000, 2005; Collins & Prochazka, 1996; Edin & Johansson, 1995) or recruiting their afferents using electrical stimulation (Collins et al., 2000; Collins & Prochazka, 1996). Previous studies utilizing electrical stimulation to create kinesthetic illusions modulated either the frequency of the stimulation to mimic the discharge of the receptors when the index finger was flexing (Collins & Prochazka, 1996), or the intensity to mimic the increased number of receptors that fire when movement amplitude is increased (Collins et al., 2000). The findings between these studies cannot be directly translated, however, as different methods of applying the stimulation were used in each study. Whereas Collins & Prochazka (1996) used an array involving 12 to 16 pairs of electrodes placed over the entirety of the dorsum of the hand, Collins et al. (2000) used two electrode pairs placed over the metacarpophalangeal (MCP) joints of digits III and IV.

To investigate the extent to which the central nervous system (CNS) uses the encoding of receptor discharge frequency (i.e., frequency coding) or the number of receptors firing (i.e., population coding) from cutaneous afferents, this study modulated the frequency and the intensity of the electrical stimulation and measured their effects on illusory movement prevalence and amplitude. The method for applying the electrical stimulation to create illusory movements utilised in this study has been described previously in abstract only (Gandevia,

1994), however, the frequency and intensity parameters of the stimulation differ between the abstract and the current study. The method involves two electrodes placed on the skin of the dorsum of the hand/wrist, to activate the superficial branch of the radial nerve—a purely cutaneous nerve that typically innervates the dorsum of the hand and lateral 2 ½ digits (Sulaiman et al., 2015). In the current study, trains of electrical stimulation were delivered to mimic the discharge patterns of these cutaneous receptors during rhythmic flexion and extension movements and create the illusion of movement in the index finger. In some trials, frequency was increased and decreased to mimic the increase in frequency that occurs with the increase in flexion of the joints (Edin & Abbs, 1991). In other trials, the intensity was increased and decreased to mimic the changes in number of receptors that discharge during movement. A larger movement affects a larger patch of skin, encompassing more receptors, and, as such, an increase in intensity activates more afferents and correlates to a larger number of receptors discharging. In other trials, both the frequency and intensity were increased and decreased simultaneously, to most closely mimic what occurs physiologically: as the movement amplitude increases, the receptors increase their discharge rate and there is an increase in the number of receptors that discharge. We hypothesised that the CNS used both frequency coding and population coding of feedback from cutaneous receptors for kinesthesia. Therefore, we predicted that modulation of either the frequency or intensity of the stimulation would create illusions of movement. As frequency and population coding are simultaneously used by the CNS during natural movements, however, we predicted that combining the modulation of frequency and intensity would create larger amplitudes of illusory movements in a larger proportion of participants than the modulation of either frequency or intensity alone. We also hypothesised that modulation of electrical stimulation would produce illusions of movement in the index finger in the direction of flexion as the modulation of the stimulation increased, and extension as the modulation of the stimulation decreased.

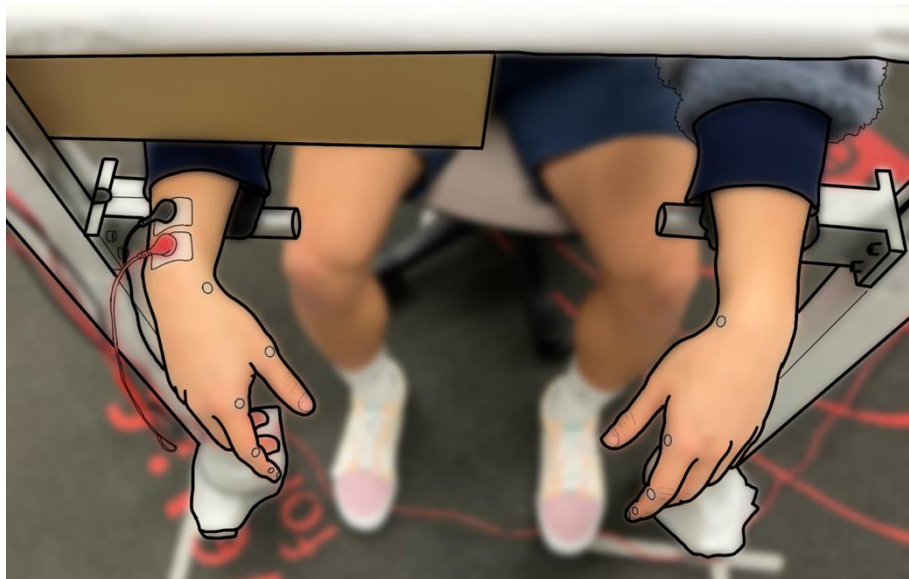
If illusions of movement can be created with either the frequency-modulated pattern or the intensity-modulated pattern, it suggests that the CNS uses either frequency coding or population coding to encode kinesthesia from cutaneous receptors, respectively. If there is a difference in the prevalence or amplitude of the illusory movements between the frequency-modulated or intensity-modulated patterns, however, this may suggest these neural codes may be incorporated in different ways when informing kinesthesia. If the method used in this study creates illusory movements in the majority of participants, it could be used to investigate other basic research questions, integrated into virtual reality, or used in rehabilitation protocols.



## 2.2 Methods

### 2.2.1 Participants

Thirty-five participants with no musculoskeletal or neurological impairments that affect the movement or sensation in the hands were recruited and provided written, informed consent. Each participant took part in one experimental session, which lasted 1-2 hours. Participants were seated comfortably with their forearms supported and hands hanging relaxed with a cardboard divider between their chest and hands to prevent them from seeing their right hand, as shown in Figure 2-1. They were informed that the purpose of this study was to “investigate how feedback from receptors in the hand produces sensations and perceptions in the hand” and were naïve to the specific hypotheses tested. One participant withdrew due to discomfort (excessive itchiness) during the stimulation and their data were excluded from the analyses. Thus, statistical analyses were performed on data from 34 participants (22 females, 12 males; 18-33 years old; 31 right-hand dominant). This study conformed to the standards set by the most recent *Declaration of Helsinki* and was approved by the Human Research Ethics Board at the University of Alberta (Pro00118263).



**Figure 2-1 Experimental Setup.**

Image of the experimental setup, showing stimulation electrodes on the right wrist (black – cathode; red – anode), and reflective markers on the wrists and index fingers. A cardboard divider blocked the view of the right (test) hand throughout the experiment.

### 2.2.2 Electrical stimulation

A Digitimer DS8R stimulator (Digitimer, Welwyn Garden City, UK) was used to administer electrical stimulation (rectangular monophasic pulses; 500 ms duration) over the superficial branch of the radial nerve (see Figure 2-1). Two self-adhesive electrodes (7/8 inch x 1 3/8 inch; Nissha Medical Technologies, Buffalo, USA) were placed on the skin over the dorsal surface of the right wrist, using anatomical landmarks. The anode was placed over Lister's tubercle on the radius, with the cathode placed ~1 cm proximally. Perceptual threshold (PT) was determined using a modified version of the staircase method (Cornsweet, 1962). Initially, pulses of stimulation (~10 second interstimulus interval) were presented at progressively increasing current until the participant reported they were certain they felt it, and this stimulus intensity was recorded as the first transition point. Intensity was then increased a pseudo-random amount to a new starting point and was then progressively decreased in a stepwise fashion until the participant reported they no longer felt the stimulation, and this was recorded as the second transition point. This process was repeated until 10 transition points were recorded and the average of the 10 points was calculated and defined as PT.

Participants received trains of stimulation in a series of 10 trials. Each trial consisted of five success stimulus trains. Each stimulus train consisted of a series of pulses delivered for four seconds with one second in between. During a given trial, the stimulation was delivered in one of four patterns: 1) Frequency-modulated: stimulation frequency increased sinusoidally from 55-250 Hz then back to 55 Hz (intensity held at PT); 2) Intensity-modulated: stimulation intensity increased sinusoidally from 1-2 times PT and back to PT (frequency held at 55 Hz); 3) Combined modulation: frequency and intensity were modulated as described above, at the same time; 4) Sham: frequency was held at 55 Hz and intensity was held at PT. During each experiment, participants received one Sham trial and three trials of each of the modulated patterns. The order of the trials was randomised for each participant.

