

**THE RELATIONSHIP BETWEEN WHOLE-BODY MOTION AND UPPER LIMB  
CONTROL FOR REACHING AND BALANCE**

**by**

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## ABSTRACT

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Two functions of the upper limb are reaching and maintaining balance. To successfully perform these roles requires a mechanism for detecting and compensating for body sway. Here I investigate this possible mechanism by using vestibular stimulation to evoke responses in both the upper and lower limbs. I demonstrate that the evoked arm movements are scaled to the degree of sensed whole-body motion, and only operate when reaching within an earth-fixed reference frame. These findings suggest that vestibular signals contribute to maintaining reach accuracy during unexpected body motion which would otherwise take the limb off-target.

I also show that the arm responds to vestibularly sensed body motion for balance. When firmly grasping a stationary support, upper limb forces are coordinated with ground reaction forces to produce a counteractive whole-body sway response. In contrast, during light grasp ( $<1\text{N}$  grip force) the arm does not actively engage in balance. Instead, it simply acts as a passive sensor to provide feedback of body motion which improves balance. Finally, even though postural control during stance has been successfully modelled as an inverted pendulum, my results suggest that the nervous system does not transform light touch feedback into a signal of rotation about the ankle joint.

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## PUBLICATIONS

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# CHAPTER 1

## GENERAL INTRODUCTION

---

### 1.1. Upper limb function and control

#### 1.1.1. The upper limb and reaching

The human upper limb comprises the bones, muscles, and joints of the arm, forearm, wrist, and hand. The evolutionary adaptation of bipedalism in man, freed the upper limb from use in balance and locomotion, and instead is an organ for grasping and manipulating. However, all primates share the ability to perform intricate reaching movements, a skill necessary for interaction with their surroundings, e.g. picking fruit from a tree. In humans reaching for an object is a goal-directed and functional motor task that integrates the nervous and musculoskeletal systems, requiring simultaneous coordination of the shoulder, elbow, and wrist joints (Liu *et al.*, 2013). Reaching, picking up, and drinking from a glass is an effortless task, but effective performance requires motor planning and continuous feedback for adjustment of the upper limb relative to glass and body. Although the exact mechanisms that control reaching are not fully understood, it is proposed that an initial crude motor plan is formed prior to the initiation of movement, and is subsequently updated online through internal feedback loops as the movement progresses (Desmurget & Grafton, 2000). For online control, we continuously update sensory input to inform us of arm trajectory/position relative to

the target and body, and adjust upper limb position and trajectory according to any error between actual and desired movement (Desmurget *et al.*, 1998). It is clear that sensory systems which provide input on upper limb and/or body orientation and motion are crucial for accurate control of upper limb movements. In Chapters 2 & 3, I explore how we utilise sensory detection of body motion to maintain reaching accuracy.

### **1.1.2. The upper limb and balance**

Although bipedalism has freed movement of the upper limb for reaching and grasping in man, it has also made us less stable compared to other mammals that predominately stand and locomote quadrupedally. To remain balanced, the body's centre of gravity must stay within the limits of its base of support. When standing, the base of support for humans, i.e. the feet, is relatively small compared to quadrupeds (only 2 feet compared to 4), constraining our body displacement within tight boundaries without becoming unstable. Standing upright has also heightened our centre of gravity further from the base of support, further reducing stability. To overcome these balance challenges inherent to standing on two limbs, balance control systems must be in place.

Although balance stabilization is no longer a *primary* function of the upper limb in healthy humans, it has retained functional use as a balance aid. The use of the upper limb for balance can be separated into two types of strategies: 'fixed-support' or 'change-in-support' strategies (Maki & McIlroy, 1997). Here, support refers to the

base of support. Therefore fixed-support strategies act to control body displacement without changing the base of support. The upper limb contributes to fixed-support balance strategies when we make rapid arm movements in reaction to a balance perturbation. Such movements use the limb as a counterweight and generate reaction torques to alter body position away from the direction of the fall and slow body motion (Allum *et al.*, 2002). Another upper limb fixed-support strategy involves grasping a support during balance perturbation. In this case, the base of support includes the feet (when standing) and the base of the external support being grasped. The arm utilises the external support by exerting force to compensate for any body motion, e.g. holding onto a handrail whilst standing on a bus, or using a walking aid. In contrast to fixed-support strategies, change-in-support strategies involve changing the base of support. The upper limb is utilised in this strategy when reaching or grasping a support after a balance perturbation (McIlroy & Maki, 1995; Quant *et al.*, 2001; Maki & McIlroy, 2006), e.g. reaching and grasping a handrail on a bus that suddenly stops. By reaching out and grasping an external support, the base of support is changed to include an external support, thus creating new limits in which body displacement must be kept. Both types of balance strategy require a sense of body orientation and motion to evoke compensatory upper limb responses to prevent loss of balance. In Chapters 4 & 5, I explore the different roles of the upper limb in balance control, and how sensory signals are integrated to maintain stability when the limb is engaged in balance.

### 1.1.3. Sensory inputs

Our knowledge and interaction with the world is based on those facets that stimulate our sensory receptors. When interacting with our environment we use a variety of sensory inputs to provide us with a sense of body and limb orientation and motion. Detection of body motion is necessary to be able to make compensatory limb movements, whether to maintain the position of a limb in space, or maintain balance. Sensory signals that provide a sense of body motion and orientation are integrated from multiple modalities.

The *vestibular* organs located in the inner ears detect head motion, and from this we derive a sense of self motion in space. Furthermore, those with vestibular loss have impaired perception of body motion (Walsh, 1961). Detection of passive body motion when standing allows us to compensate for perturbations through postural reflexes, preventing a loss of balance. The importance of the vestibular system for balance is highlighted by significant instability in patients with complete loss of vestibular function compared to healthy individuals, particularly when other sensory inputs (i.e. vision, proprioception, cutaneous etc.) are unreliable (Nashner *et al.*, 1982). We also use vestibularly sensed body motion to control upper limb movement. Bresciani *et al.* (2002c) demonstrated when reaching for a memorized earth-fixed target during passive body motion, individuals are still able to fully compensate for self motion detected by the vestibular system and maintain reach accuracy. This evidence demonstrates the role of the vestibular system in detection of self motion and the importance of this sensory input for balance and reaching.

We rely more on our ability to 'see' the world through *vision* than any other sensory input. Light reflected by our surroundings enters the eye and is focused by the lens onto light sensitive receptors of the retina. This information is delivered through the visual pathway to the visual cortex in the occipital lobe of the brain, where it is integrated and processed to form a sense of vision. This sense provides a detailed image of objects fixed or moving in our surroundings, as well as self motion relative to the external world. The recognition of visual landmarks based on prior knowledge (e.g. a tree stands vertical), contributes to a sense of self orientation. As we move through the world, objects, surfaces, and edges in the visual scene move relative to ourselves, termed 'optic flow' (Gibson, 1958). The velocity and direction of optic flow corresponds to the velocity and direction of self motion. The sense of self motion derived from the visual system is important for balance. Just closing our eyes whilst standing reduces our postural stability (Edwards, 1946). Visual illusions of self motion, known as 'vection', are apparent when only optic flow is present with no actual self motion. For example, looking out of the window at a parallel train pulling away when sat on a stationary train can give a false sensation of self motion in the opposite direction. When standing, such visual illusions evoke postural responses in compensation for a sense of motion (Lee & Lishman, 1975). Visually-evoked balance responses demonstrate how the visual system contributes to balance by providing a sense of whole-body motion.

When touching a surface, *cutaneous* receptors located in the skin detect pressure applied and any relative motion between the contact surface and our skin. Any

change in pressure or movement of the skin across a surface fixed in space indicates self motion relative to that surface. Lightly touching an earth-fixed surface improves postural stability when standing (Jeka & Lackner, 1994; 1995; Clapp & Wing, 1999; Rabin *et al.*, 1999), even if the hand provides no mechanical support (Holden *et al.*, 1994). Therefore when grasping a support the hand provides additional sensory information regarding body orientation which can be used for postural control.

*Proprioception* is generally considered to encompass the perception of limb position, movement, and force (Gandevia, 1996). For example, with our eyes closed, we can still sense the position and orientation of our arms and legs relative to our body. This sense is the product of subcutaneous receptors within the musculoskeletal system, known as 'proprioceptors', that provide constant information on muscle length and velocity of movement (i.e. spindles), muscle tension (i.e. Golgi tendon organs), and joint angle (i.e. Pacinian corpuscles and Ruffini endings). Artificial excitation of proprioceptors using muscle vibration can elicit illusions of changes in perceived limb orientation and movement. For example, when vibration is applied to the muscles of the upper limb, subjects perceive the arm has moved and adopted a new position depending on the muscle stimulated (Goodwin *et al.*, 1972). This illusion is most likely the result of sensed changes in muscle length, as muscle spindle firing rate is modulated by vibration (Goodwin *et al.*, 1972). When vibration is applied during non-visually guided reaching, the error between intended arm position and actual arm position is greatly increased compared to control trials (Capaday & Cooke, 1981). Furthermore, when patients with severe proprioceptive deficits perform reaching tasks, they make large spatial errors compared to healthy subjects (Gordon

*et al.*, 1995). These results demonstrate that upper limb proprioception has a significant role in performing successful reaching actions. As well as reaching, proprioception is useful for balance control. When vibration is applied to muscle spindles of the leg in standing subjects, postural adjustments are evoked in compensation for perceived body tilt (Eklund, 1972). When in contact with a stationary surface (e.g., light finger touch), feedback from proprioceptive receptors provide information about body movement relative to the contact surface for balance control (Rabin *et al.*, 1999). When arm proprioception is disrupted by spindle vibration during light hand touch with a stationary surface, the stability benefits of light touch are absent (Rabin *et al.*, 2008). This provides evidence that proprioception input from the upper limb has a role in balance.

The sensory inputs are integrated in the central nervous system (CNS), and combine to provide an overall sense of body orientation and motion. This information is used for balance and the control of voluntary movement, as these abilities are impaired with loss or perturbation of these sensory inputs. In the experimental chapters of this thesis, I explore how the aforementioned sensory inputs contribute to upper limb control when reaching. I also determine how they contribute to balance when the arm is in contact with a support.



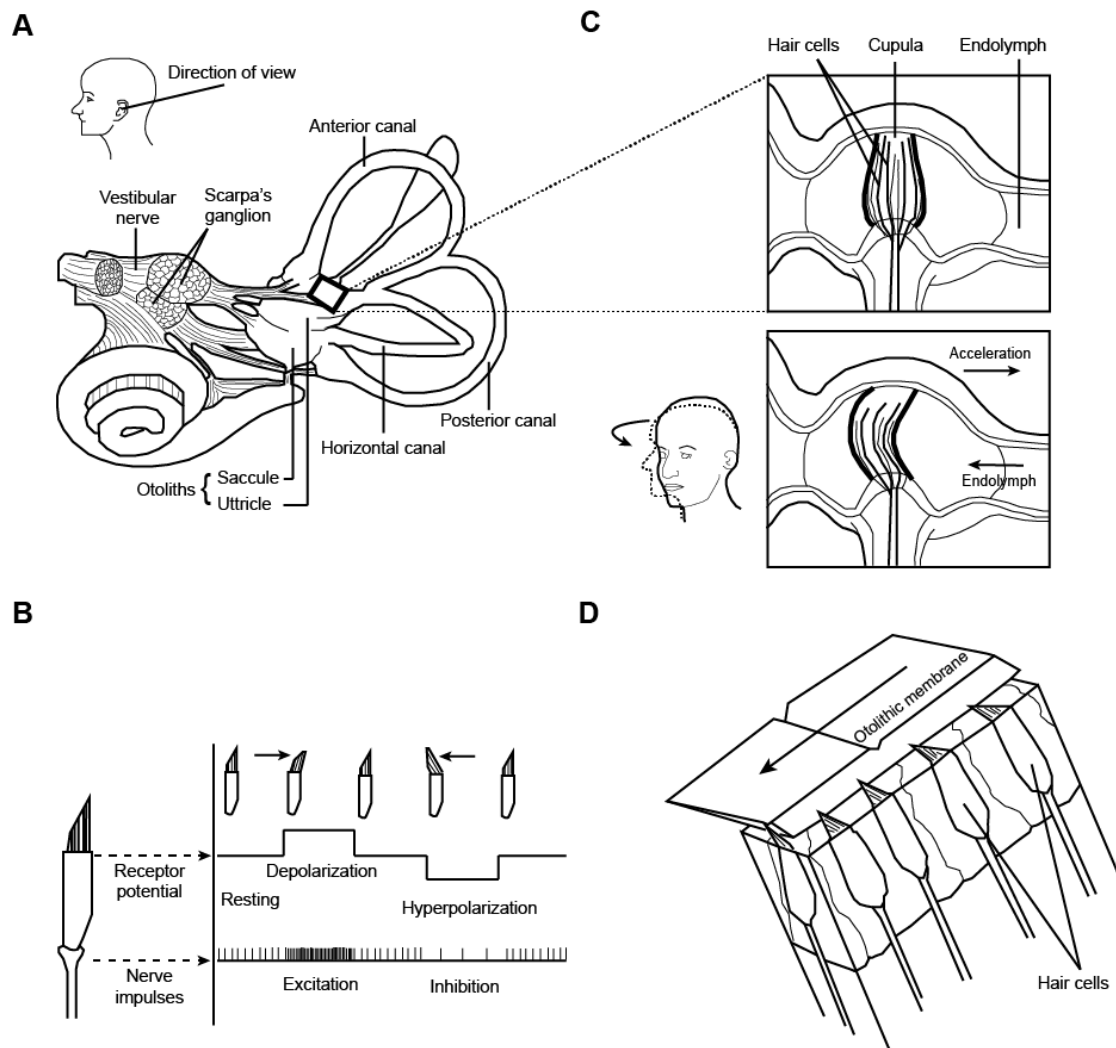
## **1.2. The vestibular system**

### **1.2.1. Anatomy and physiology**

The peripheral vestibular organs form the non-auditory section of the inner ears, and provide a sense of whole-body motion and orientation. This sense is known to contribute to balance, eye movements, upper limb movements, and even cardiovascular regulation (Yates & Miller, 1998). Located bilaterally and fixed within the skull, the vestibular end organs comprise of the semicircular canals and the otolith organs (Figure 1.1A), which are sensitive to rotational and linear acceleration, respectively. Signals from the end organs travel to the CNS via sensory afferents which form the vestibular branch of the vestibulocochlear nerve (cranial nerve VIII).

Three semicircular canals provide us with a sense of head rotation. Each canal is a looped tube of membranous labyrinth partially filled with endolymph fluid. A bulbous section at the base of the canal, the ampulla, contains the cupula. The cupula is a gelatinous diaphragm attached to the epithelium on the perimeter of the ampulla, and a number of hair cell bundles project into the cupula. Deflection of the hair cells leads to depolarization or hyperpolarization of the receptor membrane, depending on direction of deflection (Figure 1.1B). Depolarization increases the firing rate of vestibular afferents (excitation), while hyperpolarization reduces the firing rate (inhibition). The canals detect angular acceleration of the head because inertial movement of the endolymph within the canal results in forces on the hair cells causing them to deflect (Figure 1.1C). Consider head rotation in the plane of the

horizontal canal, i.e. rotation about the vertical axis. As the vestibular organs are fixed within the skull, head rotation rotates the canal. However due to inertia, the endolymph contained in the canal lags behind head rotation, therefore rotates independently within the canal in the opposite direction. In the ampulla, the motion of the endolymph applies force on the cupula, bending it towards the direction of endolymph flow. As the cupula bends, the hair cells contained within are deflected, thereby modulating the firing rate of the associated sensory afferents. The pattern of afferent firing provides us with a sense of rotational velocity and direction. Each semicircular canal is sensitive to rotations in its plane. For example, the horizontal canal sits in the horizontal plane and is therefore most sensitive to horizontal rotations. The anterior and posterior canals are orientated more vertically, approximately  $45^\circ$  from the sagittal plane. With three canals on each side of the head, angular rotation of the head is detected in three axis of rotation. The vestibular organs are mirrored bilaterally, therefore rotation stimulates partnered canals. For instance, head rotation about a vertical axis to the left excites the left horizontal canal and inhibits the right horizontal canal. Such pairing also exists for the anterior and posterior canals.



**Figure 1.1. The vestibular end organ.** A) Orientation of the vestibular end organ, semicircular canals and otoliths, within the middle ear. B) The hair cells of the canals and otoliths transduce mechanical stimuli to neural signals. Deflection of the hair cells increases or decreases afferent firing frequency (nerve impulses) depending on the direction of deflection. C) The ampulla of the semicircular canal. As the head rotates, the endolymph flows in the opposite direction due to inertial forces. The endolymph flow displaces the cupula, deflecting the hair cells. D) The hair cells of the otolith organs project into the otolithic membrane. Movement of the otolithic membrane over the membranous labyrinth, by tilting of the head or linear acceleration, deflects the hair cells. Figures adapted from Goldberg & Hudspeth (2012).

The vestibular end organs also include the otolith organs, which detect linear acceleration (Figure 1.1D). The otolith organs are the saccule and utricle, which

detect linear motion (e.g. translation) and static orientation of the head relative to gravity (e.g. head tilt). Each organ consists of a membranous labyrinth, with hair cells arranged in an elliptical patch, the macula. The hair cells are embedded in a gelatinous membrane containing calcium carbonate crystals, or otoconia, which make the membrane denser than the surrounding endolymph. Gravitational forces exert force on the otoconial matrix, which moves independent of the membranous labyrinth, deflecting the hair cells. As for the semicircular canals, deflection of the hair cells alters the vestibular afferent firing pattern depending on the direction of acceleration. The orientation of the organs and hair cells, allow detection of linear acceleration along any axis. The utricular macula is inclined backward  $\sim 30^\circ$  from horizontal and slopes away laterally by  $\sim 10^\circ$  (Naganuma *et al.*, 2003). Thus, the utricle senses linear acceleration predominately in the lateral and sagittal axis. In contrast, the saccular macula is aligned with the sagittal plane and detects vertical (including Earth's gravity) and anteroposterior acceleration. However, input from the otoliths can be ambiguous, as both linear acceleration (translation) and acceleration owing to gravity produce similar displacement of the otolith membrane. For instance, forward linear translation produces an inertial movement of the otoconial matrix backward, deflecting the hair cells in the same direction. Pitching the nose upward when stationary also displaces the matrix backward due to gravitational forces, thus generating the same neural signals as during forward linear translation. The brain integrates information from the otoliths with other sensory modalities, such as visual and somatosensory systems to interpret the otolith signal correctly. However, when other sensory input is unavailable, linear accelerations can evoke sensations of tilting. Such false sensations are known as somatogravic illusions (Stott

& Benson, 2016), which are common in aviation, as fast linear accelerations are routine and visual input can be unreliable. For example, in conditions of poor visibility, pilots have reported sensations of the aircraft pitching up during sudden forward linear acceleration during level flight, and incorrectly respond by pitching the aircraft downward.

The cell bodies of vestibular afferents, which synapse at the hair cells of the end organs, form the Scarpa's ganglion. The sensory signals travel ipsilaterally from Scarpa's ganglion to the brainstem via the vestibular portion of the VIII cranial nerve. Although a few vestibular afferents project directly to the cerebellum, most project into the four vestibular nuclei; medial, lateral, superior, and descending nuclei, located in the dorsal part of the pons and medulla. These nuclei integrate vestibular inputs with afferent signals from the visual system, proprioceptors via the spinal cord, the cerebellum, the reticular formation, and the contralateral vestibular nuclei complex.

The efferent pathways of the vestibular nuclei consist of signals sent to the cerebral cortex, oculomotor nuclei, cerebellum, spinal cord, and reticular formation. These projections are either ascending or descending. Ascending pathways project to three main areas: the cortex, oculomotor nuclei, and cerebellum. Projections to cortical regions, via the thalamus, are thought to be involved in conscious perception of spatial orientation and self motion (Lopez & Blanke, 2011). A vestibular cortical system has been proposed, with evidence from animal (Guldin & Grüsser, 1998) and human studies (Lobel *et al.*, 1998; Stephan *et al.*, 2005) demonstrating activation of

similar areas of the cortex during vestibular stimulation. Ascending projections to oculomotor nuclei initiate compensatory eye movements for head motion (e.g. the vestibular ocular reflex). The cerebellum receives input for the modulation of vestibular reflexes for posture and balance.

The main descending pathway of the vestibular nuclei is the vestibulospinal tract. The vestibulospinal tract receives input from the medial and lateral nuclei (Brodal, 2010), and relays motor commands via the spinal cord to the postural musculature for control of posture and balance. Vestibular nuclei connections with the reticular formation also provide an additional descending pathway, utilizing the reticulospinal tract (Peterson & Abzug, 1975). The vestibulo- and vestibulo-reticulospinal tracts have been suggested as pathways for vestibular control of the upper limb (Mars *et al.*, 2003).

### **1.2.2. Vestibular evoked balance responses**

Vestibular detection of head motion provides us with a conscious perception of whole-body motion and orientation in space, but also evokes compensatory responses in order to maintain equilibrium. One such vestibular-evoked response is the vestibular ocular reflex (VOR). On detection of head motion by the vestibular organs, ascending projections from the vestibular nuclei to the oculomotor nuclei produce eye movements in compensation for sensed head motion. This response occurs at a latency of less than 10ms (Aw *et al.*, 1996; 2006), allowing us to maintain the image of the external world stable on the retina during head motion.

Vestibular signals also evoke balance responses. Vestibularly sensed motion evokes excitatory and inhibitory muscle responses in the trunk and limbs via descending projections. These muscle responses generate forces and movement necessary to compensate for sensed body motion and prevent a loss of balance. The exact pathway of these responses remains unknown, with the vestibulospinal, reticulospinal (Britton *et al.*, 1993; Dakin *et al.*, 2007), and corticospinal (Marsden *et al.*, 2005) tracts proposed.

The importance of the vestibular system in balance responses is clearly demonstrated by the inability of those with loss of vestibular function to maintain balance when reliant on vestibular input. Martin (1965) asked blindfolded subjects to sit upright on a bed that was able to tilt. When the bed was rapidly tilted side to side, subjects responded with movement of the trunk and limbs to prevent themselves from falling. When the same task was asked of patients with no vestibular function, little or no compensatory postural adjustments were made, making them susceptible to falls. This evidence demonstrates the importance of vestibular-evoked postural adjustments for balance control. However, it is important to state that patients with vestibular deficits are able to effectively maintain balance when vision or stable support is available (Nashner *et al.*, 1982; Horak *et al.*, 1990). Similarly, patients with vestibular deficits have no problem walking with their eyes open, but demonstrate impaired ability to orientate locomotion with their eyes closed (Glasauer *et al.*, 1994; Borel *et al.*, 2004). Therefore, other sensory inputs (i.e.

vision, somatosensory) can provide sufficient information on body orientation and motion to prevent impaired balance control when vestibular signals are unavailable.

Stimulation of the vestibular organs, through actual motion or artificial stimuli, has been used to study vestibular-evoked balance responses. Using actual motion provides a natural vestibular stimulus. Subjects can be rotated (Bresciani *et al.*, 2002b), pulled or pushed (Fitzpatrick & McCloskey, 1994), or their support surface tilted or translated (Nashner *et al.*, 1982). However, the disadvantage of real movement is that it is difficult to modulate vestibular input in isolation, as real perturbations often stimulate multiple sensory modalities (i.e. cutaneous, proprioception) simultaneously. Alternatively, artificial vestibular stimulation provides pure modulation of vestibular signals, evoking virtual sensations of motion without any actual head or body movement. Caloric vestibular stimulation involves cold or warm water or air irrigated into the ear canal. It is believed the difference in temperature between the water/air entering the canal and the regional body temperature around the horizontal semicircular canal creates a convection current within the endolymph of the canal (Jacobson & Newman, 1997). This movement of the endolymph mimics endolymph flow during actual rotation of the head, evoking a sensation of body rotation. In response to this sensed rotation, compensatory eye movement reflexes (i.e. horizontal nystagmus) are evoked (Fitzgerald & Hallpike, 1942). Caloric vestibular stimulation is used clinically to test vestibular function. However, due to the cumbersome nature of the technique, it is difficult to use for the study of vestibular-evoked postural responses. In contrast, galvanic vestibular stimulation (GVS) is widely used to study vestibular-evoked balance responses (for a



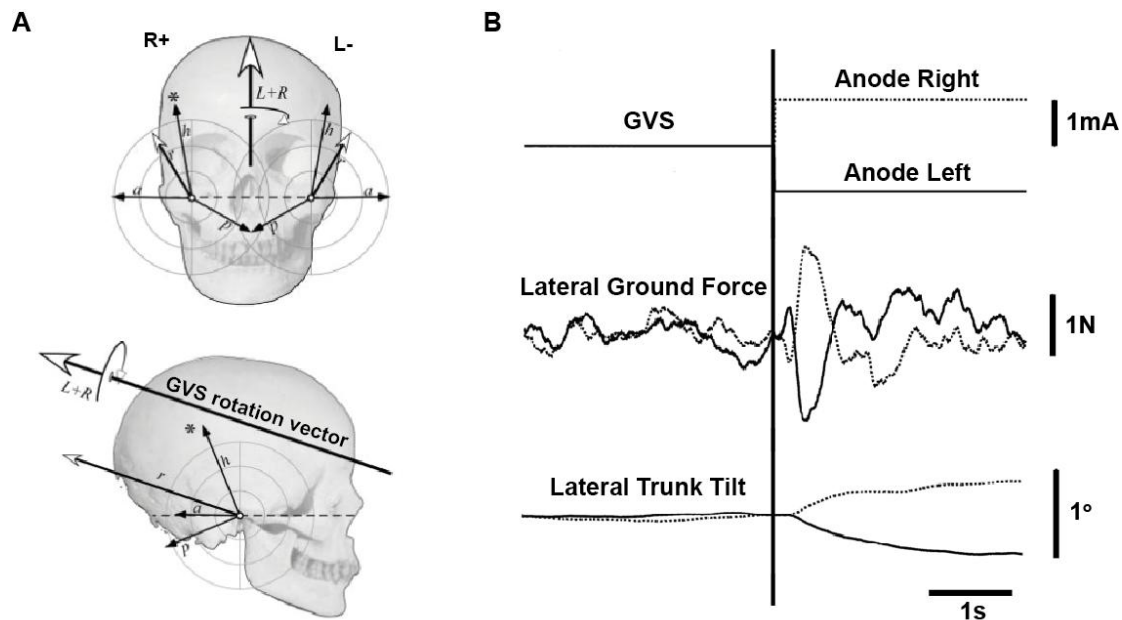
review see Fitzpatrick & Day, 2004). The first description of GVS was as early as 1790, from Italian physicist Alessandro Volta (Volta, 1923). When Volta applied the current of his voltaic pile across his own head, he reported a sensation of spinning before subsequently collapsing (the voltaic pile generated ~30V!). The spinning sensation experienced was likely the result of vestibular stimulation. The GVS technique has only been slightly refined from Volta's pioneering, if not extremely dangerous, experiments. A smaller 6V battery is used to deliver a small controlled current ( $\leq 5\text{mA}$ ) via electrodes placed on the mastoid processes behind the ears. The stimulus is typically delivered with an anodal electrode on the mastoid process behind one ear, and a cathodal electrode placed behind the other ear, i.e. bipolar bilateral GVS. When the stimulus is applied for 1 to 2s it can evoke an illusory sensation of whole-body motion. When standing, balance responses are produced to compensate for the false sensation of motion.

GVS directly modulates the firing rate of both canal and otolith afferents (Lowenstein, 1955; Kim & Curthoys, 2004), bypassing the mechanics of the vestibular end organs. Evidence suggests the site of GVS action is the spike trigger zone of the primary afferents (Goldberg & Smith, 1984; Aw *et al.*, 2008). GVS primarily excites irregular primary afferents, whereas afferents classed as regular show minimal modulation even when large stimulus currents are applied (Goldberg & Smith, 1984). Although vestibular afferent firing during GVS has not been directly measured in humans, GVS of the squirrel monkey has shown cathodal stimulation increases afferent firing, while anodal stimulation decreases the firing rate. In both cases, the

change in firing rate is linearly related to current amplitude (Goldberg & Smith, 1984).

Unlike natural stimuli, GVS is indiscriminate, stimulating the entire population of susceptible afferents regardless of the hair cells they innervate. If we consider the semicircular canals, cathodal GVS will increase the firing rate of all responsive afferents of the three canals simultaneously and equally. This will induce a virtual signal of rotation about a vector orthogonal to each canal. Based on the anatomical orientation of the vestibular organs within the skull (Blanks *et al.*, 1975), Fitzpatrick & Day (2004) estimated the rotation vector of the canal signals evoked by binaural bipolar GVS (Figure 1.2A). With anodal stimulation applied, the horizontal canal would signal head yaw to the cathode side ( $h$  vector, right ear). As the anterior and posterior canals are aligned  $45^\circ$  to the sagittal axis of the skull, the signal would include a pitch and roll component. Both would signal head roll towards the cathode, however the anterior canal would also signal nose-down pitch ( $a$  vector, right ear), while the posterior canal would signal nose-up pitch ( $p$  vector, right ear). Such equal and opposite pitch signals are unnatural and cancel out, therefore the resultant vector ( $r$  vector, right ear) is the summation of the yaw and roll components. Because the roll component is the product of both the anterior and posterior canal, while only the horizontal canal signals yaw, the resultant vector is biased towards roll. This is the same for both sides of the head. Therefore, by summing both resultant vectors on each side of the head ( $L+R$  vector), it is estimated GVS will evoke a signal of rotation about a mid-sagittal axis directed

backward and upward  $\sim 18.8^\circ$  of Reid's plane (Fitzpatrick & Day, 2004). This axis is referred to as the GVS rotation vector.



**Figure 1.2. Sensed head rotation evoked by GVS and the corresponding balance response.** A) When GVS is applied, the firing rate of the vestibular afferents from all three semicircular canals on the cathodal side (left ear, L-) are increased, and reduced on the anodal side (right ear, R+). The rotation vectors of each canal; anterior ( $a$ ), posterior ( $p$ ), and horizontal ( $h$ ), were summed to estimate the resultant vector ( $r$ ) on each side. Summation of the left and right resultant vectors ( $L+R$ ) gives the estimated rotation vector of the bilateral bipolar GVS signal. Front and lateral views are shown. *Adapted from Fitzpatrick & Day (2004).* B) Balance response to GVS during standing, measured as ground force and body movement. In compensation for a sense of whole-body rotation towards the cathodal ear, the body tilts towards the anode. To produce body movement, ground forces are generated. After GVS onset (vertical line), there is a small lateral ground force impulse at 250ms (early component), followed by a larger impulse in the opposite direction at 450ms (late component). The late component is responsible for the lateral trunk tilt towards the anode. Anode-right and -left stimuli are shown as dotted and solid traces respectively. Positive values indicate tilt and force response to the left, and negative values are to the right. *Adapted from Marsden et al. (2002).*

GVS also excites the otolith afferents. Fitzpatrick & Day (2004) estimated binaural bipolar GVS would produce a signal of linear acceleration toward the cathode side or tilt towards the anode. The tilt-translation ambiguity is due to both movements inducing the same otolith afferent firing pattern. However, the contribution of these signals to GVS-evoked responses is thought to be minimal compared to the signals from the canals (Cathers *et al.*, 2005), if playing any role at all (Mian *et al.*, 2010). Evidence to support the idea that GVS is primarily interpreted as head roll, consistent with activation of the canal afferents, comes from perceptual, anatomical, modelling, oculomotor, and balance responses (Reynolds & Osler, 2012).

When standing, GVS evokes a balance response. The ultimate product of the response is whole-body sway towards the side of anode electrode placement in compensation for a false sensation of head roll towards the cathode. To produce the body sway, lower limb muscle activity is modulated to generate lateral forces on the ground (Marsden *et al.*, 2002, Figure 1.2B). The pattern of ground force includes a short and medium latency component. The short latency component, a small deflection in ground force towards the cathode electrode, begins at ~250ms. This is followed by the much larger medium latency component at ~450ms, consisting of force generated towards the anode. The nature of the short latency component is not fully understood, but is not related to the observed whole-body sway. On the other hand, the medium latency component corresponds to the sway observed towards the anode (lateral trunk tilt, Figure 1.2B). The response is equal and opposite when the GVS polarity is reversed (i.e. anode-left and anode-right). In

Chapter 4, I investigate how the upper limb, when engaged in balance, contributes to vestibular-evoked balance responses.

### **1.2.3. Vestibular evoked orientation responses**

Sensory input from the vestibular system provides us with conscious awareness of our orientation and movement in space. The ability of the vestibular system to detect changes in our orientation and/or motion is dependent on the magnitude of these changes passing a certain threshold before detection is possible. Vestibular thresholds for the perception of body motion have been studied by applying a constant linear or angular acceleration to subjects supported (such that somatosensory cues were diminished) in different positions (Walsh, 1961; Clark & Stewart, 1970). The threshold for perception of linear acceleration, primarily detected by the otoliths, has been found to range between 1.6 and 2.5cm/s<sup>2</sup> (Walsh, 1960), while angular acceleration thresholds, primarily detected by the semicircular canals, range between 0.04 and 4°/s<sup>2</sup> (Clark, 1967; Guedry, 1974).

As well as inducing balance responses, GVS alters perceived body orientation and motion. When applied to subjects in a supine position, balance responses are absent, but subjects do report a sensation of whole-body rotation about the naso-occipital axis towards the cathodal ear (Fitzpatrick *et al.*, 2002). When GVS was applied simultaneously with actual rotation about the naso-occipital axis in supine subjects, they perceived rotation greater or less than actual rotation, depending on GVS polarity. For example, during rotation towards the cathodal ear, subjects

perceived greater than actual rotation, and when actual rotation was in the opposite direction to the cathodal ear, subjects perceived they had rotated less than they actually had (Fitzpatrick *et al.*, 2002). This effect has also been demonstrated when GVS is simultaneously applied with actual rotation whilst sitting in a rotating chair, with perceived rotation error greatest when the naso-occipital axis was aligned with the axis of chair rotation (Day & Fitzpatrick, 2005). These findings demonstrate how vestibular signals are used to provide us with a sense of body orientation and motion in space, and how this sense can be manipulated by artificially modulating vestibular input. In Chapter 3, I use this technique to alter perception of whole-body rotation and observed how the upper limb responds when reaching.

#### **1.2.4. Modulation of vestibular evoked responses**

For a given vestibular stimulus, evoked balance and orientation responses are not always the same. The magnitude and direction of vestibular evoked responses are dependent on a number of factors including; head orientation (Pastor *et al.*, 1993), state of stability (Mian & Day, 2014), the task performed (Fitzpatrick *et al.*, 1994), and input from other sensory modalities (Britton *et al.*, 1993).

