Directional Response Properties
of Muscle Proprioceptors to Postural Disturbances

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Directional Response Properties
of Muscle Proprioceptors to Postural Disturbances

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"We all agree that your theory is crazy, but is it crazy enough?"- Niels Bohr

I would like thank my family for their support and belief in me, from across the endless *kilometers* of land and sea.

I thank Stan Nakanishi for his help on experimental setup and techniques. The mohawk will be missed.

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"To dream anything that you want to dream, that is the beauty of the human mind. To do anything that you want to do, that is the strength of the human will. To trust yourself, to test your limits, that is the courage to succeed." *- Bernard Edmonds*

"The person who says it cannot be done should not interrupt the person doing it." *- Chinese Proverb*

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GLOSSARY

aBF   anterior biceps femoris

mBF   middle biceps femoris

pBF   posterior biceps femoris

MG   medial gastrocnemius

EMG   electromyogram

SUMMARY

The somatosensory system has been implicated in the compensatory response of the nervous system to postural perturbations in humans and cats. The approach elicited - dubbed the Force Constraint Strategy - through a possible combined action of proprioceptive and cutaneous feedback, determines, and adjusts for, horizontal disturbances in various directions of a supporting surface.

To understand the mechanisms underlying this strategy, we asked whether the response patterns of muscle proprioceptors correspond to those of electromyographic recordings (EMG) in the aforementioned Force Constraint experiments.

The mechanical properties of the musculoskeletal system may also play a role in the restoration of stability. Thus, we also hypothesize that a proximal muscle would be relatively tightly tuned spatially whereas the distal muscle would exhibit a more diffuse spatial response distribution. To this end we selected the *medial gastrocnemius* (MG) and *biceps femoris* (BF) muscles to serve as our proximal and distal models respectively.

Cats anesthetized using pentobarbital were set in a stereotaxic frame with the right leg positioned on a servo-controlled platform. The platform was shifted horizontally in 16 different directions according to a ramp-and-hold waveform. Intra-axonal recordings of activity from Ia afferents of BF and MG muscles were taken. Results indicate that the strategy makes use of information from the muscle proprioceptors. However, there is no differential response in tuning breadth with respect to muscle architecture.

By characterizing the role of muscle proprioceptors in the mediation of corrective responses to perturbations of balance and stability, the results from this experiment can be used to verify biomechanical models, as well as further elucidate the underlying mechanisms of motor control.

CHAPTER 1

INTRODUCTION

Sensory control of the mechanisms of posture and stability depends on various systems. The signals from these systems, including the somatosensory (proprioceptive and cutaneous signals), as well as the vestibular and visual, are integrated together (Peterka 2002). This enables the control system to determine the status of the body with regard to its equilibrium position. Any deviation from this position elicits a compensatory/restorative motor response. The integration of information from multiple input sources is very important as it helps to resolve ambiguities in perception (Horak and Macpherson 1996). A particular sensory system may produce the same response for non-unique environmental stimuli, and so information from this system alone would be insufficient to determine the body's postural state.

Research into the response of cats to horizontal disturbance of their supporting surface (Macpherson 1988a, b) has revealed that a single strategy (termed the Force Constraint Strategy) is employed in order to counteract the perturbation effects and restore the position of the centre of mass with respect to the limbs. Each hindlimb produced a ground-reaction force - in one of two directions - with amplitude modulated to the direction of perturbation. Furthermore, the muscle activation patterns, as depicted by electromyographic recordings, demonstrated that the postural response is tuned to the direction of the supporting surface perturbation. This response has also been observed in humans (Henry et al. 1998).

Vestibular System

Vestibular receptors detect acceleration of the head in a gravitoinertial reference frame, that is, a frame of reference that takes into account gravitational and inertial forces (Nashner et al. 1982). Thus, when considering movement relative to the environment (or even movement of the environment relative to the body), the otolith organs of the vestibular system sense (i) the linear acceleration produced by translation (horizontal, vertical, or lateral movement), (ii) the direction of the gravitational acceleration, and (iii) body tilt, thereby assisting in setting the spatial vertical reference. Furthermore, the vestibular system also includes semicircular canals that detect rotational acceleration associated with motion in a curved path.

Because the vestibular and visual sensors are based in the head, and movement of the head is independent of that of the rest of the body, information on the position of the trunk and limbs in space is inferred and thus incomplete. This limits the capacity for precisely coordinated large scale movements and fine motor control. Furthermore, the transmission of this information is not sufficient to account for the short latency reactions observed in EMG experiments in response to postural disturbances (Horak et al. 1990; Nashner and Berthoz 1978). The somatosensory system is required to provide complete information concerning the spatial configuration of the various body segments.

Somatosensory System

Research has demonstrated that the somatosensory system plays a major role in the determination and regulation of postural orientation and equilibrium, even in the face of

unexpected postural disturbances (Macpherson 1988a, b; Stapley et al. 2002; Thomson et al. 1991). This system includes afferents in the form of cutaneous receptors, and proprioceptors such as muscle spindles and Golgi tendon organs (Dietz 1992; Nardone et al. 1990; Nashner 1976). *This study focuses on the roles of muscle proprioceptors as candidates for regulating the responses to postural disturbances.* Therefore, the mechanisms underlying postural adjustments and the associated receptors must be examined.

Cutaneous Receptors

Cutaneous receptors, located in or near the junction of the dermis and the epidermis, can act in three main capacities: mechanoreceptors, thermal receptors, and nociceptors (Iggo and Andres 1982; Iida et al. 1999)). Depending on their location (hairy skin or glabrous skin) and function, the various receptors may be classified either as slowly adapting (which transmit impulses to the central nervous system for the duration of a constant stimulus), or rapidly adapting (which gradually decrease firing, in the presence of a steady stimulus, to a low baseline level or to extinction). The mechanoreceptors, particularly those that respond to skin movement, are the most salient to the task of postural regulation (Horak and Macpherson 1996). In experiments investigating postural responses to rotation and translation, (Ting and Macpherson 2004) proposed that the cutaneous receptors are responsible for the directional tuning of the automatic response for maintaining balance.

Muscles

Muscle fibers, specifically those of skeletal muscle, are the actuators for voluntary movement. These fibers are bound together by connective tissue and attached to bones via tendons. These extrafusal muscle fibers are innervated by the axons of alpha motor neurons and contain longitudinal bundles of myofibrils that provide the basis for producing muscle contraction. The extrafusal muscle fibers, together with their associated alpha motor neuron, are called a motor unit. Intrafusal fibers, found within encapsulated structures known as muscle spindles, are served by both sensory (spindle afferent) and motor (gamma motor neuron) axons.

The discovery of the Force Constraint Strategy, in which the limb muscles combined to produce a ground reaction force to stabilize the animal, led to work which sought to characterize the forces produced by individual muscles (Murinas 2003). Such information would be very useful in constructing a picture of muscle synergies involved in generating the whole limb response.

Limb architecture controls much of an animal's behavior (Kargo and Rome 2002; Mussa-Ivaldi et al. 1985). Thus, the anatomical and geometrical design of the musculoskeletal system may also play a role in the restoration of stability (Lieber and Friden 2000). To further understand the action of the muscles in postural regulation, researcher have implemented 3-D anatomical musculoskeletal models on the computer (Burkholder and Nichols 2000; Burkholder and Nichols 2004; Kargo and Rome 2002). The Burkholder and Nichols model describes the action of 32 muscle-tendon units and consists of 7 degrees of freedom: 3 at the hip, 2 at the knee and 2 at the ankle. This model was used to predict the endpoint forces generated by various muscles. Based on

the concordance in results among this model, the experimental ground reaction forces of Murinas 2003, and the Macpherson 1988 tuning curves, we chose to target two specific muscles: medial gastrocnemius and biceps femoris. Even though there is agreement with respect to direction, their separate architectures (BF is proximal and triarticular while MG is distal and biarticular) may dictate different spatial response distributions about the resultant (when subjected to the same type of disturbances as in the Macpherson 1988 experiment).The medial gastrocnemius is one half of the biarticular muscle which forms from two heads attached to the femur. The heads joins at the upper tibia and insert into the lateral portion of the proximal calcaneus via the Achilles tendon (Lawrence and Nichols 1999a, b). Analysis of the biomechanics showed that MG muscle exerts substantial ankle joint torques that cause plantarflexion as well as abduction.

The biceps femoris muscle consists of two heads (Chanaud et al. 1991). These heads are subdivided into three compartments, each supplied by a branch of the sciatic nerve. Thus the posterior bicep femoris is innervated by a single nerve. The anterior head is further divided into the anterior and medial biceps femoris compartments. Biceps femoris originates from the ischial tuberosity, spreads across most of the lateral surface of the thigh (Pratt et al. 1991) and inserts into the lateral margin of the patella, as well as the proximal third of the lateral tibia. Hence, biceps femoris is a large, triarticular muscle that extends the hip, flexes the knee, and laterally rotates the foot outward through similar action at the tibia.

Muscle Spindles

Structure

Muscle spindles are a mixture of muscle and sensory tissues, and so possess some attributes of each. Spindles contain specialized cells called intrafusal muscle fibers that possess areas that are striated, wherein lies the ability to contract. However, unlike other muscle, these areas are only to be found at the ends; the central regions are non-contractile. These intrafusal fibers are found within the core of muscles and are oriented in parallel with the main extrafusal fibers. There are two main types of these multi-nucleated intrafusal fiber: nuclear bag and nuclear chain (Prochazka 1996). The former are so called because the nuclei are concentrated in the center of the fiber, which swells out into a bag. Conversely, the nuclei run along the non-contractile length of the nuclear chain fiber. The nuclear bags are further sub-divided into static and dynamic varieties based on their mechanical properties. As previously stated, the muscle spindles have both sensory and motor components. Sensory information is recorded by two main fiber types. A large-diameter (12-20 um), myelinated primary sensory fiber (known as group Ia), innervates all the intrafusal fibers. The endings wrap around the central part of the intrafusal fiber in a spiral formation and are thus known as annulospiral endings. A smaller-diameter (6-12 um), myelinated secondary sensory fiber (known as group II), innervates the chain fibers and static bag only. These are located away from the central - but still in the non-contractile - region and, owing to their configuration, are called flower-spray endings. Motor input is provided by two types of small-diameter gamma motor neurons, as opposed to the large-diameter alpha motor neurons that innervate the extrafusal muscle fibers (Matthews 1964). Dynamic

bag fibers are innervated only by dynamic motor neurons while static gamma motor neurons make connections with the static bag and chain fibers. These connections are at the polar contractile ends of the intrafusal fibers.

Ia afferent enters the spinal cord dorsally, traverses the intermediate zone, and forms a monosynaptic connection with an alpha motor neuron in the ventral horn. This motor neuron innervates the homonymous muscle, that is, the very muscle containing the activated muscle spindle.

Function

The intrafusal fibers are categorized as static and dynamic because of their mechanical properties. The former respond to slow steady changes in muscle length and the latter to rapid changes in muscle length (Prochazka 1996). Thus the static bag and nuclear chain fibers - and their corresponding primary and secondary sensory endings - signal a steady-state change in length. Conversely, the dynamic bag fiber, and by extension its primary sensory ending, is highly sensitive to the velocity or rate of change of muscle length. This means that the Ia afferents code for both the length change and velocity of change, and studies have shown that the discharge frequency is directly proportional to the extent of spindle stretch. On the other hand, the group II afferents predominantly encode stretch.

The associated gamma neurons also play a role in the activity of the receptors. When gamma motor neurons are activated, they cause contraction of the polar ends, which increases the stretch on the central region. As indicated before, increased stretch results

in higher discharge frequency. Activation of gamma motor neurons can prevent

slackness in muscle spindles and may influence sensitivity (Hulliger 1984).