Before each trial, PT was reassessed by sending a single pulse. If the participant could no longer feel that pulse, stimulation intensity was increased until the participant was certain they could feel it. Most participants required an increase of a 0.1 mA, the smallest step available by the stimulator, if any increase was required. Then, participants received a "familiarization trial" of the upcoming stimulation pattern and were instructed to "focus on what you are feeling and where you feel this occurring in your hand". Sensations typically described by participants included vibration, tingling, pressure, temperature changes, skin stretch, and movement. Although movement was not emphasized, if the participant felt that their right (stimulated) hand was moving, they were instructed to keep that hand relaxed and mimic that movement with

movements of their left (unstimulated) hand. Participants were informed that they may not feel movement on every trial. If movement was perceived, however, participants were asked to describe the movement direction (i.e., flexion or extension, abduction or adduction) and location (i.e., which fingers the movements were perceived). These movement descriptions were recorded after every trial. After one familiarization trial, participants were invited to complete another familiarization trial or receive the stimulation again for the data to be collected as an official trial. Participants typically completed two familiarization trials at the start of an experiment, but this would decline to one as the experiment continued. Participants received identical instructions during data collection trials as the familiarization trials.

### 2.2.3 Motion capture and data collection

Matching movements performed by the left, unstimulated hand, were recorded using ten OptiTrack Prime 13W passive motion capture cameras (NaturalPoint Inc., Corvallis, USA). Recordings were collected using a 250 Hz framerate. Tracking of all four fingers was not possible as movement of some digits blocked the cameras from tracking them at all times. The lateral aspect of the index finger was the only finger always tracked by the cameras and, therefore, recorded. To mark the joints of the index fingers, reflective tape (Salzmann 3M Scotchlite Reflective Stickers, Salzmann Ltd., Stockport, GB) was cut into 3- or 4-mm diameter circles and placed on the lateral aspect of the centres of the wrists, metacarpophalangeal (MCP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints, and the tips of the index fingers of both hands. To differentiate between the right and left hands, extra markers were placed on the ulnar head, and the MCPs of the thumb and little finger of the right hand. All sensations reported by participants were recorded for each trial, for every participant.

### 2.2.4 Data analyses

Matching movements at the MCP and PIP joints of the left index finger were quantified and compared between the three modulated stimulation patterns and the sham. Movements at the DIP joint were not quantified for three reasons: 1) the superficial radial nerve does not typically innervate the skin over the DIP joints (Sulaiman et al., 2015) and, thus, illusory movement was not predicted at this joint; 2) the DIP and PIP joints are mechanically coupled and, as such, participants cannot independently move either joint if movement was felt at only one (unlike the MCP or PIP joints); and 3) flexion of the DIP created large distortions of the skin under the reflective markers at that joint, which increased the noise of the movement when quantification of the movements were calculated and decreased the validity of the data for this joint.

#### *2.2.4.1 Illusory movement: Number of participants*

To quantify the number of participants who experienced illusory movements, they must have felt and mimicked illusory movements during at least one trial.

#### *2.2.4.2 Illusory movement: Amplitude*

The motion capture recordings of the movements of the index finger were exported from Motive (Tracker: version 3.1.0 Beta, NaturalPoint Inc., Corvallis, USA) and synchronized with the timing of the stimulus trains using timestamps in Lab Streaming Layer (Swartz Centre for Computational Neuroscience). When the stimulation pattern was selected for the upcoming trial, an Arduino board sent the timing information into Lab Streaming Layer, which temporally synchronized the information from the Arduino and the data from Motive into a single file. The synchronized files were then analysed using an in-house software program, GaMA (Gaze and Movement Analysis), which calculated the angles of the MCP and PIP joints throughout the data collection trials.

To quantify the amplitudes of the illusory movements for each trial, the difference between the maximum and minimum angles for each train of stimulation were averaged, regardless of the number of times the participant moved their finger. For example, if participants only mimicked the illusory movements twice, rather than five times for all five trains, the average of all five trains includes those in which the movement did not occur and was calculated as the amplitude of the movement within a trial.

During data collection, seven participants experienced a twitch-like contraction of the right hand during one or more trials and mimicked the movement with their left hand. These twitches consisted of a single, large movement of one or more digits that was not synchronized with the stimulation. As these movements were not consistent with the type of rhythmic movements that were intended with the stimulation patterns, the data from the stimulation train in which they occurred was removed, and the other four trains were averaged for the data analysis.

During one trial, one participant flexed their index so much during their matching movement that the markers for the DIP and fingertip were obscured from the motion capture cameras. As the location of the DIP is required for quantification of the PIP angle, the full range of motion could not be calculated for this trial. As such, the average amplitude of movement for this trial was quantified using the only the angles that could be calculated from the dataset, rather than the full range of motion that was mimicked by the participant.

#### 2.2.4.5 Illusory movement: Direction

The direction of the matched movement was defined as the direction the joint initially moved into when mimicking the illusory movements. Four participants initially moved very slightly ( $< 1^\circ$  of movement) in the opposite direction before moving much farther into the direction that was reported. For example, one participant moved slightly into extension before moving much farther into flexion and this movement was deemed flexion for our analyses. At the end of each data collection trial, participants were verbally asked which direction they perceived the movements, which were also recorded. If a participant moved one joint in the opposite direction of the other joint, whichever joint moved the most defined the direction for the movement of the index finger. For example, if the MCP moved into extension and the PIP moved into flexion, but the PIP moved more than the MCP, the direction of the index finger was deemed flexion.

#### 2.2.5 Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics software (version 29.0.0.0, SPSS Inc., IL, USA). Cochran's Q test was used to determine whether the proportion of participants who perceived illusory movements were different between the four stimulation patterns. As one of the major questions for this project was regarding if the type of stimulation modulation affected the amplitude of movement, the data from only the participants who perceived movements at the index finger ( $n = 20$ ) were included for statistical analyses. The data for movement amplitudes was not normally distributed, as assessed by the Shapiro-Wilk's test of normality on the studentized residuals. Therefore, Friedman's Analysis of Variance by Ranks was used to determine whether there were statistically significant differences between the stimulation patterns and each joint measured (i.e., the MCP and PIP of the index finger). Pairwise comparisons used a Bonferroni correction for multiple post hoc comparisons. To test for interaction effects between the stimulation patterns, and the joints measured, the data were transformed using a logarithmic transformation, after which all variables were normally distributed, and a 4x2 two-way ANOVA was performed on the transformed data for the four stimulation patterns and the two joints. McNemar's test was used to determine whether there was a significant difference between the proportions of participants who experienced illusory movements in the direction of flexion compared to participants who experienced extension. All descriptive statistics in text and figures are reported as the mean  $\pm$  standard deviation.