The vestibular end organs are fixed in the skull, therefore vestibular signals must be transformed from head coordinates to a body reference frame before being used to generate appropriate postural responses. This principle has been demonstrated by using GVS. When GVS is applied in standing subjects, the direction of body sway is always directed towards the anodal ear. When head-on-body orientation is altered

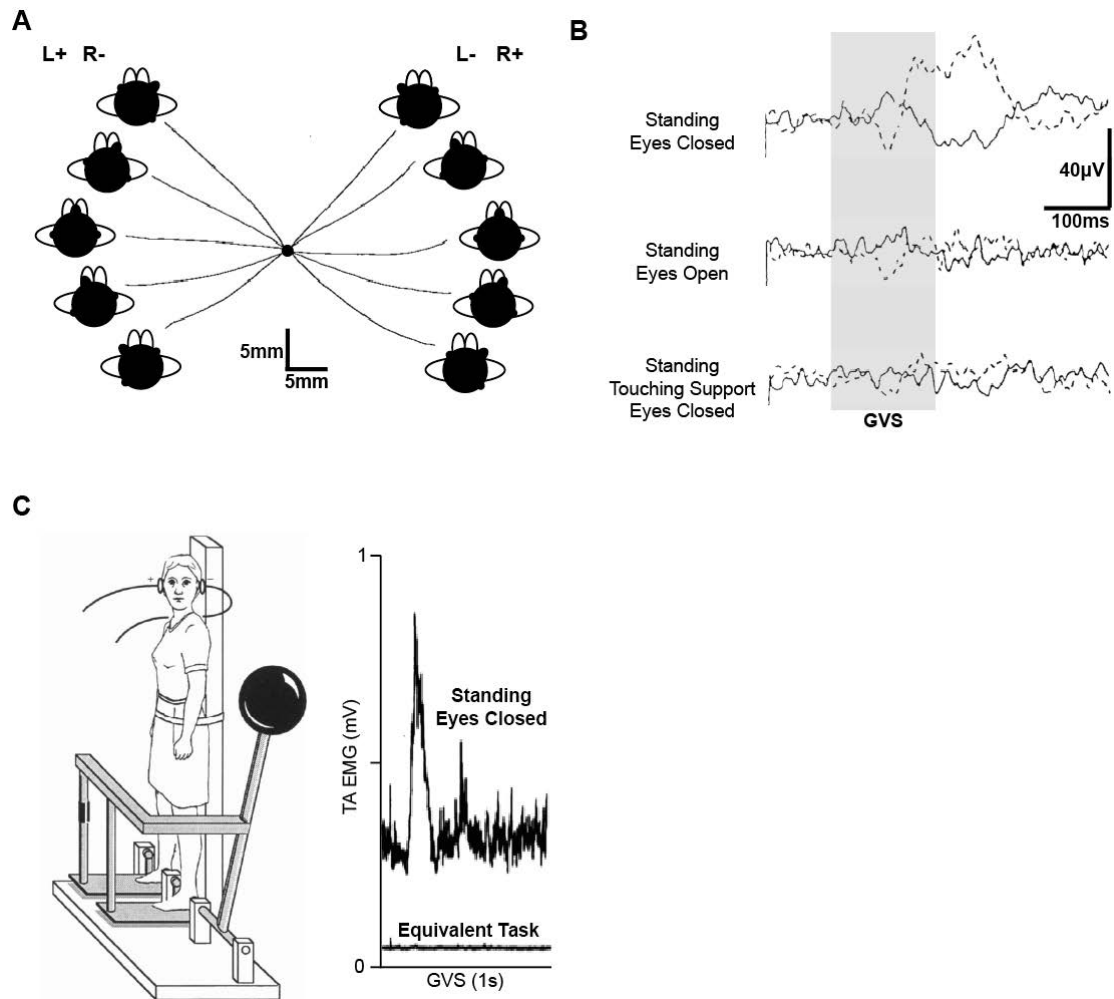
(e.g. from head facing straight ahead to head facing right), the direction of GVS-evoked sway is altered by a similar degree (Lund & Broberg, 1983; Pastor *et al.*, 1993; Mian & Day, 2009, Figure 1.3A). This ‘craniocentric’ principle extends to conscious perception of motion, with the direction and magnitude of perceived motion dependant on head orientation (Day & Fitzpatrick, 2005). Although these studies demonstrate coordinate transformation of vestibular signals for postural control, violation of the craniocentric principle has been found under conditions of anisotropic stability (Mian & Day, 2014). For instance, when stance width is increased, the body becomes more stable in the frontal plane, and the direction of GVS-evoked sway becomes biased towards the sagittal plane, resulting in a nonlinear relationship between head orientation and response direction (Mian & Day, 2014). The same anisotropic stability effect also occurs when making light fingertip contact with a stable surface to the side of the subject. However, unlike increasing stance width, light contact provides minimal mechanical support (Holden *et al.*, 1994), suggesting the anisotropic stabilizing effect of light touch is due to greater sensitivity of proprioceptive feedback in the direction of the arm (Rabin *et al.*, 1999). It has been proposed that multisensory weighting is anisotropic, with the gain of the vestibularly evoked balance response being lower in the direction of greater proprioceptive sensitivity (Mian & Day, 2014). These findings indicate that vestibular signals are integrated with respect to whole-body stability for balance control.

Vestibular-evoked responses are also modulated by the task being performed and the amount of additional sensory feedback available. For example, when GVS is applied in standing subjects, response magnitudes are greater when vision is

removed or somatosensory cues are reduced (Nashner & Wolfson, 1974; Britton *et al.*, 1993; Welgampola & Colebatch, 2001, Figure 1.3B). In contrast, having additional sensory input available from an external support reduces the magnitude of GVS-evoked responses (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994, Figure 1.3B). When lying, sitting down, or even standing supported by a backboard, lower limb muscle responses are completely absent (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994; Luu *et al.*, 2012), demonstrating that such responses are dependant on the muscles playing an active role in balance. Vestibular responses are also suppressed when subjects balance a body-equivalent inverted pendulum, whilst fully supported in a standing position (Fitzpatrick *et al.*, 1994, Figure 1.3C). In this task, the lower limbs are engaged in balance, and somatosensory cues during normal stance are mimicked, however vestibular information is incongruent. This finding suggests that not only must the muscle be contributing to balance, but also that vestibular input must be relevant to the task for a vestibular-evoked response to occur.

In the experimental chapters of this thesis, I investigate whether vestibular-evoked upper limb responses are modulated by head orientation (Chapter 4), state of stability (Chapter 4), non-vestibular sensory input (Chapter 2), and task (Chapters 2, 3, & 4), as reported for postural responses.





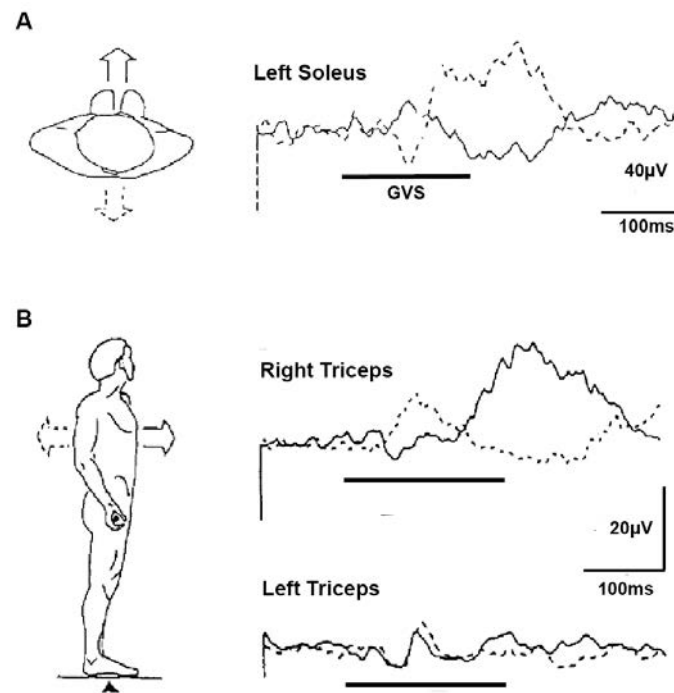
**Figure 1.3. GVS balance responses are modulated by head orientation, sensory cues, and task.** A) Direction of GVS evoked body sway at different head-on-body yaw angles (R45°, R22°, 0°, L22°, L45°, R is right and L is left). Bilateral bipolar GVS was applied at both polarities (anode-left and anode-right). Subjects stood at the central point and the traces depict whole-body sway trajectory. Sway was directed towards the anode electrode in each head position. *Adapted from Pastor et al. (1993).* B) GVS EMG (right soleus) responses are suppressed when additional sensory cues are available. Stimulus polarity was anode-left in dashed traces, anode-right in solid traces. When subjects stood with eyes closed and unsupported there was clear polarity-dependant modulation of muscle activity. Opening the eyes or touching a support considerably reduced the response, particularly the second component. *Adapted from Britton et al. (1993).* C) GVS-evoked right tibialis anterior EMG response (TA EMG) when standing with eyes closed or performing a balance equivalent task with incongruent vestibular input. Balance equivalent task: the subject stood supported in the standing position, on an unstable platform that could rotate about an axis co-linear with the ankles. Attached to the platform was a freely moving weight, similar to the load of the subject's body. The task was to balance the body equivalent load using their feet. GVS was applied with the head turned to the

side such that the GVS rotation vector was parallel with the ankle rotation. Eyes were closed throughout. *Adapted from Fitzpatrick et al. (1994).*

#### **1.2.5. Vestibular evoked upper limb responses for balance**

When holding onto a stationary support during body motion, we use the upper limb to help us maintain balance. For example, when holding a handrail whilst standing during an unsteady bus journey, the arm exerts force onto the handrail in compensation for involuntary body motion to keep us upright. The majority of research into vestibular-evoked responses has been focused on balance when standing freely, with little study on how the upper limb uses vestibular input for balance when holding onto a support during standing. Britton *et al.* (1993) applied GVS to subjects holding a fixed support as they stood on a transversely pivoting platform, such that use of the arm was the only means of maintaining equilibrium (Figure 1.4). EMG recorded at the triceps brachii, showed GVS modulated muscle activity, consistent with a compensatory balance response for a false sensation of self motion. The response was similar to the muscle activity of the lower limbs during normal standing. As with balance responses during normal standing, the upper limb response was craniocentric, and dependant on the limb contributing to balance (no response was found in the arm not being used). These findings demonstrate vestibular signals contribute to upper limb for balance responses. In Chapter 4, I further explore vestibular-evoked upper limb balance responses. Specifically, I determine how these responses are affected by grasp context, and how they are coordinated with the rest of the body for balance, as they have only been

previously studied when the role of the lower limbs has been abolished (Britton *et al.*, 1993).

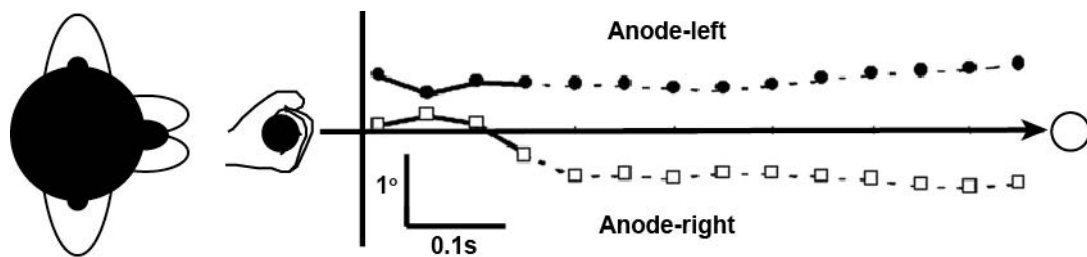


**Figure 1.4. Vestibular evoked arm response for balance.** A) EMG modulation of the left soleus during GVS whilst standing unsupported with eyes closed. The head is turned to the left, such that GVS-evoked body motion is in the anteroposterior axis. GVS polarity was anode-left in dashed traces and anode-right in solid traces. B) EMG modulation of the right and left triceps brachii during GVS when the right arm was used to maintain balance. Subjects stood on a transversely pivoted platform and maintained balance in the anteroposterior axis by grasping a fixed handle with their right hand. *Adapted from Britton et al. (1993).*

### 1.2.6. Vestibular evoked upper limb responses during reaching

When reaching for an object it is necessary to compensate for any unexpected body motion to maintain reach accuracy, e.g. reaching for a handrail when stood on a bus that suddenly accelerates. The vestibular system provides us with a sense of whole-

body motion. Therefore it has been suggested that vestibular input may be used to control the upper limb when reaching (Bresciani *et al.*, 2002a, 2005; Mars *et al.*, 2003; Smith & Reynolds, 2017). When subjects are gently spun in a rotating chair with their eyes closed, making them reliant on vestibular input to detect body motion, they are still able to maintain reach accuracy to a memorised earth-fixed target (Bresciani *et al.*, 2002c, 2005). Evidence for a link between vestibular signals and the control of reaching has also been provided by GVS. When applied whilst reaching, GVS deviates hand trajectory towards the anodal ear (Bresciani *et al.*, 2002a, 2002b; Mars *et al.*, 2003; Moreau-Debord *et al.*, 2014; Smith & Reynolds 2017; Figure 1.5). Similar to postural responses, the effect is also dependent on head orientation, with the largest magnitude observed during head-down tilt, being minimal when the head is upright (Moreau-Debord *et al.*, 2014). These vestibular evoked upper limb movements have been interpreted as compensatory for sensed whole-body displacement (Bresciani *et al.*, 2002a, 2002b; Moreau-Debord *et al.*, 2014). However the precise nature and function of these responses remains unclear. In Chapters 2 & 3, I investigate whether vestibular-evoked arm movements function to maintain reaching accuracy during involuntary body motion, determining if the responses are modulated by availability of non-vestibular sensory inputs, and the relevance of vestibular signals to the task, as shown for balance responses (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994).



**Figure 1.5. Vestibular evoked arm response during reaching.** Subjects reached for a memorized earth-fixed target (white circle) holding a manipulandum. The head was fixed-in-space to minimise body movement. GVS (anode-left or anode-right) was applied on movement onset (vertical line) and remained throughout the movement. Hand position data were normalised with respect to a control condition (no GVS). The hand trajectory deviated towards the anode electrode. Dashed lines indicate time the hand directions became significantly different between GVS polarities. *Adapted from Bresciani et al. (2002a).*

### 1.3. The upper limb as a sensor for balance control

When holding onto a stationary object during unexpected motion, the upper limb acts to maintain balance by applying forces to the contact point. As well as playing an active role in balance control, the arm also acts as a sensor, passively improving balance by providing sensory feedback about self motion.

During stance, light fingertip contact with a stationary object improves stability (Jeka & Lackner, 1994, 1995; Clapp & Wing, 1999; Rabin *et al.*, 1999). Unlike firmly holding an object, light contact provides minimal mechanical support (Holden *et al.*, 1994). The beneficial effects of light contact for balance have been attributed to sensory input from the hand being used as feedback for balance control (Jeka & Lackner, 1994, 1995; Rabin *et al.*, 1999). Cutaneous receptors in contact with the object detect any movement of the fingertip relative to the object, indicating self motion.

This improved perception of self motion facilitates more efficient postural control. When afferent signals are eliminated through anaesthesia of the finger, the benefits of light finger contact for balance are abolished (Kouzaki & Masani, 2008), demonstrating the role of the limb as a sensor.

Light contact with another person has also been found to improve balance (Johannsen *et al.*, 2009; Reynolds & Osler, 2014). As well as providing improved perception of self motion through sensory input of the finger, the very task of maintaining interpersonal light contact may also contribute to improved balance control (Johannsen *et al.*, 2011). However, light contact with a haptic device replaying recorded human body sway reduces stability (Wing *et al.*, 2011). Others have also observed increased body sway when lightly touching randomly moving objects (Jeka *et al.*, 1997; Oie *et al.*, 2002; Allison *et al.*, 2006). In contrast to touching a stationary object, body sway becomes entrained with the motion of the contact reference. In this case, it is suggested evoked sway is a compensatory postural response for a false interpretation of contact point motion as self motion (Jeka *et al.*, 1997). However, the exact nature of this interpretation remains unclear. In Chapter 5, I explore how sensory signals from the upper limb during light contact are interpreted and integrated for balance control.

## **1.4. Summary and aims**

### **1.4.1. Summary**

We use our upper limbs to interact with our environment in everyday life. Two main functions of the limb are 1) reaching for objects and 2) maintaining balance. To successfully function in these roles, a mechanism for detection of, and compensation for, unexpected body motion is necessary. When reaching, vestibular-evoked arm movements provide some support for vestibular contribution to such a mechanism. However the precise nature and function of these responses remains unclear. Vestibular-evoked upper limb responses have also been demonstrated when the limb is engaged in balance control. But it remains to be seen how these responses are integrated with the rest of the body to form a whole-body balance response. The limb also acts as a passive sensor when in contact with an object, detecting self motion. Precisely how this sensory input is integrated and interpreted for balance control is unclear.

### **1.4.2. Aims**

In this thesis, I investigate the relationship between the upper limb and whole-body motion. I first focus on reaching, and how reach accuracy is maintained during unexpected body motion. I then explore the role of the limb for balance, and how it both utilises and provides sensory signals about self motion for balance control. To

explore these areas of interest, I performed a number of experiments to achieve the following aims.

### *Reaching*

A mechanism which could detect and compensate for unexpected body motion when reaching would be beneficial for reach accuracy. Galvanic vestibular stimulation (GVS) applied during reaching has been found to alter reaching trajectories and final hand positions. This evidence provides some support that vestibular signals contribute to such a compensatory mechanism, but the precise nature and function of these responses remains unclear.

**The *first* aim of this thesis was to establish whether GVS-evoked upper limb responses function to compensate for whole-body motion.** Firstly, to effectively compensate for body motion, the evoked limb movement should be scaled relative to sensed self motion. In Chapter 2, I applied GVS to standing subjects asked to point at a target. By manipulating the amount of non-vestibular sensory input available to the subject, I could modulate sensed self motion, and observe whether the arm response was correspondingly modulated. Secondly, vestibular-evoked arm movements should only operate when the arm is being controlled in an earth-fixed rather than body-fixed reference frame. Compensation for whole-body motion would be unnecessary when reaching for a body-fixed target. In Chapters 2 & 3, I address this hypothesis by observing GVS-evoked arm movements when reaching for earth-fixed or body-fixed targets.



## *Balance*

When holding onto a stationary object the upper limb provides balance support. Vestibular-evoked upper limb responses have been observed when the limb is engaged in balance, however it remains unknown how the upper limb interacts with the rest of the body to form a coordinated balance response. Furthermore it is unknown how changing the manual interaction with the support may affect the response, as during light grasp the arm acts only as a sensor for balance control, suggesting a firm grasp is required to generate upper limb responses for a vestibular perturbation.

**The *second* aim of this thesis was to establish under what context of manual interaction the upper limb responds to vestibular perturbation for balance, and how is it coordinated with the lower limbs.** In Chapter 4, I applied GVS to standing subjects grasping a stationary support. To establish whether the response is altered by changes in hand grasp, I measured forces generated by the limb when grasping the support either lightly or firmly. I simultaneously measured forces generated at the feet to see how the lower and upper limb responses interacted. I then determined how the direction of upper limb and ground force vectors are integrated to generate body sway and whether the responses are modulated by head orientation, as previously reported for balance responses when there is no upper limb support.

As well as exerting forces to maintain balance, the upper limb also plays a passive role, providing sensory feedback about self motion beneficial for balance when in

contact with a stationary object. Body sway is evoked when lightly touching a moving object. It is thought that the motion is misinterpreted as self motion, thus producing a counteractive sway response. However, it is not exactly known how sensory feedback from light contact is integrated for balance.

**The *third* and final aim of the thesis was to establish how sensory signals from light upper limb contact with an earth-fixed object are integrated and interpreted for balance control.** Body sway has been expressed in terms of angular motion of the body about the ankle joints (i.e. an inverted pendulum). Based on this consideration, in Chapter 5 I hypothesised that self motion detected by light contact with a moving object is interpreted as angular body sway. To test this hypothesis, subjects stood lightly grasping a moving touch pad. The degree of stimulus angular motion about the ankle joints was kept constant whilst simultaneously altering the linear *translation* of the moving stimulus. In this way I could test whether the body sway response was matched to angular motion or translation. If the sway response remained tied to stimulus angle, this would suggest that sensory signals from light contact are integrated and interpreted as angular body sway.

## **CHAPTER 2**

### **MODULATION OF VESTIBULAR EVOKED UPPER LIMB MOVEMENT DURING REACHING**

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When using our arms to interact with the world, unintended body motion can introduce movement error. A mechanism which could detect and compensate for such motion would be beneficial. Observations of arm movements evoked by vestibular stimulation provide some support for this mechanism. Modulation of vestibular signals through galvanic vestibular stimulation (GVS) has been found to evoke upper limb movements when reaching for a memorized target. These vestibular-evoked responses have been interpreted as compensatory for sensed self motion. For this to be the case, the response should be scaled accordingly to the magnitude of sensed self motion, and only occur when the task requires compensation for body motion. The availability of non-vestibular sensory input is well known to attenuate GVS-evoked postural responses by reducing the false sensation of whole-body motion. This should be true of upper limb responses if they are compensatory. Subjects stood pointing at a memorized target while binaural bipolar GVS was applied. GVS evoked lateral trunk and arm movement towards the anode, with some arm-on-trunk movement. This finding suggests that the trunk and upper limb responses were coordinated to maintain pointing accuracy. To attenuate sensed self motion, additional somatosensory input was provided by fixing the subjects head in-space using a clamp. GVS-evoked trunk movement was expectedly minimal and upper limb movement was greatly reduced, although not entirely

abolished. Surprisingly, the arm-on-trunk movement was similar to that found when standing freely. These findings demonstrate that the magnitude of the arm response was relative to sensed whole-body motion, which was modulated by the amount of non-vestibular sensory cues available. Secondly, I hypothesised that vestibular-evoked upper limb responses should be dependant on the task requiring compensation for body motion. Reaching in an earth-fixed reference frame requires the arm to compensate for any self motion relative to the target, while reaching in a body-fixed reference frame does not. Standing subjects reached for either a body-fixed or earth-fixed memorized target, with GVS applied at the onset of the reach. The results suggested GVS only evoked changes in arm trajectory when reaching for the earth-fixed target, while no response was found when reaching for the body-fixed target. However, the results were not conclusive and further research is required. The fact vestibular-evoked arm movements when pointing at a target are relative to sensed self motion, and seem to only occur when reaching in an earth-fixed reference frame, suggest the upper limb response is compensatory for self motion in order to maintain reaching accuracy.

## **2.1. Introduction**

When reaching for an object it is necessary to compensate for any body movement that may take the limb off-target. The ability to correct arm movements in this way is a common requirement, e.g. reaching for a handrail while standing on an accelerating train. It requires continuous processing of hand and target position, comparing the predicted outcome of the movement to the intended target location,

and correcting for any error (Desmurget *et al.*, 1998; Desmurget & Grafton, 2000). Even without visual feedback, it is possible to maintain reach accuracy to a memorised earth-fixed target during body motion (Bresciani *et al.*, 2002c, 2005). In this case, vestibular signals may provide the sensory input used to compensate for body movement (see Blouin *et al.*, 2015 for review).

Evidence for vestibular control of arm movements has come from the use of galvanic vestibular stimulation (GVS). GVS artificially stimulates the vestibular system, producing a false sensation of movement, primarily consisting of head roll about a naso-occipital axis (Day *et al.*, 1997; Day & Cole, 2002; Marsden *et al.*, 2002; Wardman *et al.*, 2003; Day & Fitzpatrick, 2005; Reynolds & Osler, 2012). When standing, it induces sway towards the anode electrode, compensating for a sense of body displacement towards the cathode (Lund & Broberg, 1983; Day *et al.*, 1997; Marsden *et al.*, 2002; Fitzpatrick & Day, 2004). When reaching for a memorised target, GVS deviates hand trajectory towards the anodal ear (Bresciani *et al.*, 2002a, 2002b; Mars *et al.*, 2003; Moreau-Debord *et al.*, 2014). Similar to the postural response, the arm response has been interpreted as compensation for sensed whole-body displacement (Bresciani *et al.*, 2002a; Moreau-Debord *et al.*, 2014).

However, the precise nature of the link between vestibular signals and upper limb control remains unclear. Arm movements evoked by GVS have been reported to be of similar magnitude when seated versus standing (Bresciani *et al.*, 2002a, 2002b). This contrasts with findings from the postural literature, where responses to GVS are normally suppressed when sitting (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994; Day &

Cole, 2002; Day & Reynolds, 2005; Blouin *et al.*, 2007). For instance, lower limb responses are absent when seated (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994). Even when sitting quietly with the trunk unsupported (i.e. sat on a stool), GVS-evoked trunk movement is minimal compared to when standing (Day & Cole, 2002; Day & Reynolds, 2005; Blouin *et al.*, 2007). Reasons for the suppression are two-fold. Firstly, vestibular-evoked balance responses are functional and therefore task-dependent; when the balance task is minimised by sitting or lying down, vestibular information is not relevant in the same way, and GVS-evoked leg muscle activity disappears (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994). Secondly, the control of balance involves integration of multiple sensory inputs. Reliance upon vestibular input therefore depends upon the availability of information from other modalities. Removing vision (General Introduction, Figure 1.3B) or proprioception increases GVS response magnitude (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994; Welgampola & Colebatch, 2001; Bent *et al.*, 2002; Day *et al.*, 2002; Day & Cole, 2002). Conversely, addition of cutaneous information suppresses the response (General Introduction, Figure 1.3B). When sitting or lying down, all of these factors come into play; the balance task is abolished (or at least minimised), and tactile information from the chair offers an additional source of sensory information. This would explain the reduced GVS responses (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994; Day & Cole, 2002; Day & Reynolds, 2005; Blouin *et al.*, 2007). Hence, if the arm-movement response to GVS is produced to compensate for a sensed whole-body motion, one would expect it to exhibit similar suppression as postural responses, when sitting versus standing. But this is not observed (Bresciani *et al.*, 2002a, 2002b). Given this

discrepancy between arm movements versus sway responses, the underlying mechanism linking vestibular input to the upper limb remains unclear.

For GVS-evoked arm responses to be in compensation for vestibular sensed whole-body motion, the response should be: 1) relative to the magnitude of sensed self motion; and 2) only operate when reaching in an earth-fixed reference frame, as such compensation would be unnecessary when operating in a body-fixed reference frame. In this chapter I studied GVS-evoked arm responses when standing. Firstly, I measured arm responses with and without additional somatosensory input and restriction of body movement (experiment 1). By fixing the head-in-space, this provided additional non-vestibular inputs to conflict with the false vestibular input during GVS. Under these conditions, the sense of self-motion should be attenuated (Britton *et al.*, 1993). Therefore, if arm responses are relative to sensed body motion, as is the case for the sway response, it is predicted that any GVS-evoked arm movement should be attenuated when the head is fixed compared to when standing freely. Secondly, in an additional preliminary pilot experiment (experiment 2), I measured upper limb responses when reaching in an earth-fixed or body-fixed reference frame whilst standing. If arm responses are compensatory for sensed whole-body motion, such responses should only occur when moving the arm in an earth-fixed reference frame.

## **2.2. Methods**

### *Subjects*

6 subjects (24yrs  $\pm$ 3.3; 4 males; 2 females) were recruited for experiment 1. For experiment 2, pilot data from 3 subjects (25yrs  $\pm$ 2.6; 2 males, 1 female) were collected. All subjects were healthy with no known neurological conditions, and informed consent was obtained. Ethical approval was obtained from the University of Birmingham Ethics Committee and was in compliance with the Code of Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association (Declaration of Helsinki).

### ***Experiment 1***

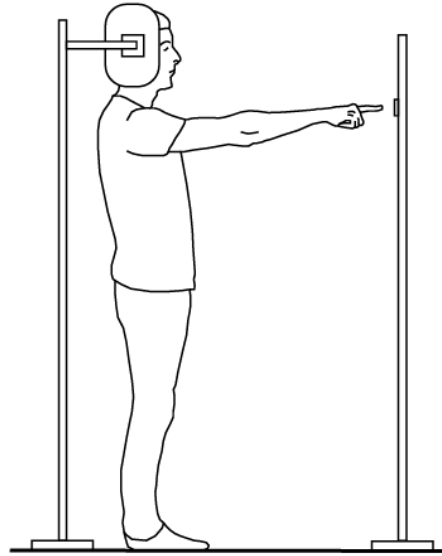
In this experiment, I investigated the hypothesis that the magnitudes of GVS-evoked arm responses are relative to the magnitude of sensed body motion, and therefore compensatory. I measured arm responses when standing freely and pointing at an earth-fixed target. I then fixed the head in space using a head clamp to provide additional somatosensory input and also restrict trunk movement, with the intention of attenuating the false sense of body motion evoked by GVS. Comparing the magnitude of GVS evoked arm movement when standing freely and restrained, I aimed to test whether the magnitude of GVS-evoked arm responses were relative to the magnitude of sensed self motion.



### *General procedure*

The experimental set-up is shown in Figure 2.1. Subjects stood with feet together, facing a target (4 x 4cm) positioned straight ahead at shoulder height. Subjects pointed at the target with their right index finger, with the arm outstretched. Motion capture sensors (recorded at 30Hz, Fastrak, Polhemus Inc., USA) were fixed to the tip of the finger and sternum, to record hand and trunk movement respectively. On hearing an audio cue, subjects closed their eyes to remove visual feedback. After 2s, in 2/3 of trials, a GVS (5s, 2mA) stimulus was applied. An equal number of anode-left (AL), anode-right (AR), and NO-GVS stimuli trials were given. GVS was applied using carbon rubber electrodes (46 x 37mm) coated in conductive gel placed on the mastoid processes in a binaural bipolar configuration. Stimulation was provided in a square wave pattern via an isolation unit (Model 2200, A-M Systems, USA).

Hand and trunk responses were measured when standing freely with no head restraint (head free). The responses were then measured with the head fixed in a clamp (head fixed) to minimise trunk movement and provide additional somatosensory input. 30 trials were completed for each condition; 3 GVS (AL, AR, NO-GVS) X 2 head restraints (head free, head fixed), giving 180 trials in total.



**Figure 2.1. Experiment 1 setup.** Subject stood with feet together, pointing with their right index finger at a target positioned at shoulder height and aligned with their mid-line. In head fixed conditions, the head was restrained in a head clamp (as shown). In head free conditions the head clamp was removed. Subjects had their eyes closed throughout each trial. Motion capture sensors were fixed to the tip of the right index finger and the sternum to record arm and trunk position respectively.

### *Analysis*

GVS-evoked arm responses were compared between head fixed and head free standing to test whether restraint of body movement and availability of additional non-vestibular sensory information (head restraint) had attenuated the magnitude of arm responses. Lateral hand and trunk position were first synchronised around GVS onset, then averaged across trials. The NO-GVS conditions were then subtracted from GVS conditions to highlight GVS effects. In addition to hand and trunk position, hand-on-trunk was also calculated by subtraction of the trunk from hand. Peak hand, trunk, and hand-on-trunk position deviation towards the anodal ear during GVS were used as a measure of response magnitude.

Hand, trunk, and hand-on-trunk velocity were derived from position data. The first time point, post GVS onset, at which velocity was  $> 2$  SD baseline (1.5s pre-GVS time window) was used as a measure of response onset.

Firstly, to test whether there was an effect of GVS polarity (AR vs. AL) on response magnitudes, data from AR conditions were inverted to remove directional effect. Large inter-individual variability in magnitudes were apparent, therefore to minimise the effect of skew and normalise the data, magnitude data were logarithmically transformed ( $\ln$ ) after being made positive (constant added, +1), before statistical analysis was performed. One-sample t-tests were used to test whether the magnitude of responses (hand, trunk, and hand-on-trunk) were significantly greater than zero (i.e., NO-GVS). To compare response magnitudes and onset timings between GVS polarities (AR vs. AL) and head restraint conditions (head free vs. head fixed), repeated measures analysis of variance (2 X 2 ANOVA) were used to test for main effects of the conditions. Hand and trunk response onset times were also compared. Significance was set at  $P < 0.05$ . Statistical analysis was completed using statistical software SPSS Statistics 19 (IBM, USA).

## ***Experiment 2***

If GVS-evoked arm responses are truly compensatory for sensed self motion, arm responses should only occur when moving the arm in an earth-fixed reference frame, and would be unnecessary, and even impair movement accuracy, when operating in a body-fixed reference frame. In this experiment I measured GVS-evoked arm responses when reaching for an earth-fixed or body-fixed target.

### *General procedure*

The experimental set-up is shown in Figure 2.2. Subjects stood barefoot with feet together. Ahead of the subject (120cm) was a rear projected screen (2.03 x 1.52m), such that the screen filled the subject's visual field. Motion capture sensors (recorded at 33.33Hz) were fixed to the back (C7) and tip of the right index finger to record trunk and arm position respectively. PLATO translucent spectacles (Translucent Technologies Inc., Canada) were worn so vision could be occluded on reach onset. A trigger was fixed to the left side of the chest and held down when the arm was in the start position before reaching. Release of the trigger indicated reach onset.

Using rear projection, a life sized avatar was presented on the screen in front of the subject (Simulink 3D animation toolbox, The Mathworks Inc., USA). The avatar was made up of a head, trunk and legs, and was adjusted to match the subject's height (Figure 2.2A). Euler angles were derived from the trunk Fastrak sensor (see Reynolds, 2011), and used to rotate the avatar in yaw, pitch, and roll, such that when the subject rotated about the ankle, the avatar mirrored their body sway. A red square target (5 x 5cm) was fixed to the avatars trunk. The target was aligned with the subject's right shoulder such that reaching from the start position (left side of subject's chest) to the target would produce arm movement primarily in the horizontal plane.

The subject's task was to reach for the target fixed to the avatar, which was either body-fixed or earth-fixed. In conditions when the reach target was body-fixed, the

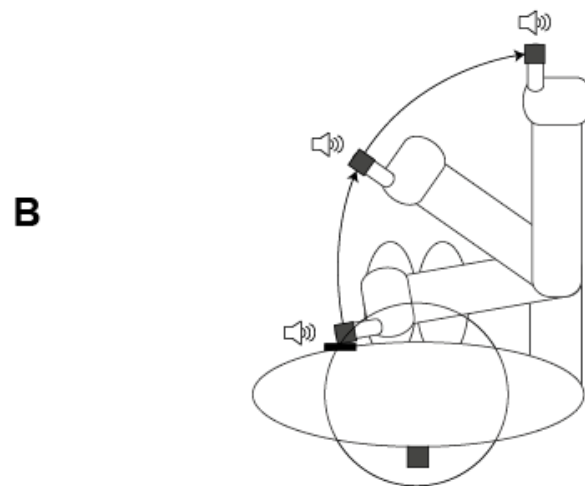
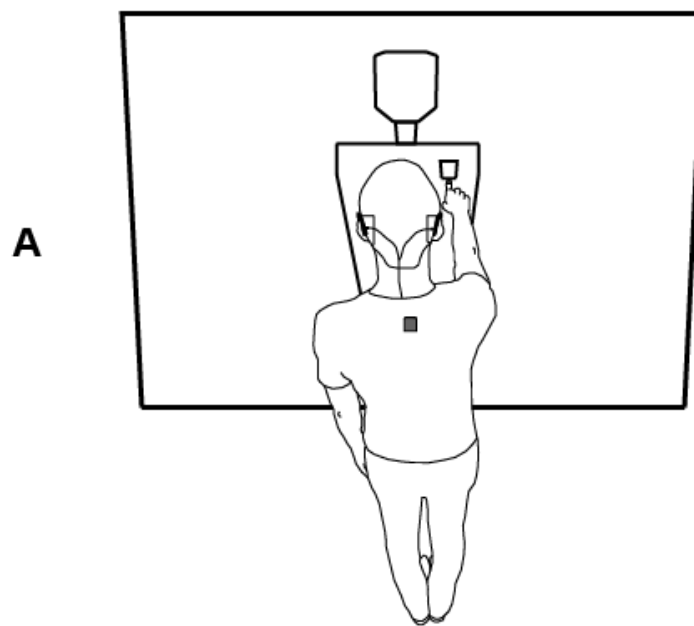
avatar mirrored the subject's movement, such that the target, fixed to the avatars trunk, moved relative to the subject's body sway. Before a trial began, subjects voluntarily swayed left and right to show that the avatar and the reach target were fixed to their movement. In contrast, in conditions when the target was earth-fixed, the avatar did not mirror the subject's voluntary movement and remained fixed in the start position, such that the subject moved relative to the target.

