MICRONEUROGRAPHIC RECORDINGS FROM CUTANEOUS

RECEPTORS FROM THE LOWER LIMB OF HUMANS

by

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Abstract

Postural control is achieved through complex interactions between different neural networks. While it is difficult to isolate the contribution of any individual system, somatosensory information from the lower limbs provides a sensitive measure of postural sway during quiet stance (Fitzpatrick and McCloskey 1994). Furthermore, these signals initiate postural responses to perturbations to permit accurate realignment of the body after a disturbance in stance (Inglis et al. 1994). One possible source of this essential information, although not clear, is thought to originate in cutaneous mechanoreceptors located in the glabrous skin of the foot sole. To date, there is limited information about the cutaneous afferents in the lower limb. The purpose of this study was therefore to document the characteristics of these receptors and to examine their potential role in postural control. Thirty-one recording sessions were performed on thirteen conscious participants between 22-50 years of age. Single unit activity was recorded from the tibial nerve at the level of the popliteal fossa with tungsten electrodes inserted percutaneously in the lower limb. Stable single unit recordings typically lasted between 10-15 minutes despite small ankle movements. Receptors were classified as slowly (SA) and fast adapting (FA) based on their response to a sustained indentation of the skin. In accordance with previous investigations the units were subdivided based on the properties of their receptive fields; small, well defined (type I) and large with obscure borders (type II). The proportion of the different receptor types (14% SAI, 15% SAII, 60% FAI, 14% FAII: n = 106) demonstrates that the glabrous skin of the foot sole potentially has a higher dynamic sensitivity than other documented skin regions (i.e. hand). The low degree of static activity in the foot sole could argue towards a sampling bias. However, the interpretation of the data is that this is of functional importance because during quiet stance maintaining stability is a dynamic task since the body is never completely motionless (Horak and Macpherson 1996).

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ABBREVIATIONS AND DEFINITION

CoP   Center of Pressure
This is the point of origin of the ground reaction force, which represents the acceleration of the body. The center of pressure does can reflect body sway.

FAI   Fast Adapting Type I
This receptor responds with a burst of impulses only at the onset and removal of the stimulus. The receptive field is small and well defined. Also referred to as a RA (rapidly adapting) receptor in literature. The name of the anatomical structure producing this response is presumed to be the Meissner's corpuscle.

FAII   Fast Adapting Type II
Similar response pattern to the FAI, however this unit has a large and obscure receptive field. These receptors are exceptionally sensitive to vibration. Commonly referred to as a PC (Pacinian Corpuscle) in the literature after the anatomical name of the receptor.

RF   Receptive Field
The region of skin from which a single sensory receptor may be activated is defined as the receptive field. A monofilament of four-to-five times the threshold force was used to outline the receptive field.

SAI   Slow Adapting Type I
Unit that responds with a continuous discharge during maintained skin indentations. These units have a small well-defined receptive field and are characterized by an irregular-firing pattern. The proposed receptor terminal is referred to as Merkel cells or discs.

SAII   Slow Adapting Type II
Although these receptors have a similar response pattern as the type I units, SAII's are defined by their regular firing pattern. They also have a larger, indistinct receptive field. Ruffini endings are the cutaneous receptors that are proposed to generate this type of response.

SNR   Signal-to-Noise Ratio
This refers to the difference between the size of the action potential and the background noise of the neurogram. This measurement is an indicator of the quality of the recording and the impedance of the electrode.

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I guess if I am writing this page, then that means that I have finally completed my thesis – but there are a number of individuals who deserve special mention if only to try and recognize the contribution that these people have had over the past two years.

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Chapter One
Introduction and Literary Review

INTRODUCTION AND LITERARY REVIEW

1.1 INTRODUCTION AND OVERVIEW:

In quietly standing humans, body sway whether spontaneous or induced, occurs primarily at the ankle joint (Horak and Macpherson 1996). It has recently been demonstrated in humans that following the loss of somatosensory inputs from the lower limb, postural abnormalities resulted from the faulty triggering and scaling of postural responses (Inglis et al. 1994). The source of this essential somatosensory information remains to be determined, and while indirect evidence points to a variety of possible candidates, no direct evidence (i.e. actual recordings of the neural signal) for the human has been provided to date.

There are several classes of receptors located within different regions of the lower limb, each with varying response characteristics, that could potentially provide sensory feedback related to postural sway during stance: 1) cutaneous receptors of the hairless or glabrous skin of the foot sole (may potentially code for the distribution of the center of pressure during standing), 2) the hairy skin covering the calf, shin and dorsum of the foot (may detail ankle and perhaps knee movement), 3) the muscle spindles and Golgi-tendon organs from muscles that act around the ankle joint and that reside in the foot (intrinsic foot muscles), and 4) the joint receptors of the ankle and foot joints. The actual receptor behaviour, their densities, distributions and how these receptors respond to movements associated with postural sway or during loading of the limb that occurs with stance, remains unknown for the human. While the roles played by these afferents and how they behave are assumed in much of the literature, and primarily based on physiological studies

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on animals, little scientific data in the human has been documented in detail concerning their potential in contributing to the control of standing posture and balance.

From the literary reviews on the role of somatosensory information in kinesthesis, it is easy to become disconcerted by the circular arguments proposed by the experiments. It seems apparent that the receptors in the skin, joints, and muscles can neither be given an exclusive role nor excluded from participation (Moberg 1983). However, within the last ten years, the role of skin in motor control appears to be receiving more attention. This stemmed from anecdotal observations where a local anesthetic was applied to the upper limb in humans, the pulling of a tendon in the hand which did not generate stretch of the muscle but caused a displacement of the skin caused the patient to report a movement sensation (Moberg 1983). The importance of cutaneous input has long been recognized in a clinical setting. In reconstructive surgery it has become prevalent to transfer undamaged skin to areas where normal cutaneous innervation has been damaged, particularly around joints (Moberg 1983).

This generates a source of input that muscle spindles cannot replace. Transferring this debate to the lower limb, it is unclear as to which source of input may predominant. During ankle movement, both the stretch of the skin and muscle receptors detailing the length of the muscles could potentially code for the position of the foot. Applying this input to standing balance, it was demonstrated that taping the skin around the ankle joint could improve foot position awareness (Robbins, Waked, and Rappel 1995). In this instance, since muscle afferents are not affected it is presumed that by taping the skin, a pre-indentation hyper-sensitizes the skin receptors to subsequent stimuli (Horch and Burgess 1975). This study implied that skin may not only be an important source of

kinesthetic input but also play a predominant role in standing balance. This hypothesis was supported by an additional observation where foot position awareness was the strongest when the subjects were barefoot. The authors concluded that the information emanating from the plantar cutaneous mechanoreceptors was required for precise foot position sense (Robbins, Waked, and Rappel 1995). Placing the plantar surface in direct contact with the weight-bearing surface subjected skin receptors in the foot sole to intense shear forces. It is believed that these pressure sensors in the foot are not only involved in the detection of foot-surface contact, but may be responsible for the control of posture and stability (Wu and Chiang 1997).

There are four different types of cutaneous receptors that have been identified in the human skin. Termed mechanoreceptors, these units are excited by local tapping, vibration, and pressure – stimuli that all involve the stretching and indentation of the skin. Of the regions of skin in which cutaneous receptors have been investigated, there are distinct differences between patterns and distributions of receptor types, including an absence of fast adapting receptors in the face. It is not clear if all four receptor types are present in the foot sole and what role these units may play in the behavioural control of standing balance. The overall purpose of this study is to document the properties of the cutaneous mechanoreceptors in the foot sole. To achieve this, a sterilized tungsten-recording electrode will be inserted into the tibial nerve at the level of the popliteal fossa.

The tibial nerve innervates the skin of the posterior knee, the calf, and the plantar surface of the foot. At the level of the knee, the position of the nerve is rather superficial, covered only by fascial tissue.

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By examining the type, distribution, and firing patterns, it will be possible to elucidate on the potential role of these receptors in the control of standing balance. In addition, the results of this study can be used to compare the glabrous skin of the foot sole with other documented cutaneous surfaces. Ultimately, the best manner in which to view this investigation is that of a foundation for future research. It is necessary to establish the characteristics of cutaneous afferents and the stability of the recordings in the lower limb in normal healthy volunteers. Once this has been achieved, subsequent experiments could investigate the response of cutaneous afferents to loading, tangential forces including frictional coefficients, and response to slip.

1.2 THE SENSORY COMPONENTS OF POSTURAL CONTROL:

The underlying components of postural control are comprised of a variety of motor coordination tasks. Examples of such objectives include the control of the position of the body's center of mass, stabilizing body segments during voluntary movement, and maintaining specific anatomical positions with respect to the body or the environment (Horak and Macpherson 1996). These tasks are not mutually exclusive. The integration of these processes results in the control of two fundamental goals, postural orientation and postural equilibrium. Postural orientation refers to the relative position of the individual body segments. Postural equilibrium is the state in which all the forces acting on the body are balanced so that the tendency is to remain in the desired position (Horak and Macpherson 1996). The relative positioning of the body segments may undergo rapid changes so the postural control system incorporates automatic responses that include anticipatory postural adjustments to maintain the desired position. Termed a postural

strategy, this involves examining the relationship between the active muscles, body kinematics, and forces generated at the joints and against the support surfaces (Horak and Macpherson 1996). Upon reflection, the postural control system is a complex neural network that includes both sensory and motor components involved in the control of an essential behavioural task.