Golgi Tendon Organs

Structure

Unlike the muscle spindle, the Golgi tendon organ lies in series with the muscle, at the

junction between the muscle fibers themselves and the tendon (Jami 1992). It consists

of a capsule innervated by a group Ib axon. Like its group I counterpart, the Ia fiber,

this is a large diameter afferent (12-20um). The Ib afferent - an unmyelinated, branched

network within the capsule - is entwined with collagen fibers belonging to the tendon.

The afferent leaves the capsule as a single myelinated nerve and makes its way to the

spinal cord. Like the spindle afferents, the GTO fibers enter through the dorsal root and

synapse at the alpha motor neurons innervating the homonymous muscle. However,

unlike the spindle afferent, this is not a monosynaptic connection. The afferent first

makes an intermediate synapse with an interneuron, which in turn synapses with a

variety of alpha motor neurons.

Function

The nerve fibers within the capsule are mechanoreceptors. Stretching of the tendon,

such as would be caused by increased muscle tension during active contraction of

extrafusal muscle fibers, straightens the collagen fascicles associated with the tendon

(Jami 1992). This exerts pressure on the Ib sensory mechanoreceptors, eliciting a firing

response whose discharge rate is directly related to the force applied (Crago et al. 1982; Houk and Henneman 1967).

Role of Proprioceptive Feedback in Postural Regulation

Detection of - and initiation of rapid responses to - perturbations in stance are dependent on proprioceptive information (Inglis et al. 1994). Among the most salient to this study is monosynaptic stretch reflex, the tonic contraction of a muscle in response to its being stretched (Liddell and Sherrington 1924). When a muscle lengthens, there is an increase in spindle discharge. As previously mentioned the afferents carrying this signal enters the spinal cord and monosynaptically activates the alpha motor neuron innervating the homonymous muscle. This causes the extrafusal fibers to tighten and attempt to shorten. This contraction in turn leads to decreased spindle firing, which reduces the excitation induced on the alpha motor neurons and hence leads to muscle lengthening. This continuous action has been thought to provide a mechanism of stiffness regulation (Nichols and Houk 1976). It has been claimed that postural responses are determined by proprioceptors projecting to supraspinal centers, rather than from spinal reflexes (Macpherson et al. 1986). Furthermore, Ting and Macpherson 2004 have strongly suggested that cutaneous receptors – and not muscle proprioceptors – are responsible for the directional tuning of the responses to perturbation. However, the Burkholder/Nichols models used musculoskeletal architecture (without need for higher/supraspinal control) as the sole basis for predicting the pulling directions (Burkholder and Nichols 2000; Burkholder and Nichols 2004). The results of this model, which have been experimentally corroborated (Murinas 2003; Macpherson

1988), strongly point to the influence of proprioceptive feedback (particularly that of the stretch reflex). Thus one cannot rule out contributions of muscle proprioceptors to the Force Constraint Strategy.

Project Goals

Muscle activation patterns and endpoint forces produced by a hindlimb during postural perturbations of a supporting surface have been modeled (Burkholder and Nichols 2000; Burkholder and Nichols 2004) and experimentally characterized (Macpherson 1988a, b). For both the medial gastrocnemius and biceps femoris muscles, the 3-D model (Burkholder and Nichols 2004) predicted horizontal plane endpoint forces directed caudally and slightly in abduction. These results corroborated the findings of Murinas 2003 in her characterization of endpoint forces generated during stimulation of the individual muscles.

The results suggest that the muscles would exhibit the highest activation when the supporting surface is made to perturb the leg in a path directed rostrally and in adduction, that is, opposite that of the endpoint force vector. This was previously borne out, for the biceps femoris muscle as a whole, by Macpherson 1998b, in the follow-up work to the identification of the Force Constraint Strategy. Another study however has obtained EMG responses to 16 directional perturbations for the separate compartments of the biceps femoris (Chanaud and Macpherson 1991).

Studies have indicated that proprioceptive signals may contribute to postural regulation strategies since certain aspects, such as orientation, are computed at the spinal circuit level (Bosco and Poppele 2001; Lacquaniti et al. 1990). Therefore, we hypothesize that,

if the muscle spindles and the pathways that parallel or include the stretch reflex contribute to the Force Constraint Strategy, then the response patterns of muscle proprioceptors will correspond to those of EMG identified in the aforementioned studies. Consequently, if this involves proprioceptive feedback rather than supraspinal control, it will be oppositely directed to the endpoint force vectors.

Intra-axonal recordings of activity from Ia afferents of biceps femoris (BF) and medial gastrocnemius (MG) muscles will be taken. The proprioceptor response patterns will then compared to that of the EMG and endpoint force patterns. The activation patterns are expected to be in a direction of perturbation that is rostral and in adduction. More specifically, with regard to the separate compartments of the biceps femoris, one would expect differing ranges of activation in accordance with the EMG responses observed by Chanaud and Macpherson 1991. That is, perturbations directed rostrally and in adduction should activate anterior biceps; perturbations directed completely rostrally or rostrally and slightly in adduction should activate medial biceps; and disturbance directed rostrally and in abduction should favorably activate posterior biceps femoris. This study will help to elucidate the possible sources contributing to postural regulation.

CHAPTER 2

METHODS

Anesthetic Preparation

Experiments were conducted on three adult cats. The cats were administered an

isoflurane/oxygen mixture in order to attain a level of anesthesia for surgery. A

tracheotomy was then performed and the airway was kept open by the insertion of an

endotracheal tube. The endotracheal tube was connected to a respirator which

maintained inspiratory and expiratory airflow at a desired level. A carotid artery was

cannulated in order to monitor blood pressure. Both common carotid arteries were tied

off rostrally to the cannulation point to reduce bleeding. A cannula was also inserted

into the external jugular and a continuous supply of fluids delivered to support

cardiovascular function (mean arterial blood pressure greater than 70 mmHg).   A 10

cc syringe of pentobarbital (Nembutal) was also connected to an access point in the tube

that fed into the vein. Administration of the inhalation agent was ceased at this point.

The amount of pentobarbital administered was adjusted to maintain a surgical level of

anesthesia (areflexic state). The core body temperature was monitored via a rectal

probe and maintained between 36 and 38 C with a heated pad and/or infrared lamp.

Preparation for Intra-axonal recording

In order to obtain recordings, it was necessary to access the dorsal rootlets. Thus, a

laminectomy was performed. Firstly, incisions were made in the midline of the back

and the left and right back muscles were dissected off the lamina on both sides at the

lumbar and sacral levels. After reaching the spine, the lamina was removed thereby exposing the dorsal and ventral nerve roots.

An incision was made into the right hind leg, the medial gastrocnemius and biceps femoris nerves dissected out from the rest and nerve cuffs placed on them. The incision was then closed with steel staple sutures.

The cat was then secured using frames for the head and spine. The head was fixed in a horizontal position with ear bars and the stereotaxic frame. The spine was stabilized with the use of hip pins (just anterior to the greater trochanter), as well as a clamp at L4 spinal process and another on L7 vertebral body. To support the upper body, a clamp was placed at the high thoracic region. The right hind limb was placed on the platform in its natural position, which is on an angle of approximately 30 in abduction. The steel sutures were removed, re-exposing the tissue. The skin flaps were positioned over the spine in such a way as to form a pool into which was poured mineral oil. This procedure prevented the tissue from drying out. The left limb was suspended in extension in order to help prevent the hip from sagging.

Decerebrate Preparation

In one animal, decerebration was utilized instead of pentobarbital anesthesia. Under isoflurane anesthesia, a midline incision was made over the skull and the overlying skin and muscles reflected. The skull was opened up, via a bilateral craniotomy (approximately 1 cm radius), to expose the parietal cortex. With a spatula, an inter-collicular (between inferior and superior colliculi) transection was made. All brain tissue, including the cortex, basal ganglia, and thalamus, was removed by aspiration.

To protect the rest of the tissue from dehydration, the floor of the skull was covered with small cotton ball soaked in saline. Over this was placed mineral-oil soaked cotton gauze. At this point the anesthetic agent was discontinued. In order to allow for blood clotting, as well as vessel contraction, the cat was left undisturbed for at least an hour after the procedure.

Data Collection/Intra-axonal Recording

The muscle was stimulated via the cuff electrode-encased nerve. Using a bipolar electrode, the rootlet with a high concentration of afferent signals originating from the target muscle was selected to examine afferent activity. A glass micropipette slowly inserted into the chosen rootlet was used to detect orthodromic potentials coming from the stimulated muscle. Identification of the afferent involved calculating its conduction velocity. The axon's conduction time between the stimulation and recording sites was measured. Hence, together with the distance between these two points (measured post-experiment), the conduction speed was determined. During the rising phase of the twitch contraction, a characteristic pause or deceleration in the firing rate was indicative of the muscle spindle while acceleration in the firing rate identified the Golgi tendon organ.

The horizontal coordinate system for translation was chosen as follows: 0 represented forward, 90 perpendicularly right, 180 back, and 270 perpendicularly left. Translation of the foot was controlled by a servomotor with lead screw drive and an encoder for feedback control, which was mounted on a rotary stage. This stage could be manually

turned to any desired degree for translation. This could be done while maintaining the platform, and hence the foot that rested on it, immobile. Owing to the manual nature of obtaining directions, the order was not random. The stage was rotated from 90 through 270 and, because the motor could be moved both forward and backward, the full complement of angles could be obtained.

Translation directions were given via modified software written in LabVIEW by Mr. William Goolsby. The motor was always directed to first move at a speed of 20mm/s, either forward or backward depending on the desired direction. The linear phase of the ramp lasted 100ms, with 50ms extra consumed in deceleration. The hold period lasted 1800ms, after which the leg was returned to its original position. The afferent response to translation of the supporting surface in 16 directions was recorded. The CED Spike 2 software package was used to collect and digitize the afferent data. The animal in its stereotaxic frame was isolated from the actual motor apparatus that moved the foot in order to reduce the effect of vibrational noise on the recordings at the dorsal root.

Analysis of Data

Instantaneous firing rate was first calculated using the Spike2 software. The parameters were chosen to capture the main aspects of the receptor's response to the perturbation. To capture the pre-perturbation phase, the average background instantaneous firing rate was recorded as this would serve as a reference against which the other parameters in future stages could be analyzed. During the perturbation itself, the muscle would display its dynamic response properties. To capture this, the strength of response

(number of spikes and peak instantaneous firing rate), as well as onset of said response (time to first spike and time of peak rate), were recorded. Finally, in the hold or plateau phase, the muscle would be expected to exhibit its steady state response, and these could be measured by the number of spikes in the steady state (in comparison with the ramp phase) or with the average steady state instantaneous firing rate (in comparison with the pre-perturbation background rate.) A spike2 script was written by Clotilde Huyghues-Despointes and me to obtain these parameters, which was then processed in MATLAB. Only units which gave data for more than 80% of the directions were examined. 18 units (11 MG and 7 BF), were eventually analyzed; 0 of those were GTOs.

CHAPTER 3

RESULTS

Afferent Identification and Classification of Parameters

Useful data was obtained only from the pentobarbital-anaesthetized animals. The afferents examined had conduction velocities ranging from 80-105 m/s, well within the range for group I. The muscle spindles were identified as being spindle afferents based upon the characteristic deceleration or pause in firing rate during the rising phase of a twitch contraction (Figure 1A). Conversely, the Golgi tendon organs were identified by and acceleration of firing during the rising phase of the twitch force (Figure 1B).

The stimulus profile followed a ramp and hold characteristic. This allowed us to obtain afferent response profiles corresponding to the pre-perturbation, the dynamic, and finally the steady state phases when the muscle stretch had ended and the muscle was being held at its new length (Figure 2).

Based on the time of the initiation of the stimulus, a Spike 2 script was used to extract data related to the desired parameters. Figure 3 depicts how these parameters were determined from the output channel (instantaneous firing rates).