Once the subject had established whether the reach target was body-fixed or earth-fixed, they stood in the start position (stood upright). After 2s of quiet standing, an audio cue signalled the subject to begin reaching for the target fixed to the avatar (Figure 2.2B). Upon the onset of reaching (signalled by release of the trigger) vision was occluded (translucent spectacles became opaque) and in 2/3 of trials GVS (2mA, 4s) was applied (as in experiment 1). To maintain the duration of the reach movement to approximately 2s, three audio cues of increasing pitch were played to indicate onset of the reach (beep 1), +1s (beep 2), and +2s (beep 3). Therefore the subject could time the movement to finish on the 3<sup>rd</sup> audio cue. The reaching action was practiced 3 times before recoding began. 6 trials were completed for each condition in a randomised order; 3 GVS (AL, AR, NO-GVS) X 2 tasks (body-fixed, earth-fixed), giving 36 trials in total.

### *Analysis*

As pilot data were collected from only 3 subjects, only descriptive analysis was carried out. Hand and trunk lateral position were analysed for individual subjects. Data were averaged across trials and fixed to time of reach onset. Trunk position was

subtracted from hand to give hand-on-trunk position. Position at end of GVS was used as a measure of endpoint position and compared descriptively between GVS conditions (AL, AR, NO-GVS) and tasks (body-fixed and earth-fixed).



**Figure 2.2. Experiment 2 setup and reach action.** A) Subjects stood with feet together facing a rear projection screen. Motion capture sensors were fixed to the right index finger and back. GVS was applied through electrodes placed on the mastoid processes. PLATO translucent spectacles were worn to occlude vision on reach onset. A trigger fixed to the left side of the chest and held down when the hand was in the start position. Projected onto the screen was a life-sized avatar with

a target fixed on the right side of the avatar's chest, aligned with the subjects shoulder. The subject's arm is shown in the endpoint position of the reach. *B*) The reaching action performed as seen from above. At the start of the trial the right index finger presses down on a trigger positioned on the left side of the chest. On an audio cue the reach begins towards the target located on the avatar. The reach duration is controlled by audio cues at 1s (arm halfway through reach) and 2s (final arm position).

## **2.3. Results**

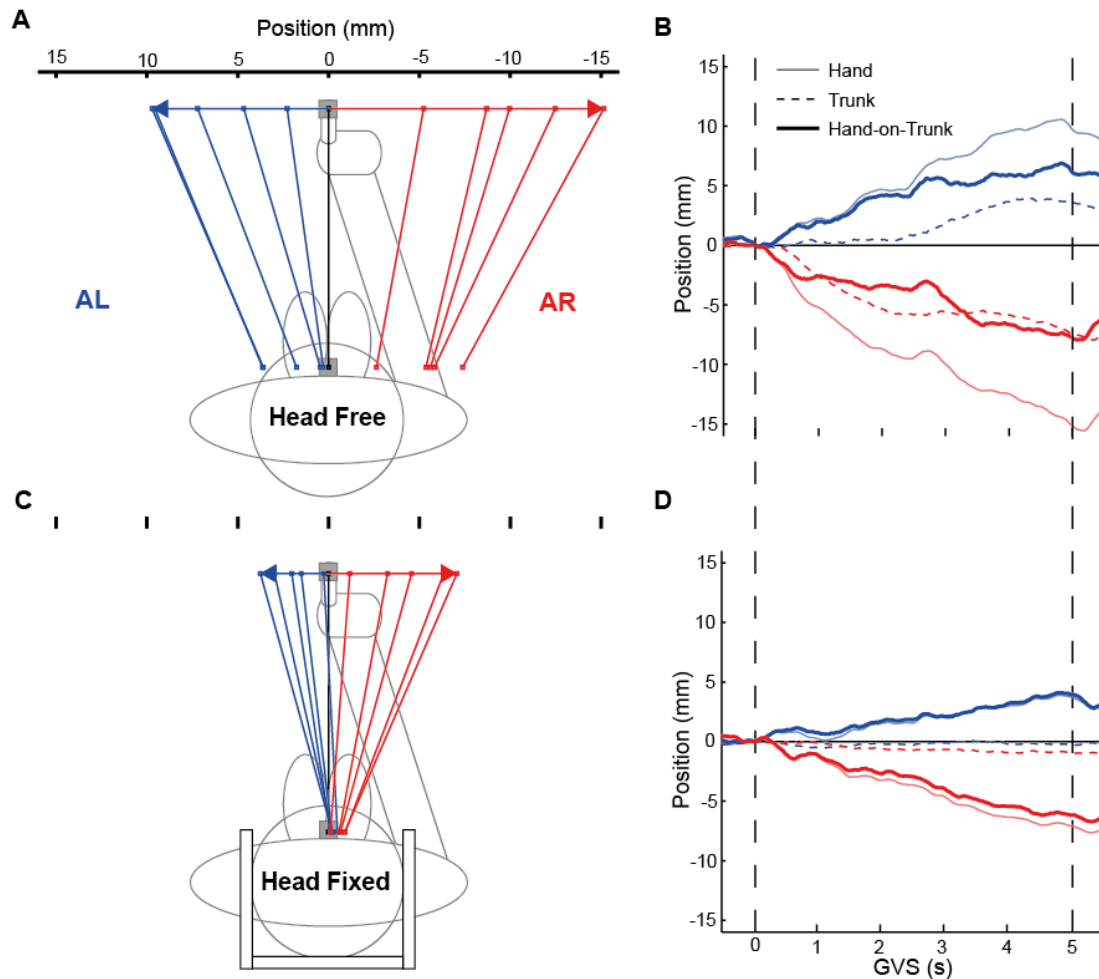
### **Experiment 1**

GVS-evoked hand and trunk responses when standing freely and standing with the head fixed-in-space were compared.

Lateral hand and trunk response during GVS for a representative subject are summarised in Figure 2.3. When the head was free of restraint (Figure 2.3A, *B*), the hand and trunk both moved laterally towards the direction of the anodal ear. Hand movement was greater than trunk movement, producing hand-on-trunk movement towards the anode. When the head was fixed in space (Figure 2.3C, *D*), trunk movement was minimal. However, hand movement towards the anode persisted, although reduced compared to the head free condition. This produced hand-on-trunk movement of a similar magnitude to the head free condition.

Average hand, trunk, and hand-on-trunk kinematics throughout GVS are shown in Figure 2.4. Average position kinematics (Figure 2.4A, *B*) reflect the representative subject data (Figure 2.3B, *D*). From the velocity traces, it is clear the hand response

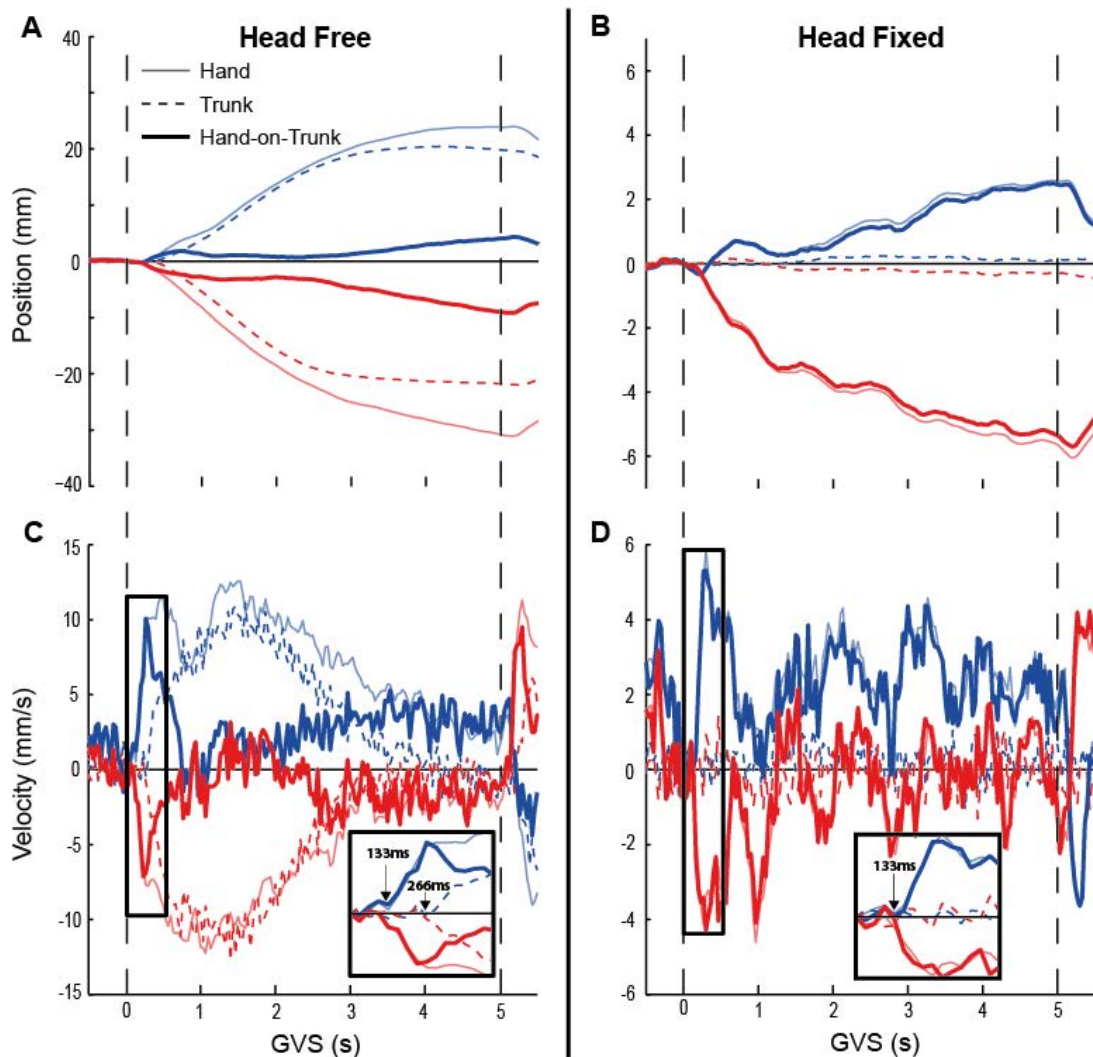
(~133ms) begins prior to any trunk response (~266ms) in the head free condition (Figure 2.4C), with similar hand response onset when the head was fixed (Figure 2.4D).



**Figure 2.3. Hand and trunk response of a representative subject.** A & C) Lateral position deviation of the hand and trunk plotted at 1s time points throughout the 5s GVS stimulus, in the head free (A) and head fixed (C) condition. Anode-left (AL) and anode-right (AR) stimulus are shown as blue and red data points, respectively. The black points show hand and trunk position at GVS onset (set to 0). The hand moves in the direction of the anode for each consecutive second of GVS, in all conditions. Lines connecting trunk and hand position show hand-on-trunk movement. In the absence of any hand-on-trunk movement the line would remain completely vertical. B & D) Lateral hand, trunk, and hand-on-trunk position throughout GVS, in the head free (B) and head fixed (D) conditions. Position is set to zero at GVS onset. Positive



and negative values indicate leftward and rightward deviation respectively. Vertical dashed lines indicate GVS onset and end.



**Figure 2.4. Average hand, trunk, and hand-on-trunk kinematics.** Lateral hand (thin solid line), trunk (dashed line), and hand-on-trunk (thick solid line) position (A & B) and velocity (C & D) during GVS with the head free (Left) and head fixed (Right). Blue and red traces separate anode-left and anode-right stimulus, respectively. Vertical dashed lines show GVS onset and offset. Positive values indicate deviation to the left, and negative to the right. Note the scales for the head fixed condition are considerably smaller than the head free. For velocity traces, the first 500ms of GVS has been magnified to highlight onset of the response.

Hand, trunk, and hand-on-trunk response magnitudes (peak position deviation towards the anode) are shown in Figure 2.5A. When the head was free, both AL and

AR GVS evoked significant hand, trunk, and hand-on-trunk responses (response magnitudes compared to 0;  $t_{(5)} \geq 4.80$ ,  $P \leq 0.005$ ).

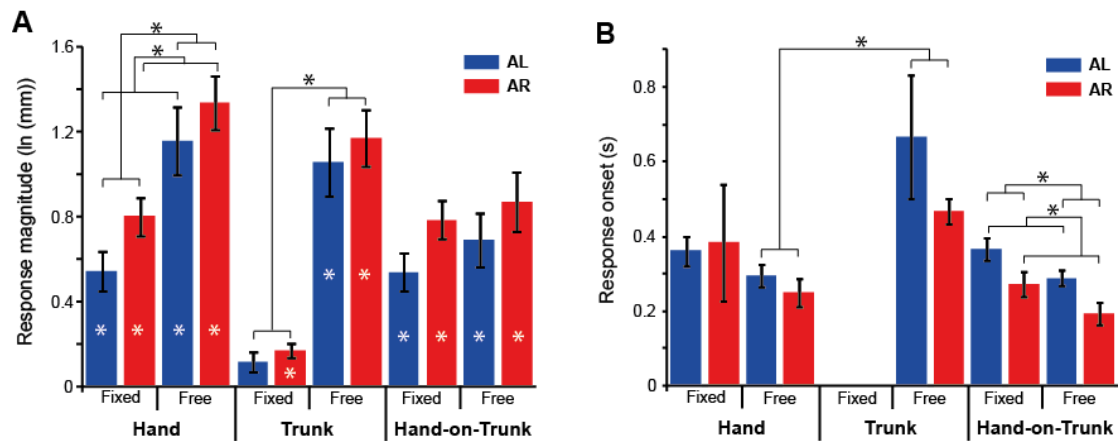
When the head was fixed, trunk responses were significantly reduced compared to the head free condition (main effect of head restraint:  $F_{(1,5)} = 28.98$ ,  $P = 0.003$ ), with response magnitudes only significantly greater than zero for AR stimuli ( $t_{(5)} = 4.39$ ,  $P = 0.007$ ), but not AL ( $t_{(5)} = 2.25$ ,  $P = 0.074$ ). However, a post-hoc power analysis (G\*Power; Erdfelder *et al.*, 1996) revealed that based on the effect size ( $d = 0.92$ ), a total of 18 subjects would have been needed to obtain statistical power (power = 0.95) for the AL condition. This suggests that limited statistical power because of the modest number of subjects ( $N = 6$ ) may be a cause in limiting the significance of this comparison, i.e., a Type II error.

There was a significant hand response present for both polarities with the head fixed ( $t_{(5)} \geq 5.15$ ,  $P \leq 0.004$ ), albeit reduced compared to the head free condition (main effect of head restraint:  $F_{(1,5)} = 20.92$ ,  $P = 0.006$ ). This hand movement produced significant hand-on-trunk responses ( $t_{(5)} \geq 4.80$ ,  $P \leq 0.005$ ) of similar magnitude to the head free condition ( $F_{(1,5)} = 2.40$ ,  $P = 0.182$ ). Therefore, restraining the head reduced the magnitude of GVS-evoked hand and trunk movement, but the magnitude of hand-on-trunk movement remained the same with or without restraint.

Surprisingly, AR responses tended to be greater in magnitude than AL responses across all conditions. However, this difference was only significant for the hand

response ( $F_{(1,5)} = 9.50$ ,  $P = 0.027$ ), but not the trunk ( $F_{(1,5)} = 3.42$ ,  $P = 0.124$ ) or hand-on-trunk response ( $F_{(1,5)} = 4.83$ ,  $P = 0.079$ ). These non-significant comparisons may also be the product of Type II error, as a post-hoc power analysis revealed that if the subject cohort was increased by 2, this would have been enough to obtain statistically significance differences in response magnitudes between GVS polarities for both the trunk and hand-on-trunk responses based on the effect sizes given (trunk:  $d = 0.83$ , hand-on-trunk:  $d = 0.98$ ).

Average response onset data (derived from velocity traces in Figure 2.4C, D) are shown in Figure 2.5B. There was no significant effect of GVS polarity ( $F_{(1,5)} = 0.02$ ,  $P = 0.904$ ), or head restraint ( $F_{(1,5)} = 2.39$ ,  $P = 0.183$ ) on the hand response onset. Mean (SD) hand onset across conditions was 0.32s ( $\pm 0.06$ ). Due to minimal trunk movement during the head fixed condition, trunk velocity did not cross the threshold for onset measurement ( $> 2$  SD baseline), therefore no response onset time was taken. In the head free condition, trunk onset was not significantly affected by GVS polarity ( $t_{(5)} = 1.08$ ,  $P = 0.330$ ). Trunk response onset was compared to the hand response onset in the head free condition. Mean trunk onset was 0.57s ( $\pm 0.14$ ), significantly later (+0.24s) than the hand response ( $F_{(1,5)} = 13.95$ ,  $P = 0.014$ ), confirming hand movement towards the anode prior to any trunk movement in the head free condition. For hand-on-trunk response onset, there was significant main effect of head restraint condition ( $F_{(1,5)} = 22.27$ ,  $P = 0.005$ ) and GVS polarity ( $F_{(1,5)} = 6.91$ ,  $P = 0.047$ ), with response onsets faster when the head was free compared to fixed, and faster during AR stimuli compared to AL.



**Figure 2.5. Average hand, trunk, and hand-on-trunk response magnitude and onset.** A) Hand, trunk, and hand-on-trunk response magnitudes (peak position deviation towards the anode) during GVS for the head free and head fixed conditions. Blue and red bars separate anode-left (AL) and anode-right (AR) stimulus, respectively. Note that response magnitudes were logarithmically transformed (ln) due to between subject variability. Anode-right data has been inverted to compare deviation magnitude. Standard error bars shown. Significant response magnitudes compared to zero (i.e., NO-GVS) are denoted by a \* within the bars. Significant differences between head restraint conditions and GVS polarity are also shown (\*). B) Time of response onset (velocity > 2SD of baseline). Significant differences between hand and trunk response onsets are shown. Note that no response onset was measured for the trunk in the head fixed condition, as trunk velocity did not meet threshold. Significant effects of head restraint condition and GVS polarity are also shown for hand-on-trunk response onset times.

## Experiment 2

GVS-evoked arm responses when reaching for an earth-fixed target and a target that was fixed relative to body position (body-fixed) were compared descriptively. Hand, trunk, and hand-on-trunk kinematics for each subject are shown in Figure 2.6.

### Hand

In all conditions, the hand moved from left to right, as it moved from the start position (left side of subject's chest) to the end position (arm outstretched aligned

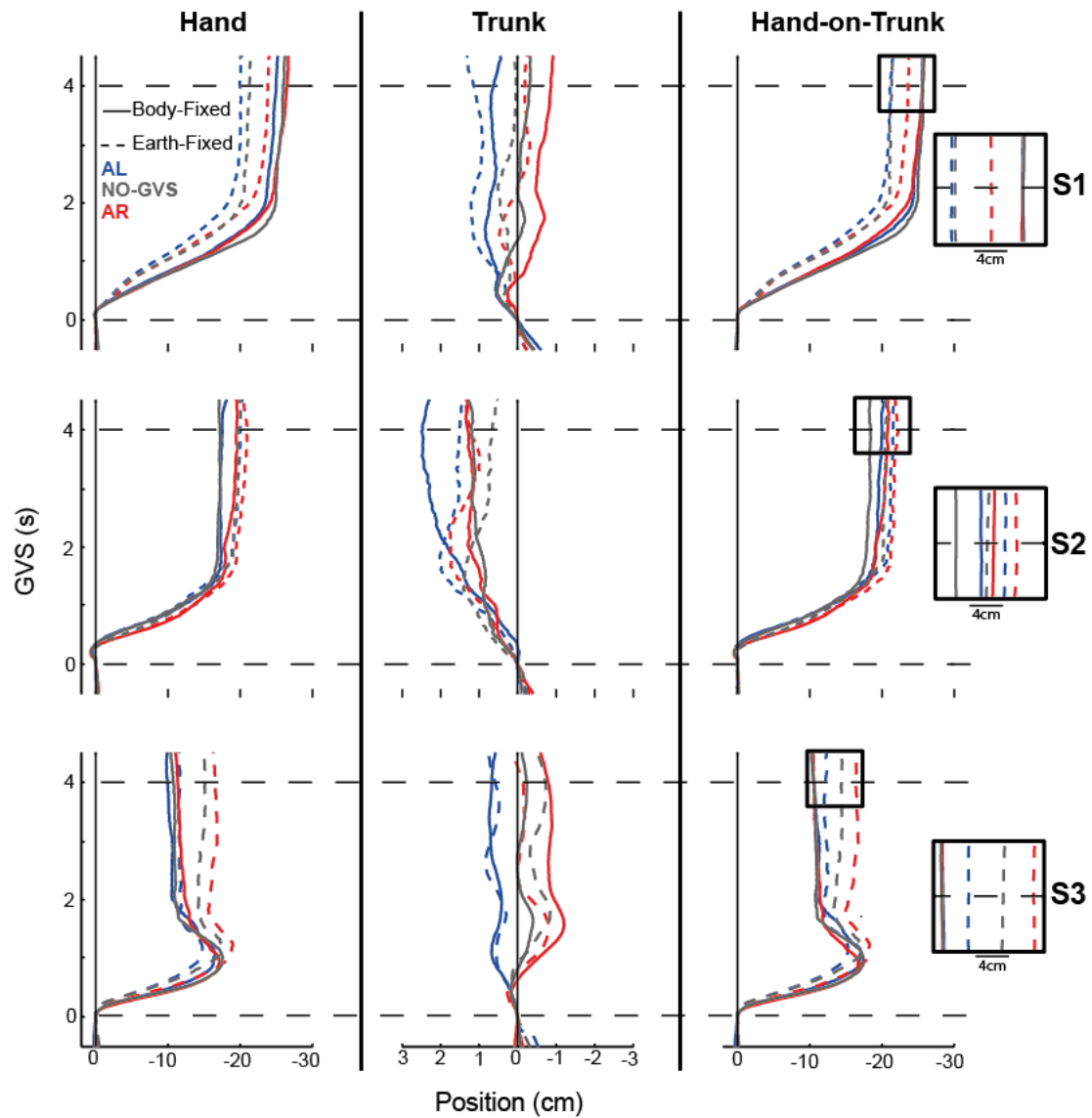
with right shoulder). In subjects 1 (S1) and 3 (S3), GVS deviated the hand towards the anode when reaching for the earth-fixed target (left column of graphs; Figure 2.6). In contrast, hand endpoint positions were similar across GVS conditions when reaching for the body-fixed target. Although subject 2 showed hand deviation when GVS was applied in both the earth- and body-fixed tasks, this deviation was not polarity-dependant, with hand endpoint position towards the right regardless of stimulus polarity.

### *Trunk*

Trunk movement was varied between subjects (centre column of graphs; Figure 2.6). In NO-GVS trials, trunk movement was minimal for S1 and 3, however S2's trunk position deviated to the left. When GVS was applied, S1 showed trunk movement towards the anode in both tasks. For S3, this was the case only for the body-fixed task. In the earth-fixed task for S3 and both tasks for S2, both AL and AR stimuli deviated the trunk to the left of the NO-GVS condition.

### *Hand-on-trunk*

For S1 and 3, there was no effect of GVS on hand-on-trunk endpoint in the body-fixed task (right column of graphs; Figure 2.6). In contrast, there was a clear polarity-dependant effect in the earth-fixed task for S3. This was less clear for S1, with AR stimuli producing a clear deviation towards the anode, but minimal deviation produced for LA stimuli. For S2, there was no GVS polarity-dependant effect in either task, with the hand-on-trunk deviating to the right of the NO-GVS condition regardless of GVS polarity or task.



**Figure 2.6. Hand, trunk, and hand-on-trunk kinematics for three subjects.** Hand, trunk, and hand-on-trunk lateral position whilst reaching for a body-fixed (solid traces) or earth-fixed (dashed traces) target, for subject 1 (S1), 2 (S2), and 3 (S3). Anode-left (AL, blue), anode-right (AR, red), and NO-GVS (grey) stimuli conditions are shown. Horizontal dashed lines indicate GVS onset and end. Positive and negative position values indicate leftward and rightward movement from start position, respectively. For hand-on-trunk data, traces at time of GVS end have been magnified to highlight any endpoint differences between tasks and GVS conditions.

### *Summary*

To summarise, there may be a task-dependant GVS effect upon hand responses when reaching, with deviation of the limb only when moving in an earth-fixed reference frame. However, this finding was not consistent across the 3 subjects. Due to intra- and inter-individual variation in GVS-evoked trunk movement, it is hard to interpret hand-on-trunk results. Therefore a new study was designed (Chapter 3) to eliminate variation in GVS-evoked trunk movement, by passively moving the body (a rotating chair) and testing task dependency of GVS-evoked arm-on-trunk movement.

## **2.4. Discussion**

When standing and pointing at an earth-fixed target, electrical vestibular stimulation evoked lateral trunk and arm movement to compensate for a false sense of motion. The hand began moving before the trunk, and continually moved relative to the trunk, suggesting a coordinated contribution of the trunk and arm to maintain pointing accuracy. When non-vestibular input was made available, the magnitude of the hand response was minimised. This modulation of the response suggests that it was scaled to the magnitude of sensed self motion, as is reported for postural responses. Surprisingly, although the trunk response was minimal when body movement was restricted, arm-on-trunk movement persisted and was of similar magnitude as when the body was free of restraint.

Hand response directions were opposite for each GVS polarity but not of equal magnitude, with overall AL stimuli responses around 70% the magnitude of AR

responses. One possible explanation for these polarity differences are the mechanical differences between moving the right arm towards the left anodal side (horizontal adduction) and right anodal side (horizontal abduction).

When standing quietly, GVS evokes trunk movement towards the anode, consistent with a compensatory postural response to maintain balance (Day *et al.*, 1997). Here, the same response occurred when standing and pointing at the target. However, I found the trunk response was not wholly responsible for arm movement, as there was arm-on-trunk movement in the same direction. This finding is similar to the results of Mars *et al.* (2003), who measured arm movement when making a forward trunk and reaching action whilst sitting on a stool (no trunk restriction). GVS caused deviations in trunk movement as well as reach endpoint. Although both moved laterally towards the anode, trunk deviation was responsible for only 60% of arm movement, therefore final arm position was the consequence of arm-on-body movement (Mars *et al.*, 2003). My results showed trunk movement was responsible for ~90% of the arm response, but nevertheless significant arm-on-body movement was observed. A possible biomechanical explanation for the arm-on-body movement is that the maximum range of lateral trunk movement may have been less than was required to fully compensate for the sensed movement. In this case additional arm-on-trunk movement would be necessary to maintain pointing accuracy. Furthermore, the arm response began significantly earlier than any trunk movement, demonstrating the arm responded independently of the trunk. The latency of EMG responses to GVS in postural muscles has been shown to increase with distance from the brain stem, with longer latencies in the leg (100ms) compared to the back (60ms)



(Ali *et al.*, 2003). Therefore the earlier arm response could be attributed to a shorter pathway between arm and brain compared to leg/trunk. However, mechanical differences between the upper limb and trunk may provide an alternative explanation. Due to the lower inertial properties of the arm versus the trunk (Chandler *et al.*, 1975), less force would be required to accelerate the arm. This may explain why arm movements were detected earlier than then the trunk. Although the arm responded earlier than the trunk, arm-on-trunk movement was continual throughout the duration of GVS (Figure 2.4A). This suggests the arm-on-body movement was in constant compensation for the sensation of motion, and not just a 'reflex' response of the upper limb at the onset of stimulation. Therefore it is likely a coordinated combination of trunk motion and movement of the arm relative to the trunk was used to maintain pointing accuracy in the face of vestibularly sensed whole-body motion (Mars *et al.*, 2003).

Alternatively, the arm-on-body movement found in my experiments could be attributed to limitations in the measurement of these responses. Firstly, because the height of the motion captures sensors that recorded trunk and hand position were not kept exactly the same (although they were similar as the hand was maintained at shoulder height and the trunk sensor was positioned on the sternum), lateral body sway about the ankle joint (i.e. an inverted pendulum) would produce greater lateral translation for the higher sensor (most likely the hand in this case) compared to the lower sensor for the same amount of angular displacement relative to vertical (i.e. standing upright). To control for any difference in sensor height, responses could have been measured as angular variables. Secondly, GVS has been found to evoke

perceptual (Day & Fitzpatrick, 2005) and motor responses (Osler & Reynolds, 2012) corresponding to a signal of yaw motion, with maximal responses when the GVS rotation vector ( $19^\circ$  above Reid's plane; Fitzpatrick & Day, 2004) is vertical, and minimal when horizontal. As the arm was extended out in front of subjects in my experiments, any trunk yaw rotation would result in lateral arm-on-trunk translation. Here, the head was in a 'natural' position facing straight ahead. Thus if we assume Reid's plane was horizontal, the GVS rotation vector would be above horizontal, suggesting a yaw component of the signal would be present. These limitations must be taken into consideration when interpreting the arm-on-body movement found in these experiments.

Previous research has shown GVS to influence upper limb movement in a variety of body postures. This occurs when reaching towards earth-fixed targets, both during sitting (Bresciani *et al.*, 2002*b*; Mars *et al.*, 2003; Moreau-Debord *et al.*, 2014) and standing (Bresciani *et al.*, 2002*a*). It has also been demonstrated when maintaining arm position in space, similar to the current experiments, but while seated in a fixed chair (Pu *et al.*, 2012). As shown here, the direction of the evoked arm movement is consistently towards the anode electrode. This arm movement is interpreted as a counteractive response to sensed body motion, to maintain arm trajectory in space. But if so, the response should scale with perception of body motion. Specifically, it should be attenuated when self motion perception is suppressed. Such attenuation has been demonstrated for postural responses to GVS, where response magnitude is inversely related to the availability of veridical sensory information (Day *et al.*, 2002). For example, opening the eyes or making light contact with an earth-fixed object

both provide no mechanical support, nor eliminate the need for balance, but do attenuate the sway response to GVS (Britton *et al.*, 1993; Day & Guerraz, 2007). Similarly, even when the trunk is unsupported (i.e. sat on a stool), trunk sway responses are suppressed when seated versus standing (Day & Cole, 2002; Day & Reynolds, 2005; Blouin *et al.*, 2007). This suggests that the magnitudes of postural responses are highly dependent on the stimulus evoking a sense of body motion, which in turn is dependent on the amount of veridical sensory information available. However, when we consider the upper limb, the existing literature is ambiguous on this crucial point. In particular, Bresciani *et al.* (2002a, 2002b) found that GVS-evoked perturbations of reach trajectory were of similar magnitude when standing versus sitting. Other authors have also demonstrated significant effects of GVS upon arm movement while sitting in fixed chairs (Pu *et al.*, 2012; Moreau-Debord *et al.*, 2014). When I fixed the head such that trunk motion was restricted, hand movement in-space was reduced ~73% compared to when standing freely. If magnitude of sensed whole-body motion was equal when the head was fixed compared to standing freely, the hand would have had to compensate the same amount in both conditions to maintain pointing accuracy. The fact this was not the case suggests sensation of body motion was attenuated by the additional somatosensory input provided by the head restraint, therefore the hand compensated less. This finding demonstrates the upper limb response is relative to sensed self motion as is found for vestibular-evoked postural responses (Britton *et al.*, 1993; Day *et al.*, 2002). However, although the upper limb response was attenuated, it was not entirely abolished. The small hand movement made when trunk movement was restricted produced arm-on-trunk movement of similar magnitude compared to when standing

without restraint. Furthermore, the response onset latency was also similar with or without trunk movement restrained. These findings are similar to previous studies that have demonstrated vestibular-evoked arm movements when trunk motion is restricted (Bresciani *et al.*, 2002*a*, 2002*b*; Pu *et al.*, 2012; Moreau-Debord *et al.*, 2014). Here, it seems even though the head was fixed in-space, a sensation of whole-body motion remained when GVS was applied, albeit smaller than when free of restraint. Because trunk movement was restricted, only the arm was able to compensate for sensed motion, hence why the arm moved on trunk. The finding that the arm-on-trunk response was the same magnitude when the head was fixed compared to when standing freely could be interpreted as the manifestation of a ‘hard-wired’ reflex. That is, a fixed relationship between vestibular input and upper limb output, regardless of other sensory cues. This seems unlikely. It may just be coincidental that the arm-on-body movement produced in coordination with trunk movement when standing free of restraint just happened to be similar to the magnitude of arm compensation required for the smaller sensed whole-body motion when the head was fixed. Alternatively, methodological limitations already highlighted may have played a role in producing artificial arm-on-body movement.

In the first experiment, there were some non-significant statistical comparisons that may have been significant if the number of participants recruited had been greater ( $\geq 8$ ), as revealed by a post-hoc power analysis. This limitation of underpowered comparisons must be taken into consideration when interpreting the statistical findings, with potential Type I and II errors being made. However, the main finding of

a large difference in magnitude of arm responses between head restraint conditions was very clear, both descriptively and statistically.

To further investigate the functional use of GVS-evoked arm responses, preliminary pilot data was collected to test whether such responses depend on the relevance of vestibular input to the task performed (experiment 2). When reaching in an earth-fixed reference frame, it is necessary to compensate for body motion relative to the target to maintain reach accuracy. On the other hand, reaching in a body-fixed reference frame requires no such compensation for whole-body motion relative to the target, thus vestibular input is irrelevant to maintain reach accuracy. If vestibular-evoked arm movements are compensatory in nature, I hypothesised they should only be observed when reaching for an earth-fixed target. For 2 out of 3 subjects, hand position was unaffected by GVS when reaching in a body-fixed reference frame. In contrast, when reaching for an earth-fixed target, GVS deviated the hand towards the anode. These results suggest GVS-evoked arm movements are dependent on the task requiring compensation for self motion. It must be stressed that this preliminary data is entirely descriptive and no statistics were applied. The fact a reaching action was made whilst standing free of any restraint, allowed balance responses to occur. Trunk movement across conditions was not consistently polarity-dependant, making interpretation of hand-on-trunk motion difficult, and may be a reason arm responses were variable between subjects. An explanation for variable trunk responses was that subjects were performing a reaching action from left to right. This action itself would have evoked balance responses (Cordo & Nashner, 1982), contaminating the whole-body movement to GVS and subsequently

any arm response. To remove any effect of balance responses on arm responses, in Chapter 3 I test task-dependency of arm responses by applying GVS simultaneously with passive body motion using a rotating chair, such that subjects feel they have been rotated further or less depending on GVS polarity (Day & Fitzpatrick, 2005). Using this method it was possible to eliminate balance responses but still evoke a false perception of whole-body motion, allowing testing of arm responses for vestibular sensed body motion, uncontaminated by postural responses.

My findings suggest vestibular evoked arm movements are relative to the magnitude of sensed self-motion and are only apparent when moving the limb in an earth-fixed reference frame. Therefore, it is likely that these vestibular evoked movements are compensatory in order to maintain reaching accuracy. However, further study is required to further understand the compensatory nature of these arm movements due to limitations in the experiments used in this chapter.

## **CHAPTER 3**

### **VESTIBULAR FEEDBACK MAINTAINS REACHING ACCURACY DURING BODY MOVEMENT**

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It has been proposed that vestibular signals are used to control reaching during unexpected body motion that would otherwise take the limb off-target. Vestibular-evoked arm movements during reaching provide some evidence for such a mechanism, however, the research to date is ambiguous on the precise nature and function of these evoked movements. For such a mechanism to be functional, it should only operate when the arm is being controlled in an earth-fixed rather than body-fixed reference frame. In the latter case, compensation would be unnecessary and even deleterious. To test this hypothesis, subjects were gently spun in a rotating chair while asked to maintain their outstretched arm pointing either towards earth-fixed (EF) or body-fixed (BF) memorised targets. Galvanic vestibular stimulation (GVS) was applied concurrently during rotation to isolate the influence of vestibular input, uncontaminated by inertial factors. During the EF task, GVS produced large polarity-dependent corrections in arm position. These corrections mimicked those evoked by real changes in chair velocity, indicating a compensatory arm response to a sensation of altered body motion. In stark contrast, corrections were completely absent during the BF task, despite the same chair movement profile and arm posture. These effects persisted when I controlled for differences in limb kinematics between the two tasks. The results demonstrate that vestibular control of the upper limb maintains the accuracy of hand placement in the face of unpredictable body

motion. Gating of the response according to the task goal emphasises its functional utility.