In a simplistic paradigm, one could evaluate postural control during quiet stance. Maintaining stability, despite the absence of an overt movement, is a dynamic and not a static task since the body is never completely stationary (Horak and Macpherson 1996). Despite a subject's desire to remain quiescent, the beatings of the heart and normal respiratory cycles have a tendency to disrupt this delicate equilibrium (Kandel, Schwartz, and Jessel 1991). The detection of this movement, or sway, is essential to the maintenance of a stable standing position. Sensory information from the visual, vestibular, and peripheral proprioceptive systems regulate quiet stance. The sensory systems are not independent channels that merely sum together at some level to result in a motor output (Horak and Macpherson 1996). Instead, the postural control system integrates and interprets the sensory information to determine the body's overall state and position. At this point, the individual role of each system is not clear.

In examining the supposed contribution of a specific sensory system, the most prevalent approaches incorporate either differential or illusive techniques (Wu and Chiang 1996). The differential model measures the effect of a specific system by eliminating that information. Elderly populations are incorporated in differential experiments, as there is the potential for significant deterioration in various sensory systems with normal aging. There are however a number of other functional changes that accompany the aging

process, which may confound the changes in the biomechanics of task performance (Wu and Chiang 1996). Using this method, it is evident that the removal of visual information gives rise to an increase in postural sway.

The illusive approach used in postural research evaluates a given system by providing the subject with deceptive information specifically designed to target the system in question. Galvanic stimulation of the vestibular system alters the discharge of the vestibular afferents, thereby altering the vestibular systems interpretation of the body's alignment (Inglis et al. 1995). The resultant of inducing this type of stimulation compelled the subjects to change their postural orientation. The interpretation of these results in conjunction with previous work was that the vestibular system might contribute to the perception of body orientation (Fitzpatrick and McCloskey 1994).

During upright stance in normal, healthy individuals, in the absence of any purposeful movement, there is surprisingly little electromyographic (EMG) activity in postural muscles (Kandel, Schwartz, and Jessel 1991). This is due to the anatomical arrangement of the body in which the knee is locked and the action of the long muscles and ligaments in the back allow the spinal column to assume its natural curve (Kandel, Schwartz, and Jessel 1991). Movement is possible at the neck, hip, and ankle joint but in this position the weight of the body is balanced and postural sway is limited to the ankle joint (Kandel, Schwartz, and Jessel 1991).

Postural sway during quiet stance occurs primarily at the ankle joint (Horak and Macpherson 1996) in which signals of rotation of the body about the ankle from somatosensory receptors could signal this information. During quiet stance, the role of somatosensory input from the lower limbs provides the most sensitive means of postural

sway with vestibular cues becoming more prominent during larger perturbations (Fitzpatrick and McCloskey 1994). It is these somatosensory signals that are important in the initiation of postural responses to perturbations whereas the vestibular signals act to modulate the amplitude of this response and signal the direction of upright to permit accurate realignment of the body after a disturbance in stance (Inglis et al. 1995). Unlike the visual and vestibular systems, it is difficult to achieve a complete and well-defined loss of somatosensory information in the lower limb. Blood pressure cuffs placed above arterial pressure points in the ankle produce ischemia in the leg, reducing transmission in large sensory afferents primarily affecting cutaneous sensation and primary muscle spindle afferents (Diener et al. 1984). The reduction in postural stability was attributed to the decreased input from the soles of the feet. This conclusion was supported in a clinical population in which patients with peripheral neuropathy, a disease that attacks large diameter cutaneous fibers demonstrated poor postural stability (Wu and Chiang 1996). Even though somatosensory input includes both skin and muscle, in this instance, the role of muscle afferents may be secondary.

Cutaneous input from the lower limb may be able to code movement from two different regions. The skin surrounding the ankle joint may provide the nervous system with information about the position of the ankle based on the stretch of the surrounding skin. Furthermore, the skin on the foot sole that is in contact with the ground may also provide essential input in postural control. An opposite force referred to as the ground reaction force counters the pressure that the body exerts on the ground. The point of origin of these ground reaction forces is referred to as the center of pressure (CoP). The movements of the CoP do not reflect sway but the overall force of acceleration of the body

(Horak and Macpherson 1996). Although cutaneous information has been investigated in different regions of the body, it is not clear at this time if cutaneous information from the lower limb is sensitive to joint angle or CoP distributions.

1.3 *THE NEURAL INTEGRATION OF CUTANEOUS INFORMATION*:

Cutaneous input enters the spinal cord at all levels, synapsing with a variety of cellular structures. Cutaneous information is potentially an important source of sensory information to be integrated in the neural network contributing to motor control. This can be directly observed by the post-synaptic influence cutaneous afferents have on motoneurons. Brief electrical stimulation of the skin can modify the recruitment order of motor units during muscle stretch (Garnett and Stephens 1981). The distribution of cutaneous fibers is not distributed evenly amidst the motoneurons. The distribution of cutaneous connections to local motoneurons is dependent upon the initial threshold of the motoneuron (Garnett and Stephens 1981). Cutaneous input can also alter motoneuron activity in an indirect manner. Cutaneous axons converge on inhibitory spinal interneurons to relieve this inhibitory mechanism preceding human movement (Iles 1996). The functional significance of these connections, regardless of direct or indirect reflex actions, would be to preferentially recruit higher threshold (more powerful) motor units, to assist in the lifting of a heavy object.

Cutaneous influence over motor signals has also been observed in the lower limb. Skin receptors can modulate motoneuron discharge in response to tonic and phasic fluctuations in pressure (Rossi and Decchi 1994). The load that the limbs are subjected to, possibly measured by cutaneous mechanoreceptors, might be used as a measure of the

current supporting function of the limb, based on which the reflex is modulated (Rossi and Decchi 1994). The reflex pattern of activation of different muscles appears to be dependent on the task or region of skin that is stimulated (Burke et al. 1991). For example, the EMG responses of lower limb musculature during a forward fall varied depending on the subject's initial stance position (Do et al. 1990). The unilateral loss of this afferent input during anesthetic block affects the biomechanical variables differently and alters the motor activity (decrease in EMG) of both legs (Thoumie and Do 1996). The reflex effects of cutaneous mechanoreceptors on motoneurons innervating lower limb muscles is dependent upon the task in which the limb is involved (Rossi and Decchi 1996). That is, when the foot is in contact with the ground, the contact force with the ground presumably excites the receptors in the foot sole, thereby altering the muscle activity in a predetermined manner. However, when the foot is not in contact with the ground, the reflex effects on muscle activation patterns are minimal, as they are not influenced by cutaneous activity.

Sensory integration of cutaneous input from the lower limb in the nervous system may demonstrate the role of skin in postural control. Although inducing ischemia in the lower limb can block large-diameter sensory afferent fibers distal to the block, it can also affect efferent-motor nerves, which may potentially influence the stability of upright stance (Wu and Zhao 1997). Early animal research examined skin in isolation and revealed a strong connection between the cutaneous receptors in the lower limbs of cats and the cerebellum. The cerebellum is intimately involved in the control of purposeful movement. The association of direct cutaneous input from the footpads was believed to demonstrate the importance of this afferent input in standing and walking activities (Leicht et al. 1977). More evidence of skin's role in standing balance was observed when a change in posture

created an increase in somatosensory information represented in the cortex (Applegate et al. 1988). This demonstrated that the CNS could gate both cutaneous and muscle afferent inputs independently according to task and relevance of the information. The integration of this information is relayed through the PNS and expressed in the CNS as a series of postural adjustments to maintain a stable upright position.

1.4 CUTANEOUS MECHANORECEPTORS:

There are three types of receptors that are encountered in the skin: thermoreceptors, nociceptors, and mechanoreceptors. The classification of these receptors is exclusively based on the properties of the afferent unit and not on their supposed role in perception (Vallbo et al. 1979). Although cutaneous sense organs are different, similarities include a dorsal root or cranial nerve neuron with peripheral terminals, a conducting peripheral nerve fiber and central terminations in the spinal cord or brain stem (Birder and Perl 1994). The mechanoreceptors are comprised of sensory units that are excited by innocuous mechanical stretch of the skin. The conduction velocity of these afferent fibers was estimated from the latency of the response to a mechanical stimulus. The speeds at which these signals are transmitted are quite rapid suggesting that cutaneous receptors are innervated by large myelinated fibers (Vallbo et al. 1979). These sensory units are divided into various classes or categories based on structural, molecular, and signaling properties (Birder and Perl 1994). Some of the noted differences included the morphology of the cell body, the molecular components, specialized endings associated with the peripheral nerve fiber, and the signals transmitted by cutaneous stimulation. A functionally defined type of cutaneous receptor can be illustrated by a particular peripheral and anatomical arrangement. The

classification of these receptors may appear arbitrary, but there is remarkable consistency in the observations through the literature (Birder and Perl 1994).

From a physical perspective, the mechanical position of a point relative to a starting position can be defined by its displacement measured in units of distance (Birder and Perl 1994). The first derivative of displacement with time is velocity. Following this, the second derivative of displacement is acceleration. Mechanical stimulation affecting the skin has elements of displacement, velocity, and acceleration, which can generate a response from the different receptors ranging from position to transient detection (Birder and Perl 1994). The present understanding of the somatosensory system has developed against the background of opposite theories of specific versus non-specificity (Hamann 1996). The concept of non-specificity assumed that all cutaneous sensation could only be interpreted through central processing. A series of action potentials transmitted through the periphery could be evaluated based on spike complexity and signal pattern in the CNS. However, the identification of skin receptors was initially regarded as support for the notion that there were specific coding parameters to a certain mechanical event. Two separate groups of post-synaptic units were classified based on mechanical responses to innocuous stimuli (Hamann 1996). Important information about the types of receptors located in the skin as well as the functional importance of their stimulus-response patterns was revealed by the anatomical investigations to follow.