## 2.3 Results

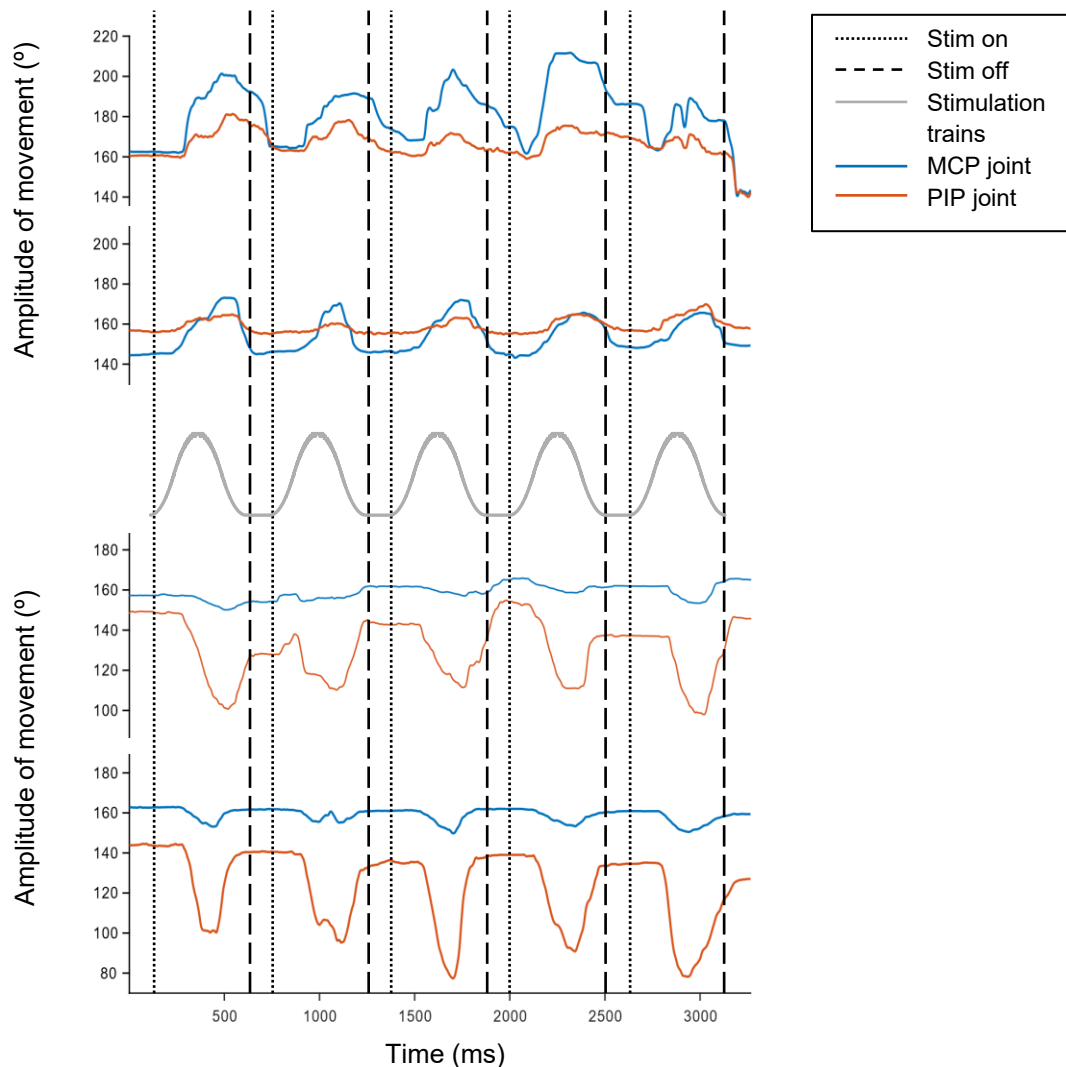
Electrical stimulation of the superficial radial nerve evoked illusory movements in the hand in 25/34 (74%) participants. Illusory movements were perceived most often in digit II (21/34; 62%) and digit I (17/34; 50%), and less often in digit III (12/34; 35%), digit IV (6/34; 18%) and digit V (7/34; 21%). The stimulation produced illusory movements in the index finger that could be quantified in 20/34 (59%) participants. The overall mean amplitudes of the illusory movements (averaged across the MCP and PIP joints) were 4.5° for the frequency-modulated trials, 6.1° for the intensity-modulated trials, 6.2° for the combined-modulation trials, and 1.0° for the sham trials. For 50% of participants who perceived movement at the index finger, the first portion of the movement was flexion, for 40% it was extension, and 10% of participants reported movements beginning in either flexion or extension.

### 2.3.1 Illusory movements: Number of participants

Electrical stimulation was delivered in three different modulated patterns and one sham pattern, which produced illusory movement somewhere in the hand in 25/34 participants. Participants mimicked these movements with the opposite (left) hand and these matching movements were recorded and quantified at the MCP and PIP joints of the index finger. Figure 2-2 displays the raw traces of the mimicked movements for four participants, in which 180° is the MCP or PIP joint is in line with the wrist and hand and larger angles indicate extension and smaller angles indicate flexion. The percentage of participants that perceived illusory movements during each type of stimulation is shown in Figure 2-3. During the frequency-modulated trials, 19/34 (56%) participants perceived illusory movements of the stimulated hand. During the intensity-modulated trials, 20/34 (59%) participants perceived illusory movements, and during combined-modulation trials, 19/34 (56%) participants perceived illusory movements. One participant (3%) perceived illusory movements in digit V during the sham trial. Cochran's Q test was used to determine that a higher proportion of participants perceived illusory movements during the frequency-modulated, intensity-modulated, and combined-modulation trials than the sham trial, and there was no significant difference between numbers of participants that perceived illusions of movement during the three modulated trials ( $n = 34$ ;  $\chi^2(3) = 34.3$ ,  $p < 0.001$ ; see Figure 2-3).

Of the 25 participants who perceived illusory movements, 21 (84%) reported that the movements included the index finger. For one participant, these movements were abduction/adduction which, when mimicked with the left hand, could not be calculated as they were parallel to the plane used to quantify the movements. As such, that participant's data were excluded and data from the remaining 20 participants were included in the final analyses.

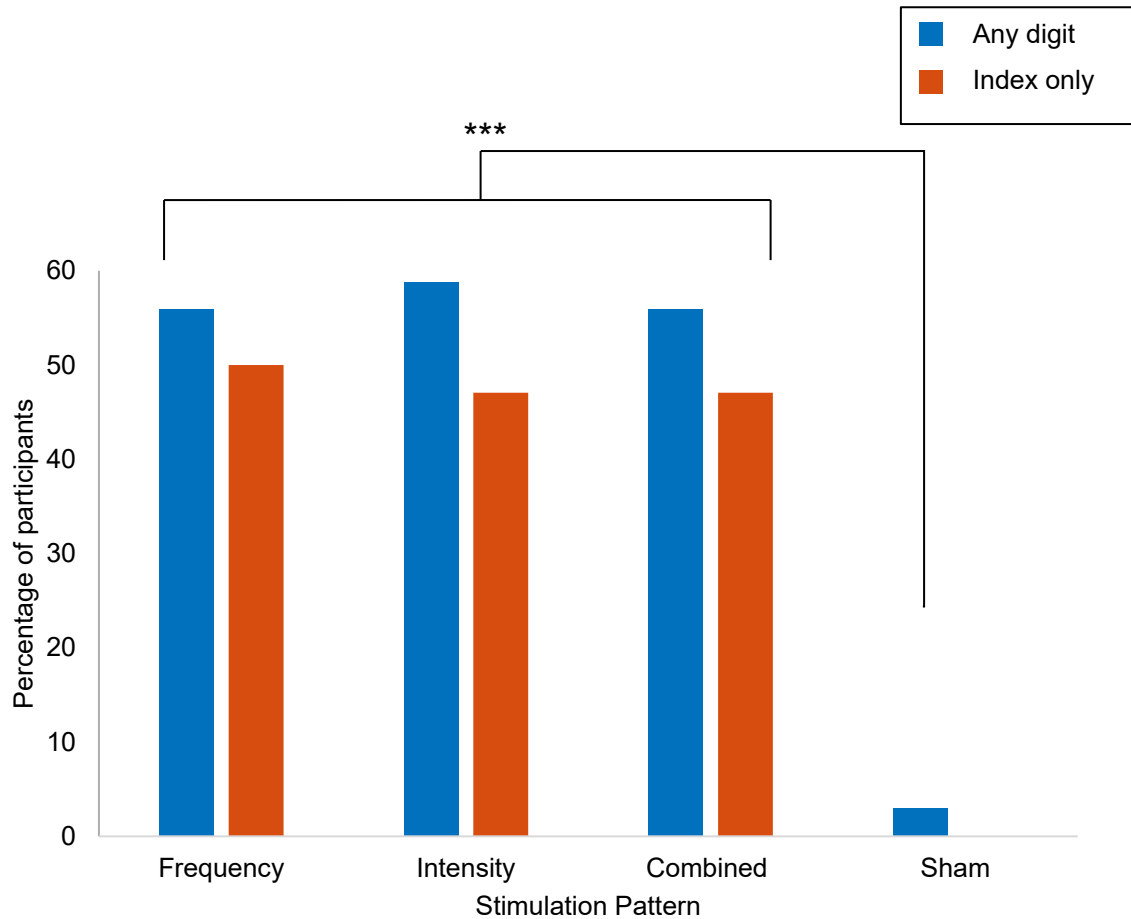
During the frequency-modulated trials 17/20 (85%) of participants perceived illusory movements in the index finger. During the intensity-modulated trials, 16/20 (80%) participants perceived illusory movements, and during the combined-modulation trials, 16/20 (80%) participants perceived illusory movements. Cochran's Q test was used to determine that participants were just as likely to perceive illusory movements during the three modulated trials ( $n=20$ ;  $\chi^2(2) = 1.20$ ,  $p = 0.549$ ). No participant reported illusory movements in the index finger during the sham trials.