General Profile Characteristics

Of the 7 biceps femoris afferents, 1 was identified as anterior BF, 1 as medial BF, and 2 as posterior BF. We were unable to identify the specific BF compartment of the other 3 afferents. 6 of these showed similar firing patterns in response to diametrically opposed directions of perturbation. Excitation (activation rates above background) was observed in response to movement in one direction with inhibition (activation rates
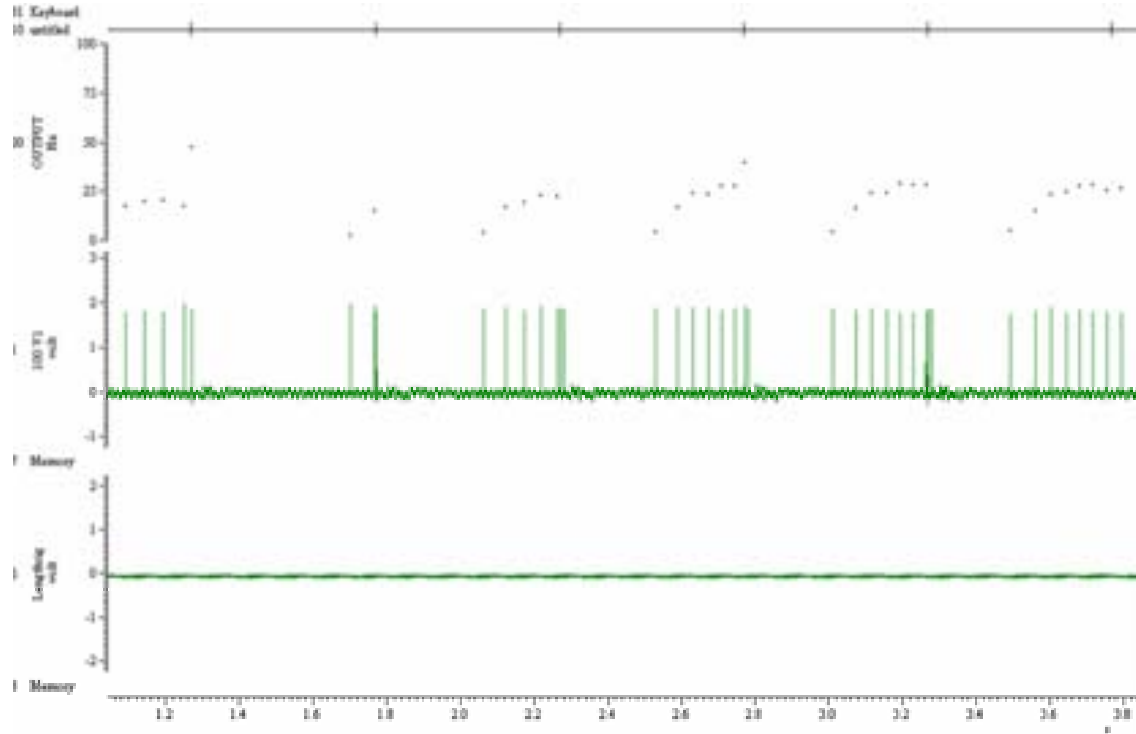
Figure 1: Determination of Receptor Type. The figures show a portion
of the processed data from the Spike 2 (Cambridge Electronic Design)
recording software. Channel 5 shows the length signal, which
indicates how far from equilibrium position is the supporting platform.
Channel 1 shows the activity recorded from the muscle receptor. In
this case this represents the resting or background activity. Channel
20 represents the instantaneous firing rate. Channel 10 represents
the instances when an impulse in sent to the muscle, as indicated by
the short vertical lines at particular intervals along the horizontal.
(A) Activity from the receptor ceased each time an impulse was applied
which, together with its identification as a Type I (conduction
velocity > 80 m/s), indicates a spindle afferent. (B) Receptor
activity increased with application of impulse. Receptor was thus
classified as a Golgi tendon organ.

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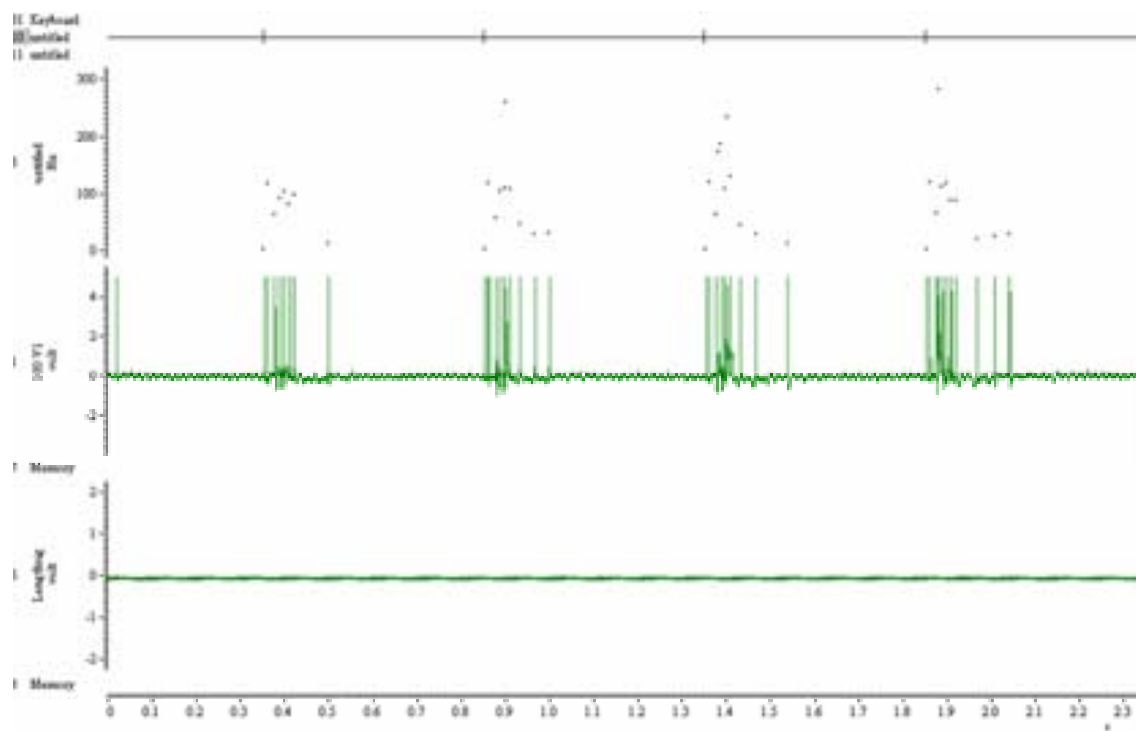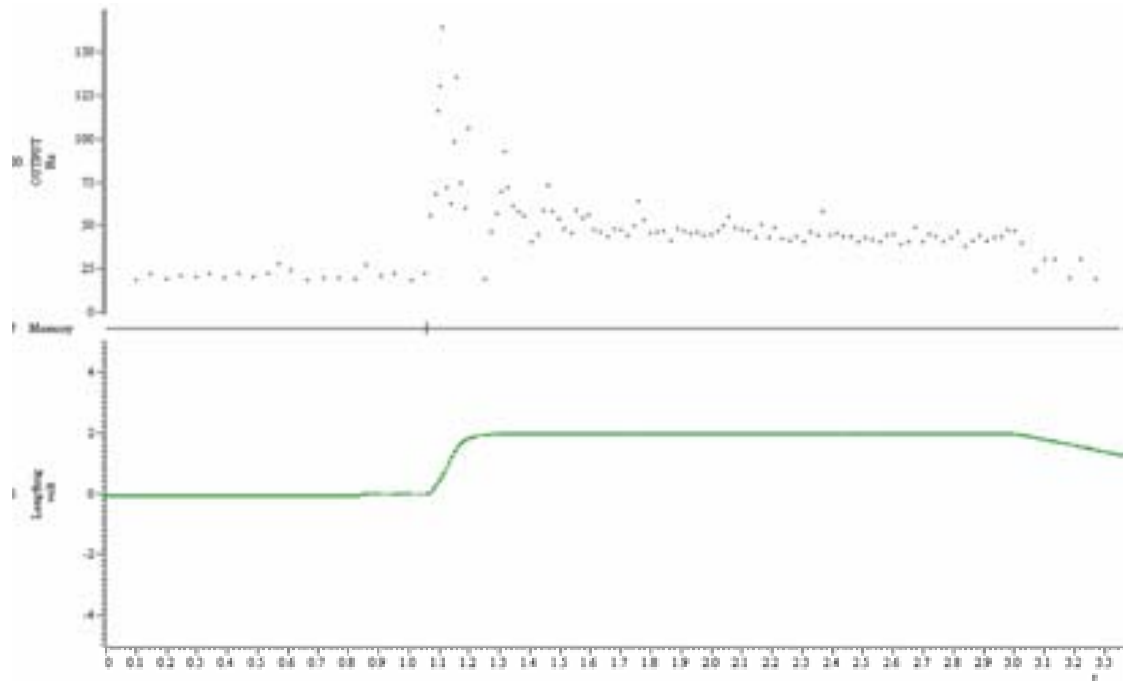
Figure 1B

Figure 2: Spindle afferent response to perturbation. Channel 5 shows the length signal profile of the three stages of the perturbation (pre-perturbation, stretch, and plateau). Channel 20 shows the instantaneous firing rates of the corresponding background, dynamic, and steady state responses of the receptor. Channel 7 shows the point at which the stretch phase began, and was used for analysis purposes.
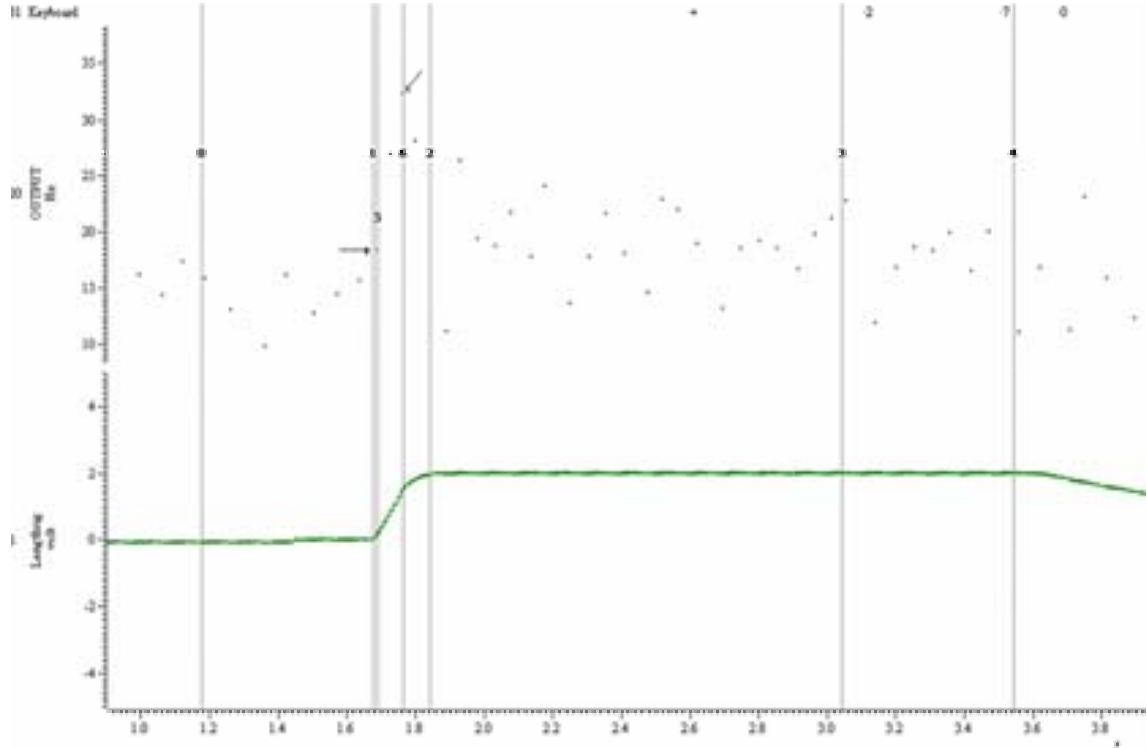
Figure 3: Reference points for the definition of parameters. As in
the previous figure, Channels 5, 20, and 7 respectively indicate the
length signal profile, the corresponding firing rate, and the point of
start of the ramp phase. The numbered vertical lines are used as
references for which to determine the value of the desired parameters.
Line 1 overlaps the point from channel seven and thus represents the
start of the ramp phase. Interval 0 to 1 (500ms) is used to obtain
the instantaneous background firing rate. Interval 1 to 2 (150ms) is
used to determine the number of spikes during the ramp. Analysis
within interval 3 to 4 (500ms) gives the number of spikes during the
steady state as well as the steady firing rate. Line 5 overlaps the
point that indicates the first spike time, also pointed out by the
lower arrow. The upper arrow indicates the point where the peak
firing rate occurs, as portrayed by Line 6.

below that of background) in the other. The remaining unit displayed brief bursts during the dynamic phase with no steady state response. The 11 medial gastrocnemius receptors, however, displayed three main types of response profiles. The first, classified as MGa, displayed profiles similar to those of the biceps afferents. The second class, MGb, exhibited dynamic and steady state responses in one direction. A weaker dynamic response is seen in the other direction as well as a lack of a steady state response. The final profile displayed identical steady state and dynamic responses to diametrically opposed directions.   Figure 4 shows an example of these profiles, together with a reference length signal.