The type and distribution of nerve endings is limited to the arrangements of the dermal and epidermal layers (Miller, Ralston, and Kashara 1958). In the middle portion of the papillary ridges, the ridge itself extends deep into the underlying dermis forming an intermediate crest (Miller, Ralston, and Kasahara 1958). Dispersed within these layers and

between the ridges is a constantly recurring triad consisting of three types of endings; free, encapsulated and branched. The free endings may be the termination of a single or branched fiber. The encapsulated endings, on the other hand, are composed of a gel-like substance that envelopes the receptor terminal. These afferents terminate in deep fibrous structures.

There are four types of receptor terminals found in mammalian skin. Expanded tips that occur in close bundles just below the epidermal border characterize Merkel's discs. The label "disc" refers to the concave, flattened appearance of these cells. They do not contain keratin and are distinct from the rest of the epidermal cells (Kandel, Schwartz, and Jessel 1991). Each Merkel cell receives one afferent that innervates many cells that are approximately 2-3 mm in diameter (Gandevia 1996). As the afferent nerve terminal pierces the basement membrane, it loses its myelin sheath and forms a thin sheet with condensed edges to maintain this position (Hamann 1996). Merkel cells have finger-like processes that extend throughout the skin. The second type of free ending located in the skin is called a Ruffini ending. In comparison with Merkel cells, these endings are located in deeper layers of the skin. Structurally, Ruffini endings are similar to GTO's (Hamann 1996). These terminals are composed of small connective tissue cylinders (6-12 mm) arranged along dermal collagen strands which are supplied by one to three myelinated nerve fibers approximately 4-6 μm in diameter (Hamann 1996). Within the cylinder, the nerve fibers once again lose the myelin sheath and branch in a shrub like pattern.

Encapsulated endings are found in the dermal layers and occur as a single (Pacinian) or multiple (Meissner) units within one papillae. Although the bare nerve terminals of these receptors are sensitive to mechanical deformation, the "onion skin"

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capsule filters any slow frequency components of the signal leaving these receptors sensitive only to very readily changing stimuli. Pacinian corpuscles (PC) are located in deep fibrous structures tightly anchored via collagen fibers at its poles enabling tension to reach the receptor (Gandevia 1996). The PC is the largest cutaneous receptor reaching up to 4 mm in length and 1 mm in diameter. A single axon terminates within a large number of concentric lamellae, which are separated by fluid filled spaces (Kandel, Schwartz, and Jessel 1991). The capsule and inner core acts as a high-pass filter causing the receptor to mediate the sense of vibration (Gandevia 1996). The other type of encapsulated ending, the Meissner corpuscle, is located at the tip of the dermal protrusion. Meissner's corpuscles are ovoid and found with their long axis aligned perpendicular to the surface of the skin within the dermal papillum (Kandel, Schwartz, and Jessel 1991). Each corpuscle is innervated by two to eight separate axons which forms a complex neural network within the receptor. In the finger, they appear every two to three ridges, but occur less frequently in the palm (Gandevia 1996).

The four anatomical structures produce different response patterns. These responses are subdivided according to the region of sensitivity, referred to as the receptive field (RF), and the rate of adaptation to a sustained stimulus. Meissner's corpuscles and Merkel cells have small receptive fields whereas Pacinian corpuscles and Ruffini endings respond to stimuli over a much wider area (Kandel, Schwartz, and Jessel 1991). Classification of RF types is based on the characteristics of size and structure. A type I RF is small and well defined whereas a field that is much larger and more obscure is a type II RF. In response to a maintained indentation within the receptors RF, it is the bare endings of the Merkel cells and Ruffini endings that faithfully code the stimulus. This is referred to

as a slow adapting response. The fluid-filled capsule surrounding the terminal of the Meissner and Pacinian corpuscles limits them to signal only the onset and removal of the stimulus. The encapsulated fibers are therefore fast adapting receptors. In accordance with this classification scheme, Merkel cells are slow adapting type I (SAI) units, Meissner's corpuscles are fast adapting type I (FAI) units (also referred to as rapidly adapting RA), Ruffini endings are slow adapting type II (SAII) units, and Pacinian corpuscles are fast adapting type II (FAII) units (also referred to as PC in the literature) (see figure 1 on page 16).

The absolute threshold of a receptor may be defined as the minimal input signal needed to generate an action potential (Johansson and Vallbo 1979). The FA/SA type I units have several points of maximal sensitivity within the field corresponding to the branching of the axon terminals within a small area of skin (Kandel, Schwartz, and Jessel 1991). Because of the superficial positioning of these receptors, they are very sensitive to mechanical indentation of the skin. The thickness of the epidermis does not appear to affect their responsiveness (Hamann 1996). Type II units have a larger area of sensitivity however within this region there is only a single point of maximal sensitivity supposedly corresponding to the single terminal end organ (Kandel, Schwartz, and Jessel 1991). These units are distributed fairly evenly across the hand but in lower percentages than their counterparts (Johansson and Vallbo 1979).

FAST ADAPTING, NO STATIC RESPONSE

SLOW ADAPTING, STATIC RESPONSE PRESENT

	SMALL WELL DEFINED RECEPTIVE FIELDS	LARGE OBSCURE RECEPTIVE FIELDS
Fast Adapting	Fast Adapting Type I (FAI)	Fast Adapting Type II (FAII)
Slow Adapting	Slow Adapting Type I (SAI)	Slow Adapting Type II (SAII)

Maintained Indentation
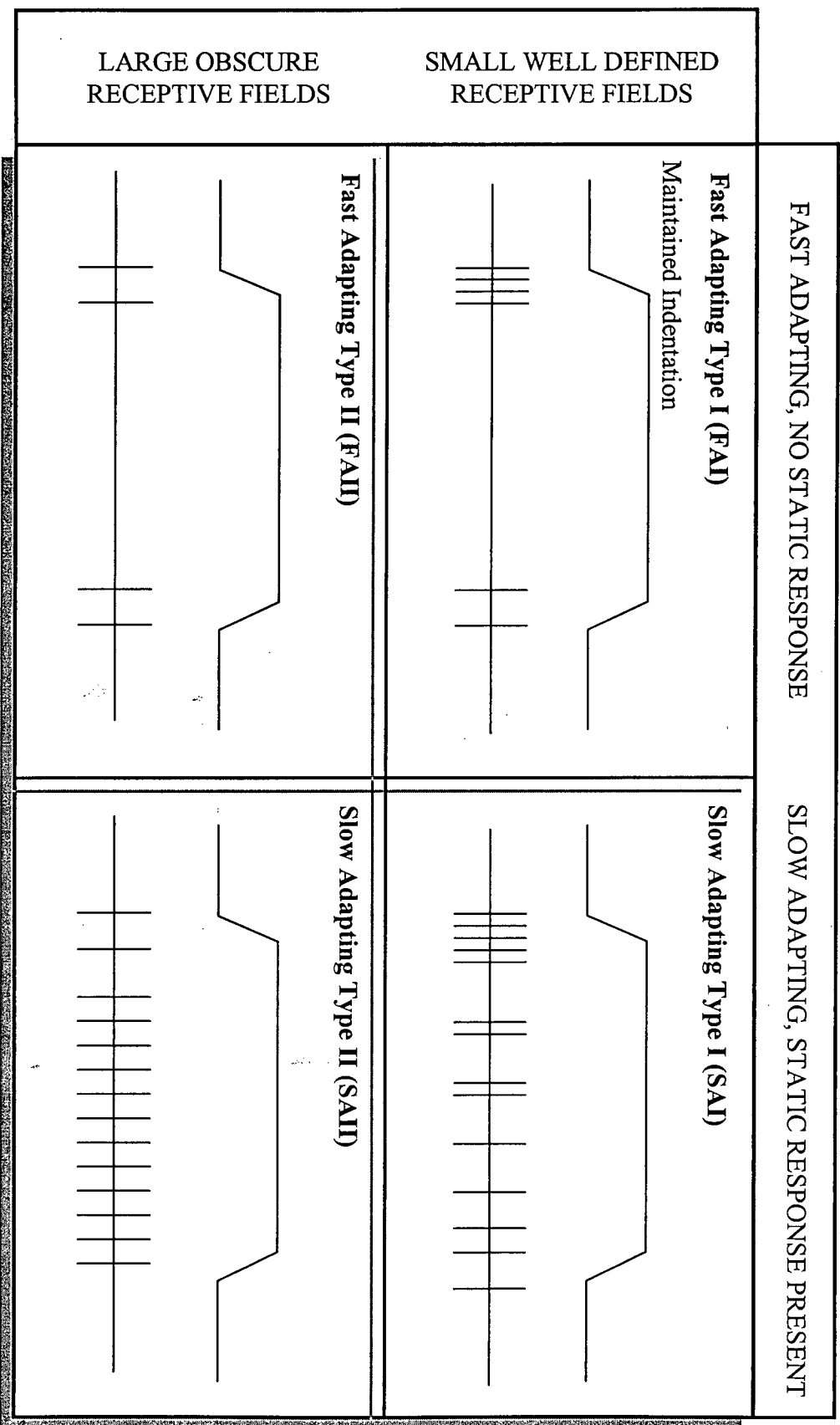
Figure 1 - Adaptation Responses of Cutaneous Mechanoreceptors

The types of cutaneous mechanoreceptors present in the human body, classified according to adaptation and receptive field properties. This figure illustrates the impulse discharge (lower trace) to and maintained ramp indentation (upper trace) for each unit. This figure has been adapted from the one found in Johansson and Vallbo (1983).