**Figure 2-2 Raw traces of illusory movements.**

Raw traces of the left (unstimulated) index finger mimicking the movements perceived in the right (stimulated) index finger of four participants. Extension of the index finger is displayed in the top two traces and flexion of the index finger is displayed in the bottom two traces. Dotted lines represent the beginning of each stimulation train and dashed lines are the end of each

stimulation train. Grey lines represent the modulated stimulation patterns. Blue lines depict the movements at the metacarpophalangeal (MCP) joints, and orange lines depict the movements at the proximal interphalangeal (PIP) joints.



**Figure 2-3 Percentage of participants perceiving illusory movements.**

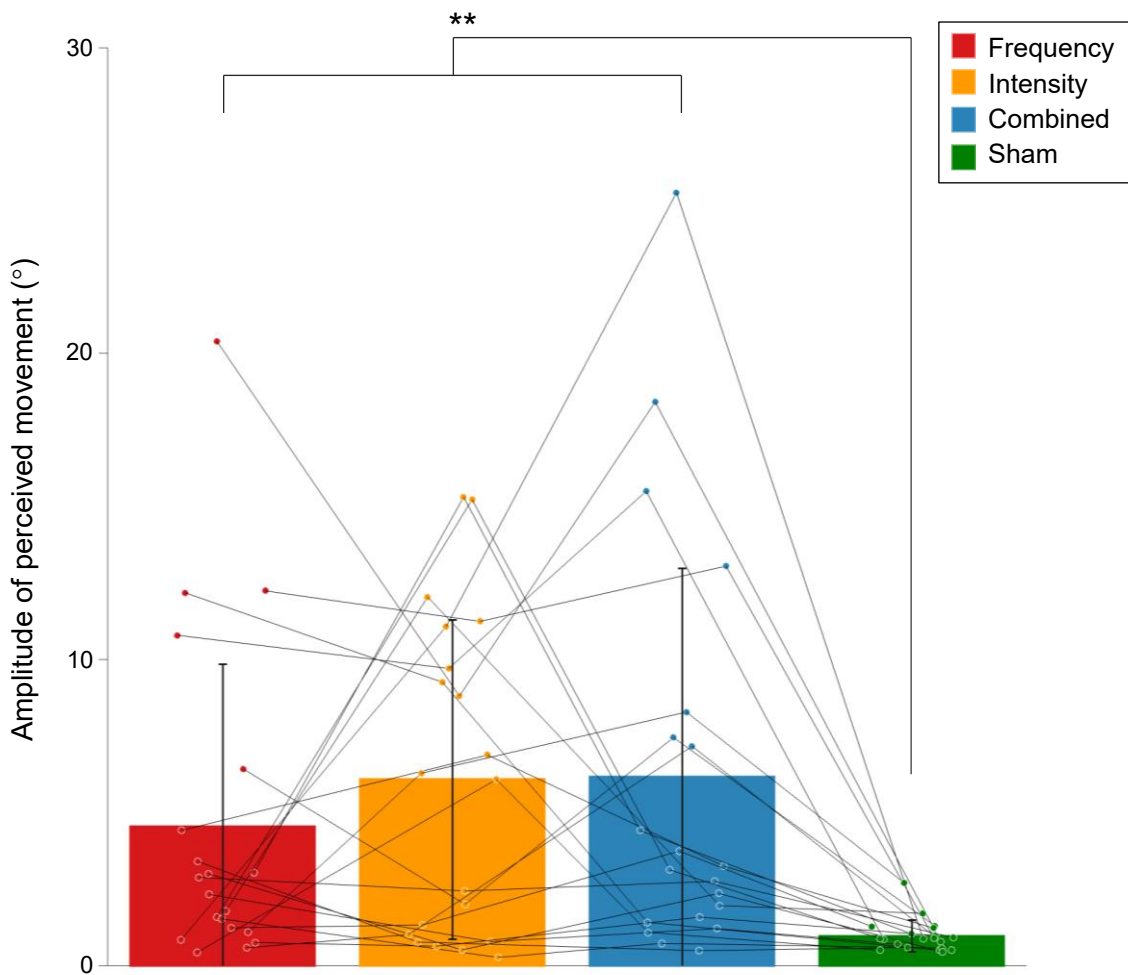
Percentage of participants that perceived illusory movements in any digit of the hand (n=34) or at the index finger only (n=20) for each type of stimulation pattern. Adjusted significance \*\*\*p < 0.001.

### 2.3.2 Illusory movements: Amplitude

As is evident from the matching movements shown in Figure 2-2, the illusory movements varied in amplitude and direction, both within and between participants. Thus, to obtain an overall measure of the illusory movement amplitude, matching movements at the MCP and PIP joints



were averaged for each participant and stimulation pattern, independent of direction, and these mean amplitudes are shown in Figure 2-4. During the frequency-modulated trials, the overall illusory movement amplitude was  $4.5 \pm 5.3^\circ$  (range 1.5 - 20.4°). During the intensity-modulated trials, the overall illusory movement amplitude was  $6.1 \pm 5.2^\circ$  (range: 1.0 - 17.7°), the combined-modulation trials illusory movement amplitude was  $6.2 \pm 6.8^\circ$  (range 1.4 - 25.3°), and the sham trials illusory movement amplitude was  $1.0 \pm 0.5^\circ$  (range: 0.4 - 2.7°). There was a significant difference in illusory movement amplitude between the sham trial and the three modulated patterns, but there was no significant difference between the frequency-modulated, the intensity-modulated, and the combined-modulation trials ( $n = 20$ ;  $\chi^2(3) = 21.4$ ,  $p < 0.001$ ).