The behavior for a biceps femoris unit observed in Figure 4 is further illustrated in Figure 5, which depicts all 16 directions of translation for one unit from an animal under anesthetic (Nembutal) preparation. Also of note is that for some diametrically opposed directions of perturbation there are robust inhibitory and excitatory responses in all directions except around 90 through to 112.5 and 270 through to 292.5 - essentially in motions orthogonal to the sagittal plane. Particularly in the directions 90 and 270, we observe activity at the end of the plateau, when the platform is returning to equilibrium position. These responses were not repeatable and so may have been artifact.

Specific Afferent Patterns of Response

The data obtained was compiled and transformed into a polar coordinate format, which uses the same coordinate system as during the experiments in order to provide a more

intuitive representation of the patterns of afferent responses to the horizontal

perturbations of the supporting surface. Figure 6, which depicts both dynamic and
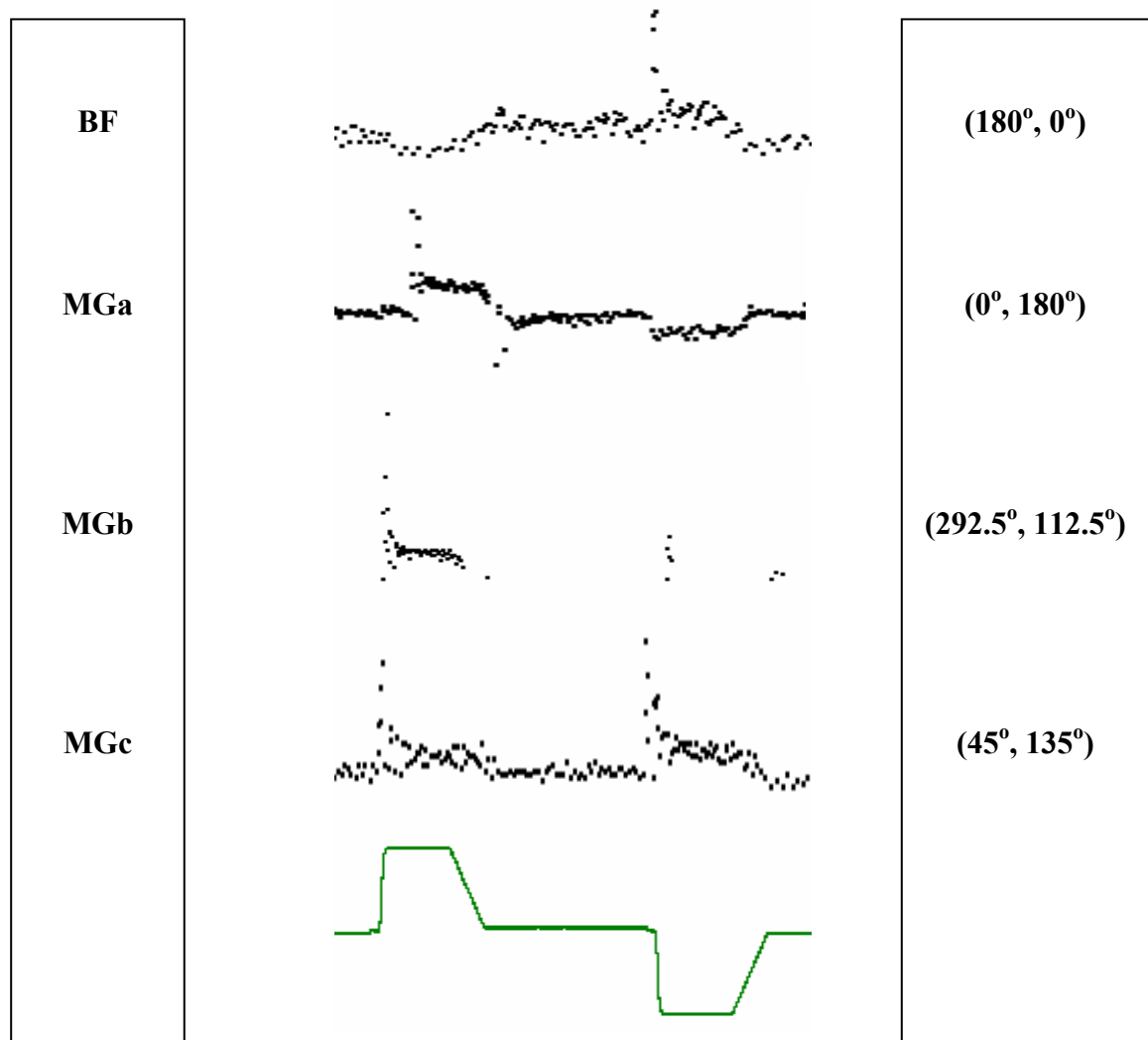
Figure 4: Multiplicity of firing patterns. The figure displays the various firing profiles observed for muscles spindles.
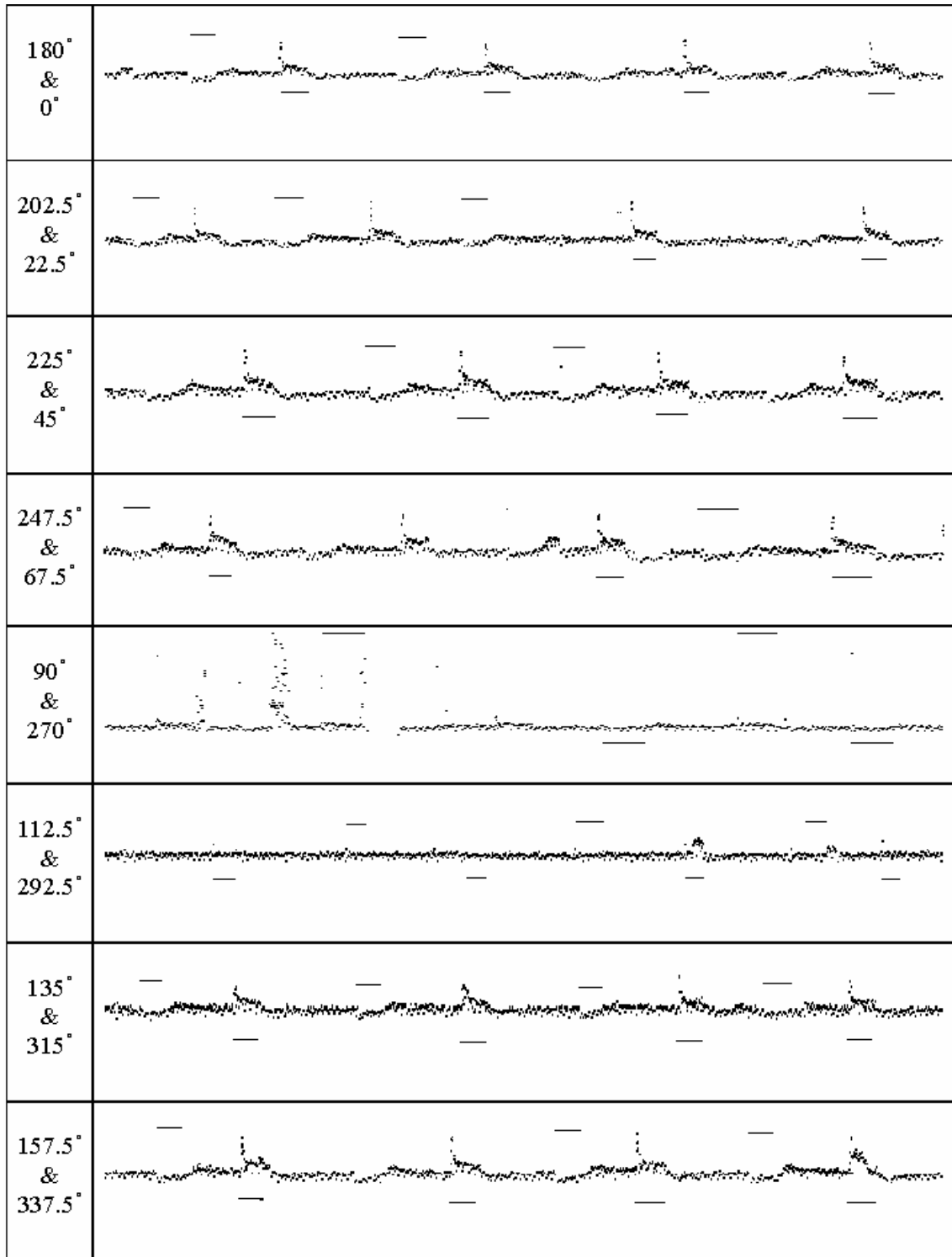
Figure 5: Complete 16-directional firing profile for a biceps unit.
The figure displays the firing patterns in response all 16 directions
of translation of the supporting surface. Horizontal bars are placed
above or below the event representing the first and second directions
respectively. Each bar is indicative of approximately a 2 sec period.
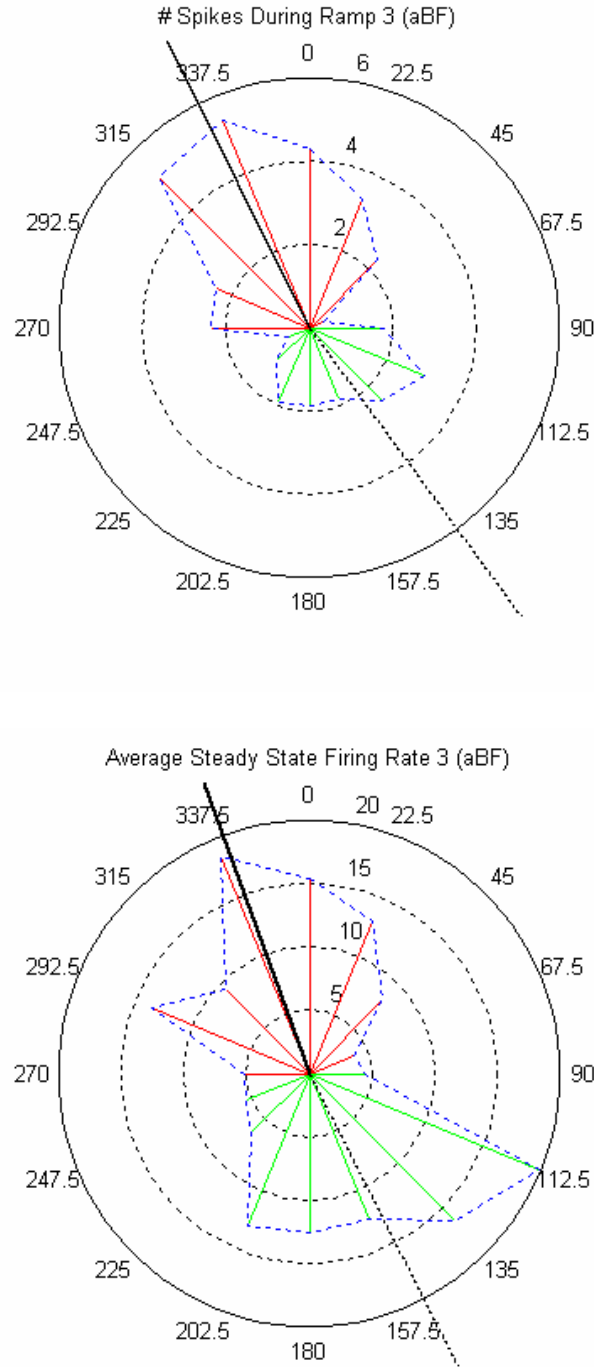
Figure 6: Individual Unit firing pattern (aBF). For a sample anterior biceps femoris muscle receptor of cat 4, the response to translations of the supporting surface is depicted. (A) The number of spikes, which serves as which serves as an indicator of the dynamic response (B) The average steady state instantaneous firing rate, an indicator of the steady state response. The red lines represent excitatory response and the green inhibitory. The solid and dotted black lines represent the resultant excitatory and inhibitory responses respectively.