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The advent of the oscilloscope and the electron microscope afforded researchers an improved recording technique and facilitated the identification of free nerve endings in the development of an understanding about sensory receptors (Hamann 1996). Despite the anatomical and physiological differences, the receptor classes have afferents with comparable conduction velocities (Gandevia 1996). Psychophysiologists investigating the relationship between the sensory experience and the neural processes demonstrated that the intensity of the stimulus and the neural response were directly related (Werner and Mountcastle 1964). Despite the importance of cutaneous information, it was not until the advent of another scientific technique that the capacity of these signals in the control of human movements could be elaborated upon.

1.5 STIMULUS-RESPONSE PROFILES OF CUTANEOUS MECHANORECEPTORS:

In an attempt to record neural activity from conscious human subjects, a technique called microneurography was developed (Vallbo and Hagbarth 1968). This technique will be described in greater detail at a later point, but briefly, it involves the insertion of a recording needle into the underlying nerve of choice. Cutaneous receptors can be stimulated at the point of origin (i.e. face, hands, or feet) and the neural signals can be recorded. Mechanical stimulation of the nerve fibers and cutaneous afferents evokes a number of responses. A paresthesia or abnormal sensation, can be evoked when the tip of the electrode mechanically irritates the nerve. The characteristics of the paresthesia can be used to define what type of nerve fiber has been stimulated. If there was a distinct sensation of pinpricks superficially in a well-defined region then cutaneous fibers were stimulated. If there was a dull aching sensation in deeper structures in a diffuse area apart

from a region of maximal sensitivity, then muscle fibers were irritated (Vallbo and Hagbarth 1968). Once inside the nerve, a mass discharge of action potentials referred to as multi unit activity is the first signal to be encountered. This activity is nonspecific as the electrode is recording signals from several different axons. The dynamic activity is typically more prominent than the static response. As the electrode is repositioned, eventually single unit activity from an individual axon can be recorded reflecting the activity of a single cutaneous mechanoreceptor.

Based on single unit recordings, it was estimated that in the hairless, or glabrous skin of the human hand there are approximately 17,000 mechanoreceptive units over which half are rapidly adapting (Johansson and Vallbo 1983). The ability for humans to detect minimal tactile stimuli in the hand is limited by the sensitivity of the peripheral sensory apparatus (Johansson and Vallbo 1979). The FA type I and II units appear to be extremely sensitive to both low (30-40 Hz) and high (300-400 Hz) frequencies respectively (Johansson and Vallbo 1979, Gandevia 1996). Type I receptors respond well to local tapping, movements across the RF, as well as low level vibration. Type II units are extremely sensitive to vibration, which has sometimes been used to dissociate between receptor types.

Slow adapting receptors respond to local pressure or indentation of the skin. The state of the receptor is changing during the adaptation as both type I and II units provide a stronger signal when a given indentation is superimposed on a pre-existing level of indentation (Horch and Burgess 1975). More specifically, SAI units respond to a perpendicular ramp and hold displacement or constant force stimulus with an initial burst of impulses that is velocity dependent, referred to as the dynamic index (Hamann 1996).

This is followed by a slowly adapting irregular discharge. The initial dynamic component enables these receptors to be very sensitive to the velocity component of a stimulus. The irregular discharge pattern produced by SAI's is unique among mammalian tonic mechanoreceptors (Horch, Whitehorn, and Burgess 1973). It is believed that an impulse originating from an individual terminal can influence the impulse generating process in another terminal thereby resetting the end organ (Horch, Whitehorn, and Burgess 1973). In comparison, SAII's have poor dynamic sensitivity and respond with a regular burst of impulses to a sustained stimulation. Surprisingly, the majority of these units in the upper limb spontaneously discharge in the absence of indentation. Upon removal of a stimulus, there is an initial silent period after which the spontaneous activity gradually reappears (Knibestol and Vallbo 1970). Imposed joint movements can be detected by these receptors indicating that SAII's may play a role in joint awareness (Edin and Abbs 1991).

Single unit recordings are subdivided according to their stimulus-response profiles. It is important to maintain a rigid classification scheme in which manual stimulus applications are delivered at a constant rate. Even when the thresholds and RF profiles are studied with manually applied nylon monofilaments, the differences between the units with distinct borders and obscure fields can be easily appreciated (Vallbo et al. 1979). The consequence of consistent stimulus application was first addressed when FA receptors were tested by a constant velocity displacement, they did not adapt as long as the velocity of distortion is maintained (Birder and Perl 1994). Rapid adaptation implies that the unit is firing only while the stimulus is moving, whereas slow adaptation indicates that the units firing behaviour is constant (Vallbo et al. 1979). This classification is based on a stimulus that is fixed in time (displacement). Another example was observed when a transient

detecting (type II) cutaneous receptor was tested with a rapidly moving stimulus with variable acceleration. In this instance the FAII unit did not adapt (Birder and Perl 1994).

1.6 THE FUNCTIONAL ROLE OF CUTANEOUS MECHANORECEPTORS:

The type of information and therefore the overall function of a region will depend upon the pattern of cutaneous afferents distribution. Upon classifying these afferent units, the RF is not a uniform entity. Its exact size, shape and geography are dependent upon the characteristics of the stimulus employed to activate the unit (Johansson 1978). A comparison of the literature, in which comparable methodology standards were employed, reveals definite differences between the innervation of the forearm skin, the face, and the dorsum of the hand (Johansson and Vallbo 1979, Edin and Abbs 1991, and Vallbo et al. 1995). The human hand is by far one of the most extensively studied regions. The hand is an organ of remarkable capacity and versatility in motor and sensory tasks and is undoubtedly dependent upon the underlying neural elements (Johansson and Vallbo 1979). One of these basic neural structures is the peripheral equipment that respond to tactile skin stimulation; the population of low-threshold cutaneous mechanoreceptors. In light of this, the majority of the information pertaining to the functional role of cutaneous afferents is derived from this region.

Recordings from skin afferents in the dorsal surface of the hand indicated that the majority of these receptors were sensitive to movement (Edin and Abbs 1991). Movements around a joint deform the skin not only overlying that particular joint, but also in the surrounding regions. The FA units typically responded to a single joint action and although they failed to respond to ongoing rotations, the bursting patterns reflected the

extremes of flexion and extension movements (Edin and Abbs 1991). The SA receptors were influenced by the activity of several joints and their responses were related to the pattern of skin stretch (Edin and Abbs 1991). From this data, it was concluded that the mechanoreceptors were strategically distributed to reflect both the static and dynamic joint positions. This was a role that was previously attributed to muscle and joint afferents. If skin could contribute to kinesthesia and position sense, then skin stretch in the absence of movement should evoke an illusory action. Each joint configuration is associated with a unique skin strain pattern distributed across the nearby skin (Edin and Johansson 1995). In the anesthetized finger joint, skin strain patterns that mimic the pattern associated with movements elicit the perception of the actual movement. At this point, the debate between the afferents involved in joint awareness becomes confusing. From previously reported data, it was demonstrated that an individual's ability to detect a small misalignment between the angles of their right and left knees was not reduced by anesthetizing the skin around the joint (Clark et al. 1979). It was postulated that just because receptors can generate signals in which proprioceptive information can be derived does not demonstrate that the CNS uses this input. Cutaneous afferents may posses a limited capacity to provide joint awareness that may likely be of significance only when muscle spindle afferents cannot contribute to kinesthesis (Burke, Gandevia, and Macefield 1988). In a second study that tried to evoke movement illusions from sensory afferents, vibration of muscle spindles proved to be a more effective stimulus than skin stretch (Collins and Prochazka 1996). This was consistent with the prevailing concept that cutaneous input contributes to human movement but may be to a lesser extent than muscle afferent input (Collins and Prochazka 1996).

Proponents of cutaneous information believe that the skin's importance in kinesthesia has been greatly underestimated in previous experiments. Skin stretch not only influences a substantial portion of the somatosensory cortex in the primate; activity of these neurons can represent the movement direction and posture of the limb (Cohen, Prud'Homme and Kalaska 1994). Although it is possible to block individual inputs with anesthesia, the experimental outcomes are merely suggestive as the removal of motor behaviour may indicate that the blocked input was only one of several inputs involved in perception (Edin 1992). A population of receptors (Edin and Abbs 1991), if represented by skin strain patterns, must convey information about joint position. To exclude cutaneous inputs during knee movement as in Clark's study, large skin areas on the leg would have to be anesthetized. It is therefore invalid to conclude that the awareness of static knee positions does not depend on the sensory input from the skin around the joint because a 15 cm band of skin around the leg was anesthetized and the subjects failed to show a deteriorated position sense (Edin and Johansson 1995). Finally, skin and mucosa receptors are the only possible source of input for sensorimotor control of facial expression and speech movements, since muscle spindles are apparently lacking in facial muscles, excluding the muscles of mastication (Edin 1992).

Regardless of the capacity or contribution of skin in kinesthesis, it is generally agreed that cutaneous input is essential in tactile manipulation. Information about the surface features is important in programming the necessary force needed to grasp an object before the initial lift (Johansson and Westling 1987). To grasp and lift may appear as two different tactile tasks, however both involve minimizing the stretch of the skin due to frictional forces. Only the cutaneous mechanoreceptors innervating the area of contact can

reveal the occurrence of relative motion between the skin and the object surfaces (Srinivasan, Whitehouse, and LaMotte 1990). The more slippery the object the higher the ratio between the grip force and the vertical load force must be (Johansson and Westling 1987). Before the lift, cutaneous afferents initiate these adjustments so that the proper force is applied (Johansson and Westling 1987). These forces need to be continuously regulated during the hold phase as too weak a grip force causes slip whereas too strong a grip may damage the object or produce unnecessary fatigue (Johansson and Westling 1984). Inherent to cutaneous afferents is sensitivity not only to force, but a directional sensitivity for the manner in which these forces are applied (Trulsson, Johansson, Olsson 1992). An automatic adjustment in grip force between the thumb and fingers was observed when the tangential force against the skin signaled a sudden change in the load force (Johansson, Lemon, and Westling 1994). All of these responses occur in a rapid fashion as to maintain stability between the hand-object interface.