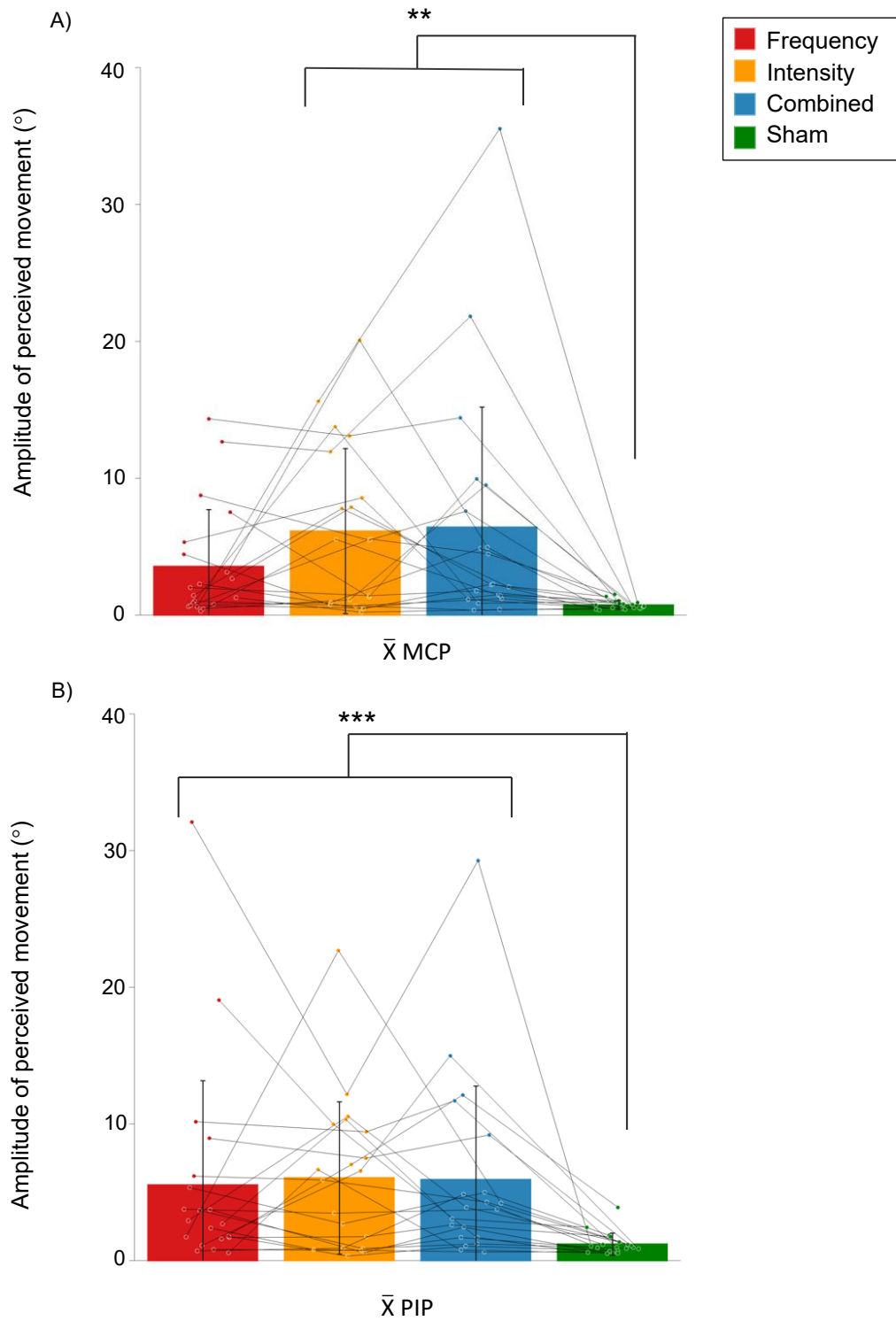


**Figure 2-4 Amplitude of illusory movements averaged between the MCP & PIP joints**

Connected dots denote data from individual participants; bars denote the mean with error bars representing the standard deviation. MCP - metacarpophalangeal joint; PIP - proximal interphalangeal joint. Adjusted significance,  $**p \leq 0.009$ .

The amplitude of the matching movements was also compared at each of the MCP and PIP joints, separately, and these data are shown in Figure 2-5. For the MCP joint (Figure 2-5 A), participants felt significantly less movement in the sham trial compared to the intensity-modulated ( $n = 20$ ;  $\chi^2(3) = 2.21$ ,  $p = 0.002$ ) and combined-modulation ( $n = 20$ ;  $\chi^2(3) = 3.67$ ,  $p = 0.001$ ) trials, but the amplitude of illusory movement was not significantly different from the frequency-modulated trial ( $n = 20$ ;  $\chi^2(3) = 2.21$ ,  $p = 0.165$ ). The frequency-modulated, intensity-modulated, and combined-modulation trials were not significantly different from one another ( $n = 20$ ;  $\chi^2(3) = 15.1$ ,  $p = 0.002$ ). During the frequency-modulated trials, the amplitude of illusory movement at the MCP joint was  $3.5 \pm 4.2^\circ$  (range:  $1.0$ - $18.6^\circ$ ). During the intensity-modulated trials, illusory movement amplitude was  $6.1 \pm 6.0^\circ$  (range:  $0.3$ - $21.5^\circ$ ), for the combined modulation trials, illusory movement amplitude was  $6.4 \pm 8.8^\circ$  (range:  $0.8$ - $35.5^\circ$ ), and for the sham trials, illusory movement amplitude was  $0.7 \pm 0.3^\circ$  (range:  $0.4$ - $1.5^\circ$ ).

At the PIP joint (Figure 2-5 B), participants felt significantly less movement in the sham trial compared to the frequency-modulated ( $n = 20$ ;  $\chi^2(3) = 3.92$ ,  $p = 0.001$ ), intensity-modulated ( $n = 20$ ;  $\chi^2(3) = 3.31$ ,  $p = 0.006$ ), and combined-modulation ( $n = 20$ ;  $\chi^2(3) = 4.53$ ,  $p < 0.001$ ) trials. There was no significant difference between the frequency-modulated, intensity-modulated, or combined-modulation trials in the amounts of illusory movements reported by participants ( $n = 20$ ;  $\chi^2(3) = 24.5$ ,  $p < 0.001$ ). During the frequency-modulated trials, the illusory movement amplitude was  $5.5 \pm 7.6^\circ$  (range:  $1.8$ - $33.0^\circ$ ). During the intensity-modulated trials, illusory movement amplitude was  $6.0 \pm 5.6^\circ$  (range:  $0.8$ - $39.6^\circ$ ), for the combined modulation trials, illusory movement amplitude was  $5.9 \pm 6.9^\circ$  (range:  $1.4$ - $51.2^\circ$ ), and for the sham trials, illusory movement amplitude was  $1.2 \pm 0.8^\circ$  (range:  $0.5$ - $3.9^\circ$ ).



**Figure 2-5 Amplitude of illusory movements in the MCP & PIP joints**

A) Amplitude of illusory movement at the metacarpophalangeal (MCP) joint. B) Amplitude of illusory movement at the proximal interphalangeal (PIP) joint. Connected dots denote individual

participant values. Bars indicates the mean and the error bars represent the standard deviation. Adjusted significance \*\* $p \leq 0.02$ ; \*\*\*  $p \leq 0.006$ .

We also tested whether there was an interaction between stimulation patterns and index finger joints. Given that the data were not normally distributed (see Methods), data were logarithmically transformed, after which all variables were normally distributed, and a two-way ANOVA was performed. This analysis identified significant main effects of joint ( $n = 20$ ;  $F(1) = 11.3$ ,  $p = 0.003$ ) and stimulation pattern ( $n = 20$ ;  $F(3) = 11.106$ ,  $p < 0.001$ ), and no significant interaction ( $n = 20$ ;  $F(3) = 2.567$ ,  $p = 0.063$ ). Pairwise comparisons using the Bonferroni adjustment were performed and the analyses determined that the illusory movements of the PIP joint were larger than the MCP joint ( $p = 0.003$ ), and that illusory movements perceived during the sham trial was significantly less than the frequency-modulated ( $p = 0.004$ ), intensity-modulated ( $p < 0.001$ ), and combined modulation ( $p < 0.001$ ) trials. There was no significant difference between the frequency, intensity, and combined trials on the amount of movement perceived in the index finger.

### 2.3.3 Illusory movements: Direction

In general, but with some exceptions (see Methods), the direction of the illusory movements was defined as the direction the index finger moved for the initial portion of the matching movements made with the left hand. For 13/20 participants who perceived measurable movements of the index finger, this initial movement was in the same direction for every trial. The other seven participants were less consistent but tended to move in one direction more than the other. Qualitatively, out of the 20 participants who perceived measurable movements of the index finger, 10 (50%) moved into flexion for most trials, 8 (40%) moved into extension for most trials, and 2 (10%) moved into either flexion or extension approximately equally.