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steady state responses from an anterior biceps unit, showed a preference towards the

337.5 direction in excitation and towards 157.5 in inhibition. The dynamic response

(Figure 6A) ranged favorably from 270 through 0 to 45 in excitation and 90 to 225 in

inhibition. This is similar to EMG data from a similar study (Chanaud and Macpherson

1991c), which gave a range of anterior BF spindle activation (in 1 cat) in the range

247.5 through 0 to 22.5 (translated into our coordinate system). The steady state

response (Figure 6B) more favorably responds in a range 292.5 through to 22.5 in

excitation and 112.5 through 225 in inhibition. Furthermore, during the dynamic phase

the excitatory response is twice as large as that of the inhibitory, as opposed to the

steady state phase where they are of similar magnitude.

Figure 7 shows the same information as Figure 6, but for a medial biceps femoris

spindle. In the dynamic stage (Figure 7A), strong excitation was observed from 292.5

through 0 to 22.5 (in agreement with the EMG range observed by Chanaud and

Macpherson 1991c), as well as from 112.5 to 247.5. Strong excitation ranged from 270

to 45 and inhibition from 67.5 to 180 during the steady state (Figure 7B).

Figure 8 displays responses from the posterior biceps spindle. There was excitation

from 0 to 90 and inhibition from 135 to 315 during the steady state (Figure 8B). During

the dynamic phase (Figure 8A), there was excitation ranging from 315 through 0 to 90,

with inhibition ranging from 135 to 270. Excitation occurred in the 337 to 90 range in

the Chanaud and Macpherson (1991c) study, in close agreement with our results.

These sample units suggest a trend from medial to lateral (on the polar plot) as one goes

from anterior to medial to posterior bicep femoris, similar to the behavior seen in the

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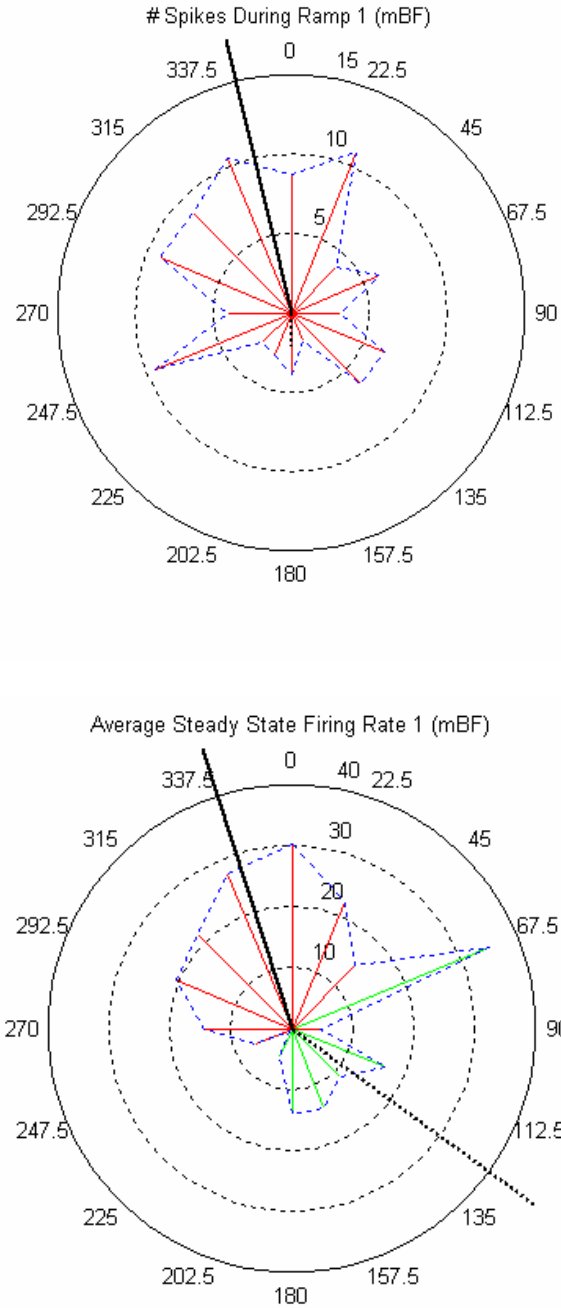
Figure 7: Individual Unit firing pattern (mBF). For a sample medial biceps femoris muscle receptor of cat 3, the response to translations of the supporting surface is depicted. (A) The number of spikes, which serves as which serves as an indicator of the dynamic response (B) The average steady state instantaneous firing rate, an indicator of the steady state response. The red lines represent excitatory response and the green inhibitory. The solid and dotted black lines represent the resultant excitatory and inhibitory responses respectively.

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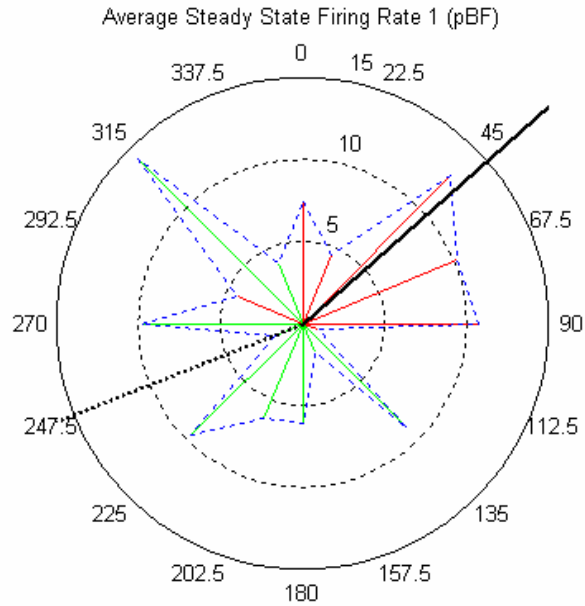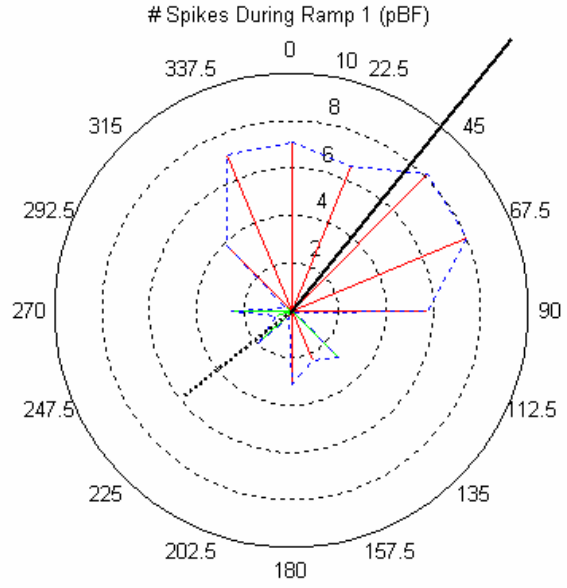
Figure 8: Individual Unit firing pattern (pBF). For a sample posterior biceps femoris muscle receptor of cat 4, the response to translations of the supporting surface is depicted. (A) The number of spikes, which serves as which serves as an indicator of the dynamic response (B) The average steady state instantaneous firing rate, an indicator of the steady state response. The red lines represent excitatory response and the green inhibitory. The solid and dotted black lines represent the resultant excitatory and inhibitory responses respectively.

EMG experiments (Chanaud and Macpherson 1991). The other biceps units, which were unidentified as to specific region, fall within these ranges.

In order to gain a sense of the general response of these receptors the data from all 7 biceps femoris muscle receptors, across cats 3 and 4, were combined (Figure 9). At steady state (Figure 9B) there is mainly excitation between the 22.5 through 0 to 292.5 range. Inhibition lies mainly in the 112.5 to 247.5 range. Mixed excitation-inhibition (wherein the excitatory regions of some units overlap the inhibitory regions of others) occurs in the 270 direction and the 45 through 90 range. The excitation profile is much more diffuse during the dynamic phase (Figure 9A), with the strongest response along the rostral-caudal plane (0-180). There is mixed excitation-inhibition in the 180 to 247.5 region.

Data for individual MG afferents was also examined. Figure 10A shows one such MG that, during the ramp, responded mainly in the 247 through 0 range with additional responses in some other directions. In the steady state phase (Figure 10B) there is excitation in the directions 45 through 0 to 270, with inhibition or no response in the 67.5 to 247.5 range.   Thus, during the dynamic phase there is activation in opposite directions but no steady state response in one of the directions, indicative of a type MGb muscle spindle response (c.f. figure 4).