Touch sensation can also involve the exploration of an object according to shape, surface features, and dimensions. Multiple recordings of cutaneous receptors from anesthetized monkeys indicated that a change in position of the stimulus on the skin resulted in a matching shift of the population response profile (Wheat, Goodwin, and Browning 1995). The size of the shift corresponded to the magnitude of the change in position. A change in object curvature, based on single unit recordings, could also elicit a response in cutaneous afferents. The SAI units appear to be the most sensitive, increasing the number of impulses as the degree of curvature increased (Goodwin, Macefield, and Bisley 1997). This corresponded to the increase in overall force exerted against the surface of the skin. As for object shape and orientation, this is probably best represented by the

spatially distributed pattern of peripheral neural discharge rates (LaMotte et al. 1998). The SA units may play a stronger role in this as they were sensitive to the amount and rate of change of indentation on the skin, compared to the FA receptors that responded only when the objects were stroked across the skin. In spite of the fact that the function of the hand is contrasted to that of the foot, it is appealing to transfer these properties to determine the function of cutaneous receptors in standing balance.

1.7 ASSUMPTIONS OF CUTANEOUS AFFERENTS IN THE LOWER LIMB:

In a case study by Oliver Sacks, the venerable doctor introduced his readers to a woman that he referred to as "the disembodied lady" (Sacks page 44). A complete deprivation of all her sensory information initially paralyzed the woman until she could learn to ambulate by using visual input as a reference. The lack of afferent information, including cutaneous sensation led to the collapse of her postural tone, difficulty in manipulating objects, and a face in which there was an absence of expression. Unlike Guillain-Barre Syndrome (GBS) that is believed to be an auto-immune disorder which attacks the myelin of peripheral nerves resulting in a reduction or block of nerve conduction (Mackel et al. 1994), this condition was purely sensory. This, along with other clinical examples has implicated cutaneous receptors as actively being involved in postural control. Unfortunately, this conclusion is based on indirect evidence from the lower or cutaneous information for other regions of the body.

From a clinical perspective, sensory disturbances are common in diabetic neuropathy in the distal extremities. Abnormal encoding patterns to mechanical stimulation were observed in cutaneous afferents in the hand even in patients who were

neurologically asymptomatic (Mackel 1989). A similar response was observed in GBS patients in whom cutaneous receptors demonstrated a limited ability of afferents to conduct high frequency trains of action potentials (Mackel et al. 1994). In both these populations, there is reduction in stability demonstrated by an increase in postural sway. The decline in available information from the foot sole includes prolonged pressure and shorter stimuli of a vibratory nature that would be used for an exploratory purpose (Janig, Schmidt, and Zimmerman 1968). The individual receptors form a neural map that is able to spatially code every pressure point against the sole allowing the CNS to constantly extract body position information and trigger appropriate responses to reduce the gap between the body position and the equilibrium position (Kavounoudias et al. 1998). In these instances, the map cannot complete a faithful representation of the distribution of force.

There are properties of cutaneous afferents that could be applicable to postural control as demonstrated by single unit recordings in the hand and face. Human periodontal mechanoreceptive afferents innervating the anterior surface responds to loads applied to the teeth (Trulsson and Johansson 1996). This exquisite sensitivity to force is further observed in the hand as it works to preserve grasp stability during changes in load force by initiating rapid and automatic modulation of the force output (Hager-Ross, Cole, and Johansson 1996). The input provides information about the region that is stimulated and the direction at which the forces are applied. A characteristic of the SAII receptors, these afferents have a preferred strain axis that could provide a sensory population vector that would reliably differentiate not only the direction of the force, but also limb position (Prochazka 1996).

Most recording techniques can only sample from one afferent at a time. A single receptor cannot provide unambiguous information about the stimulus. There are a number of cutaneous sensations associated with mechanical events; contact with body hair or skin, movement, vibration, and texture (Birder and Perl 1994). How these experiences are differentiated between is not clear. One possible suggestion was that the firing activities of neighbouring mechanoreceptors can influence the interpretation of a movement (Edin and Abbs 1991). In this example, an FAI located near a joint might respond to flexion of the finger. However the same FAI unit firing in conjunction with a distal SAII responding to remote skin stretch may signal the interpretation of abduction of the same finger. To interpret how cutaneous information transmits behaviourally usable information, the concept of a neural code was developed (Lamb 1983). The CNS extracts the relevant information based on the mean response rate, the temporal sequence of the action potentials or the spatial arrangements of the activated receptors (Lamb 1983). It is not clear how many receptors need to be activated to form this code however the specific response could be based on the total response of a population, or within a small group of afferents.

1.8 ANATOMY OF THE LOWER LIMB:

The lumbosacral plexus is comprised of the first four lumbar and sacral nerves exiting from the ventral aspect of the spinal cord. At the level of pelvic cavity the sciatic trunk emerges from the plexus. The sciatic nerve is composed of two independent divisions, the medial popliteal (tibial) and the lateral popliteal (common peroneal) which descend as a single branch as far as the lower part of the thigh. The tibial division and its

terminal branches are found in the thigh, popliteal fossa, and throughout the leg and the foot. In the thigh, it is relatively superficial, covered only by the fascia of the roof of the fossa. As the tibial nerve descends it becomes deeper as it leaves the fossa deep to and between the two heads of the gastrocnemius and beneath the tendinous arch of the soleus (Sunderland 1978). Ultimately the nerve descends behind the medial malleolus around which it passes deep to the flexor retinaculum where it divides into the medial and lateral plantar nerves. In the foot, the medial plantar nerve is the larger of the two terminal divisions. Apart from its articulation with the big toe, it also participates in the cutaneous innervation of the medial aspect of the foot (Sunderland 1978). The lateral branch is smaller, separating into the common digital plantar nerves of the foot.

The vessels and the nerve are intimately bound together in a common neurovascular bundle (Sunderland 1978). The nerve is at first lateral to the popliteal artery, then gradually crosses superficial to the vessel, being posterior to it in the middle of the fossa before passing on to and continuing down its medial side (Sunderland 1978).

Sensory and motor input is transmitted through nerve fibers, which are grouped together in a strong sheath of connective tissue called perineurium. This bundle of fibers is referred to as a funiculus. Each funiculus usually contains a variable number of motor, sensory, and sympathetic fibers, although one or two types may be absent (Sunderland 1978). It is not typical for human peripheral nerves to comprise of a single funiculus. Nerve fibers are generally composed of several funiculi which by repeatedly uniting and dividing, engage in plexus formations along the full length of the nerve (Sunderland 1978). Plexus formation results in the variations in the number and size of the funiculi, rapid changes in this pattern (maximum constant length was ~ 15 mm), regrouping and

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redistribution of nerve fibers, and variations in the relative amounts of the nerve devoted to funiculi (Sunderland 1978). An example of this type of neural intercommunication is observed in the radial nerve in which over a distance of 46 mm, there may be as many as 23 changes in the bundle pattern (Sunderland 1978).

This continuous redistribution of nerve fibers precludes the counting of the total number of fibers representing each of the muscular and cutaneous branches in a peripheral nerve. As of yet, there are no efficient methods for establishing this information. There are however a number of generalizations that have been used to describe the relative areas devoted to funiculi and the epineurium; (1) approximately 25-75% of the cross-sectional area of a nerve trunk is composed of funicular tissue depending on the nerve and the level, (2) nerves contain relatively more epineurial tissue where they cross joints, (3) the percentage cross-sectional area of a nerve trunk devoted to the funiculi is inversely related to the number of funiculi (Sunderland 1978).

With specific reference to the tibial nerve, it is not clear at this time how many fibers are contained within the neural sheath. This nerve does contain both sensory and motor fibers, which innervate a variety of structures. The sensory branch contains distributions of cutaneous, muscle (muscle spindles, GTO's), and sympathetic afferents (small diameter afferents involved in pain and temperature perception). The cutaneous innervation of the tibial nerve is to the knee via articular branches, the calf of the leg, and the plantar surface of the foot. The motor innervation is responsible for actions such as flexion of the knee (gastrocnemius), plantar flexion of the foot (gastrocnemius, soleus, tibialis posterior, popliteus), flexion of the toes (flexor digitorum longus, flexor hallucis longus, intrinsic foot muscles), and rotation of the foot.

1.9 FUNCTIONAL ORGANIZATION OF PERIPHERAL NERVES:

The existence of a functional neural organization by both modality and somatotopy is well defined and commonly accepted in the CNS, especially at cortical levels of the somatosensory system (Ekedahl, Wu, and Hallin 1998b). In contrast, there appears to be a lack of organization in the peripheral nervous system. Within the neural sheath, there are three types of fascicles, motor or muscle, sensory or cutaneous, and mixed fascicles that, contain both muscle and skin afferents. These fascicles are continuously reorganized through branching of neighbouring fibers along the length of the nerves. Fascicular plexuses formed by such rearrangements were believed to be a key feature of fascicular anatomy and was believed to demonstrate that peripheral nerve fibers were randomly organized (Wu 1996). With the major function of peripheral nerves being to propagate nerve impulses towards the CNS, there appeared to be little need for somatotopic organization.