In addition to matching illusory movements with the left hand, participants were asked to identify which direction they perceived the illusory movements. These self-reports did not always align with the matching movements. Eighteen of 20 (90%) reported they moved their index finger in the same direction for every trial. Of these reports, 10/20 (50%) were flexion, 8/20 (40%) were extension, and 2/20 (10%) were equally flexion or extension. McNemar's test was used to determine that there was not a significantly difference between the proportions of participants who perceived the illusory movement in the direction of flexion or extension ( $p =$

0.815). Five participants, however, reported movements that were opposite to the direction they mimicked in at least one trial. For example, the participant reported that they experienced flexion, however, the initial direction of their matching movements was extension.

#### 2.3.4 Qualitative descriptions

Electrical stimulation of the superficial branch of the radial nerve evoked sensations other than movement, including vibration, tingling, pressure, temperature change, or skin stretch. All participants felt either vibration (30/34; 97%) or tingling (26/34; 77%) in every trial while the stimulation was occurring. Distinction was made between vibration and tingling, where participants described vibration as 'pushing a shopping cart through an asphalt parking lot' and tingling was described as the 'hand waking up after falling asleep'. Some participants reported feeling pressure (30/34; 88%), described as a 'tapping' or 'poking' sensation on the dorsum of the hand, though they were not being touched. Other participants (15/34; 44%) described temperature changes such as a slight 'warming' or 'cooling' sensation with three participants feeling both warming and cooling sensations, though not within the same trial. These temperature sensations occurred after the stimulation was turned-off and subsided after a few seconds. Skin stretch was described by participants as a 'swelling' or 'increase in size' around a joint, or it was described as a 'pulling sensation' which included a directional component (i.e., usually towards or away from the wrist). Of the 13/34 (38%) participants who reported skin stretch, three of them felt no movement in any trial, and two of them did not report movement and skin stretch in the same trials. There were also 15/34 (44%) participants who perceived movement but did not report skin stretch on any trial.

## 2.4 Discussion

This study contributes to the body of research suggesting that the skin plays a role in kinesthesia in the human hand. Electrical stimulation was delivered to mimic the frequency coding and population coding that occurs when cutaneous receptors discharge in response to movement and evoked illusory movements in 74% of participants. A significantly greater proportion of participants perceived illusory movements when the stimulation was delivered in a modulated pattern compared to the sham stimulation. The amplitudes of the illusory movements were significantly larger when the stimulation pattern was modulated compared to the sham pattern. Contrary to our hypothesis, however, participants were not more likely to perceive larger movements when the frequency and intensity were synchronously modulated compared to the modulation of either the frequency or intensity, alone. Also contrary to our hypothesis,

there was not a significant difference between the proportions of participants who experienced the initial portion of movement in the direction of flexion compared to extension.

#### 2.4.1 Prevalence of illusory movements

Previous studies demonstrated that electrical stimulation of cutaneous afferents can create illusions of movement in the human hand (Collins & Prochazka, 1996; Collins et al., 2000). The current study had a greater proportion of participants report illusory movements (74%) compared to Collins & Prochazka (1996), who reported illusory movements at the MCP joint in 6/17 (35%) of participants, and Collins et al. (2000), who reported that electrical stimulation altered the perceived movements in 17/28 (61%) of their experimental blocks. In line with these previous studies, the current results suggest that cutaneous receptors contribute to kinesthesia of the hand.

#### 2.4.2 Amplitude of illusory movements may rely on area of skin simulated

While this study was able to produce illusory movements in a greater proportion of participants, the size of the illusory movements was not as large as those demonstrated by Collins & Prochazka (1996). In their study, when electrical stimulation was delivered alone, participants reported movements of  $11.3 \pm 16.6^\circ$  at the MCP joint. Comparatively, the current study reported smaller movements at the MCP joint, consisting of  $3.5 \pm 4.2^\circ$  for the frequency-modulated trials,  $6.1 \pm 6.0^\circ$  for the intensity-modulated trials,  $6.4 \pm 8.8^\circ$  for the combined modulation trials, and  $0.7 \pm 0.3^\circ$  for the sham trial. This could be due to the larger area of skin that Collins & Prochazka (1996) stimulated, in that their electrode array covered the entire dorsum of the hand. The current study applied the stimulation to the superficial branch of the radial nerve, which typically innervates the skin of the lateral 2 ½ digits (Sulaiman et al., 2015). In line with this hypothesis, Collins et al., (2000) applied their stimulation to a smaller patch of skin than the current study by placing the stimulating electrodes over the MCP of digit IV only and reported an average amplitude of  $1.5 \pm 1.0^\circ$  when the electrical stimulation was delivered alone. There are no studies investigating the effects of stimulation applied to varying skin area size, however, and this could be an avenue for future research.

#### 2.4.3. Kinesthesia utilises both frequency coding and population coding

Of the previous studies mentioned, one of them modulated the frequency (Collins & Prochazka, 1996), while the other modulated the intensity (Collins et al., 2000) of the electrical stimulation to create illusions of movement in the human hand. The present study had experimental trials where the frequency was modulated, the intensity was modulated, and the frequency and

intensity modulations were combined and modulated simultaneously. The frequency modulation was based off of studies demonstrating that cutaneous receptors discharge faster as flexion of the joints occurs (Aimonetti et al., 2007; Edin & Abbs, 1991; Grill & Hallett, 1995). The intensity modulation mimicked the increase in the number of receptors that discharge as the movement becomes larger (i.e., a larger area of skin becomes deformed with larger movements, which translates to more receptors firing). We predicted that an increased proportion of participants would report larger amplitudes of illusory movements during combined modulation trials, as this is what occurs naturally when movements occur, but this is not what we found; there was no significant difference in the amplitudes of movement perceived by participants between modulation patterns.

The lack of an increase in amplitude may be caused by an increase of noise in the stimulation, rather than an amplification of the signal that created the illusory movement. One reason for this could be due to the firing properties of the cutaneous receptors, and the differences in the discharge when activated naturally compared to activation through electrical stimulation. As fast-adapting receptors, Pacinian corpuscles tend to fire only at the beginning and end of a stimulus, falling silent in between. When activated by high-frequency stimulation, however, these receptors may fire continuously, increasing the amount of noise in the system that would not normally occur. In fact, studies investigating the role of Pacinian corpuscles on kinesthetic acuity have suggested that activation of these receptors may be detrimental to acuity (Weerakkody et al., 2007, 2009). Weerakkody et al. (2007, 2009) demonstrated that the application of high-frequency vibration (i.e., 300 Hz) caused a significant decrease in the ability to correctly identify whether a movement was flexion or extension, whereas low-frequency vibration (i.e., 30 Hz) had no effect, and this impairment was only seen when skin or joint afferents contributed to the detection. No impairment was demonstrated when muscle afferents were able to contribute. Interestingly, these impairments in kinesthetic acuity are also demonstrated when electrical stimulation is applied either at or above perceptual threshold. The authors suggest that it could be due to an increase in noise in the system, rather than increasing the strength of the movement signal (Refshauge et al. 2003). Pacinian corpuscles respond to high-frequency vibration and, when activated by electrical stimulation, create the sensation of vibration in the skin (McGlone & Reilly, 2010; Mountcastle et al., 1972; Talbot et al., 1968). As most of our participants (33/34; 97%) reported the sensation of vibration in at least one trial, it is reasonable to assume that Pacinian corpuscle afferents were activated with the electrical stimulation, and this may have contributed to the small amplitudes of illusory movements reported in the present study.

It is important to note, however, that electrical stimulation applied over the skin, as done in this study, activates all afferents in the skin, not just those from Pacinian corpuscles. When multiple receptor types are stimulated, the sensation of paraesthesia or tingling may occur (Vallbo et al., 1984). As 26/34 (76%) of the participants in the current study reported the sensation of tingling, it is likely that stimulation of multiple receptor afferents was the cause of this sensation. Thus, it is possible that the combined stimulation pattern, instead of creating a stronger signal by mimicking both the physiological increase in discharge rate and the increase in the number of receptors as hypothesized, increased the noise and masked the signal instead.