### **3.1. Introduction**

When reaching for an object, we must be able to compensate for any unexpected body motion that may take the limb off-target. Vestibular-evoked arm movements during reaching provide some evidence for a link between vestibular sensed self motion and upper limb control (Chapter 2). However, the precise nature and function of these arm responses remains unclear. In Chapter 2, I presented preliminary results which hinted vestibular-evoked upper limb responses are task-dependant. However, due to limitations in the methods used (see Discussion, Chapter 2), the results were inconclusive and require further investigation.

Vestibular-evoked balance responses are task-dependant (review by Forbes *et al.*, 2014). When tasked with maintaining an upright posture, galvanic vestibular stimulation evoked muscle responses are dependent on the muscles contribution to balance. For instance, lower limb muscle responses are absent when subjects are seated, or suppressed when standing subjects were fully supported by a backboard (Britton *et al.*, 1993; Fitzpatrick *et al.*, 1994; Luu *et al.*, 2012). Furthermore, vestibular responses were abolished when subjects, fully supported in a standing position (strapped to a rigid post preventing body sway related to ankle movement), used their feet to balance a body-equivalent freely moving weight (Fitzpatrick *et al.*, 1994; General Introduction, Figure 1.3C). This task mimics somatosensory cues



(proprioception, cutaneous) during normal standing but vestibular input is incongruent. This observation suggests that not only must the muscle be engaged in maintaining balance, vestibular information must also be relevant to the task for GVS to evoke a response. The task-dependent nature of vestibular-evoked balance responses is not confined to lower limbs but also applies to the upper limb. When subjects stood on an unstable platform, such that active torques around the ankle could not maintain stability, instead, holding a support was the only means of maintaining balance, vestibular evoked upper limb responses were observed in the arm holding the support, but not in the relaxed arm (Britton *et al.*, 1993). The task dependant nature of vestibular evoked balance responses demonstrates they are only apparent when vestibular input is relevant and functional to the task being performed.

Here I determine if vestibular input can help to maintain arm accuracy by compensating for whole-body motion. If this compensatory mechanism is truly functional, it should only operate when the arm is being moved in an earth-fixed reference frame. When reaching for an earth-fixed object it is necessary to compensate for whole-body motion relative the object, therefore vestibular signals are relevant to the task. Such compensation would be unnecessary, and would actually impair movement accuracy, when operating in a body-fixed reference frame. I therefore test this hypothesis by comparing the effect of GVS upon the arm when performing tasks in both reference frames.

### 3.2. Methods

Participants were required to point with their arm while seated in a rotating chair. Two experiments were performed to investigate the effect of vestibular feedback upon arm movement. In both experiments, GVS was applied simultaneously with real motion to isolate the effect of pure vestibular input upon arm movement, unaffected by inertial forces. GVS applied during real motion alters perception of motion such that subjects perceived they have moved further or less, depending on electrode polarity (Fitzpatrick *et al.*, 2002; Day & Fitzpatrick, 2005). This effect is modulated by head orientation, being greatest when the naso-occipital axis is aligned with the axis of rotation, i.e. with the head tilted up or down during yaw motion (Day & Fitzpatrick, 2005).

The purpose of experiment 1 was to investigate task-dependency of the GVS response. This involved a comparison of pointing in a body-fixed versus earth-fixed reference frame. Since arm kinematics differed between these two tasks, experiment 2 was designed to control for this difference. Additionally, experiment 2 allowed the effect of GVS to be compared against real changes in rotation amplitude.

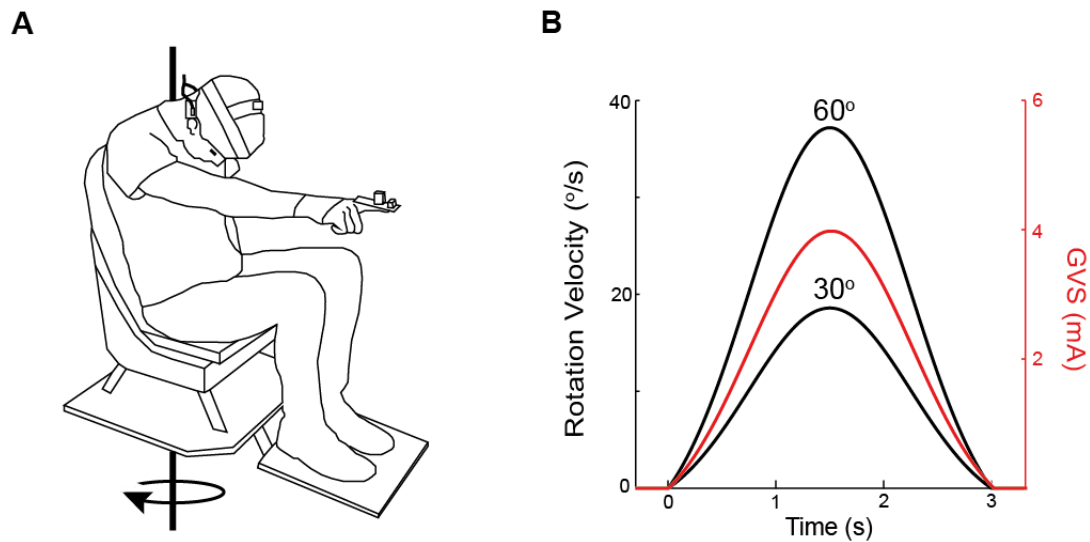
#### *Subjects*

Eight subjects completed experiment 1 (27.8yrs ( $\pm 7.4$ ); 5 males, 3 females) and experiment 2 (29.8yrs ( $\pm 5.8$ ); 6 males, 2 females). Subjects were healthy, with no known history of vestibular or neurological disorders. Ethical approval was obtained

from the University of Birmingham Ethics Committee and was in compliance with The Declaration of Helsinki, and informed consent was given.

### *Apparatus*

The experimental setup is illustrated in Figure 3.1A. Subjects sat on a motor-driven rotating chair which could be controlled with a precision of less than  $1^\circ$  (SD of displacement). They were secured by a four-point harness. Chair position and velocity were controlled and recorded at 1kHz using Real Time Windows Target in Simulink (The Mathworks Inc., USA). A motion tracking system (Fastrak, Polhemus Inc., USA) recorded arm and head movement at 33.33Hz. The arm sensor was placed over the fingertip, securely fixed to the end of a splint on the right index finger to minimise finger movement. A wrist support minimised wrist movement. During the period when vision was available at the beginning of each trial, subjects used a laser pointer attached to the same finger to guide their arm to the starting position. The head sensor was attached to the top of a welding helmet frame worn by the subject. Fastrak Euler angles were used to derive arm yaw and head pitch (see Reynolds, 2011 for further details).



**Figure 3.1. Experimental setup.** A) The subject is seated on a rotating chair with motion tracking sensors attached to the head and finger splint. A laser pointer on the splint provided visual feedback at the beginning of each trial when pointing to the target. A wrist support ensured the hand and forearm moved en bloc. GVS was applied via electrodes placed over the mastoid processes. B) Chair rotation profiles are shown for both rotation amplitudes alongside GVS current profile.

GVS currents were applied using gel-coated carbon rubber electrodes (46 x 37mm) placed over the mastoid processes in a binaural bipolar configuration. Stimuli were delivered from an isolated constant-current stimulator (Model 2200, A-M systems, USA). Peak current amplitude was 4mA for all trials, regardless of chair rotation velocity. Hence, effects of chair rotation amplitude could be analysed in isolation.

### *Experiment 1*

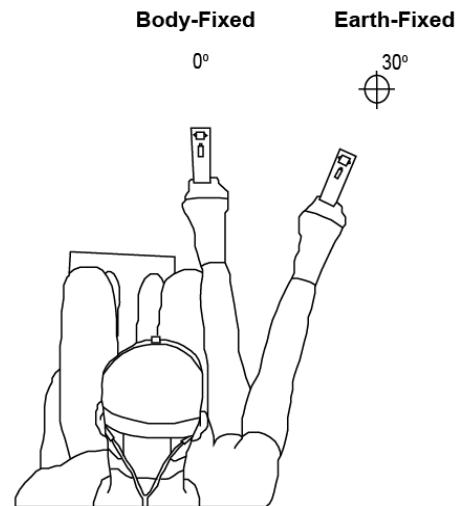
The purpose of experiment 1 was to determine if the effect of GVS depends upon the reference frame in which the arm is controlled. Earth-fixed (EF) versus body-fixed (BF) reference frame tasks were studied separately using a blocked design.

During EF trials subjects were instructed to point directly at a target attached to the wall of the room, situated  $30^\circ$  to their right (Figure 3.2). At the beginning of each trial they used the laser pointer to align their arm to this target. They then closed their eyes and tilted their head down as far as was comfortable, in order to maximise the effect of vestibular stimulation upon rotation perception. The mean angle of Reid's plane (a line joining the external auditory meatus and inferior orbital margin on each side) was  $45.23^\circ$  ( $\pm 6.02^\circ$ ) below horizontal. After 2s of baseline recording, the chair was then rotated with a Gaussian velocity profile (Figure 3.1B). Their task was simply to maintain the hand pointing towards the memorised target throughout the movement. Two magnitudes of chair rotation were used;  $30^\circ$  (peak velocity =  $18.6^\circ/\text{s}$ ) and  $60^\circ$  (peak velocity =  $37.2^\circ/\text{s}$ ), in both clockwise (CW) and counter clockwise (CCW) directions. Magnitude and direction were randomised. The duration of chair rotation was always 3.07s. A further 2s of data were recorded after rotation cessation. In  $2/3^{\text{rds}}$  of randomly-selected trials, GVS was applied simultaneously during chair rotation. The velocity signal used to drive the chair was used for the GVS stimulus, scaled to deliver a peak current of 4mA (see Figure 3.1B). GVS polarity was randomly switched to provide an equal number of cathode-left and -right trials.

BF trials were the same except for task instruction. Subjects were instructed to point straight ahead at the beginning of each trial, and to maintain the arm fixed with respect to their body throughout the movement.

Visual feedback of final arm position was not allowed for any condition.

This design resulted in 24 conditions: 2 tasks (EF, BF) x 2 directions (CW, CCW) x 3 GVS (NO-GVS, cathode-left, cathode-right) x 2 rotation magnitudes ( $30^\circ$ ,  $60^\circ$ ). 3 repeats of each condition were performed, resulting in 72 trials.



**Figure 3.2. Experiment 1 pointing tasks.** Starting position of arm in the body-fixed task ( $0^\circ$ ) and earth-fixed task ( $30^\circ$ ) during experiment 1.

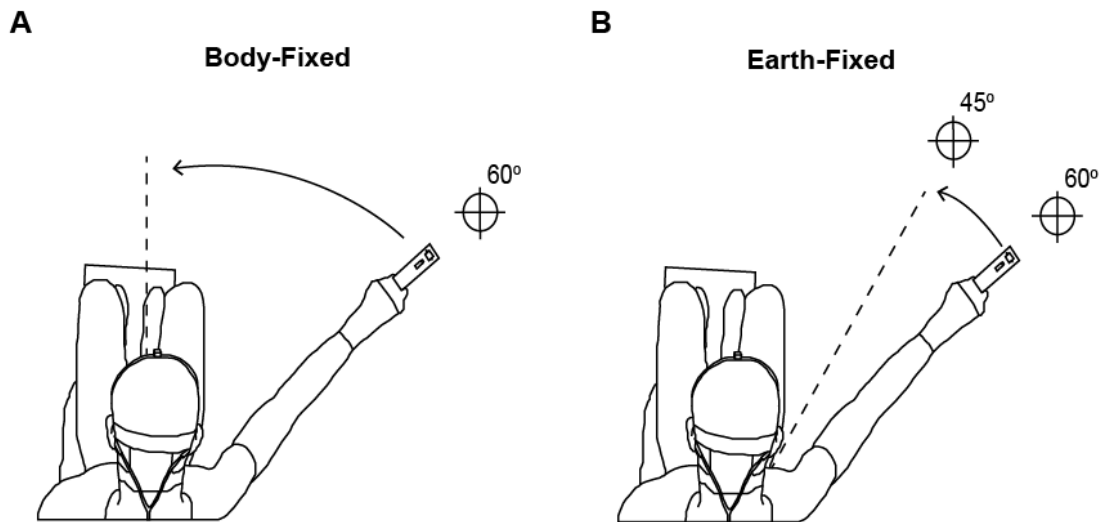
### *Experiment 2*

Experiment 1 is affected by a simple confound; the EF task requires active arm-on-body movement which is absent during the BF task. Hence, any difference in results might not be due to the different reference frames per se, but by different movement kinematics. Experiment 2 was designed to address this confound by matching arm-on-body movement between tasks.

For the BF task (Figure 3.3A), subjects started by pointing towards a target  $60^\circ$  to their right. When they felt chair motion, they were instructed to move their arm to their body mid-line (i.e. in front of their chest). They were asked to approximately

match the duration of arm movement with that of chair movement. In this way, the arm movement was approximately synchronised with chair rotation, whilst being performed in body coordinates. For the EF task (Figure 3.3B), subjects were instructed to point at the same starting target. Rather than simply maintaining the arm position here, as in experiment 1, they were asked to produce a small movement within an earth-fixed frame. Specifically, when chair rotation started they moved the arm from the  $60^\circ$  start position to a target  $45^\circ$  to their right. This ensured that some movement was performed within the EF reference frame. Chair rotation was restricted to  $60^\circ$  (peak velocity =  $37.6^\circ/\text{s}$ ) and the CW direction (experiment 1 showed no CW/CCW differences). GVS was applied in  $2/3^{\text{rds}}$  of randomly-selected trials, in the same way as for experiment 1. The head was similarly tilted downward and eyes closed throughout all trials. The mean angle of Reid's plane was  $67.24^\circ$  ( $\pm 13.34$ ) below horizontal. The design of the BF and EF tasks resulted in very well-matched movement kinematics, in terms of peak arm-on-body velocity (see grey bars in Figure 3.8D).

This resulted in a total of 6 conditions: 2 tasks (EF, BF) x 3 GVS (NO-GVS, cathode-left, cathode-right). 10 trials per condition were performed, resulting in 60 trials in total.



**Figure 3.3. Experiment 2 pointing tasks.** Starting position of arm was at  $60^\circ$  in both the body-fixed and earth-fixed pointing task. A) In the body-fixed task, the arm moved from the start position to align the arm with the subject's body midline. B) In the earth-fixed task, at the onset of chair rotation the subject moved their arm from the start position to the earth-fixed target located at  $45^\circ$ .

An obvious problem when attempting to match arm-on-body movement between EF & BF tasks, as described above, is ascertaining whether a person is following instructions; i.e. how does the experimenter know the person is genuinely attempting to point in the correct reference frame, if the movements look outwardly similar? To address this issue, I included a block of trials at the beginning of experiment 2, without GVS, where the amplitude of chair rotation was randomly altered (between  $50^\circ$ ,  $60^\circ$  and  $70^\circ$ ; equating to peak velocities of:  $31.3^\circ/\text{s}$ ,  $37.6^\circ/\text{s}$  and  $43.9^\circ/\text{s}$ ; always CW). The rationale was that this alteration should affect arm movement very differently between EF & BF tasks, but only if subjects are correctly following instructions. Specifically, rotation amplitude should only alter arm-on-body movement if moving the arm in an earth-fixed reference frame. Data from subjects who could not perform the tasks correctly (i.e. exhibit significant effect of rotation



amplitude in BF task) were excluded from further analysis (two of eight subjects were excluded, see Results). An additional benefit was to enable direct comparison of GVS-evoked arm movements with those evoked by real changes in rotation amplitude.

This resulted in 6 conditions: 2 tasks (EF, BF) x 3 rotation amplitudes ( $50^{\circ}$ ,  $60^{\circ}$  and  $70^{\circ}$ ). 5 repeats of each condition were performed, resulting in 30 trials.

### *Analysis*

All data were analysed using Matlab (The Mathworks Inc., USA). To compare the effect of conditions (GVS, tasks, rotation amplitudes) on arm response, arm displacement and velocity were measured for each condition. Arm displacement was calculated as the difference in arm-on-body position between the beginning and end of chair movement (mean yaw angle during 500ms window pre and post-movement). Arm velocity was derived by differentiating position before filtering (low-pass, 5Hz, 4<sup>th</sup> order, zero-phase-shift, Butterworth). Peak velocity was measured for each trial.

In experiment 1, CW and CCW rotations were combined due to no significant effect of rotation direction on arm displacement or velocity (see Results, experiment 1). Therefore, the conditions of experiment 1 consisted of 2 tasks (BF vs. EF), 2 rotation amplitudes ( $30^{\circ}$  vs.  $60^{\circ}$ ), and 3 GVS conditions (NO-GVS, cathode-same, cathode-opposite).

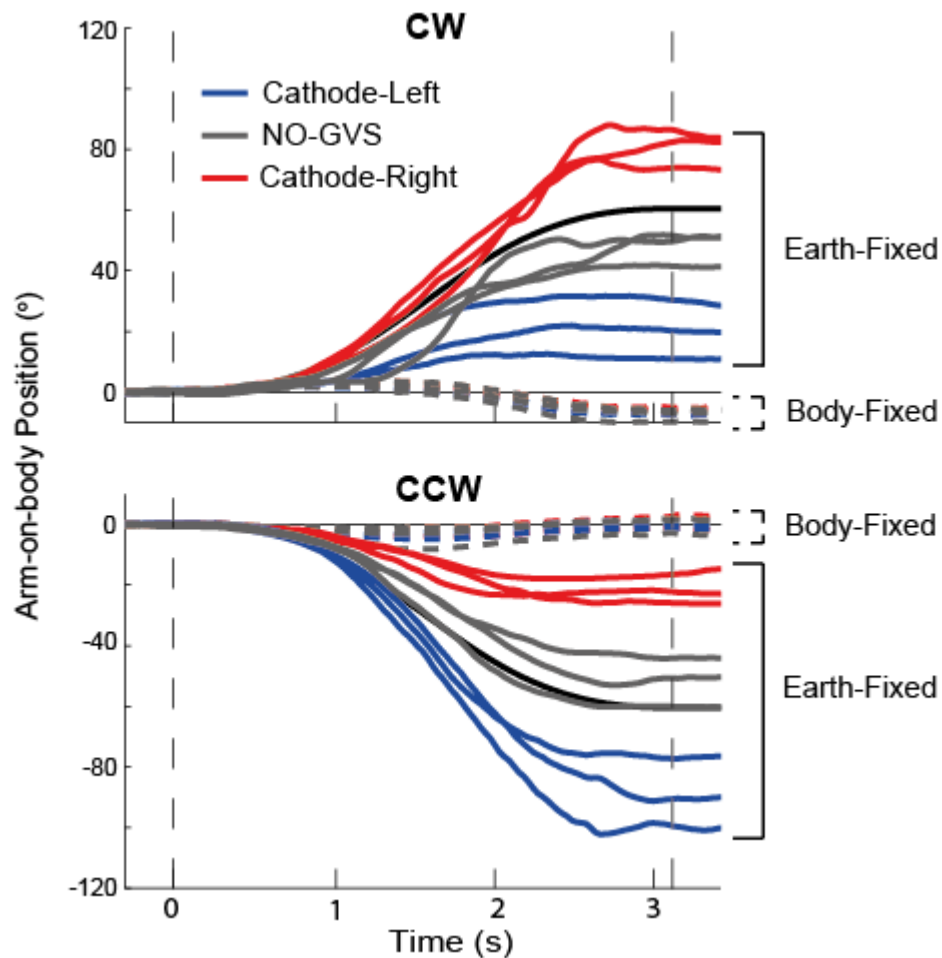
For statistical analysis of arm displacement and peak velocity, repeated-measures analysis of variance (ANOVA) was used to test for main effects and interactions between conditions (experiment 1: 2 tasks X 2 rotation amplitudes X 3 GVS; experiment 2: 2 tasks X 3 GVS, and 2 tasks X 3 rotation amplitudes). Pairwise comparisons (bonferroni corrected) were used to decompose significant ANOVA results. Paired samples t-tests were also used to compare overall arm displacement and peak velocity (difference between NO-GVS and GVS conditions) between chair rotation amplitudes (30°, 60°) in experiment 1, to see whether GVS-evoked arm movements were relative to rotation amplitude. Significance was set at  $P < 0.05$ . All statistical tests were performed using SPSS Statistics Version 19 (IBM, USA).

### **3.3. Results**

#### *Experiment 1*

Arm-on-body kinematics from a representative participant are shown in Figure 3.4 for the 60° rotation. The NO-GVS condition is shown by the grey solid and dashed lines, representing the EF and BF tasks, respectively. During the BF task the arm hovers around zero, indicating that it remained fixed with respect to the body. In contrast, during the EF condition the arm moves with respect to the body to compensate for chair rotation. This indicates that the subject moved within the appropriate reference frames. However, in the absence of GVS they exhibited a tendency to under-compensate by 10-20° in the EF task. When GVS was applied, it had markedly different effects during the two tasks. For the EF task, it increased the

amplitude of arm movement when chair movement was directed towards the cathodal ear (Figure 3.4, red solid lines for CW; blue solid lines for CCW). When chair movement was directed away from the cathode, the compensatory arm movement was smaller. In contrast, GVS had no effect during the BF task.

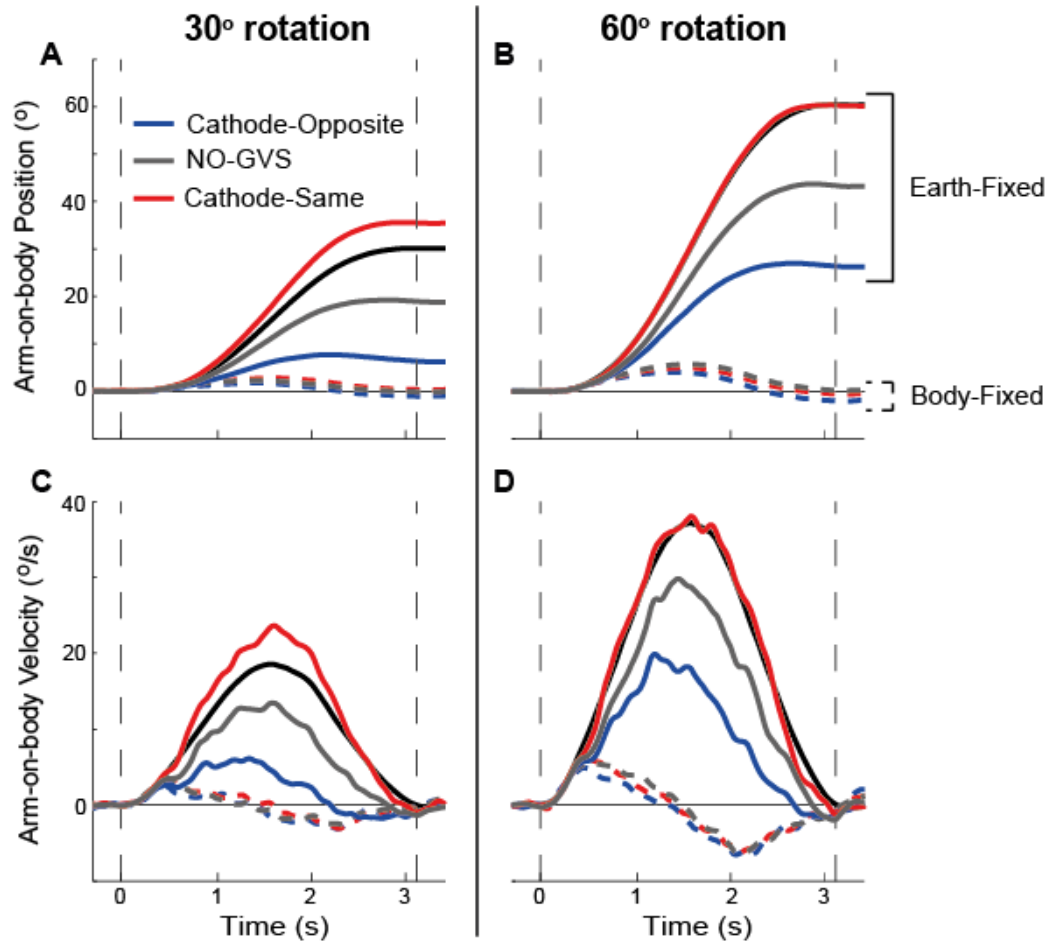


**Figure 3.4. Representative arm kinematics.** Traces depict arm-on-body orientation during 60° chair rotations. Positive values indicate leftward motion of the arm on the body. Chair orientation (in space) is shown by the solid black traces, which have been vertically flipped to aid comparison. Hence, a perfect compensatory movement during the earth-fixed condition corresponds here to an arm movement trace being identical to chair orientation. In contrast, a trace remaining at zero indicates that the arm remains completely fixed to the body during rotation. Vertical dashed lines indicate rotation onset and end. Note that in the body-fixed task, GVS conditions are overlapping.

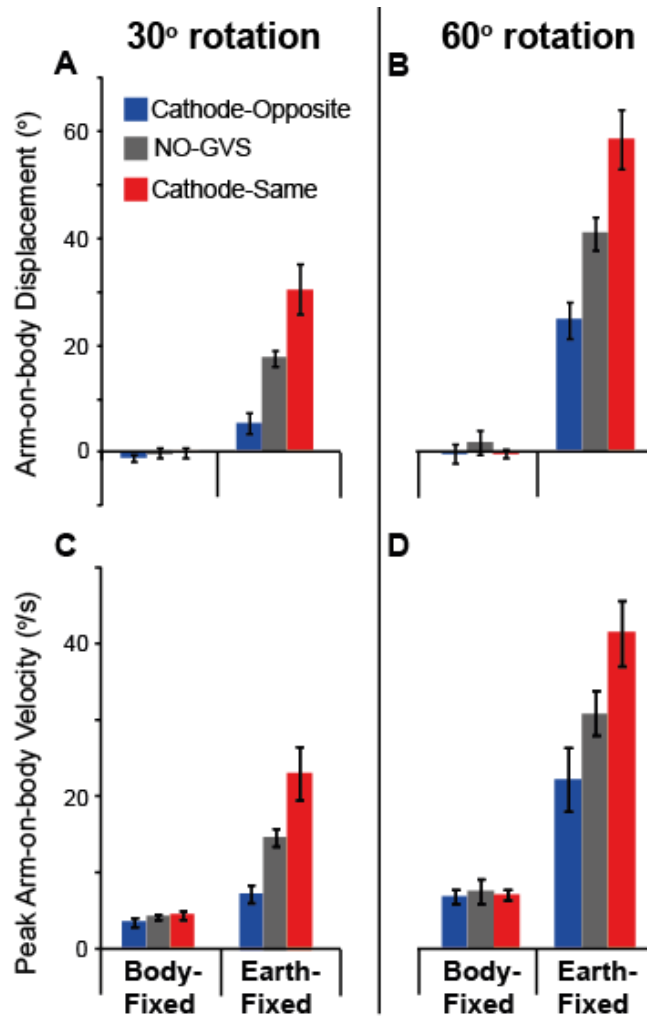
The effects observed in the representative subject can be seen on the mean traces in Figure 3.5, where arm velocity is also shown. Since rotation direction produced no significant effects upon arm displacement or peak velocity ( $F_{1,7} \leq 0.7$ ;  $P \geq 0.47$ ), both directions were combined after flipping CCW traces. GVS polarity is now referred to in terms of the cathodal electrode, being either on the same side, or opposite to, chair rotation direction. The slight velocity deflections apparent across all BF trials are consistent with inertial effects. During EF trials, the tendency to under-compensate without GVS, seen in the individual subject, is clearly apparent; mean (SD) under-shoot is  $12.4^{\circ}$  ( $\pm 4.0$ ) and  $19.4^{\circ}$  ( $\pm 8.5$ ), for  $30^{\circ}$  and  $60^{\circ}$  rotations respectively. This tendency actually causes GVS to improve performance during conditions where the cathode is on the same side as chair rotation (red traces in Figure 3.4). To statistically test whether the GVS evoked arm movements were only apparent during the EF task, as described for the representative subject, I tested for a main effect of task on mean arm displacement and peak velocity, and crucially whether there was an interaction between task and GVS (2 x 3 ANOVA). This test revealed a significant main effect of task on both arm displacement and velocity (Figure 3.6; EF vs. BF;  $F_{1,7} \geq 76.7$ ;  $P < 0.001$ ), with both exhibiting a significant interaction between task and GVS polarity ( $F_{2,14} \geq 11.1$ ;  $P < 0.001$ ). Further ANOVAs (1 x 3) used to test for main effect of GVS condition (NO-GVS, cathode-opposite, cathode-same) within each task (BF, EF) reveal that this interaction was due to the presence of a GVS effect during the EF task ( $F_{2,14} \geq 13.3$ ;  $P \leq 0.01$ ) but not the BF task ( $F_{2,14} \leq 1.9$ ;  $P \geq 0.18$ ). Furthermore, significant pairwise comparisons between GVS conditions within the EF task confirmed that the effect of GVS was polarity

dependant, with arm displacement and velocity greater during cathode-same stimuli compared to NO-GVS, and reduced during cathode-opposite stimuli (NO-GVS vs. cathode-opposite:  $P \leq 0.001$ ; NO-GVS vs. cathode-same:  $P \leq 0.012$ ; cathode-opposite vs. cathode same:  $P \leq 0.003$ ).

To see if the magnitude of GVS evoked arm displacements from NO-GVS conditions during the EF task were different between rotation amplitudes ( $30^\circ$  vs.  $60^\circ$ ), I measured the arm displacement difference between the cathode-same/opposite and the NO-GVS conditions, and combined the polarities to give an overall measure of GVS effect for both the  $30^\circ$  and  $60^\circ$  rotations. Paired samples t-tests were used to test for differences between rotation amplitudes. GVS evoked significantly greater arm deviation from baseline for the  $60^\circ$  rotation ( $30^\circ$ :  $12.5^\circ \pm 2.7$ ,  $60^\circ$ :  $16.9^\circ \pm 2.8$ ;  $t_{(7)} = 6.4$ ;  $P < 0.001$ ). However, in terms of percentage change (percentage difference between GVS and NO-GVS conditions), the effect of GVS was significantly smaller for the  $60^\circ$  rotation ( $30^\circ$ :  $72.2\% \pm 14.0$ ,  $60^\circ$ :  $41.6\% \pm 5.8$ ;  $t_{(7)} = 3.4$ ;  $P = 0.012$ ). Peak arm velocity showed a similar pattern, with rotation amplitude having no influence upon absolute difference ( $30^\circ$ :  $8.2^\circ/\text{s} \pm 1.3$ ,  $60^\circ$ :  $9.6^\circ/\text{s} \pm 2.5$ ;  $t_{(7)} = 0.72$ ;  $P = 0.5$ ), but having a large effect upon percentage difference ( $30^\circ$ :  $61.3\% \pm 11.3$ ,  $60^\circ$ :  $33.5\% \pm 7.7$ ;  $t_{(7)} = 2.9$ ;  $P = 0.022$ ). This suggests that GVS summates with, rather than multiplies, real movement sensations.



**Figure 3.5. Mean arm kinematics.** Traces depict mean arm-on-body position and velocity for both rotation amplitudes. CCW data have been reversed before combining with CW data. Positive values indicate leftward arm movement during CW rotations (and rightward arm movement during CCW rotations). Chair position and velocity are also shown in solid black for comparison. Vertical dashed lines indicate rotation onset and end. Note that in the body-fixed task, GVS conditions are overlapping.



**Figure 3.6. Mean arm displacement and peak velocity.** Arm displacement was calculated as the difference in arm-on-body orientation between the beginning and end of the trial. Peak velocity was taken as the maximum value of the differentiated position trace during the movement. Standard error bars are shown.

### *Experiment 2*

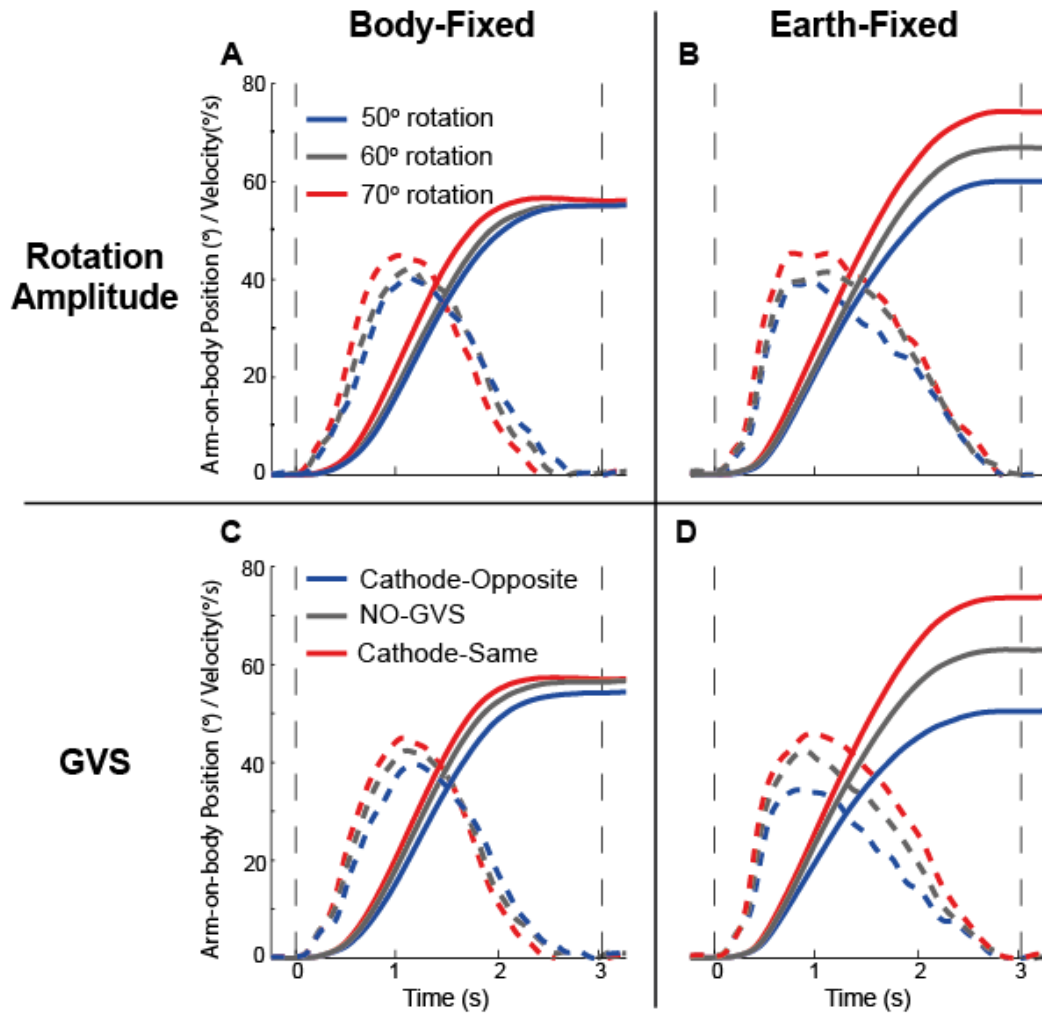
Experiment 2 addressed the confound of different arm kinematics between BF and EF tasks. Here, the tasks were altered to produce a similar arm-on-body movement. To determine if subjects were performing in the correct reference frame, I first randomly altered chair rotation amplitude between 50°, 60° and 70° in the absence of GVS. This should only affect arm-on-body motion during the EF, but not BF, task. However, within subject ANOVAs (BF task x 3 rotation amplitudes for each subject)

found two (of eight) subjects did exhibit a significant difference in hand displacement in the BF task ( $F_{2,8} \geq 4.91$ ;  $P \leq 0.041$ ), and were therefore excluded from further analysis. Mean kinematics for the remaining subjects are shown in Figure 3.7A and B. For arm displacement there is a significant interaction between rotation amplitude and task (Figure 3.8A; 2 tasks x 3 rotation amplitudes:  $F_{2,10} = 34.1$ ;  $P < 0.001$ ). A breakdown of this result reveals this is due to compensatory arm movements being larger with increasing chair motion during the EF task (EF task x 3 rotation amplitudes:  $F_{2,10} = 34.7$ ;  $P < 0.001$ , pairwise comparisons:  $50^\circ$  vs.  $60^\circ$ ,  $P = 0.015$ ;  $50^\circ$  vs.  $70^\circ$ ,  $P = 0.008$ ;  $60^\circ$  vs.  $70^\circ$ ,  $P = 0.004$ ) but not BF task (BF task x 3 rotation amplitudes:  $F_{2,10} = 1.0$ ;  $P = 0.40$ ). However, peak arm velocity does not exhibit the same interaction (Figure 3.8C;  $F_{2,10} = 0.23$ ;  $P = 0.80$ ). There is however a significant main effect of rotation amplitude on arm velocity during both tasks ( $F_{2,10} \geq 4.13$ ;  $P \leq 0.049$ ), although pairwise comparisons reveal no significant differences between rotation amplitudes for either task ( $P \geq 0.13$ ). The reason for this displacement/velocity discrepancy can be seen in the mean velocity traces for the BF task (dashed traces in Figure 3.7A). During the  $70^\circ$  rotation, arm velocity is initially higher (than the  $60^\circ$  rotation) but then immediately reduces for the remainder of the movement. The reverse is true for the  $50^\circ$  rotation. So while peak arm velocity is affected by rotation amplitude during the BF task, final arm position is preserved. This indicates that subjects moved in the appropriate reference frame.