The firing profile of the combination of medial gastrocnemius receptors (Figure 11) is, to a large extent, bidirectional during the dynamic phase of the response; the highest levels of activation occur in the ranges 45 through 0 to 270 and 90 to 202.5. The steady state response, however, was displayed excitation in the range 45 through 0 to 270. Inhibition occurs in the range 67.5 to 202.5.   There is a large inhibitory response in the
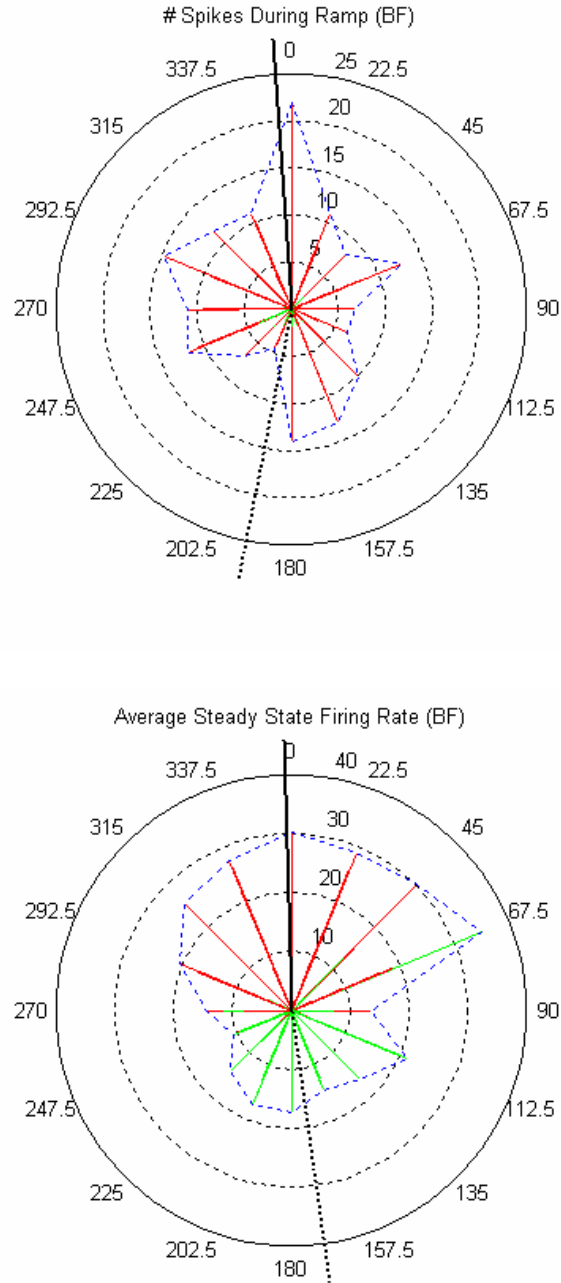
Figure 9: Combined Firing pattern of all Units (BF) across cats. The responses of all 7 units from cats 3 and 4 were combined in order to obtain a typical/general profile. (A) The number of spikes, which serves as which serves as an indicator of the dynamic response, (B) The average steady state instantaneous firing rate, an indicator of the steady state response. The red lines represent excitatory response and the green inhibitory. The solid and dotted black lines represent the resultant excitatory and inhibitory responses respectively.
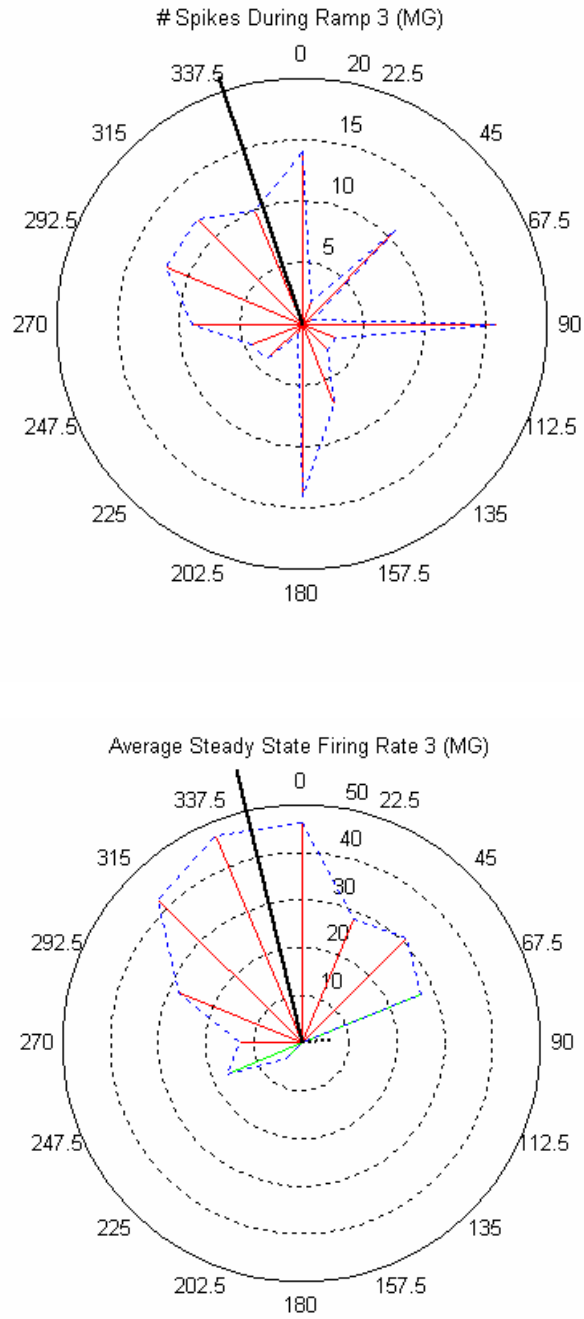
Figure 10: Individual Unit firing pattern (MG). For a sample medial gastrocnemius muscle receptor, the response to translations of the supporting surface is depicted. (A) The number of spikes, which serves as which serves as an indicator of the dynamic response (B) The average steady state instantaneous firing rate, an indicator of the steady state response. The red lines represent excitatory response and the green inhibitory. The solid and dotted black lines represent the resultant excitatory and inhibitory responses respectively.

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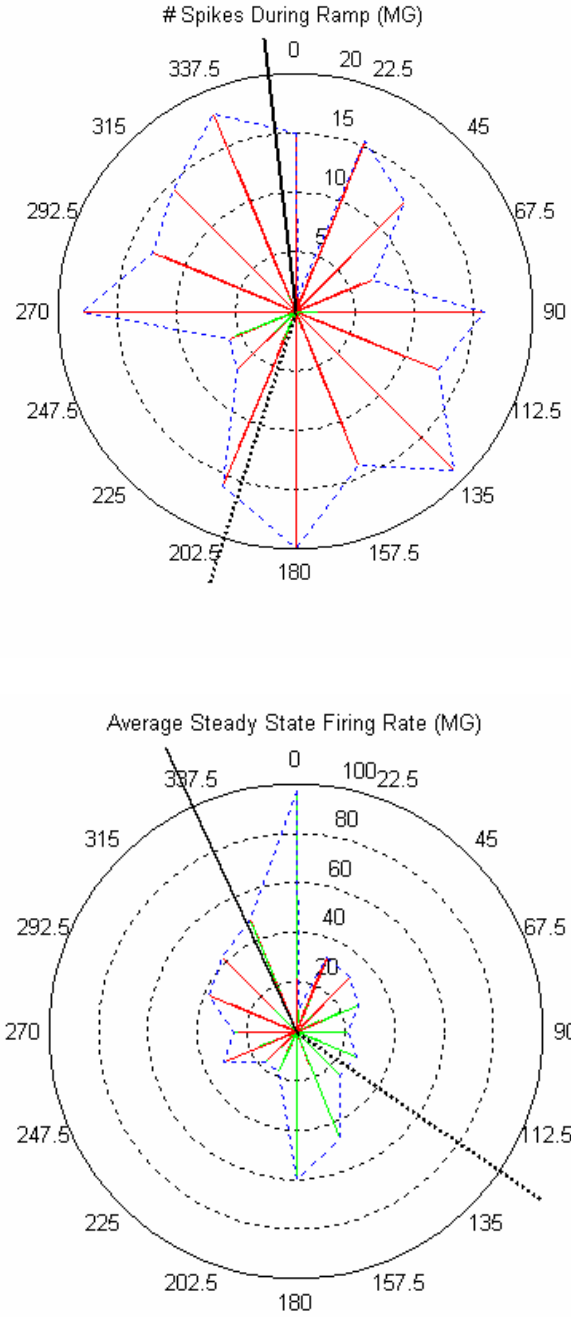
Figure 11: Combined Firing pattern of all Units (MG) across cats. The responses of all 11 units from cats 2, 3 and 4 were combined in order to obtain a typical/general profile. (A) The number of spikes, which serves as which serves as an indicator of the dynamic response, (B) The average steady state instantaneous firing rate, an indicator of the steady state response. The red lines represent excitatory response and the green inhibitory. The solid and dotted black lines represent the resultant excitatory and inhibitory responses respectively.

0-180 direction (rostral-caudal), owing to a large spike in the background response along that direction in 1 unit.

Only excitatory responses were obtained for some of the units since these did not have background firing. 67% of MG units had no background firing compared to 14% of BF units of Nembutal anaesthetized cats.

CHAPTER 4

DISCUSSION

Summary of Findings

A sample biceps femoris muscle spindle exhibited one pattern in response to perturbation while MG exhibited three main types of patterns. A single anterior BF unit showed an activation preference when the leg was perturbed inward and forward, and inhibition in the opposite direction during both the dynamic and steady states. The posterior biceps, on the other hand, preferentially activated to movement directed rostrally and outward. The medial biceps unit was preferentially activated with movement in a rostral direction. A general pattern of steady state response, as determined from all units across cats, showed excitation when the paw was shifted rostrally (292.5 to 22.5). Inhibition was observed for movement caudally (112.5 to 247.5). Mixed excitation-inhibition, due to overlapping patterns of individual units, occurred in the lateral-medial plane (45 to 90 range and in the direction of 270). The excitation pattern in the dynamic phase occurred over a wider range (with strongest response along 0-180). Mixed excitation-inhibition was observed in the other directions (180 to 247.5).

A sample individual MG unit showed excitation in many directions during the dynamic phase but became more sharply tuned in the steady state phase. There was a similar trend towards this behavior in the mBF and pBF units, but not so in the aBF. The fact that the broadest tuning occurred in the more distal muscles (MG or pBF) may be suggestive of some instability in the distal limb. In the steady state phase, there was excitation when the paw was moved in the directions from 45 to 270. Inhibition or no

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response was seen in the rest of the directions (67.5 to 247.5). The general dynamic response exhibited a bidirectional pattern of activation with respect to the perturbation directions. The general steady state response showed excitation in the range 225 through to 45 (resultant rostral-adduction) and inhibition mostly in the opposite direction (90 to 202.5).

Assumptions and Limitations

We perturbed a single hindlimb in investigating the source of the postural control strategies. However, such a strategy appears to depend on the integration of sensory feedback from all four limbs (Macpherson 1988a). Thus, our study may not give a full picture of the behavior we seek to characterize. The paw itself was attached to the platform with cyanoacrylate glue to ensure paw stability and maintain the natural foot position. Fixation of skeleton in the stereotaxic frame, apart from allowing easy access to the dorsal root neurons, was meant to restrict motion and so aid in providing stability. This did not prove sufficient as was noted both in the first experiment, which utilized a decerebrate preparation, and in the others whereby responses were observed when returning the platform to its original position from non-preferential activation directions (c.f. Figure 5). In the directions 90, 270, 112.5 and 292.5, the spindle responds to movement in an inconsistent and non-robust manner. In other directions, the responses were repeatable suggesting that these are reflective of the major directional properties of the proprioceptor. The coordinate system was chosen with respect to the sagittal axis of the cats (also known as body-centered). Another axis would have been with respect to the actual axis of the limb (or limb-centered), since the paw is turned out at an angle

from the sagittal. Does this matter in the central nervous system interpretation? One would argue that this is not the case since the assignment of a coordinate axis is essentially arbitrary and the spinal circuitry is concerned with the level of response to the direction of perturbation whether this direction is assigned the value 0 or 30. Most cats have a turnout angle of $20^°$-$30^°$ (Murinas 2003) so that the pBF unit response would correspond approximately to the limb axis. More importantly though, to make meaningful comparisons of results and draw conclusions, it was thought best to maintain a similar reference frame as that used in previous studies (Macpherson 1988). In intact animals there is supraspinally modulated activation of gamma motor neurons that ensures adequate muscle tonus in the limb. The activation is depressed, however, in the pentobarbital preparation. Lack of muscle tone could have resulted in movement artifact (c.f. Figure 5). This artifact may have led to bidirectional excitation at the outset of perturbation, as well as activation in additional directions during the dynamic phase (Figure 10A).

The receptors were identified based on their conduction velocities and their level of firing in response to muscle contraction caused by motor nerve stimulation. While group I can be reliably separated from group II afferent based on the conduction velocities (group I > 70m/s), difficulties arise when attempting to distinguish between groups Ia and Ib. Golgi tendon organs may not appreciably increase, nor will spindles decrease, their firing if the stimulus strength does not elicit significant muscle contraction. However, too high a stimulus could evoke such a powerful contraction that the unit is lost due to excessive movement in the dorsal root recording site.

Spike number and average firing rate (which depends on number of spikes) were used as measures of proprioceptor response. Previous study that involved recording impulses from rat motor neurons during muscle stretch (Haftel et al. 2004) has demonstrated the validity of these measures.

Functional Implications

The anatomical structure and muscle insertion of both muscles suggest that their endpoint forces should be backward and outward (in abduction). The endpoint forces noted for BF and MG, obtained via muscle stimulation (Murinas 2003) and computational models (Burkholder and Nichols 2004), both support this. Thus one would expect the greatest direction of muscle activation, assuming a stretch reflex-evoked response, to be in the diametrically opposite direction: forward and in adduction (about 337.5). The EMG tuning curves obtained from perturbation of the limb was compatible with this prediction (Macpherson 1988b; Ting and Macpherson 2004).