As the superficial branch of the radial nerve is a nerve that innervates only skin on the dorsum of the hand (Sulaiman et al., 2015), it is unlikely that afferents from muscles or joints were stimulated. There are, however, other cutaneous afferents that may have been activated with the stimulation. A $\delta$  fibres and C-fibers, both of which carry different types of nociceptive information, have higher thresholds of activation (i.e., 5-10 times and 15-20 times threshold of mechanoreceptors, respectively; Vallbo et al., 1979). However, as the highest intensity administered was two times perceptual threshold, and participants did not report any burning, sharp or pricking pain, which is commonly associated with the stimulation of these afferents, it is unlikely that they were activated during this study.

Contrary to our hypothesis, almost half of the participants reported extension of the index finger rather than flexion. Some of the participants reported difficulty identifying which direction the perceived movement was occurring, with five participants reporting the opposite direction in which they moved their finger. This aligns with a previous paper, where participants had greater difficulty identifying the direction of movement when electrical stimulation was applied to the same digit that was being moved (Refshauge et al., 2003).

Due to the small amplitude of these illusory movements, participants reported little confidence that some movements had actually occurred. Some of the reasons given by participants included difficulty matching a movement they did not intentionally create, and the realization that they did not normally pay this much attention to their hands. This meant they were uncertain if some of the sensations were regular occurrences that they never previously noticed, or if they were caused by the stimulation.

## **2.5 Conclusion**

The method of transcutaneously stimulating the superficial branch of the radial nerve used in this study was able to create illusory movements in a greater percentage of participants than previous studies utilising more complicated and cumbersome approaches of applying



electrical stimulation of the skin. These results add to the current body of literature suggesting that cutaneous receptors can play a role in informing kinesthesia. Although the movements were small, many studies have demonstrated that integrating other methods of kinesthetic stimulation can increase the amplitude and believability of illusory movements (Blanchard et al., 2011, 2013; Collins et al., 2000, 2005). The parameters used with this method were also limited. There was only one range used for either the frequency or intensity patterns and, as such, there could be many ways to manipulate these parameters to investigate how these varying stimulus parameters might affect the illusory movements perceived by participants.

### Chapter 3: General Discussion

The project presented was designed to investigate the role of cutaneous receptors in kinesthesia by using a simple method of stimulating the skin to create kinesthetic illusions in the hand. Throughout this thesis, kinesthesia is defined as the ability to sense the position and movement of the body and its limbs, without visual input. Previous reviews on the subject state that mechanoreceptors in the muscle, specifically muscle spindles, play the primary role in kinesthesia, but note that mechanoreceptors in the skin are likely to play a role as well (Proske & Gandevia, 2009, 2012, 2018). How the CNS uses frequency coding and population coding provided by cutaneous receptors, however, is still relatively unknown.

Studies investigating muscle spindles have demonstrated that these receptors use both frequency coding and population coding to inform the CNS about kinesthesia. Primary endings of the spindle increase their discharge rate in response to both a change in the length of the muscle and the velocity at which this change occurs (Roll et al., 1989; Roll & Vedel, 1982). This change in discharge rate of a neuron to encode a property (e.g., change in position or velocity) is known as frequency coding. It has been noted, however, that individual muscle spindles can only encode about 15° of movement (Cordo et al., 2002), and multiple muscle spindles are more accurate at discriminating changes in muscle length than single afferents, especially when groups are made up of more than one afferent type (Bergenheim et al., 1995, 1996). These results demonstrate what is known as population coding—where more than one receptor or type of receptor discharges to inform the CNS about a parameter (e.g., change in position or velocity). It is likely that the CNS requires both frequency and population coding—with multiple receptors contributing information about the static position of the limb and the velocity in which it is moving—to encode kinesthesia. Interestingly, studies by Aimonetti et al. (2007, 2012) have demonstrated that cutaneous afferents and muscle afferents use similar coding properties and, as such, feedback from cutaneous receptors may be just as sensitive as muscle spindles at encoding kinesthesia.

To investigate *how* the CNS utilises the signals provided by frequency coding and population coding from cutaneous afferents, this project used electrical stimulation with three stimulation patterns to discern their effects, if any, on the prevalence and amplitude of illusory movement. The reasoning is this: if electrical stimulation of cutaneous afferents can create kinesthetic illusions of movement, then it supports the idea that their natural discharge during movement informs kinesthesia; as has been shown with vibration of muscle spindles to evoke illusions in participants. To mimic frequency coding, a frequency-modulated stimulation pattern

was used; in which the stimulation frequency was sinusoidally increased and decreased with the intensity held at perceptual threshold. To mimic population coding, an intensity-modulated pattern was used; in which the stimulation intensity sinusoidally increased and decreased with the frequency held at 55 Hz. To most closely resemble what occurs physiologically, we added a third modulation pattern, in which both the frequency and intensity were synchronously modulated, as cutaneous receptors increase both the discharge rate and the number of firing receptors, simultaneously, as movement amplitude increases. We predicted that electrical stimulation of the skin would create illusory movements in the hand, suggesting that cutaneous receptors play a role in kinesthesia. We also predicted that the combined-modulation pattern would produce illusory movements in a larger proportion of participants and create larger amplitudes of illusory movements than either the frequency-modulation or the intensity-modulation alone. Finally, we predicted that participants would experience the illusory movement in the direction of index finger flexion, as the stimulation modulation was increased, and finger extension, as the stimulation modulation was decreased.

Previous studies have utilised electrical stimulation applied to cutaneous afferents to create illusory movements in the human hand. While Collins & Prochazka (1996) modulated their stimulation frequency and Collins et al. (2000) modulated their stimulation intensity, these studies used differing applications of electrical stimulation and, as such, their results cannot be directly compared. To apply their stimulation, Collins & Prochazka (1996) used a large array of 12 pairs of electrodes with differing frequency ranges applied to differing pairs of the electrodes across the entire dorsum of the hand. On the other hand, Collins et al. (2000) used four pairs of electrodes placed over the dorsum of the MCPs joints of digits III and IV. Thus, the current project set to investigate these ideas of frequency- and intensity-modulation by stimulating the superficial branch of the radial nerve via electrodes applied to the wrist, rather than arrays of electrodes applied to the back of the hand.

In line with our first prediction, most of our participants (25/34; 74%) perceived illusory movements in the fingers of the hand in at least one trial. It should be noted that 20/34 (59%) of participants experienced flexion or extension of the index finger, which were the movements quantified for data analyses. Overall, this is a larger proportion compared to previous studies, where Collins & Prochazka (1996) reported illusory movements in 6/17 (35%) of their participants and Collins et al. (2000) reported illusory movements in 17/28 (61%) of their experimental blocks. These findings suggest that cutaneous receptors do play a role in kinesthesia in the hand, and that the CNS uses both frequency coding and population coding from cutaneous receptors in the hand for kinesthesia. Contrary to our second prediction,

however, participants were equally likely to perceive illusory movements during the frequency-modulated, intensity-modulated, or combined-modulation trials, and there was no significant difference in the amplitude of movements between these modulations. Studies exciting cutaneous afferents, through the use of vibration on the skin, electrical stimulation, or natural stroking of the skin, have demonstrated that excess information from the skin reduces kinesthetic acuity, rather than facilitating it (Refshauge et al., 2003; Weerakkody et al., 2007, 2009), which could be what is happening in this study.

Contrary to our third prediction, that the initial portion of the illusory movements would be in the direction of flexion, participants were equally likely to move their finger into flexion or extension. Only 13 participants moved in the same direction for every trial and, of these, over half of them (8/13; 61%) moved in the direction of flexion. This begs the question as to why so many participants perceived (8/20; 40%) or mimicked (5/13; 38%) extension for every trial. While it is likely that the quantification of the movement direction has its flaws (see Section 3.1 Limitations, below), it is interesting to note that almost half of the participants perceived the movement as extension. Before this method of applying electrical stimulation is further utilised to create kinesthetic illusions, investigation as to how participants perceive the direction of finger movements could be explored.