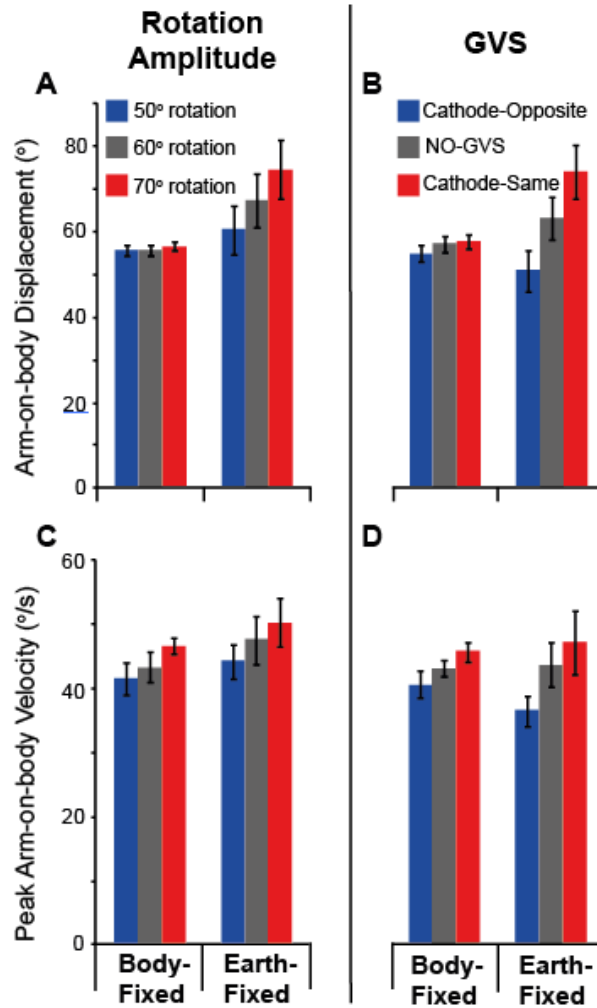
For these well-behaved subjects the effects of GVS were studied in a separate block of trials, with arm movement shown in Figure 3.7C and D. During the baseline no-GVS condition, peak velocities are closely matched between BF and EF tasks ( $43.0 \pm$



3.7°/s (BF) &  $43.6 \pm 9.8^\circ/\text{s}$  (EF); see also grey bars in Figure 3.8D). Despite this, GVS had different effects upon arm displacement (GVS-task interaction:  $F_{2,10} = 18.21$ ;  $P < 0.001$ ). A breakdown of this interaction (within task ANOVAs; 1 task x 3 GVS) confirms that GVS had no effect upon arm displacement during the BF task (Figure 3.8B;  $F_{2,10} = 3.89$ ;  $P = 0.057$ ). This contrasts with the EF task where compensatory arm movements were larger (smaller) with the cathode on the same (opposite) side as chair motion ( $F_{2,10} = 15.08$ ,  $P < 0.001$ ; pairwise comparisons: NO-GVS vs. cathode-same,  $P = 0.045$ ; NO-GVS vs. cathode-opposite,  $P = 0.014$ ; cathode-same vs. cathode opposite,  $P = 0.034$ ). However, similar to the effect of rotation amplitude, there was a main effect of GVS on peak arm velocity during both tasks (Figure 3.8D;  $F_{2,10} \geq 6.12$ ;  $P \leq 0.018$ ). In this case, mean peak arm velocity was higher during cathode-same trials, and smaller during cathode-opposite trials, although pairwise comparisons revealed no significant differences between rotation amplitudes for either task ( $P \geq 0.07$ ). Again, during the BF task these changes were immediately compensated by velocity reversals, thus preserving final arm position (dashed traces in Figure 3.7C).



**Figure 3.7. Effects of altered rotation amplitude and GVS upon arm control.** Traces depict mean arm-on-body position (solid) and velocity (dashed) for rotation amplitude conditions (A, body-fixed; B, earth-fixed) and GVS conditions (C, body-fixed; D, earth-fixed). Vertical dashed lines indicate rotation onset and end.



**Figure 3.8. Mean arm-on-body displacement and velocity.** Arm displacement was calculated as the difference in arm-on-body orientation between the beginning and end of the trial. Peak velocity was taken as the maximum value of the differentiated position trace during the movement.

### 3.4. Discussion

Galvanic vestibular stimulation (GVS), when applied concurrently with real motion, caused deviations in arm orientation when attempting to point towards an earth-fixed target. These deviations mimicked those evoked by real chair rotation. Hence, they reflect a mechanism which uses vestibular feedback to compensate for unpredictable body motion. The absence of compensatory arm movements when

reaching in a body-centred reference frame emphasises the purpose of the mechanism. In this case, body motion is no longer relevant for movement accuracy and no compensation is required.

During earth-fixed pointing subjects consistently under-compensated in the absence of GVS. In the first experiment, arm movement was around  $2/3^{\text{rds}}$  the magnitude of chair rotation. This cannot be due to biomechanical limitations, since the arm was capable of moving further when GVS was applied. Although the precise cause is unclear, under-estimation of whole-body motion perception for velocities greater than  $\sim 10^\circ/\text{s}$  has been previously reported (Day & Fitzpatrick, 2005). Peak chair velocity here was always in excess of this value, being  $\geq 18^\circ/\text{s}$ . The consequence of the under-compensation was that GVS actually improved performance above baseline during the EF task.

In experiment 1, when subjects attempted to continuously point at an earth-fixed location whilst being rotated, compensatory arm movements were systematically modified by GVS. With the cathode on the same side as chair rotation, arm movements were larger. With reversed electrode polarity or rotation direction, GVS made arm movements smaller. These observations can be interpreted in the context of established perceptual effects of GVS. Day and Fitzpatrick (2005) studied rotation perception using similar methodology, applying GVS concurrently with real rotation. When they asked subjects to return themselves to the perceived start point, the pattern of errors revealed that GVS increased or decreased movement sensation, depending on polarity. For example, with the head tilted down and the cathode over

the right ear, subjects perceived a clockwise rotation as being further than actually experienced. Under the same conditions of head posture, polarity and rotation direction, my results show that GVS increased the magnitude of the compensatory arm movement. Specifically, it caused the arm to move further in a direction opposite chair rotation. The magnitude of the evoked arm movement was similar for  $30^\circ$  and  $60^\circ$  rotations, suggesting that the sensory effect of GVS summates with, rather than multiplies, real movement sensations. To ensure that the stimulating current affected rotation sensation, I tilted the head down such that Reid's plane was  $\geq 45^\circ$  below horizontal. This was done to align the GVS head rotation vector closer towards the axis of chair rotation (Reynolds & Osler, 2012). Given that this vector was approximately  $20^\circ$  below Reid's plane (in head coordinates; Day & Fitzpatrick, 2005; Osler & Reynolds, 2012), this places the GVS vector  $\sim 25^\circ$  above vertical, or less (in room coordinates). By taking the cosine of this angle, I estimate this head orientation would produce  $\sim 91\%$  of the maximum possible effect of GVS upon yaw rotation perception. So, although I did not measure movement sensation or perception, the experiment was deliberately engineered to produce the largest influence of GVS upon yaw rotation sensation. The results are therefore consistent with an arm movement which compensates for this false sense of body movement.

In the first experiment, when subjects were asked to point within a body-fixed reference frame, GVS had no effect. In this case, they simply maintained their outstretched arm fixed with respect to their body. As they were rotated, GVS was applied but did not influence final arm position. Abolition of the response in this way supports the idea of a functional mechanism linking vestibular feedback to arm

control. For example, when scratching our nose while standing, we must control the arm in a body-fixed reference frame. There is no need to compensate for body sway; this might direct a finger inappropriately into an eye. In contrast, when reaching for a handrail while standing, the arm must take into account (and compensate for) any ongoing body movement to reach its intended target. The results show that a simple change in task goal is sufficient to reduce the effect of vestibular input on arm movement.

However, the difference between the EF and BF tasks of experiment 1 might not be attributable to different reference frames per se, but by the profoundly different movement kinematics required of the two tasks. The BF task involved zero arm-on-body movement and might be considered a non-task. This lack of movement could be responsible for the absence of a GVS effect, in itself. Experiment 2 was designed to address this confound by attempting to match arm-on-body kinematics. The results corroborated those of the first experiment. Final arm orientation was altered by GVS during the EF but not BF task, despite arm-on-body velocity being matched between tasks. Furthermore, experiment 2 confirmed that the effect of GVS was very similar to that caused by real changes in rotation amplitude. Figure 3.7 *A-D* shows that arm kinematics are similar in both quality and quantity for both interventions. This similarity confirms that arm movements evoked by GVS reflect a mechanism compensating for a sensation of altered rotation amplitude. But while GVS didn't affect final arm displacement during the BF task, the same is not true for peak arm velocity. The dashed red trace in Figure 3.7*C* shows that, with the cathode electrode on the same side as chair movement, peak arm velocity increased slightly.

This was immediately followed by a decrease in velocity, such that final arm position was unaffected. Swapping polarity caused the opposite effect (dashed blue trace in Figure 3.7C). This suggests that, while the overall movement goal was successfully achieved in body-fixed coordinates, there was a tendency to act in earth-fixed coordinates during the early phase of the movement, despite the instruction. This was also apparent during real changes in chair rotation (dashed traces in Figure 3.7A). During real changes in chair rotation, inertial effects could explain this tendency; as the chair rotates faster the inertia of the arm might result in greater arm-on-body movement. However, this cannot explain the effect of GVS upon arm velocity. In this case the mechanics are identical, the only change being sensory input. This therefore suggests a general tendency to act in an earth-fixed reference frame during the ballistic phase of an arm movement, even when the final goal of that movement is defined in body coordinates. This early component of the arm response may be immune to cognitive influence, as has been suggested for body sway responses (Guerraz & Day, 2005; Reynolds, 2010). Nevertheless, this tendency was very small in comparison to the overall kinematic differences between BF and EF tasks; final arm position was ultimately maintained during the BF task. Experiment 2 therefore confirms that vestibular control of the upper limb can be modified purely by changing the task goal.

Previous research, including the findings of the previous chapter (see Chapter 2), have also demonstrated GVS-evoked upper limb responses (Bresciani *et al.*, 2002a; Moreau-Debord *et al.*, 2014). As shown here, these responses occur when reaching for earth-fixed targets and are directed towards the anode, consistent with a

compensatory response for vestibular-sensed motion in the opposite direction. However, in contrast to postural responses, previous research has suggested that arm-on-body responses are similar regardless of the amount of perceived body motion, by providing more or less veridical sensory cues, e.g., standing versus sitting (Bresciani *et al.*, 2002*a*, 2002*b*). When I attempted to attenuate the sensation of self motion by restraining trunk movement and providing additional veridical sensory information in standing subjects, the arm-on-body response was of similar magnitude compared to when subjects stood freely (although arm-in-space movement was greatly reduced by the addition of non-vestibular cues, see Chapter 2). Bresciani *et al.* (2002*a*, 2002*b*) demonstrated that GVS-evoked arm responses when reaching for an earth-fixed target were of similar magnitude when subjects were seated versus standing. Other authors have also demonstrated arm responses when seated in fixed chairs (Pu *et al.*, 2012; Moreau-Debord *et al.*, 2014). One clue to this anomaly may be the magnitude of the reported responses. Here, GVS altered arm orientation on body by up to  $17^{\circ}$  compared to the no-GVS condition (equating to 177mm for an arm of 600 mm length). Arm-on-body movement in Chapter 2 when trunk movement was restrained, as in this study, was substantially lower than this ( $\leq 6\text{mm}$ ). Previously reported effects when seated are also at least 1 order of magnitude lower ( $\leq 1.56^{\circ}$  in Bresciani *et al.*, 2002*b*;  $\leq 23\text{mm}$  in Mars *et al.*, 2003;  $\leq 68\text{mm}$  in Moreau-Debord *et al.*, 2014). The likely cause of these differences in response magnitude is posture. In all of these studies the head was fixed-in-space, precluding the possibility of any head and/or body motion, with the exception of Mars *et al.* (2003) where subjects sat on a stool with the trunk free. In the case of Bresciani *et al.* (2002*a*, 2002*b*), a bite-bar was used to constrain the head, both



during sitting and standing. This would provide both mechanical stability and sensory input. In this case, the difference in posture between standing versus sitting may be irrelevant, since the body motion which normally accompanies a standing posture was prevented. This may explain why there was minimal difference between the two postures, and would also explain the relatively small influence of GVS. In my experiment, the body was rotating in space, and GVS was superimposed upon this natural motion. During the earth-fixed condition, this caused a relatively large change in arm trajectory. This is likely due to the paucity of veridical sensory information which would otherwise conflict with GVS-evoked sensations i.e. there was no contact with earth-fixed objects. It therefore seems logical to interpret the observed arm movements as compensatory responses to this false sense of body motion.

## CHAPTER 4

### COORDINATION OF UPPER LIMB AND GROUND REACTION FORCES FOR VESTIBULAR CONTROL OF BALANCE

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Vestibular stimulation evokes upper limb responses when using the arm to balance. Here I determine how these responses are affected by grasp context, and how the direction of the evoked force vector is coordinated with the rest of the body to generate a whole-body balance response. Galvanic Vestibular Stimulation (GVS) was used to evoke balance responses under three conditions of contact with an earth-fixed object: No contact (NC), Light grasp (< 1N) (LG) and Firm grasp (FG). As grasp progressed along this continuum, I observed an increase in GVS-evoked lateral hand force, with a simultaneous reduction in ground reaction force through the feet. During LG, hand force was secondary to the GVS-evoked body sway, indicating that the arm was performing a mostly passive role. In contrast, during FG the arm became actively involved in driving body sway, as revealed by an early force impulse in the opposite direction to that seen in LG. I then examined how the direction of the hand and feet force vectors changed with head yaw ( $\pm 0$ ,  $+45^\circ$  &  $-45^\circ$ ). During FG the GVS-evoked ground reaction force vector became skewed compared to NC, consistent with previous findings on sway anisotropy. However, this was effectively cancelled by an oppositely-directed skew in the hand force vector, such that the overall body sway response remained aligned with the inter-aural axis, thus maintaining the craniocentric principle. These results show that forces generated by

the upper limb in response to vestibular input are activated by grasp context and are coordinated with ground reaction forces to maintain balance.

#### **4.1. Introduction**

Evidence for vestibular control of arm movement when reaching for an earth-fixed target has been shown in Chapters 2 & 3. For reaching, I determined the limb uses vestibular signals to compensate for self motion. As balance also requires compensatory postural adjustments for unexpected body motion, it may be the case that the use of vestibular signals for reaching is transferable to balance. However, there is little research on vestibular control of the arm when it is providing balance support.

Holding onto a solid object improves standing balance. This can be due to improved sensory information and/or mechanical support, depending upon the nature of the manual contact. For example, light touch with a fixed object can reduce sway even though mechanical support is minimal (Jeka & Lackner, 1994; Kouzaki & Masani, 2008). Here, the upper limb only provides somatosensory feedback of body sway. Firmer grip can additionally provide mechanical support in the case of a loss of balance, exerting larger forces through the hand to keep the body upright (Maki & McIlroy, 2006). Hence the arm plays a dual role for balance, as both sensor and motor.

Upper limb motor output for balance has previously been demonstrated using

Galvanic Vestibular Stimulation (GVS). When standing, GVS evokes sway towards the anode electrode, compensating for a false sensation of body movement towards the cathode side (Lund & Broberg, 1983; Day *et al.*, 1997; Marsden *et al.*, 2002; Fitzpatrick & Day, 2004). GVS has been shown to evoke upper limb responses when forced to use the arm for balance (Britton *et al.*, 1993). Britton *et al.* (1993) recorded EMG activity of the leg and arm during GVS (General Introduction, Figure 1.4). To evoke arm responses, subjects stood on an unstable platform in such a way that active torques around the ankle could not maintain stability. Instead, holding a support was the only means of maintaining balance. GVS evoked the same pattern of EMG modulation in the arm (triceps brachii) as was observed in the leg during normal standing. The response, both in the leg and arm, consisted of an initial small deflection in muscle activation (early component), followed by a larger deflection in the opposite direction (late component). It was the late component that was responsible for producing whole-body movement in compensation for a false sense of motion in the opposite direction. The upper limb response was only present in the arm that was actively engaged in maintaining stability. Although small GVS-evoked EMG modulation was found in the relaxed arm, the response was not of the same pattern, or stimulus polarity dependant. Whether such responses would be observed during normal stance, and if so, how the response is coordinated with the rest of the body for balance control, remains open to question. Furthermore, whether the response would be altered by changes in hand grasp is unknown. During light grasp (< 1N), the arm acts mainly as a sensor and does not provide active mechanical support, which suggests that a firmer grasp may be required to generate active responses to a vestibular perturbation for balance.

Another aspect of the GVS-evoked balance response is its dependence on head orientation. When standing normally, GVS-evoked sway responses are directed towards the anodal ear. They are said to be 'craniocentric', such that turning the head on the body alters response direction by a similar degree (Lund & Broberg, 1983; Hlavacka & Njiokiktjien, 1985; Pastor *et al.*, 1993; Mian & Day, 2009). This behaviour demonstrates the conversion of vestibular information from a head- to body-centred reference frame. This principle has been demonstrated for whole-body sway and ground reaction forces when standing unsupported (Lund & Broberg, 1983; Pastor *et al.*, 1993; Mian & Day, 2009; Reynolds, 2011). However, the upper limb force vector evoked by GVS when holding a fixed support has not been studied. Recent evidence suggests the craniocentric principle may be less rigid than previously thought. Mian & Day (2014) showed the direction of GVS-evoked body sway is dependent on the state of baseline stability. When stance width is increased, the body becomes more stable in the frontal plane, and the direction of GVS evoked sway becomes biased towards the axis of instability, i.e. the sagittal plane. Changing head orientation results in a nonlinear relationship between head orientation and sway response direction. As well as changing stance width, lightly touching a stable surface produces anisotropy in stability, therefore altering vestibular-evoked sway direction (Mian & Day, 2014). Such deviations from the craniocentric principle may also apply to the upper limb balance response.

Here I address these issues by studying force responses evoked by GVS in the upper limb when holding onto a fixed object. I ask the following questions. Firstly, does the

magnitude and direction of GVS-evoked upper limb force depend upon grasp context? Secondly, is the direction of this force vector systematically altered by head orientation in a craniocentric fashion? Finally, how well is upper limb force integrated with the ground reaction force vector, and how does this affect whole-body sway? To answer these questions I asked volunteers to adopt different grasp strengths and head orientations while I measured force and body sway responses to GVS.

## **4.2. Methods**

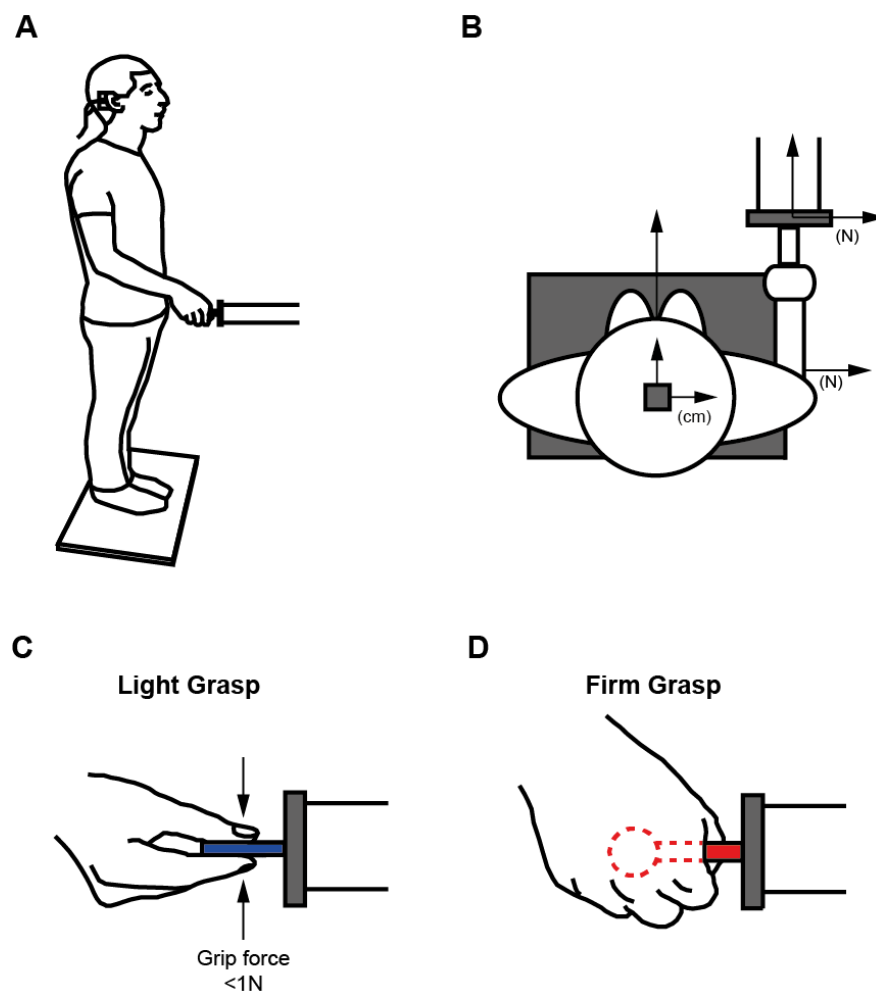
### *Subjects*

10 subjects completed experiment 1 (27.2yrs  $\pm$ 5.2; 7 males, 3 females) and 8 subjects completed experiment 2 (25.4yrs  $\pm$ 4.1; 7 males, 1 female). Subjects were healthy, with no known history of vestibular or neurological disorders, and written consent was given. Ethical approval was obtained from the University of Birmingham Ethics Committee and was in compliance with The Declaration of Helsinki.

### *Apparatus*

The experimental setup is illustrated in Figure 4.1. Subjects stood barefoot with feet together on a force plate (Kistler 9286AA, Kistler Instrumente AG, Switzerland). The end effector of an earth-fixed support with an embedded tri-axial force sensor (HapticMaster, Moog FCS, Netherlands) was positioned forward/right (35cm forward of the ankle, 35cm right of body mid-line) 45° ahead of the subject, at a height of 110cm. A motion tracking sensor (Fastrak, Polhemus Inc., USA) was attached to the

top of a welding helmet frame worn by the subject and recorded body movement. All signals were recorded at 100Hz. Note that forces refer to forces acting on the body. Fastrak Euler angles were used to derive head yaw (see Reynolds, 2011 for further details). GVS stimuli were delivered by an isolated constant-current stimulator (Model 2200, A-M systems, USA) to gel-coated carbon rubber electrodes (46 x 37mm) placed over the mastoid processes in a binaural bipolar configuration.

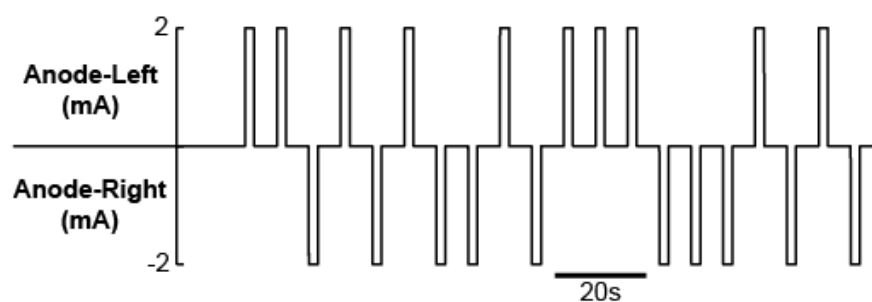


**Figure 4.1. Experimental setup.** A) Subject stood barefoot on force plate with eyes closed, grasping a fixed support. GVS was applied via electrodes placed over the mastoid processes. B) Setup from above. The end effector of the support was positioned forward/right  $45^\circ$  to the subject. Upper limb force was measured by a force sensor embedded in the support. A motion capture sensor is shown positioned on top of the head used to derive head-on-body orientation and whole-body

movement. C) Light grasp (from above): thumb and forefinger gently grasp a grip force sensor. D) Firm grasp (from above): A sphere is firmly grasped in the palm of the hand.

### *General Protocol*

Each trial consisted of 15s of quiet standing, before a series of 20 GVS stimuli (2mA, 2s duration) were delivered, with a gap of 5s between each stimulus (Figure 4.2). An equal number of anode-right and -left stimuli were delivered in a random order. Two trials were completed for each condition.



**Figure 4.2. Vestibular stimuli.** Each trial began with 15s of quiet standing with no GVS. This was followed by a series of 20 GVS stimuli (2mA, 2s duration), with a 5s gap between each stimulus. 10 anode-left (positive) and 10 anode-right (negative) stimuli were delivered in a random order. Total trial duration was 155s. The trial was repeated twice for each condition.

To measure GVS-evoked responses, signals were synchronised to the time point of GVS onset, and averaged for each condition. Responses to anode-left and anode-right currents were found to be equal and opposite (see Experiment 1, Results). Therefore the polarities were combined after inverting anode-left data, for all further analysis.



### *Experiment 1*

In experiment 1 I wanted to determine how the GVS-evoked upper limb response is altered by the nature of the manual interaction with the support.

Subjects either stood freely (No-Contact), lightly grasping the support with thumb and forefinger (Light-Grasp, Figure 4.1C), or firmly grasping the support with their right hand (Firm-Grasp, Figure 4.1D). In Light-Grasp (LG) conditions, a force sensor (50 x 50 x 8mm; F306 Disc Loadcell, Novatech Measurements Ltd., UK) was used as the end effector, allowing measurement of grasp force. Subjects were instructed to lightly grasp the effector with their right thumb and forefinger. Before data recording, subjects were shown a live trace of their grasp force, to practice maintaining grasp < 1N for the LG condition. In Firm-Grasp (FG) conditions, a solid sphere (diameter = 40mm) was used as the effector. Subjects were instructed to firmly grasp the sphere in the palm of their right hand. In the No-Contact (NC) conditions, the arms were positioned relaxed in front of the subject. The head was always aligned facing forward and eyes were closed throughout. Each trial (Figure 4.2) was repeated twice for each of the 3 grasp conditions (NC, LG, and FG) in a randomised order.

It is established that when standing, the GVS-evoked ground force response consists of an early (~250ms post stimulus onset) and late (~450ms post stimulus onset) component (General Introduction, Figure 1.2B). It is the late component that is responsible for producing whole-body movement in compensation for a sense of whole-body motion (Marsden *et al.*, 2002). As a measure of ground force response

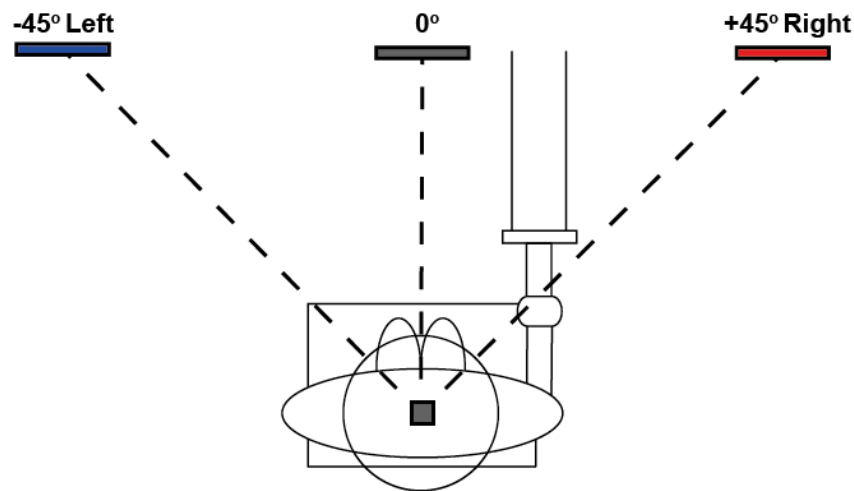
magnitude, peak lateral force towards the anode ear (consistent with the late component) was measured. To compare upper limb force between LG and FG, response magnitude was measured for FG, and the time this occurred was used to measure the response for LG. Time of peak change in force (i.e. the derivative) after stimulus onset (Marsden *et al.*, 2005) was used as a measure of response latency.

## *Experiment 2*

After establishing that GVS-evoked upper limb responses only occur during FG in experiment 1 (see Results), I wanted to see how the upper limb contributes to the direction of the whole-body sway response. The directions of the ground and upper limb force responses, and direction of overall whole-body sway (derived from Fastrak sensor position attached to the head), were measured. Head-on-body orientation was altered to see how the craniocentric properties of GVS-evoked postural responses would affect the upper limb response direction and subsequent body sway. I also looked at how grasping a support alters stability during quiet standing and its influence on GVS response direction.

Three targets (30 x 30cm) were positioned ahead of the subject (70cm). One target was aligned with the subjects' mid-line (0°), and the other two positioned 45° to the left and right (Figure 4.3). Subjects were instructed to orientate their head such that their nose was aligned to one of the targets (head centre, left, or right). Two grasp conditions were tested; NC and FG (same FG as experiment 1, Figure 4.1D). Once the head was positioned correctly, the subjects closed their eyes and the trial began

(Figure 4.2). 2 repeats for each of the 6 conditions were recorded, as follows: 3 head orientations (centre, left, right) X 2 grasp conditions (NC, and FG), a total of 12 trials.



**Figure 4.3. Head orientation targets.** Targets were positioned in-line with the subjects' midline ( $0^\circ$ ),  $-45^\circ$  to the left, and  $45^\circ$  to the right. Subjects were asked to align their nose with the centre of one of the targets before each trial.

*Quiet standing body sway:* 15s of quiet standing was recorded at the start of each trial. Direction of sway was determined by fitting a 95% confidence ellipse to ML/AP body position data (Sparto & Redfern, 2001; Figure 4.8; large ( $a$ ) and small ( $b$ ) ellipse vectors are shown). The angle between the largest ellipse vector and the ML axis was taken as the direction of sway, constrained to  $0^\circ$  to  $+180^\circ$ . Ellipse eccentricity ( $a / a^2 * b^2$ ) was used as a measure of baseline sway asymmetry, and ellipse area ( $\pi ab$ ) as a measure of sway variability.

*GVS response directions:* To measure the direction of GRF and upper limb force vectors, antero-posterior (AP) and ML forces were taken at the time point of peak rate of change corresponding to the late component of the GVS response ( $\sim 250$ -

500ms after GVS onset, Marsden *et al.*, 2002) (Fig. 5A). AP and ML forces were first differentiated ( $d$ ) and combined [ $v(d(ML^2)+d(AP^2))$ ] to give rate of change in force. Response direction was calculated as  $\tan^{-1}(ML/AP)$ . Separately we also summed the GRF and upper limb force traces and measured the combined force vector direction. To measure direction of whole-body movement during GVS, AP and ML body position were first combined and differentiated [ $d(v(ML^2+AP^2))$ ] to give body movement velocity. AP and ML body position were then taken at the time of peak velocity (Fig. 5B) and whole-body movement direction calculated [ $\tan^{-1}(ML/AP)$ ].

#### *Statistical analysis*

*Linear data (experiment 1 & 2):* Repeated-measures analysis of variance (ANOVA, experiment 1) and paired samples t-tests (experiment 2) were used to test for main effect of grasp conditions (experiment 1: no-contact vs. light grasp vs. firm grasp; experiment 2: no-contact vs. firm grasp). Pairwise comparisons (bonferroni corrected) were used to decompose any significant main effects of grasp condition in experiment 1. To test for significant hand force responses in experiment 1, one-sample t-tests were used to compare peak hand forces to zero (i.e., no-contact). SPSS Statistics Version 19 (IBM, USA) was used for statistical testing and significance was set at  $P < 0.05$ .

*Directional data (experiment 2):* Descriptive statistics (mean, SD) specific to circular data (Zar, 2010) were used to analyse angular direction of body sway during quiet standing and GVS response directions. The mean direction is only meaningful when the sample of angles is not a uniform circular distribution. Therefore mean direction

was only calculated after the Rayleigh test for uniformity rejected a uniform distribution ( $P < 0.05$ ; Zar, 2010). To determine difference between more than two conditions (i.e. 3 head orientations), ideally a repeated-measures ANOVA designed for circular data would be used. However, to my knowledge, no such test exists. I therefore used the Moore's test for paired circular data (Moore, 1980), the equivalent of a paired samples t-test used for linear data, to test for differences between conditions (test statistic =  $R'$ , significance set at  $P < 0.05$ ). Means, SDs, and Rayleigh test for circular data were analysed using CircStat toolbox for MATLAB (Berens, 2009).

### **4.3. Results**

#### ***Experiment 1***

There was no significant effect of stimulus polarity (anode-right vs. anode-left) on response magnitude for ground force ( $F_{(1,9)} = 1.6$ ,  $P = 0.23$ ) or upper limb force ( $F_{(1,9)} \leq 0.001$ ,  $P = 0.10$ ). Therefore the polarities were combined after inverting anode-left data.

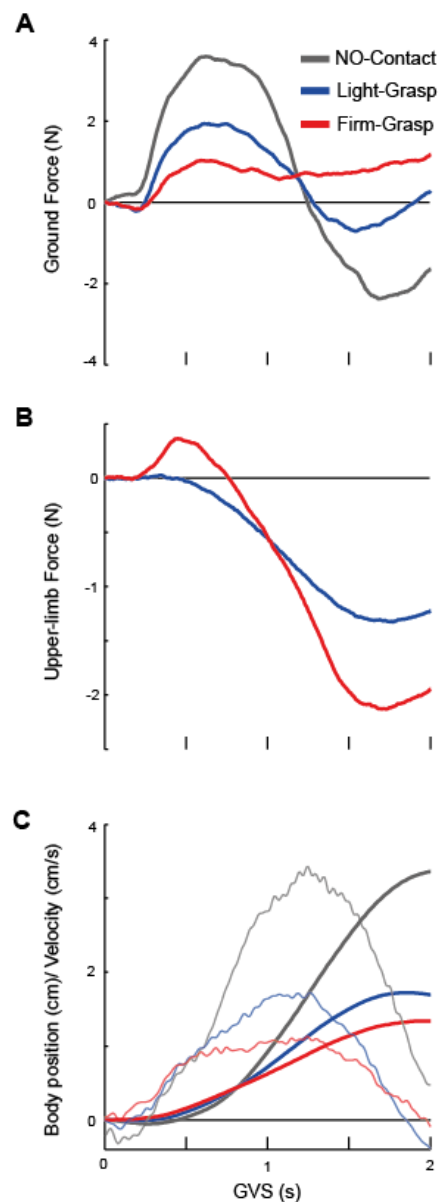
Figures 4.4 and 4.5 show the mediolateral ground force, upper limb force, and body position response during GVS for an individual subject and the average for all subjects, respectively. When GVS was applied during NC, ground force was generated towards the anode, peaking at ~600ms (Figure 4.4A, 4.5A). This is consistent with the late component of the GVS response previously described. Analysis was focused on the late component, as this is responsible for generating

whole-body movement (Marsden *et al.*, 2002). There was a main effect of grasp condition on peak ground force ( $F_{(2,18)} = 14.33$ ,  $P < 0.001$ ). Pairwise comparisons revealed mean ( $\pm$ SD) ground force response was significantly reduced during LG (mean grasp force =  $0.60\text{N} \pm 0.55$ ) and FG compared to NC (NC:  $1.97\text{N} \pm 1.32$  vs. LG:  $0.83\text{N} \pm 0.56$ ,  $P = 0.018$ ; NC vs. FG:  $0.64\text{N} \pm 0.55$ ,  $P = 0.005$ ), although there was no significant difference between LG and FG ( $P = 0.70$ ).