Electrical impulses in a nerve are generated at the specialized sensory region of the cutaneous fibers referred to as the receptive surface. A mechanical stimulus activates specialized protein molecules allowing ion channels in the membrane to open. The increase in permeability allows the ions to move across the membrane according to both their electrical and concentration gradients. These proteins consequently transform the mechanical indentation into a flow of ionic current that produces a change in the resting potential of the cell membrane (Rothwell 1994). The magnitude of this change, also known as the receptor potential, is graded in both amplitude and duration. The transuding proteins are restricted to the receptive surface of the sensory neurons and therefore, the receptor potential is a purely local signal that spreads passively along the axon (Rothwell

1994). The magnitude of this signal decreases with distance from its origin. However, if this signal reaches the first node of Ranvier in the peripheral nerve and the current is greater than the membrane potential, a net depolarization occurs. This initiates the first action potential, which can then propagate along the nerve fiber. The only function of the receptor potential is to trigger the action potential (Rothwell 1994). The greater the depolarization, up to a point, the greater the frequency of action potentials (Rothwell 1994). The magnitude and duration of the receptor potential are therefore determining the action potential frequency in the afferent fiber.

The nodes of Ranvier are uninsulated regions within a nerve, only 2 to 3 μm in length, where ions can flow with ease between the extracellular fluid and the axon. Previously believed to be randomly dispersed throughout the nerve, there appears to be some evidence that they may in fact be a defined pattern for the placement of these nodes. The location of these nodes would be vital to the continuous flow of action potentials since this is the only area within a nerve that impulses can be generated. Recording of these signals in the human median nerve demonstrated a clustering of these areas within a restricted region of sensory nerve fascicles (Hallin, Ekedahl, and Frank 1994). This was not the first study to dispute the concept of random patterning in the periphery. It appeared that small clusters of fibers in the cutaneous nerves of cats demonstrated a partial clustering according to sensory modality (Roberts and Elardo 1986). This somatotopic organization may also extend to the individual receptor terminals in the skin. While recording with a specialized concentric electrode inserted into the upper limb, a high proportion of a specific receptor type was recorded at a given instance. The outcome of statistical measures indicated a clustering of sensory fibers by receptor type for the FAI

and SAI units, whereas SAII and FAII units were coupled together within the same fascicle (Wu, Ekedahl, and Hallin 1998a, Ekedahl 1996, and Wu et al. 1998).

Research from improved recording techniques appears to demonstrate that peripheral nerve fibers are somatotopically organized and modality oriented (Ekedahl et al. 1998b). Not only are the individual fascicles segregated according to modality, but also the ultrastructure of the nerve is according the clustering of nodes of Ranvier. The result of such an organizational pattern is that neighbouring afferents in the nerve tend to supply the same restricted area of skin with RFs that overlap (Ekedahl et al. 1998a). The functional purpose of this arrangement in the periphery would be to relieve higher order structures from segregating and grouping appropriate signals (Ekedahl et al. 1998b). The establishment of peripheral nerve fiber organization has led to a greater understanding of how the CNS may use their firing patterns of different populations of cutaneous receptors to resolve various aspects of tactile discrimination.

1.10 MICRONEUROGRAPHY:

The development of microneurography was prompted by the interest in studying the somatosensory and proprioceptive mechanisms in organisms with an intact sensory system and volition, particularly in human subjects (Vallbo et al. 1979). Initially invented in Sweden in the mid 1960's, microneurography has been used in investigating sensations attributed to cutaneous, joint, and muscle afferents. These include tactile and nociceptive cutaneous activity, efferent sympathetic discharges, cutaneous thermosenstivity, and oral mechanoreceptivity. Microneurography has established a significant clinical niche in the assessment of autonomic outflow both in health and in disease such that almost half of the

major papers in which this technique is now used cover this field (Gandevia and Hales 1997).

The technical setup for microneurography requires an appropriate electrode, pre-amplifier, and amplifier. The underlying position of the nerve is first located based on its surface anatomy and response to electrical stimulation. A small electrode is inserted into the nerve and manipulated into the individual fascicles until discernable action potentials are recorded. Electrodes are typically made out of tungsten and approximately 200 μm in diameter. This material and dimension provides enough flexibility to attenuate to small movement of the tissues occurring along the electrode shaft (Vallbo et al. 1979). A thinner electrode would be too flexible and consequently would bend upon pressure from the surrounding tissues. The preamplifier is located close to the microelectrode and isolates the subjects from any unusual surge in electrical activity. Furthermore, the preamplifier relays the signal between the amplifying unit, which controls the delivery of electrical pulses, and the electrodes.

Recordings are derived from insulated monopolar electrodes that have a tapered recording surface (~ 5 μm). The insulation is gradually stripped away automatically as the tip passes through extra- and intraneural tissues (Wu 1996). The degree of insulation, or impedance of the electrode is a possible measurement of the quality of the electrode. Too high of an impedance will restrict the range or the amount of activity that the electrode will be able to record. If the impedance is too low, then the electrode will be able to record mass discharges from surrounding fascicles. This will make it difficult to be able to distinguish between the action potentials of different units. Searching for afferent fibers continues using physiological activation of the relevant receptors until a single unit is

satisfactorily identifiable above the background noise or other afferents (Gandevia and Hales 1997). The recording bandwidth can be adjusted to minimize the background activity. Typically, a high pass filter of 100-300 Hz and a low-pass filter of 10 kHz are used. This will allow signals between these two frequency cut-off levels to be recorded in the neural signal or neurogram. Signals beyond these levels will be automatically discarded.

Before the main purpose of the experiment can be fulfilled, the source and the type of action potentials need to be accurately identified (Gandevia and Hales 1997). Action potential amplitude is a function of the square of the diameter of the axons so that the impulses of small myelinated axons can be difficult to discriminate from the background noise (Burke 1997). If a receptor can be located by probing the muscle, the tendon, or by joint movement, the axon is most likely an afferent (Burke 1997). The pattern of discharge during an electrically evoked twitch contraction of the receptor bearing muscle, known as a twitch test, is an indicator than an axon is derived from either a muscle spindle or GTO. By subjecting the unit to a series of identification tests, the unit can be provisionally classified into muscle spindle primary and secondary afferents, and GTO's (Edin and Vallbo 1990). The response features, based on statistical likelihood functions is an easy and efficient manner in which to classify these muscle afferents and thereby exclude the possibility that signals are derived from cutaneous afferents.

There have been a number of objections raised pertaining to this technique. In summary, the main concern is that the electrodes are manually manipulated until single unit activity can be isolated. These adjustments cause a distortion and fragmentation of the tissues in contact with the needle. Furthermore, the relationship between the size of the

needle and the nerve fascicle diameter is so great that the likelihood of contacting a single fiber should be brought into question (Wall and McMahon 1985). Instead, the suggestion was that the large electrode pushed against the nerve fibers creating a pressure blockage, which enable the recording of unit potentials. To refute this claim, two independent studies demonstrated that at least 75-80% of the single units recorded during an experiment conducted past the electrode, refuting the conduction block hypothesis (Vallbo 1976, Inglis et al. 1996). When the electrode impales the nerve fiber the positive impulse is single peaked. When the impalement progresses and gives rise to a more pronounced intracellular recording, a notch or positive double peak appeared in the action potential (Vallbo 1976). Initially it was suggested that the double peak was the result of two simultaneously recordings overlapped, however this was proven not to be the case (Torebjork 1970). It was concluded that the first peak originated from the activity in the nearest node of Ranvier upstream of the electrode, while the second peak originated from the closest node downstream (Vallbo 1976). If the needle was continually advanced once this shape was observed, gradually there was a greater separation in the two positive peaks until finally the second peak disappeared. It was concluded that at this point, a conduction block was present (Inglis et al. 1996).

The microelectrodes underwent a significant change with the advent of the concentric needle design. The tip of the needle was altered from a taper to blade-like appearance. Changing the recording surface in this manner enabled the researcher to vary the number and specific locations of the recording surface. The recording ability was no longer dependent on the degree of insulation that surrounded the recording surface with this type of design. Although the tip of this needle penetrated the neural sheath, the

recording surface was now elevated and was extraneural. Similar double-peaked positive waveforms were obtainable with the design, which suggested the micro-recordings were not dependent upon the needle being intraneural. Credence was afforded to these observations because of the strong correlation with recordings in animals in which the recording preparations were surgically obtained (Wu 1996). Proponents of these electrodes believe that these recordings are more stable and specific in comparison with the conventional tungsten design (Wu, Hallin, Ekedahl 1997).

Regardless of the individual arguments centering around this technique, it is clear that microneurography is a powerful tool in the assessment of functional relations between neural impulses and the resulting sensory experiences (Hagbarth 1993). This technique permits a unique window to the neural traffic carried by peripheral nerves by recording the individual action potentials. A current limitation with microneurography relates to the low yield of the data. In a typical experiment lasting 4-5 hours, it is unusual to maintain a stable recording for more than 15 minutes, averaging five units per session (Vallbo et al 1979). This may discourage the application of microneurography in the investigations of special or diseased populations. With improved recording procedures and efficient methods for classifying afferent fibers, microneurography will continue to be a vital component in establishing the role of various sensory receptors in motor control.