While the method used in the present study created illusions of movement in a larger cohort of participants compared to previous studies, the amplitudes of the illusory movements are neither the largest nor the smallest reported to date. While Collins & Prochazka (1996) reported  $11.6 \pm 16.6^\circ$  (mean  $\pm$  SD) and Collins et al. (2000) reported  $1.5 \pm 1.0^\circ$ , the present study produced illusory movements of 4-6° on average. The differences in illusory amplitudes may be due to the area of skin stimulated. As Collins & Prochazka (1996) applied electrical stimulation to the entire dorsum of the hand and Collins et al. (2000) applied stimulation to only the skin over the MCP joints of digits III or IV. The present study stimulated nerve branch which innervates a smaller area of skin compared to Collins & Prochazka (1996), but a larger area than Collins et al. (2000). Due to the differences in methodology between the studies, however, a future study investigating the relationship between area of skin stimulated and amplitudes of illusory movement would need to be performed.

Before this technique is used for other research purposes, such as investigating whether stimulation of the skin can create illusions regarding the kinesthetic position sense or in applications, which are described below, it is recommended that discerning the ideal modulation patterns for stimulation of cutaneous afferents, derived from the frequency coding and population coding naturally produced by these receptors, be further explored.

### 3.1 Limitations

This project tested the differences between frequency-modulation and intensity-modulation on the prevalence and amplitudes of illusory movements by stimulating cutaneous afferents in the hand. While the findings of this project suggest that this method can be used to create these illusions, before it can be used in this way, some limitations need to be addressed.

Physiologically, we predicted that an increase in the frequency-modulation translates to an increase in discharge rate and that an increase in the intensity-modulation translates to an increase in the number of cutaneous receptors firing. Without utilising microneurography to directly record from these receptors, there is no way of knowing for certain if these afferents are responding in this way. However, as this project is stimulating the afferent rather than the receptor, simultaneously recording responses from the afferent may be difficult at best and interfere with the results at worst.

This study was the first of its kind to use motion capture to record and quantify the movements of the fingers for kinesthetic illusions. Due to its sub-millimeter precision, this methodology was both a blessing and a curse for quantifying the amplitude of finger movements. As a blessing, using passive motion capture required that reflective stickers be applied to the centre of the joints. These stickers were small, only 3 or 4 mm in diameter, and participants generally forgot they were wearing them, suggesting that their placement on the skin did not interfere with the perceptions created by the stimulation. As the cameras were placed in a way that most movements were always tracked, even the smallest movements created by participants were recorded and quantified. Unfortunately, this meant that unwanted or unexpected movements were also recorded. Any shift in posture, even rhythmic breathing movements, was captured by the cameras. Some participants data were very noisy, moving up to five degrees despite reporting that they perceived and mimicked no movement in their trials. Other participants were very still and reported movements, however, only one or two degrees of movement were quantified on the cameras. This made quantification of the amplitudes of movement difficult, as there was no cleaning or smoothing of the data that could be performed to remove the unwanted artifacts in some participants while keeping the smaller amplitudes of movements in others. As a reminder: each stimulation pattern (i.e., frequency-modulated, intensity-modulated, or combined-modulation) was experienced three times. Each of these patterns was made up of five trains of stimulation. Therefore, to try and rectify this issue, the average movement of all fifteen stimulation trains was reported as the amplitude of illusory movement for each participant.

Another limitation of this study was quantifying the direction of movements. Defining a movement as flexion or extension of the index finger seems like a simple task. As the movements were small and rarely smooth, however, discerning direction of the index finger could be quite difficult. To make matters worse, not every participant moves their joints the same way when mimicking these movements. Although not reported in Chapter 2, 11/20 (55%) of participants moved their MCP joint in the opposite direction as their PIP joint and whether the overall movement of the index finger is matched with movement of the MCP or PIP seems to vary between participants. Asking the participants which direction they perceived the movements helped with some trials, however, some participants were not certain about the direction they perceived, either. One reason for this included the small amplitude of movement, as participants were not certain they were even moving. Other participants reported that it was difficult to match or describe a movement that had not been intentionally created. Another participant responded that their finger was doing both flexion and extension, as it had to move back and forth to replicate the movements felt and were unable to choose a single direction.

Participants had difficulty matching the movements, not only in their direction, but in their timing as well. Although participants were allowed to experience the upcoming stimulation pattern as a familiarization trial before the data was collected, and participants were invited to experience the familiarization as many times as they liked, there is a latency between the timing of the stimulation and the timing of the movements. As a reminder, the amplitude of the movement was derived from the difference between the largest angle and the smallest angle within each stimulation train. Therefore, if the latency between the beginning of the stimulation train and the participant's initial movement was large enough, some of the most extreme amplitudes of the movement may have aligned with the rest between stimulation trains and was not part of the amplitude calculation for that train. Alternatively, as the modulation of the stimulation had both an increase and a decrease for every stimulation train, participants may not have reached the peak of their perceived movement when the stimulation began to decrease, resulting in participants changing direction before the movement had reached its maximum perceived amplitude. As the movements are illusory, there is no way of knowing how accurately participants were able to match the movement.

Some participants perceived illusory movements during the trial, but only mimicked the movements during one or two trains of the stimulation. As all five trains were averaged for each trial, regardless of how many times a participant mimicked the movement, it is likely that some of the larger movements have been averaged into smaller amplitudes during quantification.

### **3.2 Future Directions**

Once these limitations have been addressed, this method could be used to further research the role of the skin in kinesthesia. One project could be to investigate the role of the skin in the kinesthetic position sense. As the slowly-adapting mechanoreceptors, Merkel cell complexes and Ruffini endings, continuously discharge when a change in position is held, different ranges of frequency could be administered to discern their effects on a position-matching task. Like previous studies investigating the position sense, researchers could move the participant's finger into a new position and ask the participant to match that position with or without the electrical stimulation. This would side-step some of the larger limitations in this project, as participants would not need to report the direction of their movements, but simply match them. This project would also help to discern how well participants match their index fingers with the contralateral limb during this stimulation method. By moving participants into a known position and then asking them to match that position with and without the stimulation, it could shed some light onto how well participants were able to match the illusory movements evoked in this project.

Kinesthetic studies have also demonstrated that when stimuli from multiple sources are applied together, the resulting illusions are stronger (i.e., amplitudes of movement are larger, and the illusions are more believable to participants) than either of the stimuli applied separately (Blanchard et al., 2011, 2013; Collins et al., 2000, 2005; Honda et al., 2023). Some researchers are beginning to integrate kinesthetic illusions into virtual reality to enable participants to *feel* as though they are moving through a virtual space, when they are not moving at all (Tanaka et al., 2020). Kinesthetic stimulations, such as vibration, are also being explored in rehabilitative settings, with practitioners combining these methods with clinical therapy to try and improve outcomes for individuals with sensory deficits resulting from stroke or Parkinson's disease (Malwanage et al., 2024; Ribot-Ciscar et al., 2017; Takahashi et al., 2022).

### **3.3 Summary**

This thesis investigated the role of cutaneous receptors in kinesthesia. We applied electrical stimulation to the skin to create kinesthetic illusions in the hand to test hypotheses regarding the frequency coding and population coding of the CNS. Previous research has modulated the frequency or the intensity of electrical stimulation and produced illusions of movement in the human hand. This project was the first to investigate frequency-modulation, intensity-modulation, and the synchronization of modulating both parameters in electrical stimulation and their effects on the amplitude of illusory movements in the hand. While this study did not find a

significant difference between these stimulation patterns, illusory movements were perceived in a larger percentage of participants compared to previous studies. Future studies could be performed to refine this technique, which could enable larger amplitudes of illusory movement or larger proportions of participants experiencing the same direction of movement.



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