During LG, upper limb force simply reflected the direction of evoked body movement (blue trace; Figure 4.4B, 4.5C). Although a small deflection in mean upper limb force towards the anode can be seen during LG (Figure 4.5C), peak upper limb force ( $0.02\text{N} \pm 0.07$ ) was not significantly different from 0 ( $t_{(9)} = 1.09$ ,  $P = 0.30$ ; Figure 4.5D). In contrast, during FG (red trace; Figure 4.4B, 4.5C) the upper limb did generate force towards the anode, with mean peak upper limb force ( $0.17\text{N} \pm 0.13$ ) significantly greater than 0 ( $t_{(9)} = 4.18$ ,  $P = 0.002$ ). This response was similar to the ground force response during FG (red trace; Figure 4.4A, 4.5A); a force impulse consistent with generating body movement in the opposite direction of sensed self motion. The onset latency of the upper limb response during FG ( $256\text{ms} \pm 84.1$ ) was not significantly different from the ground force ( $267\text{ms} \pm 45.0$ ;  $t_{(9)} = 0.36$ ,  $P = 0.73$ ).

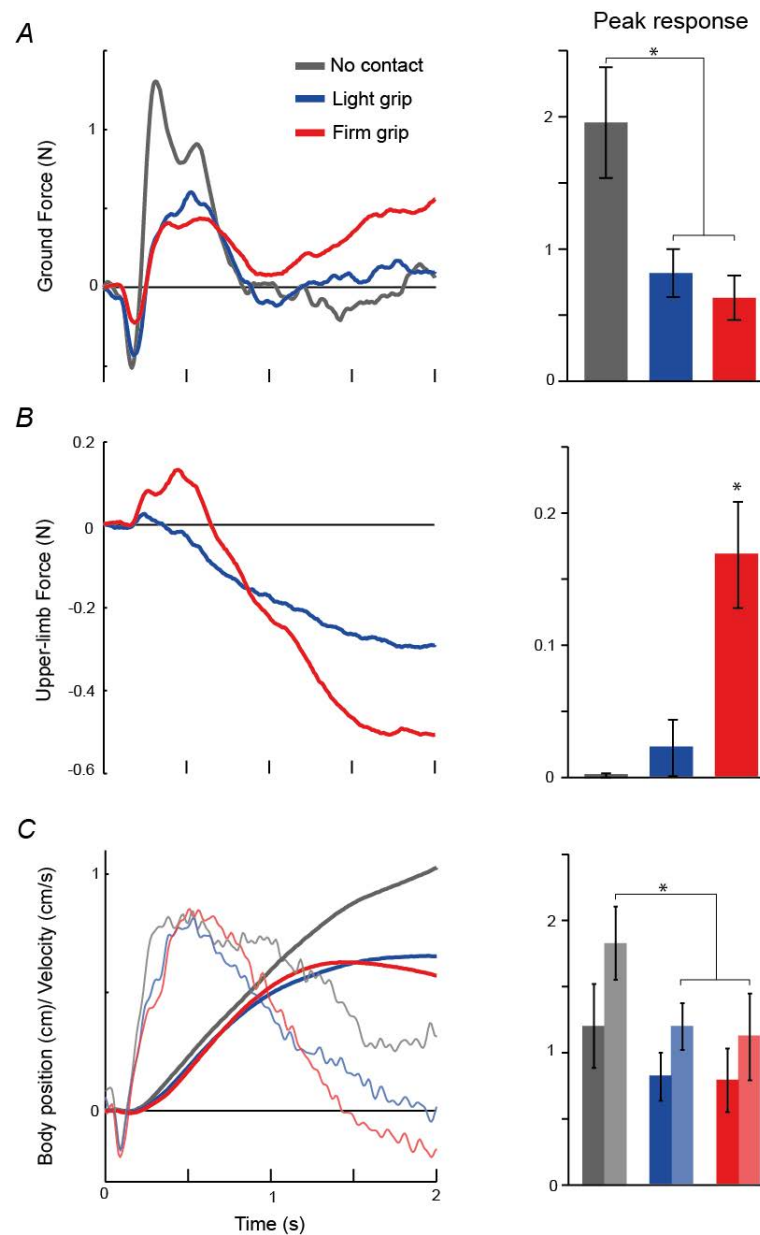
During NC, there was whole-body movement towards the anode electrode (Figure 4.4C; 4.5E). As shown for an individual subject, body movement and velocity were reduced during LG and further reducing during FG (Figure 4.4C). Although, there was no significant main effect of grasp on mean ( $\pm$ SD) peak body position (NC:  $1.21\text{cm} \pm 1.01$ ; LG:  $0.83\text{cm} \pm 0.57$ ; FG:  $0.80\text{cm} \pm 0.75$ ;  $F_{(2,18)} = 2.83$ ,  $P = 0.09$ ), there was a

significant effect of grasp on peak body velocity ( $F_{(2,18)} = 5.82$ ,  $P = 0.01$ ; Figure 4.5F). Pairwise comparisons revealed mean ( $\pm$ SD) body velocity was significantly reduced during LG and FG compared to NC (NC: 1.83cm/s  $\pm$ 0.87 vs. LG: 1.20cm/s  $\pm$ 0.56,  $P = 0.022$ ; NC vs. FG: FG: 1.13cm/s  $\pm$ 1.05,  $P = 0.015$ ), although there was no significant difference between LG and FG ( $P = 0.195$ ).



**Figure 4.4. Ground force, upper limb force, and body movement for an individual subject.** A) Mediolateral ground force response during GVS in the 3 grasp conditions,

for a individual subject. *B*) Mediolateral upper limb force response during light and firm grasp. *C*) Mediolateral body position (thick traces) and velocity (thin traces).



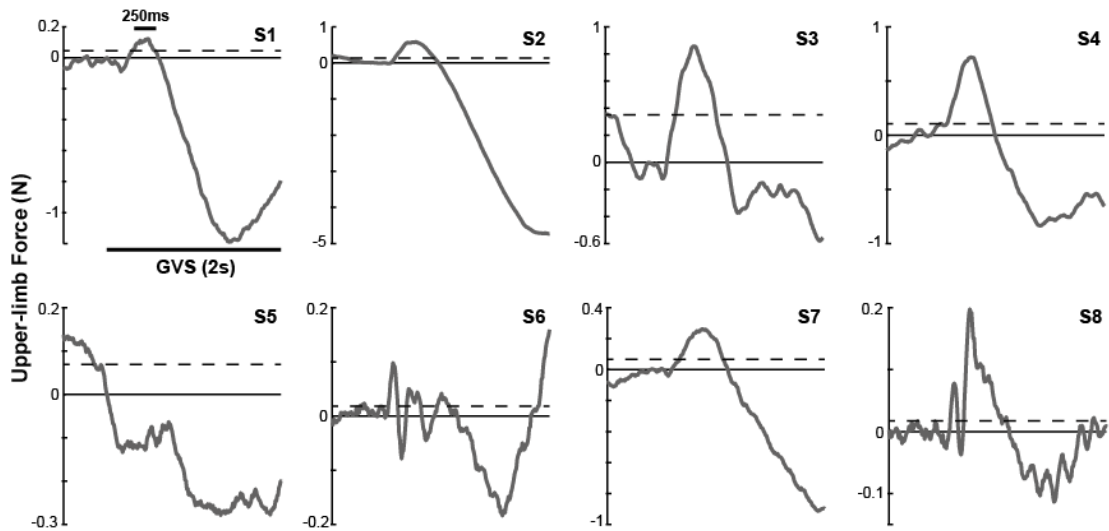
**Figure 4.5. Mean ground force, upper limb force, and body movement response.** *A* & *B*) Mean mediolateral ground force response during GVS in the 3 grasp conditions and corresponding peak ground force response towards the anode (SE bars shown). Significant pairwise comparisons are shown ( $P < 0.05$ ). *C* & *D*) Mediolateral upper limb force response during light and firm grasp, and corresponding peak upper limb response. An asterisk denotes conditions where peak upper limb force was significantly greater than zero. *E* & *F*) Mediolateral body position (thick traces) and velocity (thin traces) and corresponding peak body position (dark bars) and velocity (light bars). Significant pairwise comparisons are shown ( $P < 0.05$ ).



## ***Experiment 2***

In experiment 1, the upper limb produced a force response consistent with compensation for sensed whole-body motion only when firmly grasping the support. Experiment 2 studied the directional nature of this response, with a NC condition included for comparison of ground reaction forces.

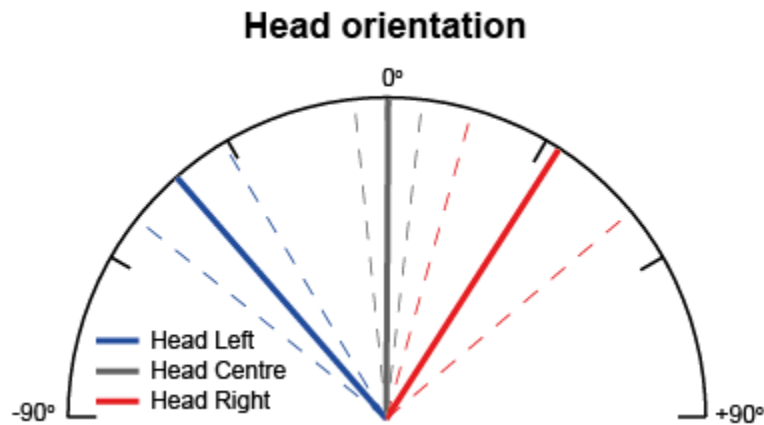
To analyse the directional nature of the upper limb response, I first determined if subjects generated an upper limb response consistent with the response found during FG in experiment 1, i.e. force production towards anode. Figure 4.6 shows the upper limb response of all 8 subjects during FG in the head centre condition, i.e. the same as the FG condition in experiment 1. If subjects were generating an active upper limb response, mediolateral upper limb force should be produced towards the anode (red trace, Figure 4.5C). However, based on the criteria I set (upper limb force towards the anode  $> 2SD$  of 500ms baseline, for at least 250ms), 2 of 8 subjects (subjects 5 & 6) did not demonstrate an active upper limb response, therefore removed from subsequent analysis. Directional analysis was completed on the remaining 6 subjects.



**Figure 4.6. Individual subjects' upper limb force response with the head centre.**

Lateral upper limb force during GVS with the head centre (grey line) for all 8 subjects (S1-8). In experiment 2 I was concerned with the direction of the upper limb response, therefore I first determined which subjects produced an active response, i.e. force production towards the anode electrode (as during FG in experiment 1, Figure 4.5C), and subsequently removed subjects who did not. The criteria used to determine if an active upper limb response was present, was lateral upper limb force should be generated towards the anode (upward)  $> 2SD$  baseline (500ms before GVS, dashed line) for at least 250ms, in the head centre orientation. Subjects 5 (S5) & 6 (S6) did not generate this upper limb response, therefore removed from subsequent directional analysis.

There was no significant effect of grasp condition on head orientation ( $R'_{(6)} \leq 0.15$ ,  $P > 0.05$ ). Therefore grasp conditions were combined in Figure 4.7. Head yaw angle was significantly different between head orientation conditions ( $R'_{(6)} \geq 1.83$ ,  $P < 0.05$ ). Mean ( $\pm SD$ ) yaw angles were; head centre =  $0.4^\circ \pm 6.1$ , head left =  $-41.0^\circ \pm 10.4$ , and head right =  $32.7^\circ \pm 17.1$ .

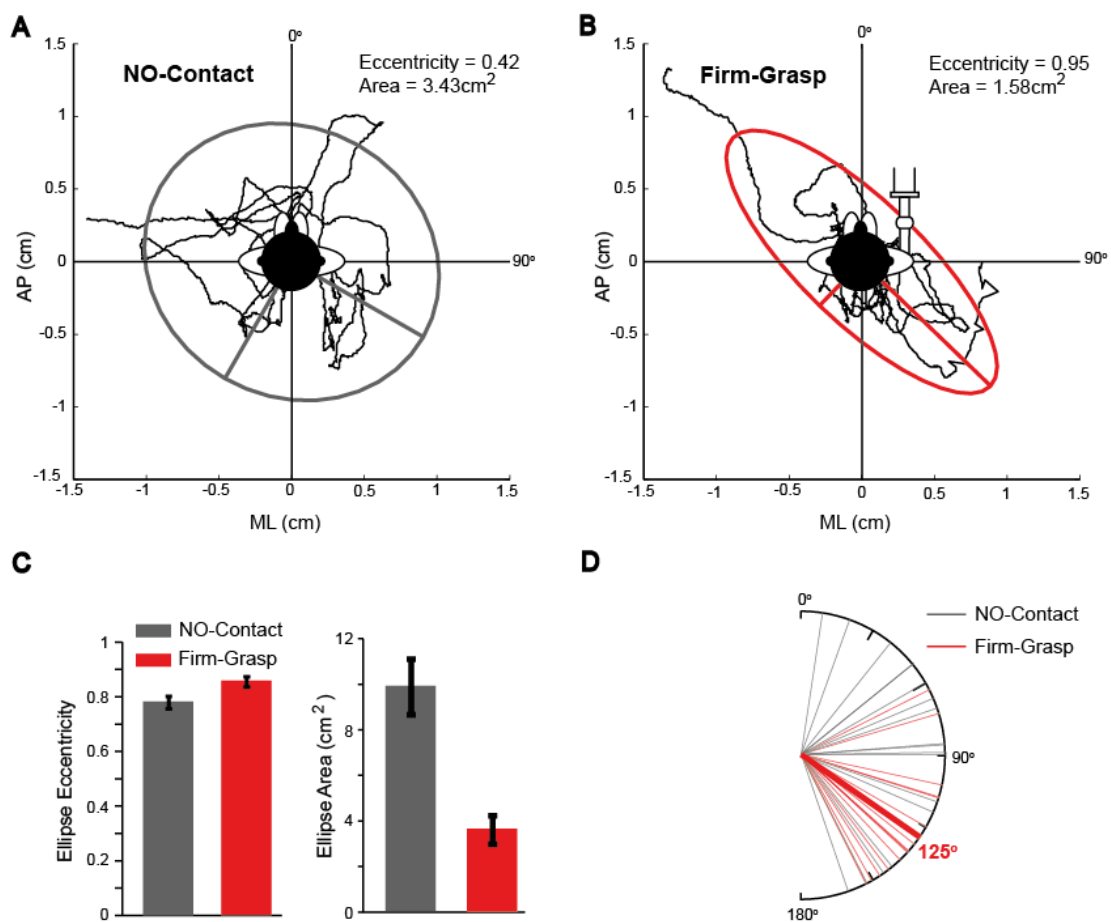


**Figure 4.7. Head orientation.** Mean head yaw angle for the 3 head orientations (solid lines). Standard deviation shown (dashed lines). Positive and negative angles indicate the head on body position was to the right and left, respectively.

Previous research has shown that the direction of GVS-evoked whole-body sway is biased towards the axis of instability when stability is anisotropic (Mian & Day, 2014). Finger contact with a stable surface has been shown to produce anisotropy in stability, subsequently altering GVS response direction (Mian & Day, 2014). I therefore analysed baseline body sway to see if FG produced anisotropy in stability, and how this may affect the direction of GVS responses during FG. Figures 4.8A and B shows body sway (derived from the motion capture sensor fixed to the head) when standing during NC and FG, respectively, for a representative subject. During NC, body sway was in no specific direction. In contrast, FG tended to alter the direction of body sway orthogonally to the hand position. FG also reduced sway variability (ellipse area).

Average body sway data during quiet standing were combined for all head orientations, and differences between the grasp conditions analysed. Figure 4.8C shows average ellipse eccentricity and area. A significant effect of grasp on

eccentricity ( $t_{(17)} = 2.35$ ,  $P = 0.03$ ) and area ( $t_{(17)} = 6.18$ ,  $P < 0.001$ ) confirmed body sway became more directional and smaller in magnitude during FG. Figure 4.8D shows direction of sway in the grasp conditions. A Rayleigh test confirmed angle of sway direction was uniformly distributed when there was NC ( $P = 0.36$ ), and became non-uniformly distributed during FG ( $P < 0.001$ ), with a mean ( $\pm$ SD) angle of  $124.9^\circ$  ( $\pm 24.1$ ).

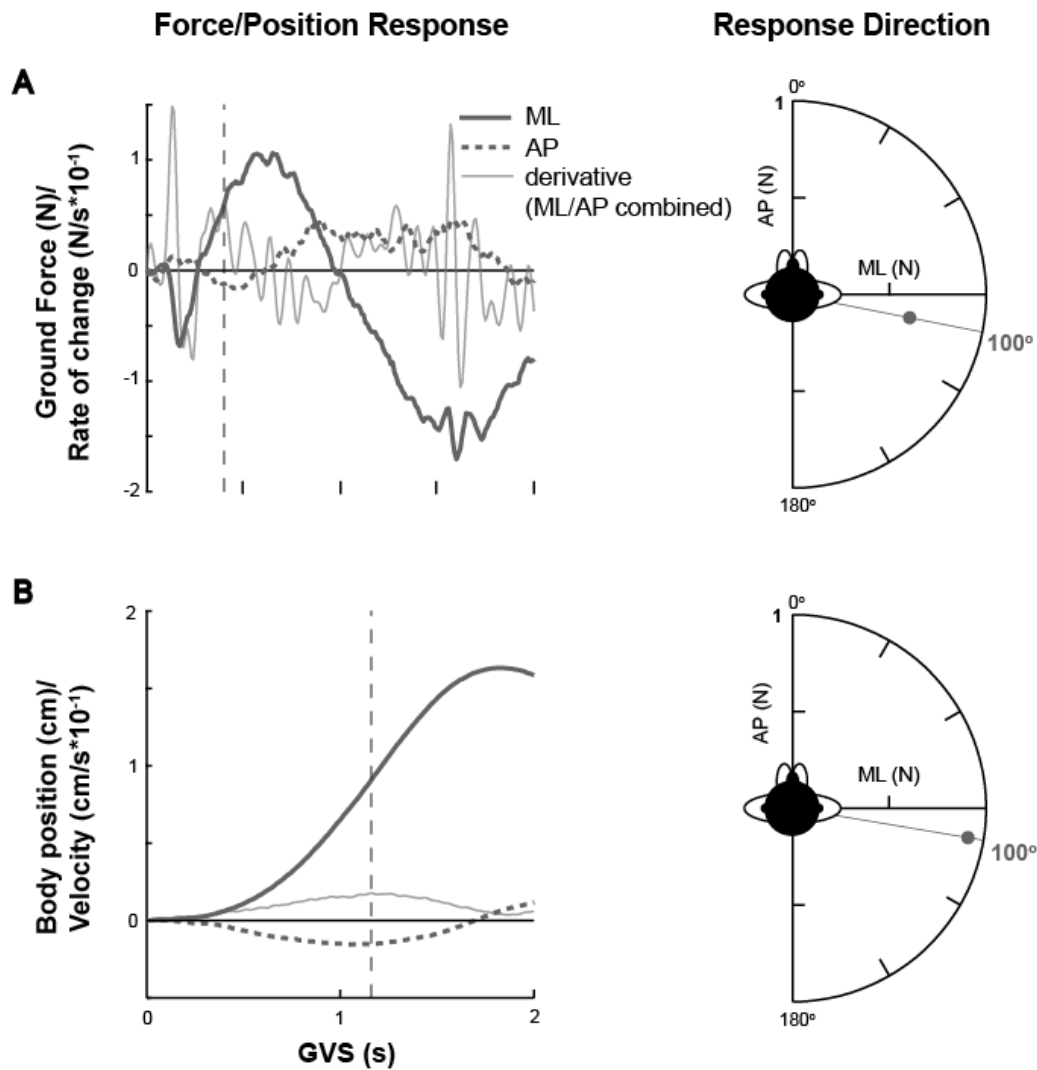


**Figure 4.8. Body sway direction during quiet standing.** A & B) 95% confidence ellipse fitted to a representative subject's body sway (derived from motion capture sensor fixed to subject's head) in mediolateral (ML) and anteroposterior (AP) axis during 15s of quiet standing with head centre ( $0^\circ$ ), during NO-Contact and Firm-Grasp, respectively. Large and small ellipse vectors are shown. Ellipse eccentricity and area values are given. C) Mean ellipse eccentricity and area for grasp conditions, SE bars are shown. D) Individual subject mean angle of sway during quiet standing for grasp conditions (thin lines). It was clear that during NO-Contact the body sway

direction was evenly distributed from  $0^{\circ}$  to  $180^{\circ}$ , therefore mean direction was meaningless. In contrast, during Firm-Grasp, the majority of subjects sway direction was concentrated between  $100^{\circ}$  and  $170^{\circ}$ , therefore sway direction was not uniformly distributed and the mean angle taken (thick red line).

#### *No Contact*

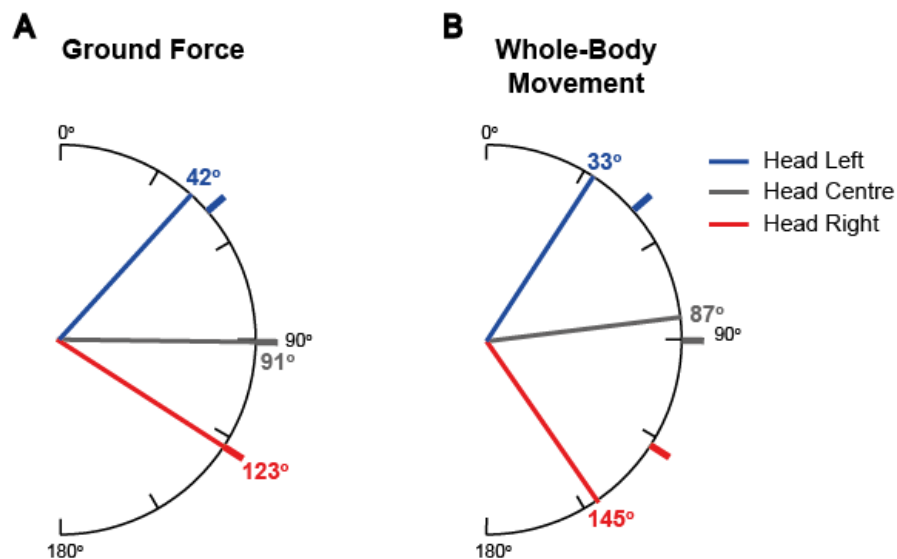
Figure 4.9 summarises the ground force (*A*) and body position (*B*) response during GVS in the NC condition with the head centre for a representative subject. The ground force response consisted of a ML shift in force towards the anode, with minimal force modulation in the AP axis. When the ML and AP ground force responses were measured at the time of peak rate of change in force (derivative of ML and AP combined), the direction of the response was  $100^{\circ}$ , therefore approximately aligned with the subject's inter-aural axis ( $\sim 90^{\circ}$ ). Body movement reflected the ground force response, with movement towards the anode in the ML axis and minimal movement in the AP axis. Therefore body movement was also directed at  $100^{\circ}$ .



**Figure 4.9. NO-Contact: Individual subject's responses with the head centre.** Ground force (A) and body position (B) in the AP (dashed trace) and ML (solid trace) axis during GVS. AP and ML traces were combined and the derivative calculated to give rate of change in ground force/body velocity (derivative (ML/AP combined)). AP and ML response were measured at the time of peak change in force/velocity (vertical dashed line) and plotted against each other (grey dot, response direction). The angle of response direction was derived from these values:  $\text{atan2}(\text{ML response}, \text{AP response})$ .

Mean GVS response direction in the 3 different head orientations tested during NC is shown in Figure 4.10. All GVS responses were significantly directional (non-uniformly distributed) as determined by a Rayleigh test ( $P \leq 0.01$ ). When the head was facing straight forward (head centre) the mean ( $\pm$ SD) ground force response was directed

towards the anode at  $90.8^\circ$  ( $\pm 21.7$ ), approximately aligned with the inter-aural axis ( $\sim 90^\circ$ ). Whole-body movement reflected the ground force response, directed  $87.1^\circ$  ( $\pm 21.8$ ) towards the anode. When the head was orientated to the left or right, the ground force response direction was significantly altered by a similar amount (head left =  $42.3^\circ \pm 32.9$ ,  $R'_{(6)} = 1.35$ ,  $P < 0.05$ ; head right =  $123.1^\circ \pm 16.4$ ,  $R'_{(6)} = 1.14$ ,  $P < 0.05$ ). This was the same for whole-body movement direction (head left:  $32.9^\circ \pm 4.3$ ,  $R'_{(6)} = 1.42$ ,  $P < 0.05$ ; head right:  $145.3^\circ \pm 20.3$ ,  $R'_{(6)} = 1.41$ ,  $P < 0.05$ ).



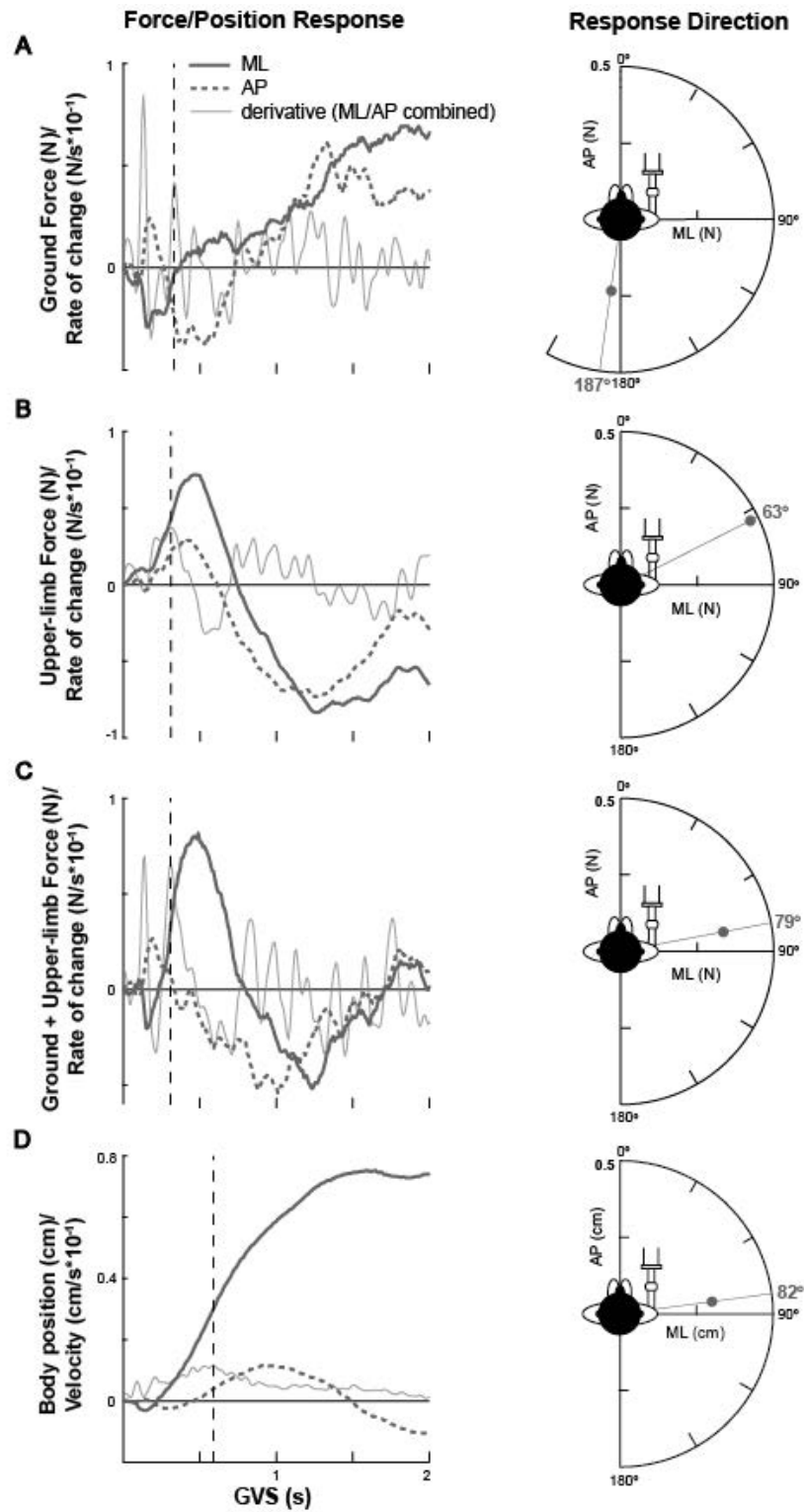
**Figure 4.10. NO-Contact: Mean response directions.** Ground force (A) and whole-body movement (B) response directions during GVS with the head orientated to the left (blue), centre (grey), and right (red). Outer ticks indicate average inter-aural axis (orthogonal to head orientation, Figure 4.7) for each head orientation.

#### *Firm Grasp*

Figure 4.11 summarises the ground force (A), upper limb force (B), ground and upper limb forces summed (C), and body position (D) during GVS in the FG condition with the head centre for a representative subject. The ground force (Figure 4.11A) was

predominately deflected backward (AP axis) and slightly towards the cathode (ML axis), producing a response direction of  $187^{\circ}$ , no longer aligned with the inter-aural axis. In contrast, the upper limb (Figure 4.11*B*) generated force towards the anode, but also slightly forward. This produced an upper limb response directed at  $63^{\circ}$ . When the ground and upper limb force ML and AP response were summed (Figure 4.11*C*), the direction of the summed response was  $79^{\circ}$ . Although the ground force response was directed away from the inter-aural axis and biased towards the axis of instability (subjects' direction of sway during quiet standing was  $133^{\circ}$ ), the direction of whole-body movement (Figure 4.11*D*) was directed  $82^{\circ}$ . Therefore, whole-body movement direction was close to the direction of summed ground and upper limb forces, and approximately aligned with the inter-aural axis, as found during NC.





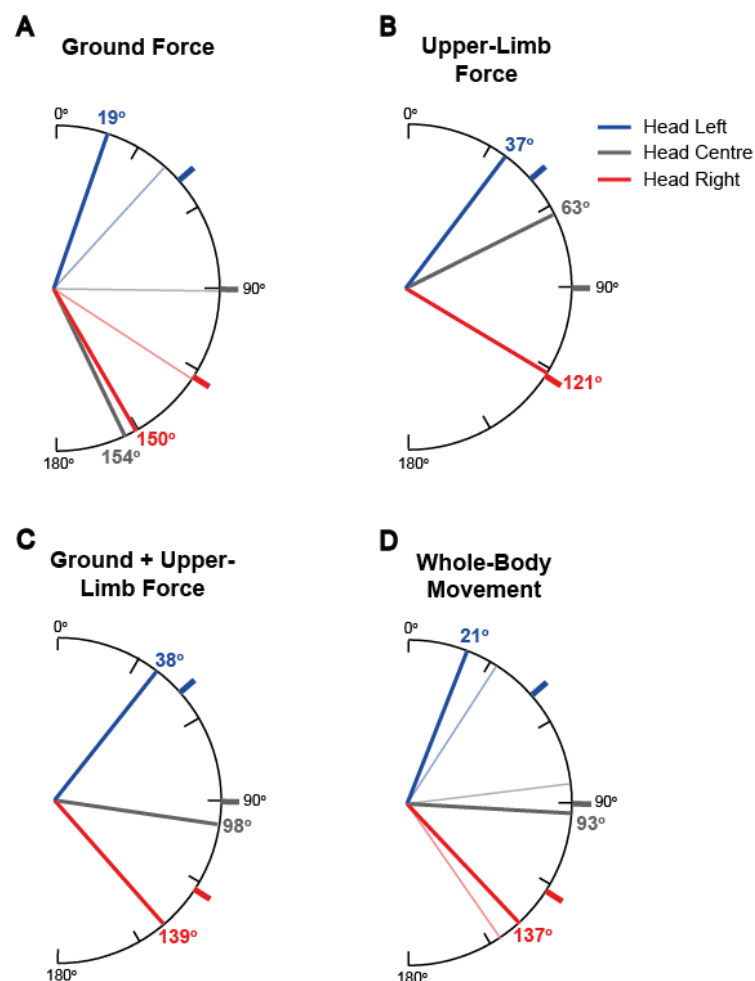
**Figure 4.11. Firm-Grasp: Individual subject's responses with the head centre.** Ground force (A), upper limb force (B), ground and upper limb force summed (C), and body position (D) response in the AP (dashed trace) and ML (solid trace) axis during GVS. Rate of change and velocity of ML and AP combined (derivative (ML/AP combined)) is shown for forces and position data, respectively. Response directions were derived as described in legend for Figure 4.9.

Mean GVS response direction for the 3 head orientations during FG is shown in Figure 4.12. All GVS responses were significantly directional as tested by a Rayleigh test ( $P \leq 0.01$ ). With the head centre, the ground force response direction (Figure 4.12A) was  $154.2^\circ (\pm 34.6)$ . This was significantly altered by  $\sim +63^\circ$  compared to the NC condition ( $R'_{(6)} = 1.25$ ,  $P < 0.05$ ), and became aligned towards the direction of baseline sway during quiet standing ( $125^\circ$ , Figure 4.8D). However, ground force response direction was not significantly different from the NC condition with the head left or right (head left:  $19.2^\circ \pm 29.8$ ,  $R'_{(6)} = 0.71$ ,  $P > 0.05$ ; head right:  $149.9^\circ \pm 15.4$ ,  $R'_{(6)} = 1.00$ ,  $P > 0.05$ ).

With the head centre, upper limb force response direction (Figure 4.12B) was  $63.4^\circ \pm 12.1$ , approximately orthogonal ( $\sim 91^\circ$ ) to the ground force direction. Orientating the head to the left or right significantly altered upper limb response direction towards the inter-aural axis (head left:  $37.0^\circ \pm 22.4$ ,  $R'_{(6)} = 1.18$ ,  $P < 0.05$ ; head right:  $121.0^\circ \pm 32.9$ ,  $R'_{(6)} = 1.37$ ,  $P < 0.05$ ).

When the ground and upper limb force responses were summed (Figure 4.12C), the direction of the summed forces was approximately aligned with the inter-aural axis. With the head centre, the summed force direction was  $98.4^\circ \pm 46.7$ . This was altered towards the inter-aural axis when the head was orientated to the left ( $38.3^\circ \pm 51.2$ ) or right ( $138.7^\circ \pm 56.1$ ), although this effect was only significant when orientated left (head left:  $R'_{(6)} = 1.15$ ,  $P < 0.05$ ; head right:  $R'_{(6)} = 1.06$ ,  $P > 0.05$ ).