At first glance, the results observed in the medial gastrocnemius do not appear to fit this mold. However, as previously mentioned there is a limitation that affected the outcome of the results: the muscle spindle possesses a very transient response to the sudden movement that is not part of the postural stabilization strategy. This may be an intrinsic physiological response or, more likely, the response from the low threshold spindles to tiny vibrations induced by movement of the supporting surface. Based on the tuning curves, the former seems especially relevant to the distal units. While this activation would not have any adverse effect on the excitatory responses, it will act to reduce the

magnitude of the inhibitory responses. However, since this is associated with the movement and hence the dynamic stage, the magnitude of inhibitory response during the steady state phase should be larger. Indeed this is observed. As noted in the results the magnitude of the inhibitory responses of the anterior biceps unit was approximately half that of its excitatory responses during the dynamic stage. In the steady state it was of comparable magnitude. The other units display similar behaviors.

Another consideration is the lack of background signal in two-thirds of the MG units and one of the BF units. The lack of background actually compounds the first problem. If there is no background, there can be no inhibitory signal since attributes such as the number of spikes and firing rates cannot be negative. If this is the case, or there is a low enough level of background signal, the activation due to non-specific movements of the passive limb during perturbation could overwhelm the inhibitory signal. This would result in multi-directional excitation patterns. Hence, without a sufficient level of background, the inhibitory response is not expressed. This behavior is observed in many of the MG spindles. One cannot say for sure whether, owing to its distal architecture (making it less movement constrained), its smaller size, or to its greater proximity to the motor, MG was more greatly affected by these vibrations than the comparatively massive BF muscle. Nonetheless the effect is still evident in the sample medial biceps spindle response displayed. This spindle actually has a resultant inhibitory vector in the 180 direction but, with a low background level, its response is drowned by excitatory signals.

These effects should not influence the direction of the response, though, and in, fact

they do not. The MG units show activation that is approximately about the 337.5-157.5

axis (rostral-adduction to caudal-abduction) during the dynamic stage (Figures 10A and

11A). This is more pronounced during the steady state phase where these effects are

not present (Figures 10B and 11B). As previously noted, the large inhibitory response

seen about the rostral-caudal direction was due to an abnormal spike in the background

activity along the same direction.

Each identified type of biceps femoris spindle displayed activation patterns that

corresponded to those of Chanaud and Macpherson (1991) EMGs. Even those biceps

which could not be specifically identified in terms of compartment exhibited activation

patterns that were completely encompassed by the biceps femoris range of EMG

response. There was only one exception to this behavior. Although measurements for

this afferent were taken in enough directions to allow it to be included in the analysis,

the responses were not robust enough (no background signal and no steady state

response) to make any solid conclusions.

During the dynamic phase the afferent responses are more diffuse, particularly for the

MG afferents. Yet, by the time they reach the plateau of steady state, the pattern is

much more repeatable along their preferred direction of activation. This might suggest

that, since it was not susceptible to the aforementioned artifactual errors, the steady

state response provides a more reliable indication of the directional tuning which

occurred during the dynamic phase. *The correspondence between results from the*

separate compartments of the biceps femoris strongly supports the hypothesis. In most

cases, the results from the medial gastrocnemius also support the hypothesis. Even though the BF muscle is diffuse in its attachments, the directional information given, by each compartment, is very precise. The breadth of the response curves is on the same magnitude as that of the medial gastrocnemius units. *This result does not support the hypothesis that the distinct architectures of the muscles would lead to differential responses with respect to tuning breadth.*

While we do not have results of GTOs to compare, (their response properties might be expected to be similar), we would expect them to provide information related to the force of the perturbation. When combined with the dynamic spindle information, they may help the nervous system to initiate the appropriate level of counteraction. Given the conduction velocities of cutaneous receptors, their possible input would more likely be combined with the steady state response of the spindle to perform fine adjustments. There exists strong correspondence between our results and previous experiments (Burkholder and Nichols 2000; Burkholder and Nichols 2004; Macpherson 1988b; Ting and Macpherson 2004). We thus *propose that muscle spindles play a critical role in the Force Constraint Strategy, and this postural response is mediated, at least in part, by pathways that parallel the stretch reflex. In addition, the extent of tuning is independent of the muscle architecture.* These results indicate that the stretch reflex is compartmentalized in biceps femoris.

Significance

Research on posture carries great implications for comparative biology. Mechanisms that underlie certain aspects of motor control, as well as responses to certain stimuli,

may be conserved across species. This knowledge would be extremely helpful to the

medical sciences, particularly in the area of rehabilitative medicine. Studies have

shown that parts of the nervous system, such as the spinal cord, can regain locomotor

function following spinal cord injury. This has been demonstrated not only in cats

(Edgerton et al. 1997), but also in rats (Timoszyk et al. 2005) and monkeys (Courtine et

al. 2005; Edgerton et al. 2004). Systems are continuously evolving to make use of this

ability in humans as well, such as with robot-assisted training (Hornby et al. 2005).

Patients who have suffered motor incomplete spinal cord injuries and undergone this

treatment have improved their walking gait, including speed and endurance.

Data obtained from postural studies can also be used to construct models, both robotic

(Sellers et al. 2004) and computational (Cheron et al. 2003), which can then be

manipulated and employed to test various hypotheses and predict the outcome of

diverse situations. The development of an ambulatory robot able to navigate stairs and

hallways would represent a great boon to the service industry. As for computational

models, these can be integrated with other models, such as of the motor cortex, to

develop more reliable neural prosthetics.

Future Directions

A first step in further understanding the spinal mechanisms underlying posture would be

to carry out experiments in which combinations of limbs are perturbed and the

responses of all four limbs can be recorded in anaesthetized or decerebrate preparations.

Furthermore, these results should be compared with data from intact animals.

Experiments have shown that the force constraint strategy disappears when the cat's limb is perturbed at shorter stances than usual (Macpherson 1994a). Thus, even though our experiment may help to explain the link between muscle spindle responses and those of EMG, the translational mechanisms from muscle activity to force output still remain to be determined.

Future experiments could also examine the response properties of the GTOs and cutaneous receptors, specifically with regard to obtaining a more complete picture of how the diverse sources of input are utilized by the central nervous system. The shearing forces induced on the foot pads by movement of the supporting surface effectively activate the more slow-reacting receptors (Ferrington 1985). Such movement also causes stretching and deformation of the skin, to which the cutaneous and deep mechanoreceptors are sensitive (Edin 1992). Research has suggested that these receptors do encode information related to both the direction (Macpherson 1994b) and velocity (Greenspan 1992) of the disturbance. Finally, studies should be performed to examine the compartmentalization of feedback from the different regions of biceps femoris to the spinal or other circuitry involved in postural stability.

APPENDIX

(E2D06)   Background Rate 1 (MG)

(E2D06)   First Spike Time 1 (MG)

(E2D06)   # Spikes During Ramp 1 (MG)

(E2D06)   Peak Firing Rate 1 (MG)

(E2D06)   Peak Firing Rate Time 1 (MG)

(E2D06)   Average Steady State Firing Rate 1 (MG)

(E2D07)   Background Rate 1 (MG)

(E2D07)   First Spike Time 1 (MG)

(E2D07)   # Spikes During Ramp 1 (MG)

(E2D07)   Peak Firing Rate 1 (MG)

(E2D07)   Peak Firing Rate Time 1 (MG)

(E2D07)   Average Steady State Firing Rate 1 (MG)

(E2D08)   Background Rate 1 (MG)

(E2D08)   First Spike Time 1 (MG)

(E2D08)   # Spikes During Ramp 1 (MG)

(E2D08)   Peak Firing Rate 1 (MG)

(E2D08)   Peak Firing Rate Time 1 (MG)

(E2D08)   Average Steady State Firing Rate 1 (MG)

(E3D03)   Background Rate 1 (MG)

(E3D03)   First Spike Time 1 (MG)

(E3D03)   # Spikes During Ramp 1 (MG)

(E3D03)   Peak Firing Rate 1 (MG)

(E3D03)   Peak Firing Rate Time 1 (MG)

(E3D03)   Average Steady State Firing Rate 1 (MG)

(E3D05)   Background Rate 1 (MG)

(E3D05)   First Spike Time 1 (MG)

(E3D05)   # Spikes During Ramp 1 (MG)

(E3D05)   Peak Firing Rate 1 (MG)

(E3D05)   Peak Firing Rate Time 1 (MG)

(E3D05)   Average Steady State Firing Rate 1 (MG)

(E3D06)   Background Rate 1 (MG)

(E3D06)   First Spike Time 1 (MG)

(E3D06)   # Spikes During Ramp 1 (MG)

(E3D06)   Peak Firing Rate 1 (MG)

(E3D06)   Peak Firing Rate Time 1 (MG)

(E3D06)   Average Steady State Firing Rate 1 (MG)

(E3D07)   Background Rate 1 (MG)

(E3D07)   First Spike Time 1 (MG)

(E3D07)   # Spikes During Ramp 1 (MG)

(E3D07)   Peak Firing Rate 1 (MG)

(E3D07)   Peak Firing Rate Time 1 (MG)

(E3D07)   Average Steady State Firing Rate 1 (MG)

(E3D08)   Background Rate 1 (MG)

(E3D08)   First Spike Time 1 (MG)

(E3D08)   # Spikes During Ramp 1 (MG)

(E3D08)   Peak Firing Rate 1 (MG)

(E3D08)   Peak Firing Rate Time 1 (MG)

(E3D08)   Average Steady State Firing Rate 1 (MG)

(E3D09) Background Rate 1 (MG)

(E3D09) First Spike Time 1 (MG)

(E3D09) # Spikes During Ramp 1 (MG)

(E3D09) Peak Firing Rate 1 (MG)

(E3D09) Peak Firing Rate Time 1 (MG)

(E3D09) Average Steady State Firing Rate 1 (MG)

(E3D10)   Background Rate 1 (mBF)

(E3D10)   First Spike Time 1 (mBF)

(E3D10)   # Spikes During Ramp 1 (mBF)

(E3D10)   Peak Firing Rate 1 (mBF)

(E3D10)   Peak Firing Rate Time 1 (mBF)

(E3D10)   Average Steady State Firing Rate 1 (mBF)

(E4D01)   Background Rate 1 (BF)

(E4D01)   First Spike Time 1 (BF)

(E4D01)   # Spikes During Ramp 1 (BF)

(E4D01)   Peak Firing Rate 1 (BF)

(E4D01)   Peak Firing Rate Time 1 (BF)

(E4D01)   Average Steady State Firing Rate 1 (BF)

(E4D05) Background Rate 1 (BF)

(E4D05) First Spike Time 1 (BF)

(E4D05) # Spikes During Ramp 1 (BF)

(E4D05) Peak Firing Rate 1 (BF)

(E4D05) Peak Firing Rate Time 1 (BF)

(E4D05) Average Steady State Firing Rate 1 (BF)

(E4D08)   Background Rate 1 (MG)

(E4D08)   First Spike Time 1 (MG)

(E4D08)   # Spikes During Ramp 1 (MG)

(E4D08)   Peak Firing Rate 1 (MG)

(E4D08)   Peak Firing Rate Time 1 (MG)

(E4D08)   Average Steady State Firing Rate 1 (MG)

(E4D09)   Background Rate 1 (MG)

(E4D09)   First Spike Time 1 (MG)

(E4D09)   # Spikes During Ramp 1 (MG)

(E4D09)   Peak Firing Rate 1 (MG)

(E4D09)   Peak Firing Rate Time 1 (MG)

(E4D09)   Average Steady State Firing Rate 1 (MG)

(E4D10)   Background Rate 1 (aBF)

(E4D10)   First Spike Time 1 (aBF)

(E4D10)   # Spikes During Ramp 1 (aBF)

(E4D10)   Peak Firing Rate 1 (aBF)

(E4D10)   Peak Firing Rate Time 1 (aBF)

(E4D10)   Average Steady State Firing Rate 1 (aBF)

(E4D14)   Background Rate 1 (pBF)