1.11 CUTANEOUS AFFERENTS AND STANDING BALANCE:

From a review of the literature, it is apparent that cutaneous sensory information is an important variable in the control of standing balance. There are strong projections from skin to all levels of the motor system, including the spinal cord, cerebellum, and motor

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cortex (Edin 1992). These connections account for the indirect manner in which skin may influence postural control. An example of this coupling was observed when the thresholds and activation patterns of muscles in the lower limb were altered during skin stimulation (Garnett and Stephens 1981, Burke et al. 1991). The afferent signals originate from four distinct receptor terminals that are found throughout the layers of the dermis. Collectively termed mechanoreceptors, these receptors are comprised of both rapidly and slowly adapting units that respond to the stretch of the skin. Although there is some discrepancy as to the degree in which cutaneous input is used in establishing limb position, it is apparent that these receptors play a role in kinesthesis. Furthermore, these receptors are sensitive to a variety of stimulus features such as size, friction, movement, and force exerted against the skin. Despite the individual response of given mechanoreceptors, it is the overall population that establishes the functional role of the cutaneous afferent in a particular region of skin. That is, an SAI responds in the same manner in the face as it does in the hand. However, the skin of the hand and face are different from the hairy skin in the arm, which suggests that these regions may be regarded as specialized sensory regions with unique innervation features (Vallbo et al. 1995). These characteristics have been prematurely applied to the skin of the lower limb. It is believed that the wide distributions of cutaneous mechanoreceptors in the foot sole are utilized in the control of standing balance. Statements in the literature like this one are misleading as there is limited information about both the cutaneous afferents in the hairy skin of the leg and the glabrous skin of the foot sole (Hagbarth and Vallbo 1968 and Ribot-Cisar, Vedel, Roll 1989). Improved recording procedures have revealed important characteristics about peripheral nerve fibers and the type of information that is transmitted through the fascicles.

It would be possible to record the impulses from cutaneous nerve axons derived from the mechanoreceptors in the foot sole using microneurography. These recordings would provide direct evidence of the potential role cutaneous mechanoreceptors in the glabrous skin of the foot might play in the control of standing balance.

1.12 AIMS OF THIS STUDY:

Microneurographic studies have examined different aspects of the functional human anatomy. To date, there is limited information about the lower limbs, particularly with respect to the cutaneous mechanoreceptors in the tibial nerve. Previous studies have demonstrated that cutaneous information from receptors in the foot sole may play an important role in the control of standing balance (Wu and Chiang 1997, Kavoundoudias, Roll and Roll 1998). The overall purpose of this study was to document the properties of the cutaneous afferents in the lower limb of humans. The individual goals of this study have been outlined below:

1) *To establish the stability of recordings in the lower limb.*

By examining such components as the average length of single unit recording periods, saliency of multi-unit recordings and the amount of movement a subject can generate before the recording is lost, the overall stability can be examined. This will also include measuring the average nerve depth, the ease to which the needle can be adjusted in the nerve, and the overall comfort level of the subject during the experiment. This information will be used to assess the feasibility of performing microneurographic recordings in the tibial nerve during standing.

2) *To create an anatomical map of the cutaneous mechanoreceptors in the foot sole.*

From the recordings in the foot sole, a map of the location of the receptors and the RFs will be created. The data set will include a measurement of the glabrous skin area and the baseline values (means for thresholds, firing frequencies, and RF sizes) for each receptor group. Based on the number of units and the measurement of the glabrous skin size, the relative densities for the receptors and regions can be calculated. These values can then be used in comparison with other body regions such as the upper limb and face (Knibestol 1973, Johansson et al. 1988, Edin and Abbs 1991).

3) *To establish what potential role the cutaneous afferents in the foot sole have with regards to movement control.*

It has been postulated that cutaneous mechanoreceptors are actively involved in the sensory feedback during movement (i.e. the gait cycle). To gain an understanding of the role these receptors might have there should be a demonstrable response to skin stretch or joint movement in the ankle or toes. Furthermore, there should be some evidence of on/off contact coding to differentiate between when the foot is involved in the swing phase and the stance phase.

4) *To establish what potential role the cutaneous afferents in the foot sole have with regards to postural control.*

Cutaneous mechanoreceptors can accurately discriminate between differences in pressure between an object and the surface contact of the hand. Translated to the lower limb, it is

reasonable to assume that this pressure discrimination may be able to discern the position of the center of pressure. To elucidate on this issue the receptors will be evaluated during periods of sustained indentation and detection of discrete indentations passing through the RFs. The response from a single afferent will be used to infer how this signal contributes to a population code (Lamb 1983) that can potentially monitor the position of the center of pressure.

Chapter Two
Methods and Procedures

METHODS AND PROCEDURES:

2.1 EXPERIMENTAL SETUP:

Thirty-one recording sessions were performed on thirteen healthy volunteers (7 males, 6 females) between 22-50 years of age (mean 29.6 years). Participants had to wait a minimum of four weeks between successive experiments on the same limb to minimize post-treatment symptoms. Subjects were excluded due to any history of neurological or neuromuscular complications. Furthermore, individuals who were taking anti-coagulating medications or immunosuppressants were also excluded from this study. Informed consent was obtained and the University's ethics committee approved the procedures.

Subjects were placed on their stomachs in a prone position on an adjustable bed. The position of the bed was adjusted to ensure that the subject was both comfortable and relaxed. Subject relaxation was important to reduce any unwanted background muscle activity that could contaminate the neural signal. In this position both legs were extended and the test limb was elevated on a support. This created a slight flexion at the knee and ankle joint so that the foot sole was facing upward. A white analgesic cream, called Ametop (4% Tetracaine), was applied to the back of the knee (ametop gel is a fast-acting anaesthetic that reduces the sensation attributed to the needle insertion). A layer of dressing was wrapped around the knee for 30 minutes to allow the treatment to take effect. Once the dressing and excess cream was removed, small Semmes-Weinstein nylon monofilaments were applied to the back of the knee to assess the effect of the anesthetic. The skin on the back of the knee was then cleansed with an Isopropyl Rubbing Alcohol (70% Isopropyl Alcohol 50 mg/ml) Solution. Any hair was removed with a clean, standard safety razor.

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2.2 NEUROPHYSIOLOGICAL TECHNIQUE:

A surface stimulating electrode was placed on the back of the knee to locate the superficial position of the tibial nerve. A Grass S48 Stimulator (between 30-90 V) delivered electrical pulses at a rate of 1 Hz. The twitch response of the triceps surae muscle group was used to assess the location of the nerve. This area was outlined on the skin with a marker. To locate the nerve subcutaneously, a sterile stimulating reference electrode was inserted into the popliteal fossa over the outlined region while an electric current was delivered intermittently. The microelectrodes were 0.2 mm in diameter and 55-65 mm in length with a standard profile tip (Fred Haer type 26-10-11). As the tip of the needle was manipulated closer to the nerve, a smaller amount of voltage was needed to elicit a twitch response. The location of the nerve was identified when a twitch was elicited at a level lower than five volts, or a mechanical sensation was evoked signaling that the tip of the electrode had penetrated the neural sheath. These mechanical sensations are called paresthesias. If the predominant sensation is that of pinpricks in a localized area, then the tip of the needle has penetrated a cutaneous fascicle (Hagbarth and Vallbo 1968). A motor or muscular fascicle branch would elicit a deep dull sensation that would be rather difficult to localize (Hagbarth and Vallbo 1968). When the stimulating electrode penetrated the nerve, the electrode was withdrawn slightly to prevent further sensations from being evoked. The stimulating electrode served as a visual reference for guiding the recording electrode into the nerve.

A sterile recording microelectrode was inserted approximately one centimeter proximal and parallel to the subcutaneous reference electrode (stimulating electrode) (see figure 2 on page 43). The verbal responses of the subjects about sensations experienced

Enlarged View of Tip

Uninsulated

Skin

Recording Electrode   Reference Electrode

Peripheral Nerve

Fascicle
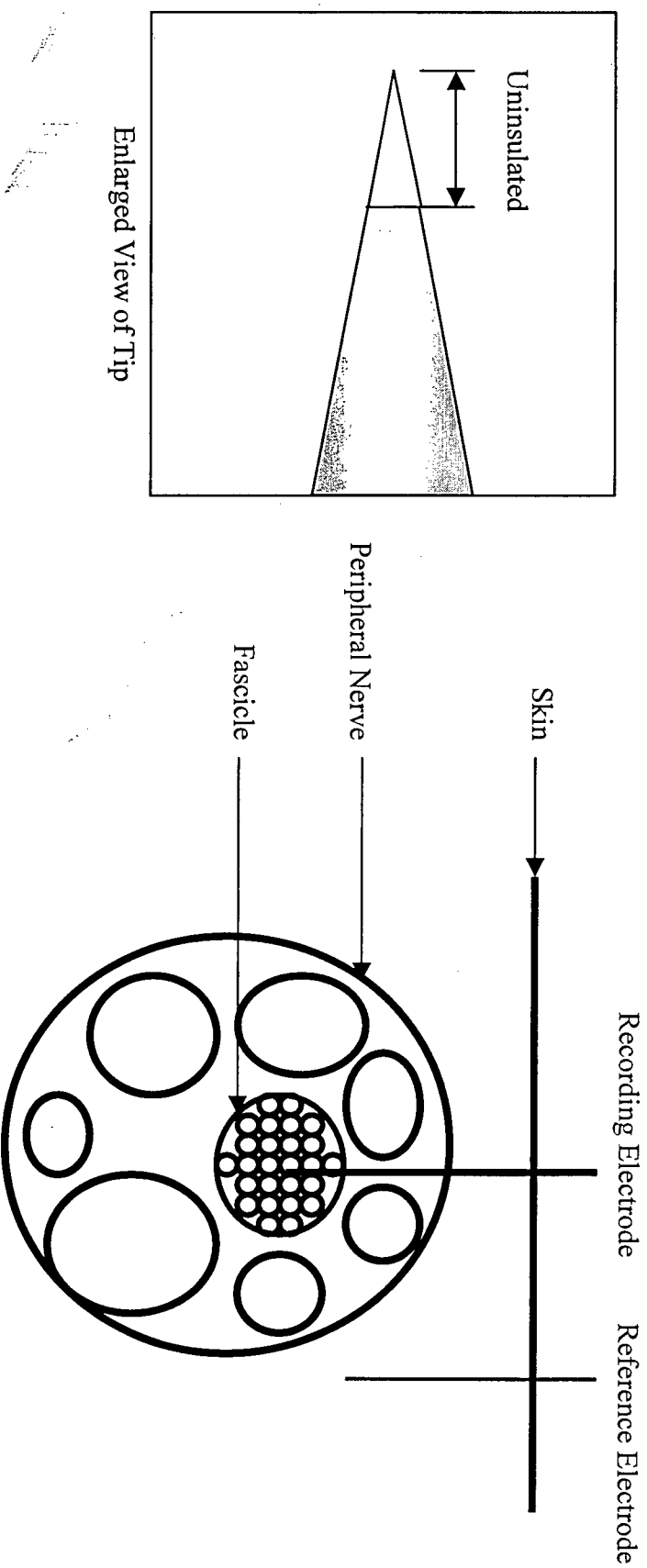
Figure 2 The Neurophysiological Technique