Although the direction of the ground force response was altered during FG compared to NC, the direction of whole-body movement was unaffected (Figure 4.12D). When the head was centre, body movement was directed  $93.3^\circ \pm 24.5$ . This was not significantly different to the direction of body movement in the NC condition ( $R'_{(6)} = 0.67$ ,  $P > 0.05$ ). This was also the case when the head was orientated to the left or right (head left:  $21.4^\circ \pm 31.4$ ,  $R'_{(6)} = 0.48$ ,  $P > 0.05$ ; head right:  $136.8^\circ \pm 11.8$ ,  $R'_{(6)} = 0.93$ ,  $P > 0.05$ ). Hence, the overall direction of evoked body sway was the same regardless of grasp condition.



**Figure 4.12. Firm-Grasp: Mean response directions.** Direction of GVS-evoked responses for ground force (A), upper limb force (B), ground and upper limb force responses summed (C), and whole-body movement (D), for the 3 head orientations

during Firm-Grasp (thick lines). Response directions during NO-contact (thin lines) are shown for comparison between grasp conditions. Outer ticks indicate average inter-aural axis (orthogonal to head orientation, Figure 4.7) for each head orientation. Note for upper limb force (B) and ground + upper limb (C), only Firm-Grasp condition is shown as no upper limb response was recorded in the NO-Contact condition.

#### **4.4. Discussion**

With the exception of Britton *et al.* (1993), previous demonstrations of vestibular influence on the upper limb have been restricted mainly to the study of reaching movements, when the arm is not actively engaged in balance (Bresciani *et al.*, 2002a; Mars *et al.*, 2003; Pu *et al.*, 2012; Blouin *et al.*, 2015; Smith & Reynolds, 2016). Here I applied GVS to subjects who were standing normally while holding onto a fixed object. I observed stimulus-related forces generated by the upper limb. These forces were systematically altered by grasp type and head orientation, and were coordinated with ground reaction forces to move the body in a direction intended to compensate for the vestibular perturbation.

When standing quietly, GVS evoked a ground force response, consistent with a balance response to compensate for a sense of body movement in the opposite direction. GVS-evoked balance responses are known to be smaller during light finger touch with a stationary surface (Britton *et al.*, 1993), even though this provides minimal mechanical support (Holden *et al.*, 1994). One reason for this is GVS responses are inversely related to the amount of veridical sensory information available that contradicts the false vestibular input. For instance, when standing with

eyes open, balance responses are greatly attenuated compared to when the eyes are closed (Britton *et al.*, 1993; Day & Cole, 2002). In the case of light finger touch, touching a stable surface provides somatosensory feedback on body orientation referenced to the contact point, reducing GVS-evoked balance responses. Here, subjects lightly grasped a support with thumb and forefinger with a pinch force below 1N. In this situation, GVS evoked a relatively slow, continuous and uni-directional build-up of lateral hand force for the duration of the stimulus (blue trace, Figure 4.5C). This force was directed towards the cathodal ear (acting on the body). Given that GVS evokes sway towards the anodal ear, this upper limb force would act to resist the whole-body response to the vestibular perturbation. Therefore, during light grasp the arm did not drive the GVS sway response, but reflected it. In other words, the arm seemed to behave like a passive spring, simply registering cutaneous forces due to body motion. Such cutaneous input would explain why the ground force and sway response was smaller during light grasp compared to the no-contact condition. During firm grasp subjects used their whole hand to firmly grip a ball and handle. This changed the nature of the upper limb response, with the appearance of an early force impulse in the opposite direction to that of light grasp (red trace, Figure 4.5C). This impulse is in the same direction as the ground reaction force, acting to drive the body towards the anodal ear. Hence, a simple change in grasp is enough to convert the arm from a passive sensor to an active motor. Subsequent to the early impulse, the force reversed direction and began to resemble the pattern observed during light grasp, albeit larger. The absence of the early force impulse during light grasp could simply be due to a lack of strength associated with that particular grasp. However, the maximum upper limb forces were similar during firm

(~0.38N) and light (~0.25N) grasp (Figure 4.5C). This suggests that the grasp-induced change in behaviour is not purely due to strength limitations. Instead, the change in grasp context may be a cue for the nervous system to transform the arm from a passive sensor to an active contributor in the balance process.

In Chapter 2, when the limb was used to compensate for self motion whilst pointing at a target, I found GVS-evoked upper limb responses occurred earlier than trunk responses. However, the present data suggests ground and upper limb responses were produced at the same time. The difference is likely due to task. Here the upper limb was used for balance, compared to maintaining reach accuracy. Britton *et al.* (1993) found the onset of EMG responses, consistent with the early component, were earlier in the arm than the leg, when the respective limb was used for balance. However, the late component of the response responsible for actually generating body movement was earlier in the leg than the arm. It is suggested that individual limb balance responses form part of a patterned, functional response for balance, with muscles activated in a distal to proximal sequence (Nashner, 1977; Britton *et al.*, 1993).

When standing quietly, body sway responses to GVS are directed towards the anodal ear, and therefore aligned with the inter-aural axis. When the head-on-body orientation is altered, the direction of the response remains aligned with the inter-aural axis, therefore response directions are described as craniocentric (Lund & Broberg, 1983; Hlavacka & Njiokiktjien, 1985; Pastor *et al.*, 1993; Mian & Day, 2009). This principle was true for the responses measured in the absence of no upper limb

contact, with the ground force and body-sway response directions approximately aligned with the inter-aural axis for three different head orientations. When firmly grasping the support, the upper limb force vector was also significantly affected by head orientation, but the relationship was not systematic. In particular, the head-centre and head-right vectors were heavily skewed in a counter-clockwise direction (Figure 4.12B). To understand the cause and consequences of this skew, we must consider the direction of the simultaneous ground force vectors.

Touching a stable surface not only reduces body sway when standing, but also alters the directional state of stability (Mian & Day, 2014). Mian & Day (2014) found lightly touching a surface positioned to the side of the subject (sagittal plane) biased the direction of body sway towards the frontal plane, i.e. the axis of less stability. When GVS was applied, the evoked sway response direction was also biased towards the frontal plane. This is in contrast to the craniocentric properties of the GVS response direction when standing with no touch contact. Why this occurred is unclear. One explanation could be that multisensory weighting was anisotropic, such that the gain of the vestibular-evoked response was lower in the direction of higher somatosensory sensitivity (sagittal plane in this case) than in the orthogonal direction (Mian & Day, 2014). In our experiment the support was positioned  $45^{\circ}$  right and ahead of the subject. Grasping the support directed body sway during quiet standing approximately orthogonal to the support ( $125^{\circ}$ ). In turn, the direction of the GVS ground force response was altered. With the head centre, the ground force response direction was altered by  $+63^{\circ}$  (Figure 4.12A). The ground force response was no longer craniocentric, instead biased towards the axis of baseline

sway. However, there was minimal, non significant, changes in ground force response direction when the head was orientated left or right. Mian & Day (2014) measured GVS-evoked body-sway response directions under anisotropic stability in a number of head-on-body orientations. In this case, anisotropic stability was caused by increasing stance width. By widening the subject's stance, they became more stable in the sagittal plane, and less stable in the frontal plane. When GVS was applied, the body-sway response was biased to the axis of lesser stability (frontal plane), but only when the vestibular signal was both in the frontal and sagittal planes, i.e. when the head was orientated with the inter-aural axis between the sagittal ( $90^\circ$ ) and frontal plane ( $0^\circ$ ). When the inter-aural axis was directly aligned with the frontal or sagittal plane, there was minimal effect of anisotropic stability on the response direction. In our study, when the head was centred, the inter-aural axis ( $90^\circ$ ) was between the axis of lesser stability (baseline sway =  $125^\circ$ ) and axis of most stability (orthogonal to baseline sway =  $35^\circ$ ). However, when the head was turned to the right, the inter-aural axis ( $123^\circ$ ) became approximately aligned with the axis of lesser stability, and when turned to the left the inter-aural axis ( $49^\circ$ ) was approximately aligned with the axis of most stability. This explains why the effect of anisotropic baseline stability on ground force response direction was minimal and non significant when the head was orientated to the left or right, and largest when the head was centred.

To discover the consequences of deviations in ground force response during firm grasp for the overall response to GVS, I summed upper limb and ground forces and derived the force vectors. The summed vectors bear a stronger resemblance to the



ground force vectors during no contact (Figure 4.12C). This suggests that the skew deviations observed in the upper and lower limbs may cancel each other to some extent. The ultimate effect of such a cancellation process would be to preserve the direction of body sway, which it is exactly what I observed. Figure 4.12D clearly shows that GVS sway response was similarly craniocentric for both the no-contact and firm grasp conditions. Such cancellation was not apparent in the findings of Mian & Day (2014), who examined the GVS-evoked summed force response during light touch. However, our observations during light grasp show that the arm does not generate active forces in response to GVS during such low-force contact. This suggests that the cancellation of skewed forces between upper and lower limb only occurs if the upper limb is an active participant in driving the response to the vestibular perturbation. Under these circumstances the principle of craniocentricity is preserved. This interaction between the upper and lower limbs suggests they do not act independent of one another, but are components of a functional whole-body balance response.

In summary, I have demonstrated vestibular-evoked forces in the upper limb which are designed to counteract a false sense of body motion. Under conditions of light contact, the observed hand forces did not produce the body sway response, but were consequential to it. A sufficiently firm grasp was required for the hand to generate forces which drive the body sway response to GVS. Under these conditions, the hand forces were coordinated with the ground reaction forces to move the body in the same direction as seen without involvement of the upper limb.

## CHAPTER 5

### SENSORY INTEGRATION OF LIGHT CONTACT

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Light hand contact with a stationary object is known to improve stability when standing. The hand acts as a sensor for the detection of self motion relative to the contact point, and this feedback is used for balance control. A moving contact point has been found to drive postural sway. In this case, it is thought that motion of the contact reference is misinterpreted as self motion, evoking compensatory postural sway. However it remains unclear how exactly sensory signals from light contact are integrated to provide a sense of self motion for balance control. Body sway has been expressed in terms of angular motion of the body about the ankle joints (i.e. an inverted pendulum). Based on this consideration, I hypothesised that self motion detected by light contact is integrated in the form of angular body sway. To test this hypothesis, subjects stood lightly grasping a touch pad that moved along a circular arc about the ankle joints. The touch pad motion was presented at two different heights and therefore different radial distances. By maintaining the same angular touch pad motion at the two heights, touch pad *translation* amplitude was simultaneously altered. Therefore, for the same angular deviation about the ankle at the higher height, the absolute translational motion of the touch pad was greater. Therefore it was possible to test whether the body sway response was relative to angular motion or translation. Different stimulus amplitudes were also tested. I found body sway was entrained with touch pad motion. However, when the touch pad height was altered, such that amplitude of angular motion was maintained, but

translation amplitude was increased, the magnitude of body sway was greater. Furthermore, the gain of the response, and stimulus-response correlation, were closely coupled with stimulus translation across a number of amplitudes. These findings suggest sensory input from light contact was not interpreted as angular deviation in body orientation relative to the floor, as hypothesised. Instead, the sway response was relative to linear translation of the contact point.

### **5.1. Introduction**

When standing, lightly touching a stationary object has been found to improve stability (Jeka & Lackner, 1994, 1995; Clapp & Wing 1999; Rabin *et al.*, 1999). Light fingertip contact provides minimal mechanical stabilization, and the beneficial effects of light contact (LC) are abolished when the finger is anesthetised (Kouzaki & Masani, 2008). This demonstrates the benefits of LC for postural control are due to sensory effects. Fingertip contact provides cutaneous (i.e. fingertip force) and proprioceptive (i.e. upper limb orientation) sensory information on body orientation and movement relative to the contact point. These sensory signals must be integrated with other sensory inputs (i.e. ankle proprioception, vestibular signals, vision) to generate an internal representation of body motion for balance control.

As well as LC with a stationary object, contact with a moving object (Jeka *et al.*, 1997; Oie *et al.*, 2002; Allison *et al.*, 2006; Wing *et al.*, 2011), or another person (Johannsen *et al.*, 2009, 2011; Reynolds & Osler, 2014), has also been shown to effect postural control. While interpersonal light touch improves balance (Johannsen *et al.*, 2009,

2011; Reynolds & Osler, 2014), LC with a rhythmically oscillating surface evokes greater body sway (Jeka *et al.*, 1997; Oie *et al.*, 2002; Allison *et al.*, 2006; Wing *et al.*, 2011). In this case, body sway becomes entrained with contact point motion. It is thought that the body sway is a compensatory postural response for a false interpretation of contact point motion as self motion. For instance, if the contact point is assumed to be stationary, forward movement of the surface relative to the body will be interpreted as backward body sway relative to the contact reference, therefore compensatory forward sway is observed. Furthermore, characteristics of the entrained body sway are coupled to the frequency (Jeka *et al.*, 1997; 1998; Wing *et al.*, 2011) and amplitude of the stimulus (Oie *et al.*, 2002; Allison *et al.*, 2006).

During upright stance, postural sway has been biomechanically expressed in terms of angular motion of the body around the ankle joints, i.e. an inverted pendulum (Winter *et al.*, 1998; Gage *et al.*, 2004). Dependant on the inverted pendulum model, the main sensory contributions during balance control (if vision is eliminated by closing the eyes); ankle proprioception and vestibular input, are in essence angular variables referenced to the floor (Peterka, 2002). Based on these considerations, I hypothesize that sensory information from an external contact reference during LC is integrated in the form of angular body sway, derived from the relative motion of the body with respect to the contact reference. Therefore during LC with a moving touch pad (TP), evoked body sway should be dependent on the angular motion of the TP, i.e. how many degrees the TP moves along the arc of a circle around the ankle joint in the sagittal plane. Based on this hypothesis, I predict TP motion presented at two

different heights should evoke the same sway responses, if the motions at the two heights are matched for angular motion, even if they differ in terms of *translation*.

## **5.2. Methods**

8 subjects were recruited (aged: 27yrs  $\pm$ 2.5; height: 174.9cm  $\pm$ 10.8; 4 males, 4 females). Subjects were healthy, with no known history of balance or neurological disorders, and informed written consent was given. Ethical approval was obtained from the University of Birmingham Ethics Committee and was in compliance with The Declaration of Helsinki.

### *Experimental setup*

Subjects stood barefoot with feet together on a force plate (Kistler 9286AA, Kistler Instrumente AG, Switzerland). Ground reaction forces were recorded from the force plate at 100Hz. Subjects were asked to lightly grasp ( $< 1\text{N}$ ) a TP (grip force sensor) with their right thumb and forefinger (Chapter 4, Figure 4.1C). The TP was fixed to a haptic device (HapticMaster, Moog FCS, Netherlands) capable of movement in three dimensions. TP position was recorded at 100Hz. The start position of the TP was positioned forward/right (35cm forward of the ankle, 35cm right of body mid-line) of the subject (the same position used in Methods, Chapter 4). Motion tracking sensors (Fastrak, Polhemus Inc., USA) were attached at the hip (greater trochanter) and trunk (C5), to give position of the lower and upper body segments respectively (recorded at 50Hz). In all trials subjects had their eyes closed. To distract subjects

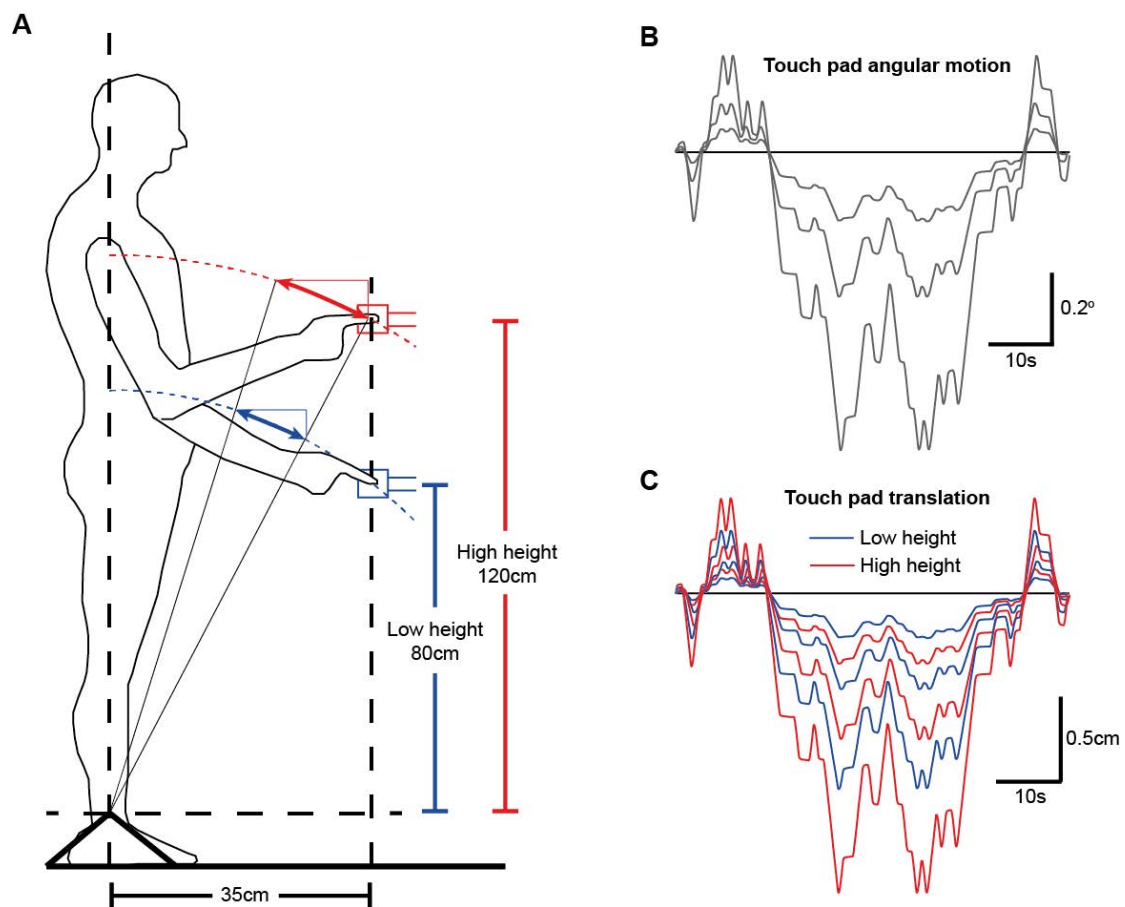
from the balance task and reduce auditory orientation cues, subjects listened to non-musical audio through headphones.

### *Light contact stimulus*

The aim of the experiment was to test whether sensory feedback from an external contact point is integrated in the form of angular body sway. If this is the case, body sway should be relative to TP angular motion in the sagittal plane with the rotation axis through the ankle joint. The angle of the TP (relative to the ankle joint) depends on its absolute distance (i.e. radius) from the ankle joint (Figure 5.1A). As shown in Figure 5.1A, the larger the radius, the more absolute motion of the TP is required per unit of angular motion. By maintaining the exact same TP angular motion at different radiuses (producing a different translation), it is possible to determine whether body sway was relative to angular motion of the TP (i.e. no difference between radiuses) or its translation.

The TP angular motion was a pseudorandom waveform, based on a pseudorandom ternary sequence (PRTS; Davies, 1970). The duration of each PRTS cycle was 24s. The stimulus was matched for the same angular motion at two TP heights (height above the ankle joint, Figure 5.1A); a low height (80cm) and a high height (120cm). As a stimulus amplitude effect on the sway response has been demonstrated in the literature (Oie *et al.*, 2002; Allison *et al.*, 2006), I also wanted to test for this effect. Three stimulus amplitudes were tested; low [LO:  $0.29^{\circ}$  peak-to-peak (pp)], medium (MED:  $0.57^{\circ}$  pp), and high (HI:  $1.15^{\circ}$  pp) (Figure 5.1B). To match angular TP motion at two heights, absolute TP translation was greater when positioned at the high height,

for the same angular motion amplitude. This meant there were 6 translation amplitudes (Figure 5.1C). The start position of the TP was always 35cm forward/right for both height conditions. The stimulus cycle was repeated 12 times in a trial, with total trial duration of 288s. Movement of the TP was controlled via Simulink (The Mathworks Inc., USA).

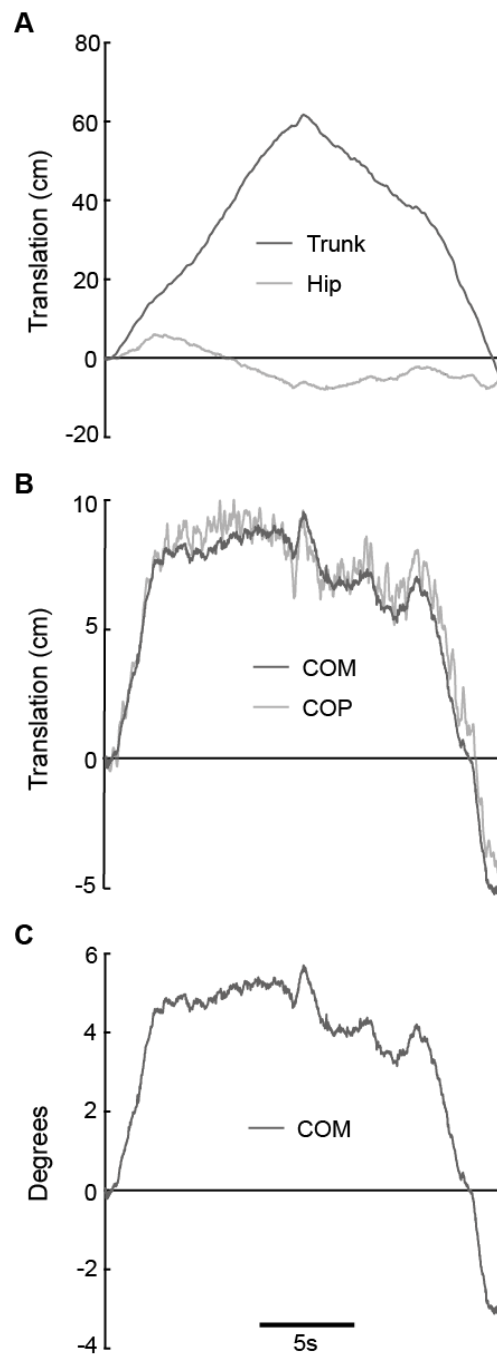


**Figure 5.1. Light contact stimulus.** A) The touch pad is positioned forward (35cm from ankle joint) and right (35cm from body mid-line) of the subject, at a low height (80cm above ankle joint, blue) and a high height (120cm, red). Angular touch pad motion about the ankle joint is shown as dotted lines for each height. For the same angular deviation, translation is greater at the high height (arrowed lines). B) Angular motion for the three stimulus amplitudes (low, medium, high). Angular motion was the same for both height conditions. C) Touch pad translation for 3 stimulus amplitudes in the low (blue traces) and high (red traces) height conditions. To match angular motion at the two heights, translation was greater at the high height for the same stimulus amplitude. Therefore there are 6 stimulus translation amplitudes.

### *Calculation of centre of mass*

Whole-body centre of mass (COM) angle and translation relative to the ankle joint in the antero-posterior (AP) axis provided the main measures of the sway response. The method used to calculate COM is described by Assländer & Peterka (2014). Hip and trunk translation (Figure 5.2A), and centre of pressure (COP; Figure 5.2B) displacement (derived from ground reaction forces) were measured during a calibration trial, whereby subjects performed slow movements at the hip and ankle joints (see Peterka, 2002). COP was taken as a vertical projection of COM (Brenière, 1996), and linear regression analysis was used to determine the relationship between hip and trunk displacement and COM. Using the parameters from the linear regression, COM translation (Figure 5.2B) during experimental trials was derived from hip and trunk translation. COM angle (Figure 5.2C) was then calculated from COM translation and COM height, with COM height estimated from anthropometric measures (Winter, 2005).





**Figure 5.2. COM derived from position markers and COP.** A) Translation of the hip and trunk markers during the calibration routine; a slow forward movement of the whole-body about the ankle joint, followed by forward bending at the hip, and the movement reversed. B) Centre of pressure (COP) translation and the derived centre of mass (COM) translation. C) COM angle relative to the ankle joint. Data were taken from a representative subject.

### *Analysis*

Data were recorded and analysed using Matlab (The Mathworks Inc., USA). Analysis was completed for stimulus angular motion and COM angular response to determine if the response was matched to TP angular motion. The same analysis was then performed on stimulus translation and COM translation (AP axis) to determine if the response was matched to translation. For the angular motion of the stimulus, there were 2 heights (low and high) and 3 amplitudes (low, medium, high). However, the translation of the stimulus was greater at the high height for the same angular motion amplitude, thus there were in fact 6 translation amplitudes, referred to as translation amplitudes 1-6 (1 = smallest, 6 = largest; Figure 5.1C). Data from the first stimulus cycle were discarded to avoid uncontrolled transient effects. The data were then averaged across the remaining 11 stimulus cycles. The amplitudes of the stimulus and the resulting COM response were calculated using the root mean square (RMS). The gain of the response relative to the stimulus was calculated as  $\text{RMS}(\text{COM}) / \text{RMS}(\text{stimulus})$ . Stimulus-response cross correlations were performed, and the timing and magnitude of the peak correlation ( $r$ ) were measured. Repeated-measures analysis of variance (ANOVA) was used to test for main effect of stimulus height and stimulus amplitude using SPSS Statistics 19 (IBM, USA). Pairwise comparisons (bonferroni corrected) were used to decompose significant main effects. Significant was set at  $P < 0.05$ .

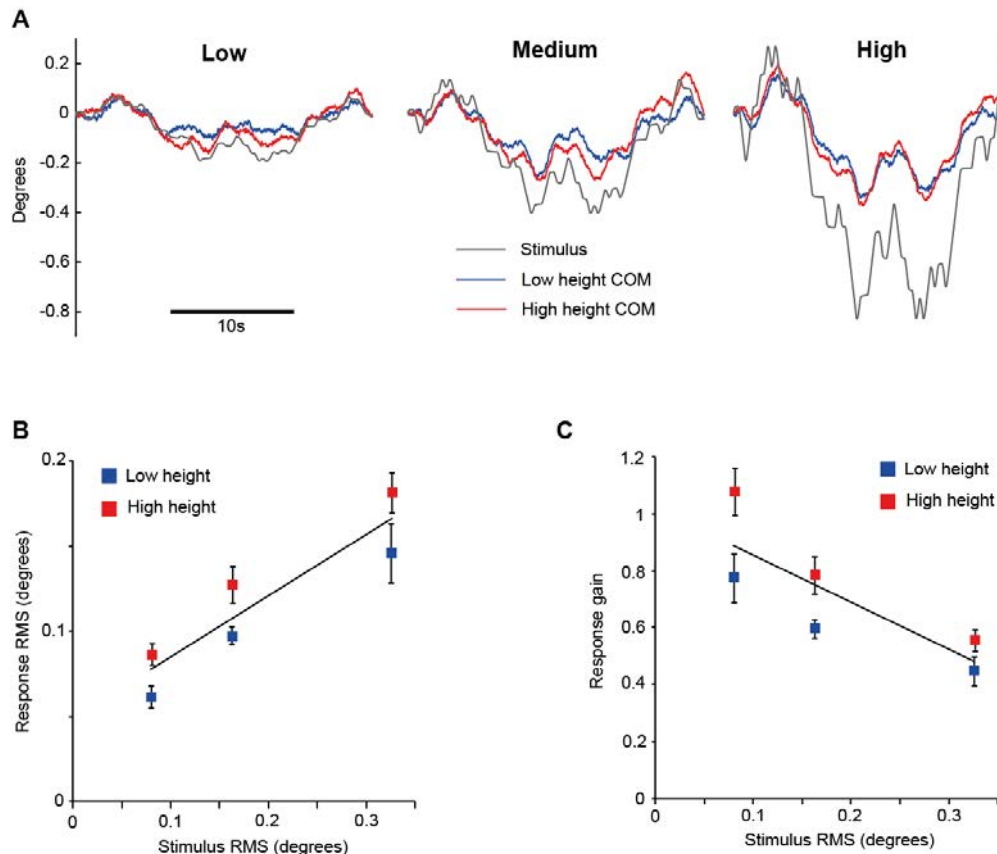
### 5.3. Results

#### *Angular stimulus*

Figure 5.3A shows mean touch pad (TP) angular motion and COM angular response at the low and high TP heights for three stimulus amplitudes (RMS); low (LO:  $0.08^\circ$ ), medium (MED:  $0.16^\circ$ ), and high (HI:  $0.33^\circ$ ). When lightly grasping the TP (mean grasp force =  $0.57\text{N} \pm 0.49$ ) COM angle was entrained with the stimulus at a latency of  $\sim 300\text{ms}$  (Figure 5.4C). The magnitude of sway is shown in Figure 5.3B. As the stimulus amplitude was increased, the magnitude of the response was also increased. This effect was present for both height conditions, with a significant main effect of stimulus amplitude ( $F_{(2,14)} = 37.50$ ,  $P < 0.001$ ). Pairwise comparisons confirm that the COM response was greater as the stimulus amplitude increased (LO vs. Med,  $P < 0.001$ ; LO vs. HI,  $P = 0.001$ ; MED vs. HI,  $P = 0.006$ ). Although the TP angular motion was the same for both heights (within each stimulus amplitude), the magnitude of the sway responses were greater at the high height, with a significant main effect of touch pad height ( $F_{(1,7)} = 11.69$ ,  $P = 0.01$ ). This result contradicts my hypothesis that the sway response should be relative to touch pad angular motion.

Although the amplitude of COM sway increased with stimulus amplitude, this was non-linear, with the gain actually reduced with increasing stimulus amplitude (Figure 5.3C). This effect was the same for both the low (LO:  $0.78 \pm 0.24$ ; MED:  $0.60 \pm 0.09$ ; HI:  $0.45 \pm 0.15$ ) and high (LO:  $1.08 \pm 0.23$ ; MED:  $0.78 \pm 0.19$ ; HI:  $0.56 \pm 0.10$ ) TP heights, with a significant main effect of stimulus amplitude ( $F_{(2,14)} = 29.29$ ,  $P < 0.001$ ; pairwise comparisons: LO vs. Med,  $P = 0.003$ ; LO vs. HI,  $P = 0.003$ ; MED vs. HI,  $P =$

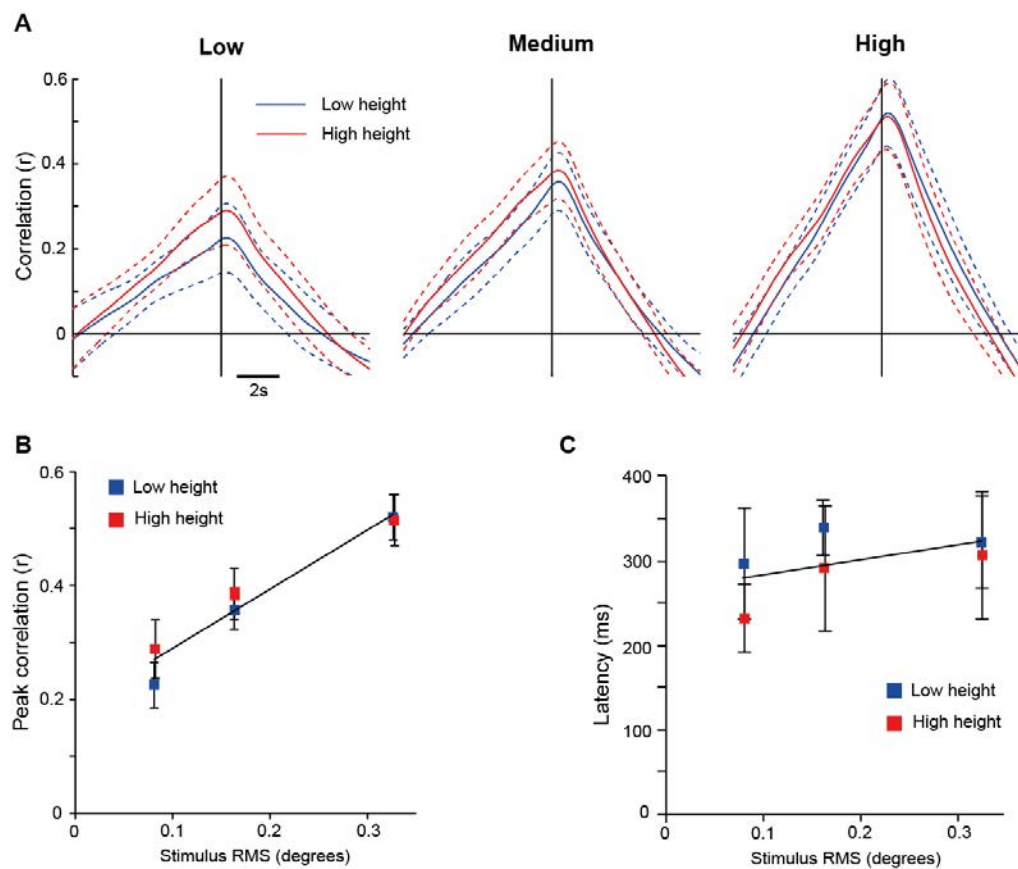
0.005). There was also a significant main effect of TP height on response gain ( $F_{(1,7)} = 13.25$ ,  $P = 0.01$ ), with gains greater for the high height compared to the low height for the same stimulus amplitude.



**Figure 5.3. COM response for angular stimulus.** A) Group mean COM angle response at the low (blue) and high (red) touch pad heights. Positive and negative values show the TP and subjects were moving forward and backward, respectively. TP angular motion relative to the ankle joint was the same at both heights. Three stimulus amplitudes (RMS) were tested; low ( $0.08^\circ$ ), medium ( $0.16^\circ$ ), and high ( $0.33^\circ$ ). B) Mean ( $\pm$ SE) COM angle response (RMS) plotted against stimulus (RMS) for both heights. Line of best fit is plotted. C) Mean ( $\pm$ SE) response gain for both heights.

Figure 5.4 shows mean results of stimulus-response cross correlations performed for angular motion. A perfect correlation ( $r = 1$ ) would suggest mechanical coupling between stimulus and response. Mean correlation ranged between 0.2 and 0.6

(Figure 5.4B). The stimulus-response correlation (mean peak  $r \pm \text{SD}$ ) was higher when the stimulus amplitude was greater, for both the low (LO:  $0.23 \pm 0.11$ ; MED:  $0.36 \pm 0.10$ ; HI:  $0.52 \pm 0.13$ ) and high (LO:  $0.29 \pm 0.14$ ; MED:  $0.39 \pm 0.13$ ; HI:  $0.52 \pm 0.13$ ) TP heights, with a significant main effect of stimulus amplitude ( $F_{(2,14)} = 29.01$ ,  $P < 0.001$ ; pairwise comparisons: LO vs. Med,  $P = 0.002$ ; LO vs. HI,  $P = 0.001$ ; MED vs. HI,  $P = 0.021$ ). However, there was no significant difference in peak correlation between heights for the same stimulus amplitude ( $F_{(1,7)} = 1.18$ ,  $P = 0.31$ ). Response latency was similar across all conditions, with no main effect of stimulus amplitude ( $F_{(2,14)} = 0.94$ ,  $P = 0.32$ ) or height ( $F_{(1,7)} = 1.13$ ,  $P = 0.32$ ). Mean response latency ( $\pm \text{SD}$ ) was 298.8ms ( $\pm 162.1$ ) across all conditions.



**Figure 5.4. Cross correlations for angular stimulus and COM response.** A) Traces show group mean  $r$  values  $\pm 95\%$  confidence intervals for the low (blue) and high

(red) TP height for the three stimulus amplitudes tested. The horizontal and vertical lines show zero correlation and zero response latency, respectively. *B*) Mean ( $\pm$ SE) peak correlation plotted against stimulus RMS in the low and high height. Line of best fit plotted. *C*) Mean ( $\pm$ SE) response latency for low and high height.