(E4D14)   First Spike Time 1 (pBF)

(E4D14)   # Spikes During Ramp 1 (pBF)

(E4D14)   Peak Firing Rate 1 (pBF)

(E4D14)   Peak Firing Rate Time 1 (pBF)

(E4D14)   Average Steady State Firing Rate 1 (pBF)

(E4D19)   Background Rate 1 (pBF)

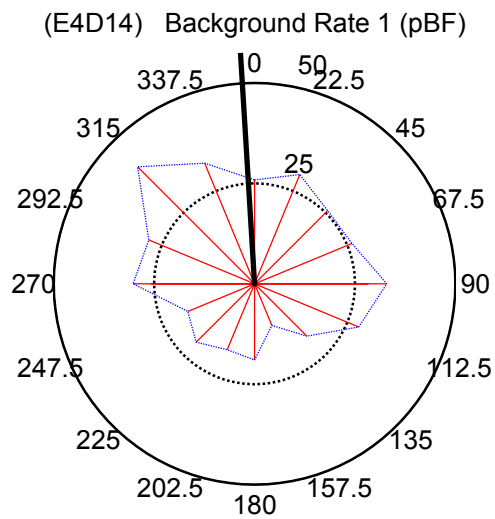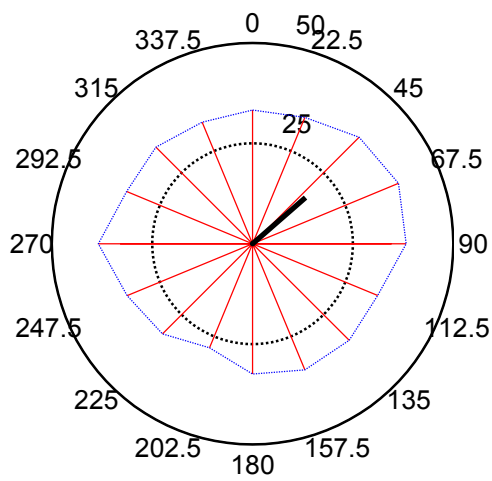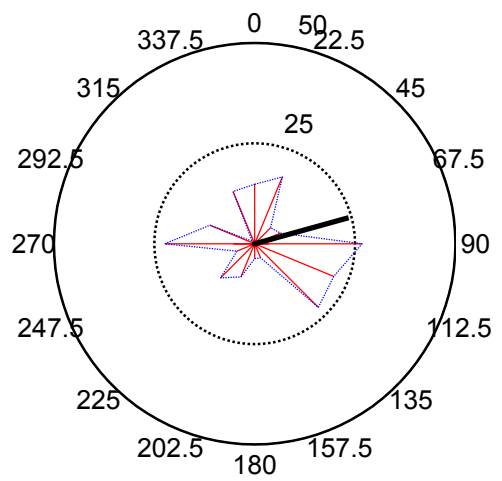(E4D19)   First Spike Time 1 (pBF)

(E4D19)   # Spikes During Ramp 1 (pBF)

(E4D19)   Peak Firing Rate 1 (pBF)

(E4D19)   Peak Firing Rate Time 1 (pBF)
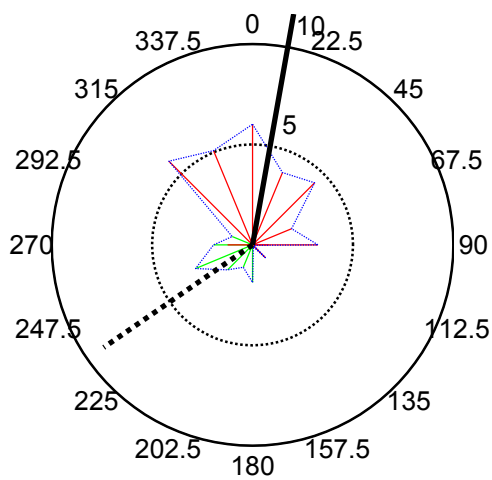
(E4D19)   Average Steady State Firing Rate 1 (pBF)

(E4D22)   Background Rate 1 (BF)
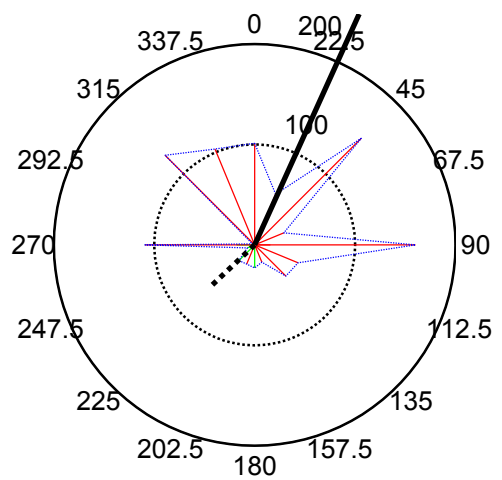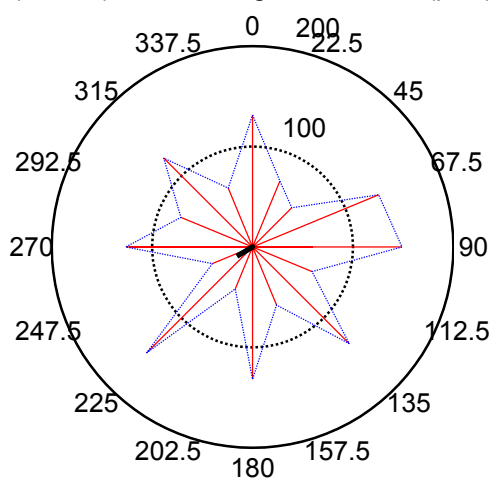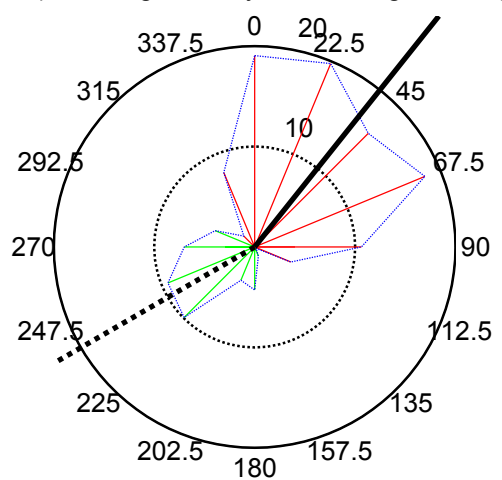
(E4D22)   First Spike Time 1 (BF)

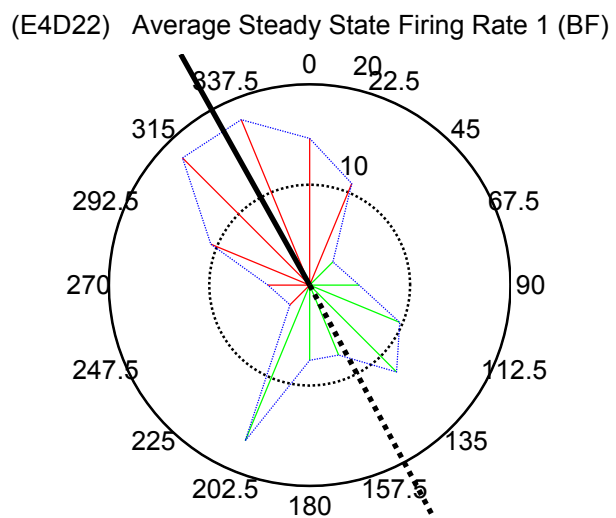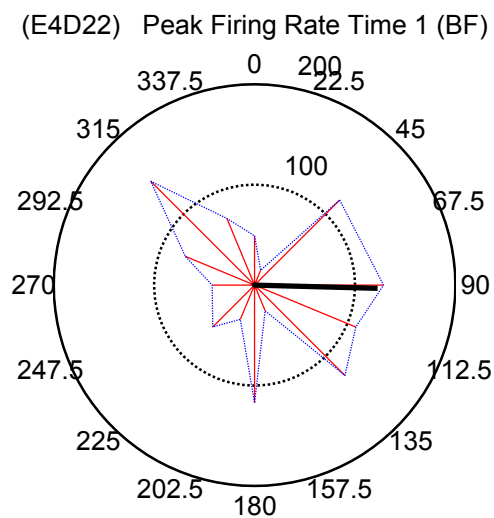(E4D22)   # Spikes During Ramp 1 (BF)
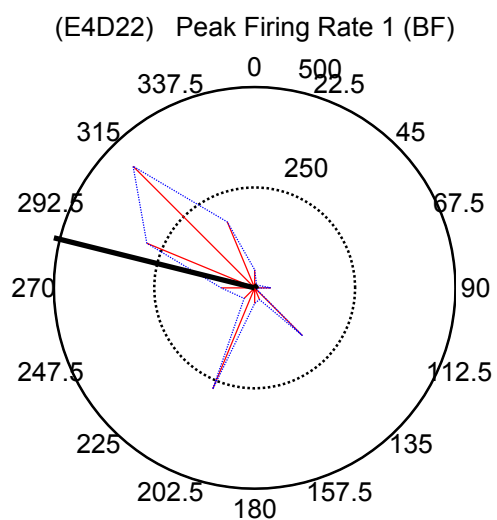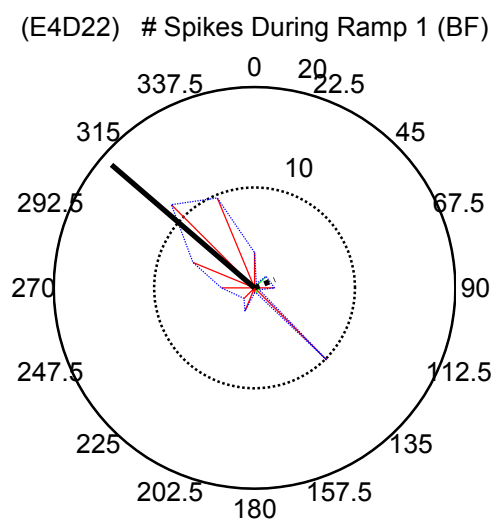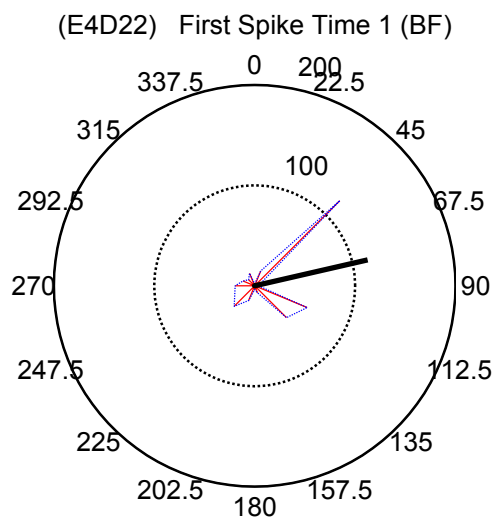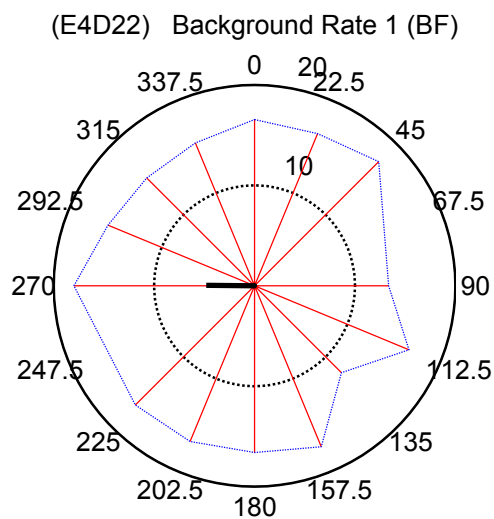
(E4D22)   Peak Firing Rate 1 (BF)

(E4D22)   Peak Firing Rate Time 1 (BF)

(E4D22)   Average Steady State Firing Rate 1 (BF)

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