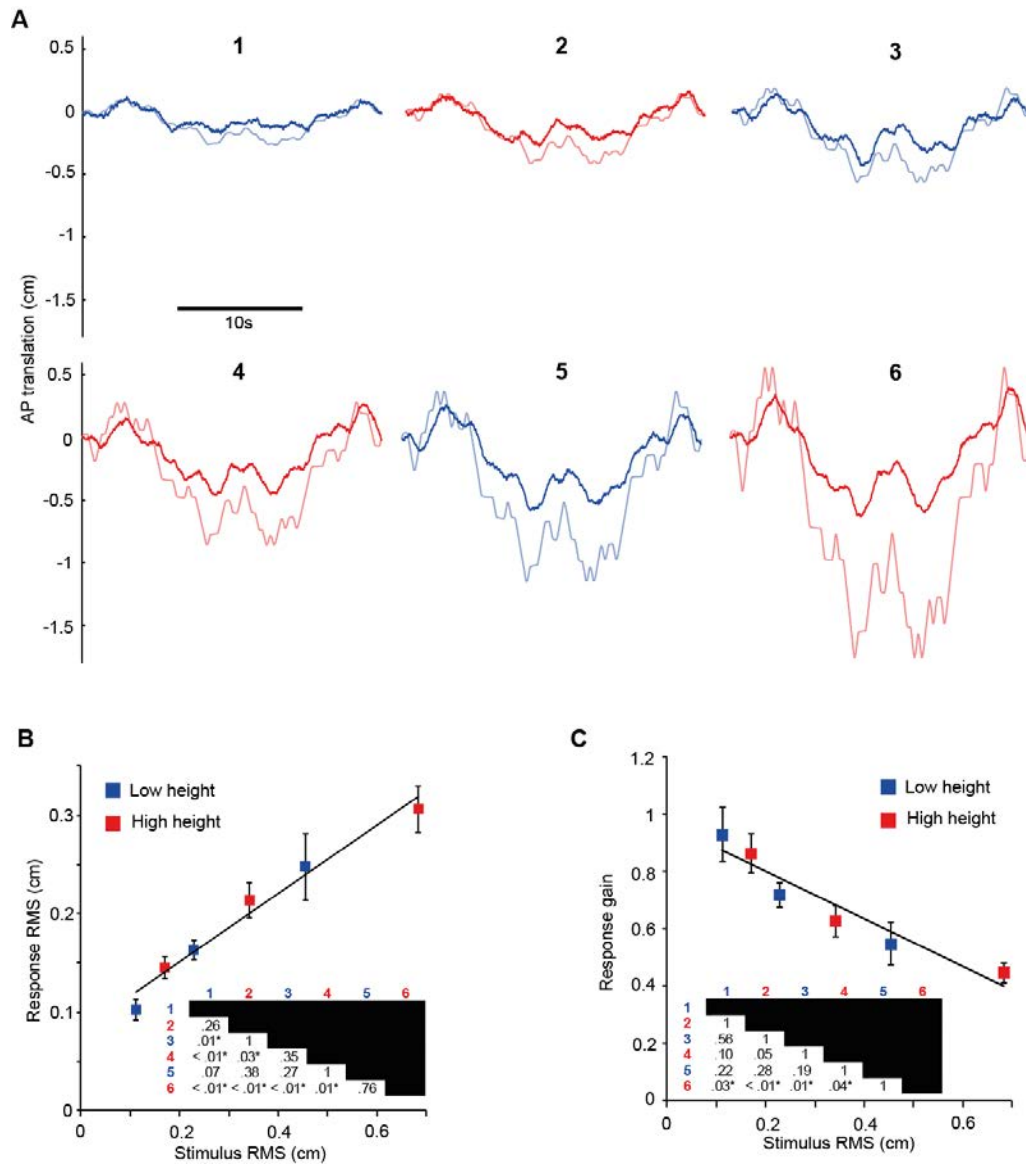
### *Translation stimulus*

Finding an effect of TP height on body sway for the same amplitude of TP angular motion (Figure 5.3) demonstrated the body sway response did not match stimulus angle. The main difference between height conditions was the amplitude of stimulus translation. The analysis was therefore repeated on the stimulus and response data in terms of translation.

There were a total of six amplitudes of translation (RMS) (light traces, Figure 5.5A); amplitude 1 (0.11cm), 2 (0.17cm), 3 (0.23cm), 4 (0.34cm), 5 (0.45cm), and 6 (0.68cm).

Figure 5.5A shows COM translation for the six translation stimulus amplitudes. The COM response (RMS  $\pm$ SD) increased with stimulus amplitude, ranging from 0.1cm to 0.3cm for the lowest and highest amplitudes, respectively (Figure 5.5B). There was a significant main effect of stimulus amplitude on COM translation ( $F_{(5,35)} = 20.84$ ,  $P < 0.001$ ). Pairwise comparisons between stimulus amplitudes for response magnitudes are shown in the table on Figure 5.5B. These comparisons confirm the trend for an increase in response magnitude for increasing stimulus amplitude, although not all comparisons are significant. The gain of the response was reduced as the translation amplitude increased, with a reduction of 52% from the lowest amplitude (0.93) to

the highest amplitude (0.45; Figure 5.5C). The main effect of stimulus amplitude on response gain was significant ( $F_{(5,35)} = 11.53$ ,  $P < 0.001$ ), with pairwise comparisons tabulated in Figure 5C.

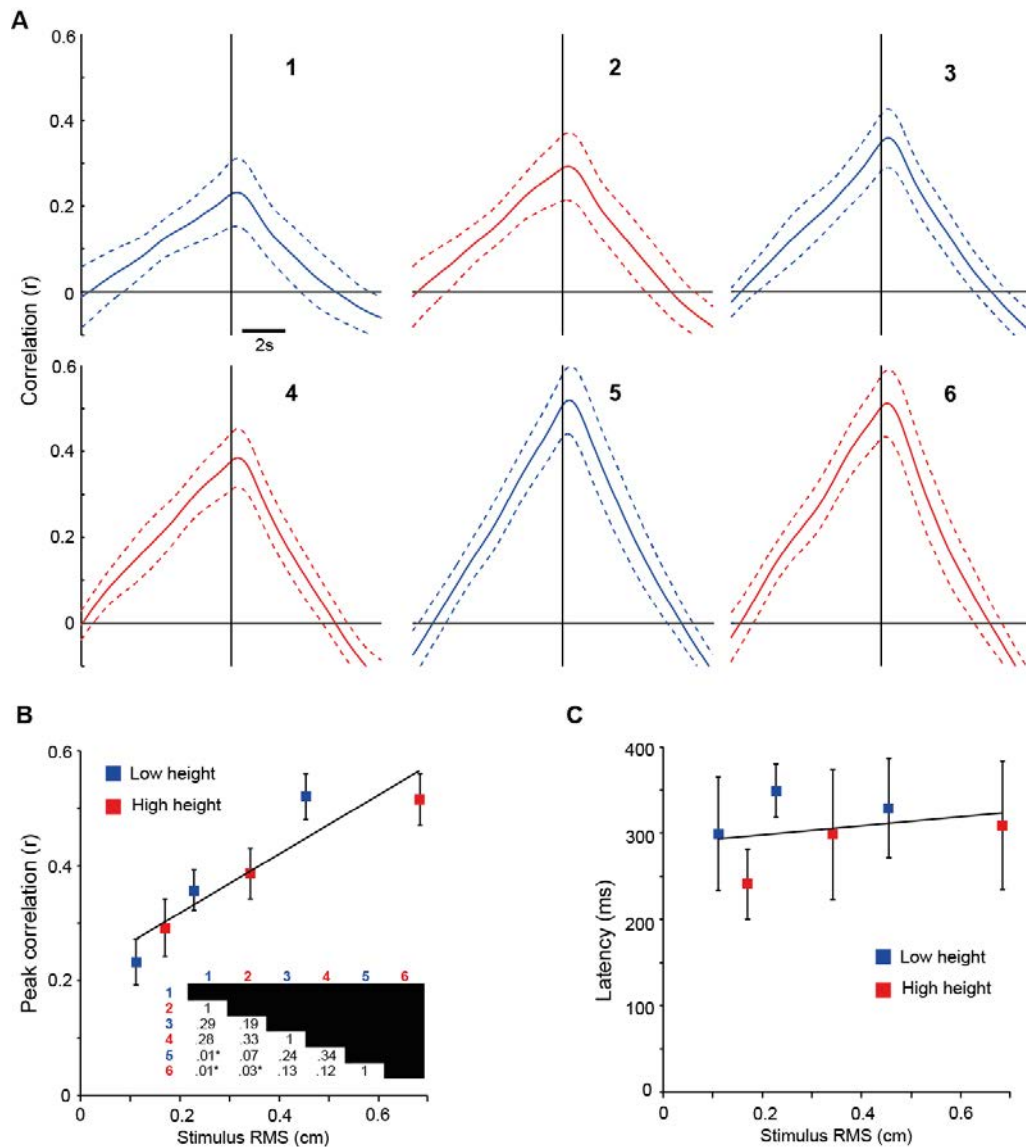


**Figure 5.5. COM response for translation stimulus.** A) Group mean COM translation at the low (blue) and high (red) touch pad heights. To maintain the same stimulus angle at the two heights, stimulus translation had to be greater in the higher height (see Figure 5.1A). Therefore TP translation was greater at the higher height (light red line) for the same angular motion amplitude (low, medium, high) at the low height (light blue line). Therefore there were a total of six translation amplitudes (1-6). B) Mean ( $\pm$ SE) COM translation plotted against TP translation for both heights. Line of

best fit is plotted. There was a main effect of stimulus amplitude on response amplitude ( $P < 0.001$ ) and pairwise comparisons are shown in a table (\*significant) C) Mean ( $\pm$ SE) response gain for both heights. There was a main effect of stimulus amplitude on response gain ( $P < 0.001$ ) and pairwise comparisons are shown in a table.

The cross correlation results between stimulus translation and COM response for the six stimulus amplitudes are shown in Figure 5.6. There was a significant main effect of stimulus amplitude on peak correlation ( $F_{(5,35)} = 14.56$ ,  $P < 0.001$ ). Correlation between the stimulus and body sway (peak  $r \pm$ SD) tended to increase with stimulus amplitude, from 0.23 for the lowest stimulus amplitude to 0.52 for the highest amplitude (Figure 5.6B). Pairwise comparisons between stimulus amplitudes for peak correlations are shown in the table on Figure 5.6B. These comparisons confirm the trend for an increase in stimulus-response correlation for increasing stimulus amplitude, although not all comparisons are significant. As for the COM angular response, there was no significant main effect of stimulus amplitude on response latency ( $F_{(5,35)} = 0.54$ ,  $P = 0.75$ ), with a mean ( $\pm$ SD) latency of 305.4ms ( $\pm$ 162.8) across all conditions (Figure 5.6C).





**Figure 5.6. Cross correlations for stimulus translation and COM response.** A) Traces show group mean  $r$  values  $\pm 95\%$  confidence intervals for the 6 stimulus translation amplitudes (1-6). The low and high TP heights are shown as blue and red data points, respectively. The horizontal and vertical lines show zero correlation and zero response latency, respectively. B) Mean ( $\pm$ SE) peak correlation plotted against stimulus RMS. Line of best fit plotted. There was a main effect of stimulus amplitude on peak correlation ( $P < 0.001$ ) and pairwise comparisons are shown in a table (\*significant) C) Mean ( $\pm$ SE) response latency. There was no effect of stimulus amplitude on latency.

#### 5.4. Discussion

As the contact point moved, body sway became entrained with its motion. The entrainment of body sway with an external stimulus has been demonstrated before, being interpreted as a compensatory response for a false sensation of self motion relative to the contact reference (Jeka *et al.*, 1997; Oie *et al.*, 2002; Allison *et al.*, 2006; Wing *et al.*, 2011). However, I found body sway was not relative to the angular motion of the contact point about the ankle joints. This finding suggests somatosensory input from light contact (LC) was not simply interpreted as angular deviation in body orientation relative to the floor, as I hypothesised. Instead, my results showed body sway was actually closely coupled with linear *translation* of the contact point.

The body sway response was different for the same angular motion of the contact point at two different radiuses (heights) from the ankle, with the response always greater when the touch pad was positioned further from the ankle. This was the case for all stimulus amplitudes (low, medium, high). This finding demonstrated that the sway response was not coupled with angular motion of the stimulus, and somatosensory input from LC was not interpreted as angular deviation of the body. To match the degree of angular motion of the contact point at different radiuses, the translation of the stimulus had to be greater when the touch pad was positioned further from the ankle. When the stimulus conditions were analysed with respect to linear motion, there was a much clearer relationship between stimulus amplitude and body sway magnitude (compare Figures 5.3B and 5.5B). This suggests that the

sway response was closely coupled with *translation* of the contact point, and the effect of the radius of the stimulus angular motion was likely the result of this coupling. Why the body sway response was coupled with translation of the contact point, as oppose to angular motion, is unclear. For body sway about the ankle joint, modelled as an inverted pendulum (i.e., body rotation about the ankle joints) (Winter *et al.*, 1998; Gage *et al.*, 2004), it would seem logical that any deviation from upright would be detected as angular deviation about the ankle joints. However, based on my results this was not the case for somatosensory input when touching a moving object.

I also found a decrease in response gain with increasing stimulus amplitude (Figure 5.5C). This has been demonstrated for postural responses to other types of sensory perturbations; somatosensory (platform tilts; Peterka, 2002; Maurer *et al.*, 2006; Assländer & Peterka, 2014), visual stimuli (Ravaioli *et al.*, 2005); and somatosensory-visual interactions (Oie *et al.*, 2002; Allison *et al.*, 2006). This is therefore an established property of human postural control that has been attributed to sensory reweighting (Peterka, 2002). If we consider each source of sensory input that provides information on body orientation has a weight, the weight of that sensory input determines how much influence it has on our internal representation of body orientation. Sensory reweighting refers to the reweighting of sensory inputs for changes in external conditions, e.g. stimulus amplitude. Under our experimental conditions (standing with eyes closed and listening to audio), the primary sensory inputs on body orientation were; ankle proprioceptors, vestibular sensors, and somatosensory input from LC. Based on the concept of sensory reweighting, the

reduction in response gain for increased stimulus amplitude, suggests that LC became a less reliable indicator of self motion as the stimulus amplitude increased, and sensory input from vestibular and/or ankle proprioceptors were weighted more heavily. Oie *et al.*, (2002) combined a LC stimulus (oscillating touch pad) with a visual stimulus (moving scene) to further demonstrate sensory reweighting for varying stimulus amplitudes. By altering the amplitude ratio of the LC and visual stimuli, they were able to demonstrate that the gain of the response to each stimulus was relative to its amplitude. For example, as the LC stimulus amplitude was increased, and visual stimulus amplitude decreased, the response gain for the LC stimulus was reduced, while increased for the visual stimulus. This demonstrates the ability of the nervous system to continually re-weight sensory inputs as we experience changes in our environment, to optimize our postural control. My results support these findings, and demonstrate sensory reweighting is relative to stimulus translation but not angle relative to the ankle joint.

In contrast to response gain, the correlation between the stimulus and response was greater when the stimulus amplitude was increased. The cross-correlation results revealed an in-phase coupling between LC and body sway, with a response latency of ~300ms (Figure 5.6C), consistent with findings in the literature (Wing *et al.*, 2011). Greater correlation between stimulus and response indicates higher fidelity of the response relative to the stimulus. Maurer *et al.*, (2006) also demonstrated a tendency for an increase in correlation with increasing stimulus amplitude (the stimulus was force applied to the torso). This effect is likely due to a greater overall amount of sensory information when the stimulus was greater in amplitude. For

example, the shear forces at the fingertip, and upper limb movement, would have been greatest when contact point motion was at the highest amplitude. Therefore, greater sensory information on the nature of the stimulus motion is available, and the ability to match the pattern of stimulus motion improved, even though the response gain was reduced.

In summary, lightly touching a moving object evoked postural responses in compensation for a false sense of self motion. Unlike vestibular input and ankle proprioceptors, I have shown somatosensory input from LC was not interpreted as angular body sway about the ankle joint. Instead the sway response was coupled with translation of the LC reference. Further research is required to understand how and why we respond to stimulus translation rather than angle.

## CHAPTER 6

### GENERAL DISCUSSION

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#### 6.1. Discussion of experimental chapters

In this thesis, I have presented four experimental chapters which have investigated the relationship between the upper limb and whole-body motion. In Chapters 2 & 3 I investigated how sensory signals, specifically vestibular input, are used to maintain accuracy of the limb when reaching for an object during unexpected body motion. While in Chapters 4 & 5, I focused on the function of the arm as a balance aid, determining how it acts upon sensory signals to maintain our balance, as well as providing passive balance control through sensory feedback.

##### 6.1.1. Vestibular control of reaching

When reaching, modulation of vestibular signals has been found to evoke arm movements that change the trajectory and endpoint of the limb (Bresciani *et al.*, 2002*a*, 2002*b*; Mars *et al.*, 2003; Moreau-Debord *et al.*, 2014). In Chapters 2 & 3, I investigated the functional nature of these limb responses. Specifically, my aim was to determine if the responses are compensatory for vestibular sensed whole-body motion.

Vestibular-evoked changes in arm trajectory when reaching for a memorized earth-fixed target have been demonstrated both in standing (Bresciani *et al.*, 2002*a*) and

sitting (Bresciani *et al.*, 2002b; Mars *et al.*, 2003; Moreau-Debord *et al.*, 2014) postures. These responses have been interpreted as compensatory for sensed whole-body motion relative to the target. If this is indeed the case, the magnitude of arm movement should be scaled to the magnitude of sensed body motion. Specifically, responses should be attenuated when sensed self motion is suppressed. Such attenuation has been demonstrated for postural responses, with the magnitude of responses reduced with the addition of non-vestibular sensory cues (Day *et al.*, 2002). However, this principle is ambiguous for upper limb responses when reaching. Bresciani *et al.* (2002a, 2002b) reported similar response magnitudes when standing versus sitting. In this case, a bite-board was used to restrict trunk movement during stance. Even so, it is reasonable to expect sitting would provide a greater amount of somatosensory feedback compared to standing, thus reducing perceived whole-body motion. They reported GVS-evoked arm movements of  $\leq 1.56^\circ$  (16mm for an arm length of 600mm). Other authors have also demonstrated GVS-evoked arm movement while seated with trunk movement restricted ( $\leq 10\text{mm}$  in Pu *et al.*, 2012;  $\leq 68\text{mm}$  in Moreau-Debord *et al.*, 2014). When I applied GVS to standing subjects with head and trunk movement restrained (Chapter 2), GVS-evoked arm movement was  $\leq 6\text{mm}$ . When subjects stood free of any restraint, the arm movement was five times greater ( $\leq 32\text{mm}$ ). In this case, trunk movement was responsible for 90% of arm movement. Obviously trunk motion can be attributed to a balance response (Day *et al.*, 1997). However, arm-on-trunk movement suggests the trunk and arm movement were coordinated to maintain pointing accuracy (Mars *et al.*, 2003), and arm movement was not merely secondary to a postural response. Interestingly, the arm responded earlier than the trunk. This may be due to a shorter

pathway between the arm and brain, compared to more distal muscles of the trunk and lower body (Ali *et al.*, 2003). On the other hand, it could be due to biomechanical factors, with the arm having much lower inertia than the body (Chandler *et al.*, 1975). Overall these findings suggest that when somatosensory input from the restraint (head clamp) was removed, sensed self motion relative to the target was greater, thus the upper limb compensated more. Therefore the upper limb response was relative to sensed whole-body motion, providing evidence the limb utilises vestibular signals to compensate for body movement.

A limitation of using a head clamp as a method of providing additional non-vestibular sensory information is that it also restrains any trunk movement. Therefore, it could be that GVS-evoked arm movements were relative to the magnitude of actual body movement, i.e., the arm just followed trunk movement. However, I found the arm moved independently of the trunk, suggesting this was not the case. A better method for testing the effect of non-vestibular sensory input on GVS-evoked arm responses would have been to provide different amounts of sensory cues on self motion without preventing body movement, e.g., vision, light touch, audio. Such cues could be introduced in a graded manner to test the hypothesis that increasing the amount of veridical sensory information available during GVS would reduce compensatory arm movements as sensed self motion is attenuated.

The fact that significant arm movements persisted with the head restrained, suggests whole-body movement was still perceived, albeit to a lesser extent. It may be that GVS-induced perception of self motion is attenuated by the addition of



somatosensory inputs, but never entirely abolished. This may explain why Bresciani *et al.*, (2002*a*, 2002*b*) found no difference in response magnitude between standing with a bite-board versus sitting. The bite-board alone could have provided enough somatosensory input to maximally attenuate sensed self motion, with the addition of extra somatosensory cues when seated, unable to further reduce the response.

Interestingly, vestibular-evoked arm-on-trunk movement was of similar magnitude when standing freely compared to when body movement was restrained. As previously discussed, when standing freely, arm-on-trunk movement was likely due to a coordinated trunk and arm response to compensate for sensed body motion. When trunk movement was restricted, only the arm was able to compensate for sensed self motion, so hand-on-trunk movement was inevitable. The observation that the response was of the similar magnitude regardless of restraint may be coincidental. It could be interpreted as a hard-wired reflex, such that the arm moves on the trunk by a fixed amount regardless of sensed motion, although this seems unlikely. Limitations in the method used to measure arm-on-body movement may explain GVS-evoked arm-on-trunk movement in my experiment. Measures of arm and trunk movement were constrained to the mediolateral axis and did not take into account any rotation of the body. Whole-body rotation at the ankle joint (i.e. roll) and/or rotation of the trunk (i.e. yaw) would result in greater lateral arm movement in-space compared to the trunk when the arm is held outstretched in front. Therefore, it is possible that the GVS-evoked arm-on-trunk movement discovered in my experiment was just an artefact of the methods used.

Another potential limitation of this experiment was a relatively small sample size ( $n = 6$ ). In some cases, statistical comparisons that were not significant may have been significant if the sample size was increased (post-hoc power analysis). Underpowered statistical testing introduces the possibility of incorrect rejection (Type I error) or acceptance (Type II error) of the null hypothesis.

To further understand whether vestibular-evoked arm movement was compensatory for whole-body motion, I hypothesised that such responses should only operate when reaching in an earth-fixed, rather than body-fixed, reference frame, since the latter situation requires no compensation for whole-body motion. In Chapter 2, preliminary data collected in standing subjects suggested that GVS-evoked upper limb responses were only apparent when reaching for an earth-fixed target. However, the results were inconclusive and difficult to interpret. Because subjects were standing, GVS evoked a balance response as well as arm movement, making it hard to dissociate the two. To observe upper limb responses in isolation from postural responses, in Chapter 3 I observed responses in seated subjects. By applying GVS simultaneously with actual body motion (chair rotation), it was possible to alter subjects' perception of self motion (Day & Fitzpatrick, 2005). When pointing at an earth-fixed target, the arm compensated for perceived body motion. These responses were almost identical to compensatory arm movements when actual chair velocity was altered unexpectedly. In contrast, when pointing to a body-fixed target, GVS had no effect on arm movement. This alteration of the evoked arm movement purely by a change in the intended target location suggests a cognitive influence upon vestibular control of the upper limb.

Interestingly, the early component of the arm movement response to body rotation was very similar when moving in a body- and earth-fixed reference frame (with and without GVS), although final arm positions were different between tasks. Therefore although the overall movement goal was successfully achieved in the tasks, there was a tendency to act the same during the early phase of the movement, despite the task instruction. This suggests the early component of the arm response may be free of cognitive influence, as has been suggested for balance responses (Guerraz & Day, 2005).

In summary, my findings provide further evidence for vestibular contribution to upper limb control when reaching during unexpected self motion. By demonstrating that vestibular-evoked arm movements are scaled according to the magnitude of sensed whole-body motion, and only operate when reaching in an earth-fixed reference frame, I conclude that these responses are compensatory for sensed whole-body motion in order to maintain reach accuracy.

### **6.1.2. The upper limb for balance**

After establishing that we use sensory signals to maintain reaching accuracy during unexpected body motion, in Chapters 4 & 5 I explored the role of the limb for balance, and how it both utilises and provides sensory signals about whole-body motion for balance control. In Chapter 4 I investigated vestibular-evoked upper limb responses for balance when holding a stationary object. The aim of this chapter was

to establish under what context of manual interaction the limb responds to vestibular signals for balance, and how contribution from the upper limb is coordinated with the lower limbs to form a whole-body response. While in Chapter 5 I was interested in the role of the upper limb as a sensor for balance control, with the aim of understanding how sensory signals from light contact are integrated and interpreted for balance control.

To my knowledge, Britton *et al.* (1993) are the only authors to observe vestibular-evoked upper limb responses for balance. In this case, subjects firmly grasped a handrail whilst standing on an unstable platform, such that applying forces to the handrail was the only means of staying upright. GVS modulated triceps brachii muscle activity consistent with hand forces intended to move the body in the opposite direction from the perceived body motion. However, holding a handrail whilst the lower limbs are disengaged from balance is not representative of everyday life, since both the upper and lower limbs normally contribute to balance. It was therefore unclear how the upper limb contributes to a whole-body balance response and is integrated with the rest of the body during normal stance. Furthermore, whether the context of manual interaction with the support (i.e. grip) would modulate the upper limb response was unknown, as during light grasp the hand acts primarily as a sensor. This suggests that a firmer grasp may be necessary to generate significant responses.

In Chapter 4, I applied GVS to subjects standing on a flat surface, either lightly or firmly grasping a fixed object. During light grasp the hand applied no force consistent

with moving the body in the opposite direction to sensed self motion. Instead, the observed change in hand force simply reflected the body sway. However, body sway and ground reaction forces were reduced compared to no contact. This is consistent with the arm providing additional cutaneous feedback for detection of self motion. As discussed, the addition of veridical sensory input is known to attenuate GVS responses. Therefore during light grasp the limb just acted as a passive sensor, as opposed to an active participant in the balance response. In contrast, when firmly grasping the support, the upper limb generated a force impulse to drive body sway towards the anode electrode. This was coordinated with a simultaneous ground reaction force impulse acting to drive the body in the same direction. Therefore, simply changing the nature of the grasp converted the limb from a passive sensor to an active participant in the balance response. This was not merely due to an inability to generate sufficient force in the light grasp position, since the limb generated similar maximum force compared to firm grasp, just not to drive body sway. This finding suggests that the change from light to firm grasp altered central recognition of the limb from a passive sensor to active contributor for balance. It is possible that cutaneous feedback from the hand is used to determine whether the hand could/should actively participate in balance control.

On the other hand, the very task of maintaining grip force  $< 1\text{N}$  in the light grasp condition may have also influenced the GVS-evoked responses. Riley *et al.*, (1999) demonstrated that when subjects are told that touching a surface is irrelevant to the experimental task, body sway is no different to when standing with no hand contact. In contrast, subjects who are directly instructed to maintain hand contact with the

same surface did have reduced sway. Therefore somatosensory information made available during light contact was not the primary contributor to the reduction in postural sway, but instead the demands of the task were the main influence on postural control. This alteration in the postural benefits of light touch by a change in task instruction suggests a cognitive influence upon light contact for balance.

During firm grasp, force generated at the hand and feet occurred simultaneously. But when pointing at a target (Chapter 2), I observed that the arm response occurred earlier than the trunk response. I speculated this was due to a shorter pathway between the upper limb and the brain, compared to the trunk and lower limbs. Britton *et al.* (1993) found the earliest GVS-evoked EMG responses in the triceps brachii appeared 20ms earlier compared to the soleus, when the respective muscles were used for balance. If a synchronous discharge from a common supraspinal structure is assumed for arm and leg responses, the difference in response timings could be simply attributed to the distance between the respective muscles and the brain (Britton *et al.*, 1993). However, these early responses are not responsible for generating the whole-body movement found. In contrast, the late component of the muscle response begins 22ms earlier in the leg than the arm (Britton *et al.*, 1993). It is suggested these responses form part of a patterned, functional response, activated in a distal to proximal sequence (Nashner, 1977; Britton *et al.*, 1993). I found no difference in the latency of the late component between upper limb force and ground force at the feet, when both upper and lower limbs were engaged in balance control. It may be that when both are contributing to balance, upper and lower limb forces must be generated simultaneously to produce a coordinated,

functional balance response. However, because I did not measure EMG responses, it is hard to compare response latencies with findings from Britton *et al.* (1993). Nevertheless, it seems likely that the latencies of GVS-evoked upper limb responses are dependent on the functional role of the limb.

During normal stance, GVS sway responses are directed towards the side of anode electrode placement. When the head is turned, the direction of the response remains aligned with the inter-aural axis, and is therefore craniocentric (Lund & Broberg, 1983; Mian & Day, 2009). I confirmed this principle, by observing that the direction of the ground reaction force vector and body sway responses were approximately aligned with the inter-aural axis. When three head orientations were compared during no contact, these responses remained fixed in head coordinates. During firm grasp, however, the upper limb force vector was also affected by head orientation, but was not aligned with the inter-aural axis. To interpret the direction of these responses, the simultaneous ground force vectors must be considered.

It has been shown that the craniocentric principle is violated when baseline stability is anisotropic (Mian & Day, 2014). It was demonstrated that changes in the mechanical state of the body (e.g. increasing stance width), or sensory input from contact with an external surface, produced anisotropy in body stability. This biased the GVS sway response towards the axis of least stability, being no longer directly related to head orientation. I found that firm grasp produced anisotropy in baseline stability, becoming less stable in the plane orthogonal to hand position. This was likely due to an altered mechanical state of the body, as well as sensory feedback

from contact. This skewed the ground reaction force response towards the plane of least stability, but only when the vestibular signal contained components in both the less stable plane and more stable plane of the body (i.e. the inter-aural axis was neither aligned with the hand position, nor orthogonal to it). Therefore, during firm grasp the ground force response violated the craniocentric principle as described by Mian & Day (2014). However, when the ground force and upper limb forces were summed, the combined vector was very similar to the ground force vectors during no contact. This suggests the upper and lower limb force vectors are integrated to preserve the direction of body sway. This was indeed the case, the body sway response was unaffected by anisotropy in baseline stability, and remained directed along the inter-aural axis regardless of head orientation, thus maintaining the craniocentric principle. One potential limitation of the methods used in this experiment was my use of a motion capture sensor fixed to the head to derive body sway. However, GVS has been shown to produce very similar sway responses when measured either at the head or trunk (Day *et al.*, 1997). Overall, the interaction between the upper limb and ground force vectors demonstrates upper limb contribution to a coordinated balance response for a vestibular perturbation.

The fact that neither the upper limb or ground force responses were aligned with the inter-aural axis (i.e. in the same direction as the body sway response) suggests individual components of the balance response remain modulated by the state of body stability, although overall whole-body sway was craniocentric. Further research is required to investigate how the state of body stability is integrated with vestibular signals to generate balance responses.



In addition to acting upon sensory signals for balance control, the upper limb also plays a passive role, providing sensory feedback of body motion. It is well known that light manual contact with a stationary surface improves balance control (Jeka & Lackner, 1994, 1995; Clapp & Wing 1999; Rabin *et al.*, 1999), even when the limb provides minimal mechanical support. In Chapter 4, when GVS was applied to subjects lightly grasping a stationary support, the upper limb did not generate forces to compensate for sensed whole-body motion. However, the sway response was reduced in magnitude compared to no contact with the support. This effect can be attributed to the limb being used as a sensor for detection of self motion relative to the contact point (Rabin *et al.*, 1999). In this case, self motion detected by the limb was in contradiction to the false vestibular signals induced by GVS. Such veridical sensory input during GVS is known to attenuate balance responses (Britton *et al.*, 1993; Day *et al.*, 2002). This suggests vestibular signals are integrated with sensory input from the upper limb for a sense of self motion, important for balance. However, quite how the CNS interprets and integrates light contact sensory input remains unclear.

The final aim of this thesis was to establish how sensory signals from light contact are integrated and interpreted for balance control. Light finger contact with an oscillating contact point evokes body sway entrained with the motion of the contact reference (Jeka *et al.*, 1997; Oie *et al.*, 2002; Allison *et al.*, 2006; Wing *et al.*, 2011). The sway is believed to be a balance response for a false interpretation of contact point motion as self motion. Human balance during stance has been biomechanically

modelled as angular body sway about the ankle joints, i.e. an inverted pendulum (Winter *et al.*, 1998; Gage *et al.*, 2004). Based on this consideration, in Chapter 5 I hypothesised that detection of self motion from light contact with an external stimulus is interpreted as angular body sway about the ankles. As expected, when standing subjects lightly grasped a touch pad that moved about an equal radius relative to their ankle joints, their sway became entrained with the profile of the stimulus. However, when the angular movement of the touch pad was kept constant, but its linear *translation* was increased, the magnitude of the sway response was greater. Therefore the balance response was not matched to the angular motion of the stimulus. Contrary to my hypothesis, it seems that sensory signals from light contact were not interpreted as angular deflection of the body about the ankle. Instead, the balance response was closely related to the amplitude of contact point translation. These findings suggest we do not reference contact point motion as angular motion relative to the ankle for postural control, but generate a balance response relative to contact point translation in space. Why this is the case is unclear. It may be important to consider the velocity component of contact point motion in future research, as some authors have demonstrated both position and velocity coupling of body sway to somatosensory stimuli (Jeka *et al.*, 1998).

By altering the amplitude of the light contact stimulus, I was able to demonstrate an effect of stimulus amplitude on response gain. As the amplitude of the stimulus increased, the gain of the sway response was reduced. This result supports findings for various other somatosensory and visual stimuli (Oie *et al.*, 2002; Peterka, 2002;

Ravaoli *et al.*, 2005; Allison *et al.*, 2006; Maurer *et al.*, 2006; Assländer & Peterka, 2014). This effect has been attributed to sensory reweighting. As the stimulus amplitude is increased, input corresponding to the stimulus for detection of self motion is deemed less reliable and greater weight is placed on other sensory inputs. I also demonstrated an effect of stimulus amplitude on stimulus-response correlation, with higher correlation as amplitude increased. This finding suggests that even though we trust input from light contact as an indicator of self motion less when the stimulus is increased, the fidelity of the response is improved. This is likely due to a greater overall amount of fingertip sensory stimulation when the amplitude of contact point motion is greater.

It has been suggested that instructing participants to maintain a constant level of light contact with a moving object constitutes as a manual tracking task, and that postural motion may function to facilitate manual tracking performance as oppose to purely being a balance response to sensed self-motion (Riley *et al.*, 1999). In my experiment, participants were instructed to maintain light contact with a touch pad and no information was given about whether or not this would move. Thus, although there was not an explicit instruction for manual tracking of the touch pad, tracking was required in order to maintain light contact as instructed. Therefore it is important to consider task instructions when interpreting postural responses to light contact. To test whether or not body sway during light touch with a moving object is in response to sensed self-motion or just facilitating manual tracking, an experiment could be designed such that participants are in contact with a moving object but

regard the contact as irrelevant to their performance in the experiment, as has been done for contact with a stationary object (Riley *et al.*, 1999).

In summary, I have further demonstrated the active and passive roles of the upper limb for balance during unexpected body motion. The role played by the upper limb is dependent on the context of manual interaction. When active, the upper limb generates forces in coordination with the rest of the body to produce body movement in compensation for vestibular sensed whole-body motion. When passive, the limb acts as a sensor for the detection of self motion for balance control. However, it seems sensory signals from the limb are not interpreted as angular body sway.

## **6.2. General conclusions**

I am now able to draw a number of general conclusions from this body of work. When we reach for an object, vestibular signals contribute to maintain reach accuracy during any body motion that may take the limb off-target. This mechanism is dependent on the task requiring compensation for body motion relative to the target, and compensatory arm movements are scaled to the magnitude of sensed whole-body motion. When making contact with a fixed object, the limb contributes to balance control. The context of manual interaction with the object determines the limb's role as either a passive sensor or active participant. As an active participant, the limb generates forces in compensation for vestibular perturbation that contribute to a coordinated whole-body balance response. While as a passive

sensor, the limb provides sensory detection of self motion for balance control. However, it is unlikely that these sensory signals are integrated and interpreted as angular body sway.

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