This figure illustrates two components of microneurography. Once the location of the nerve has been identified an insulated recording electrode is inserted through the skin. The recording surface is at the distal end of the electrode. The electrode is manipulated through the neural sheath and into a fascicle until single unit activity can be recorded.

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due to needle manipulations were essential in correct electrode placement. The path to the nerve, including penetration of the neural sheath, typically resulted in minimal sensations. The electrode was manually inserted and carefully positioned into the tibial nerve at a variable depth between 15-37 mm (mean depth 26 mm). The impedance of the microelectrode in situ was between 50-360 (mean 150) kΩ at 1 kHz.

The hand of the experimenter stroked the skin on the plantar sole of the foot and posterior lower leg in order to stimulate the underlying cutaneous receptors. A tapping action was used to excite the fast adapting receptors while a stroking action of maintained pressure would activate more slowly adapting receptors. These movements were varied in order to eliminate any bias between receptor selection. To classify specific mechanoreceptors, Semmes-Weinstein nylon monofilaments ranging between 0.05 to 200 g (0.5 mN to 2000 mN) were applied to the skin surface. The location of the receptor was defined as the point of lowest mechanical threshold. A monofilament of four-five times threshold force was used to outline the RF for a given unit (Johansson, Vallbo, and Westling 1980, Edin and Abbs 1991). In order to preserve the field for classification purposes, washable marker outlined the skin defining the RF. In identifying the receptor's adaptation properties, a monofilament of approximately four-to-five times the threshold will be placed at the origin of the receptor for a brief period (up to 10 seconds). A longer sampling period was needed to dissociate between slowly adapting receptors. Vibration sensitivity was assessed with a dual-setting Panasonic Electrical vibrator. For some of the units, force sensitivity was measured online with a hand-held force transducer (1601 Series Digital Transducer Indicator).

2.3 CLASSIFICATION OF SINGLE UNITS:

Once the electrode entered a nerve fascicle within the nerve sheath, the microelectrode was manipulated manually in small increments until single-unit activity of sufficiently high signal-to noise ratio was isolated (2-4:1). The neural data was discarded if recordings were lost before being characterized in terms of adaptation properties and threshold level. These discharge properties yielded important information in identifying that particular receptor. The fast adapting type I units were defined by a response to skin indentation with a burst of impulses only at the onset and removal of the stimulation. These units had a small, well-defined RF that was rounded or elongated. In comparison, fast adapting type II units were classified by a similar response pattern but were much more sensitive to distant taps and vibration. A much larger RF with indistinct borders characterized these units. Slow adapting units were defined by a continuous discharge during maintained skin indentations. Slow adapting type I units had a small well-defined RF. Slow adapting type II units were classified by a more indistinct RF. These units were also classified by a response in which skin stretch in a preferred direction can excite these receptors.

The neural activity was sampled by a custom built Yale Microneurography Amplifier (amplified by 10-25 k). This signal was filtered with a band-pass setting of 300 Hz to 10 kHz. Audio presentation of the neural signal was sampled by a Grass AM8 Audio Monitor. Single unit spikes were captured and displayed on-line using an oscilloscope (BK Precision 20 MHz Analogue Model 2522B) with a 10-ms time base. For analysis of action potential morphology, commercially available software (Spike2) was used to record the neural signal. The neural data was sampled (between 25-50 kHz) and

converted from analogue to digital format using a Cambridge Electronics Design 1401-micro interface.

2.4 MEASUREMENT OF THE SIZE OF THE GLABROUS SKIN REGIONS:

In order to measure the size of the various skin regions transparent paper was applied to the sole of the foot. Five subjects (2 males, 3 females) between 24-38 years of age (mean 27 years old) participated in this aspect of the study. The subjects shoe sizes (men's equivalent) ranged from size 7 to 12 (mean shoe size of 9). The boundary of the glabrous skin and the flexure lines were marked on the paper with a pen. The outline was placed against a grid so that the overall area could be measured. The size of the glabrous skin area was plotted against the product of the length and width of the foot.

Chapter Three
Results

RESULTS

3.1 MULTI-UNIT ACTIVITY:

With the recording electrode inside the nerve but between axons, mass discharge or multiunit activity was recorded. This represents nonspecific activity from a variety of axons that surrounded the recording surface of the electrode. Multiunit activity reflected the position of the needle in the overall nerve. The foot sole was divided into eight regions that included each of the five the toes, and the medial and lateral divisions of the front footpads, arch, and heel. By assessing the multiunit activity in these various regions, it was possible to outline the fascicle innervation territories. Multiunit activity could be evoked in predominantly the medial or lateral aspect of the foot corresponding to the medial and lateral plantar nerve divisions in the tibial nerve. Recordings of multiunit discharge demonstrated little activity in the absence of intentionally applied stimulation. This activity was evoked from skin regions that included extensions onto the calf and the anterior surface of the foot. Upon stimulation, the dynamic response strongly predominated over the static response with distinct on- and off-discharges during maintained indentations. The bursts of activity were reflected in the neurogram with a signal-to-noise ratio of 2:1. In some of the recordings, sympathetic activity accompanied the multiunit discharges. Sympathetic activity was distinct from cutaneous signals with a prominent negative component in the morphology of the action potentials. Efferent sympathetic activity is often encountered in recordings from skin and muscle nerve fascicles (Vallbo et al. 1979). The spontaneous resting activity occurred in highly repetitive patterns separated by periods of neural silence that varied in strength and duration (Vallbo et al. 1979). Sympathetic reflex responses can be evoked in skin nerves

by respiratory and arousal stimuli. When the subject was asked to hold their breath, the sympathetic bursts increased in duration and strength corresponding to the decrease in available oxygen. This increase in bursting behaviour was also demonstrable to a loud noise that evoked a startle response in the subject. This efferent activity reflects the skin's electrical resistance, vascular resistance, and blood pressure by transmitting impulses that produce a vasoconstriction response in the effector organ (Vallbo et al. 1979).

3.2 SINGLE UNIT RECORDINGS:

The recorded action potentials were identified according to shape based on previous published criteria (Vallbo 1976, Inglis et al. 1996). The quality of the recording varied depending on the impedance of the electrode as observed in the SNR (2-5:1). The recognition of wave shape was important as this revealed information about the position of the electrode in relation to the axon. An impulse with a prominent negative component was typical of an extra-mylenic recording. When the principal phase of the action potential was positive, the recording surface of the electrode was inside the myelin of the nerve fascicle. Over 85% of the recorded units had a prominent positive phase. In addition, identification of wave shape assisted in distinguishing the single unit from that of another unit or from multiunit recordings such as sympathetic activity. The ability to discriminate action potentials is crucial in microneurography. A positive double peaked spike typically characterized single unit recordings, with two prominent positive peaks in the initial positive phase. The double peak results as a function of the microelectrode recording the potential from the nodes of Ranvier on either side of the impaled internode (Inglis et al. 1998). The time between the two positive peaks is an indication of the

conduction time across the impaled internode. As the distance between the two peaks gradually separates until only a single positive peak is present the position of the electrode has created a conduction block in the axon (Inglis et al. 1998).

To establish single unit recordings during testing sessions, the receptor was excited and the generated action potentials were recorded. Ten consecutive unit recordings were aligned according to the maximum peak amplitude and superimposed on one another (see figure 3 on page 51). Despite minor variations in the background noise, these samples displayed similar form and amplitude. Impulses can be distinguished through the use of a template. The commercial software (Spike2) examined the neural data and identified the different shapes found in the signal. A template was then created where every time a particular waveform was encountered; it could be labeled according to the template. A mean unit potential was expressed that looked identical to the sample. This confirms that single unit activity was recorded in this study. The fact that stimulation of a receptor elicited action potentials that corresponded in amplitude, duration and form is essential to the examination of the receptor's physiological attributes.

Stable single unit recordings lasted between 5 to 36 (mean 13.5) minutes despite small ankle movements. The mean recording is slightly arbitrary because there were a number of recordings that were terminated by the experimenter after approximately 10 minutes. In these instances, all the relevant information was obtained from that particular unit and the experimenter therefore repositioned the electrode in search of another recording, thus terminating the unit prematurely. Recording sessions were limited to approximately two hours of intraneural recording time to minimize post-experimental
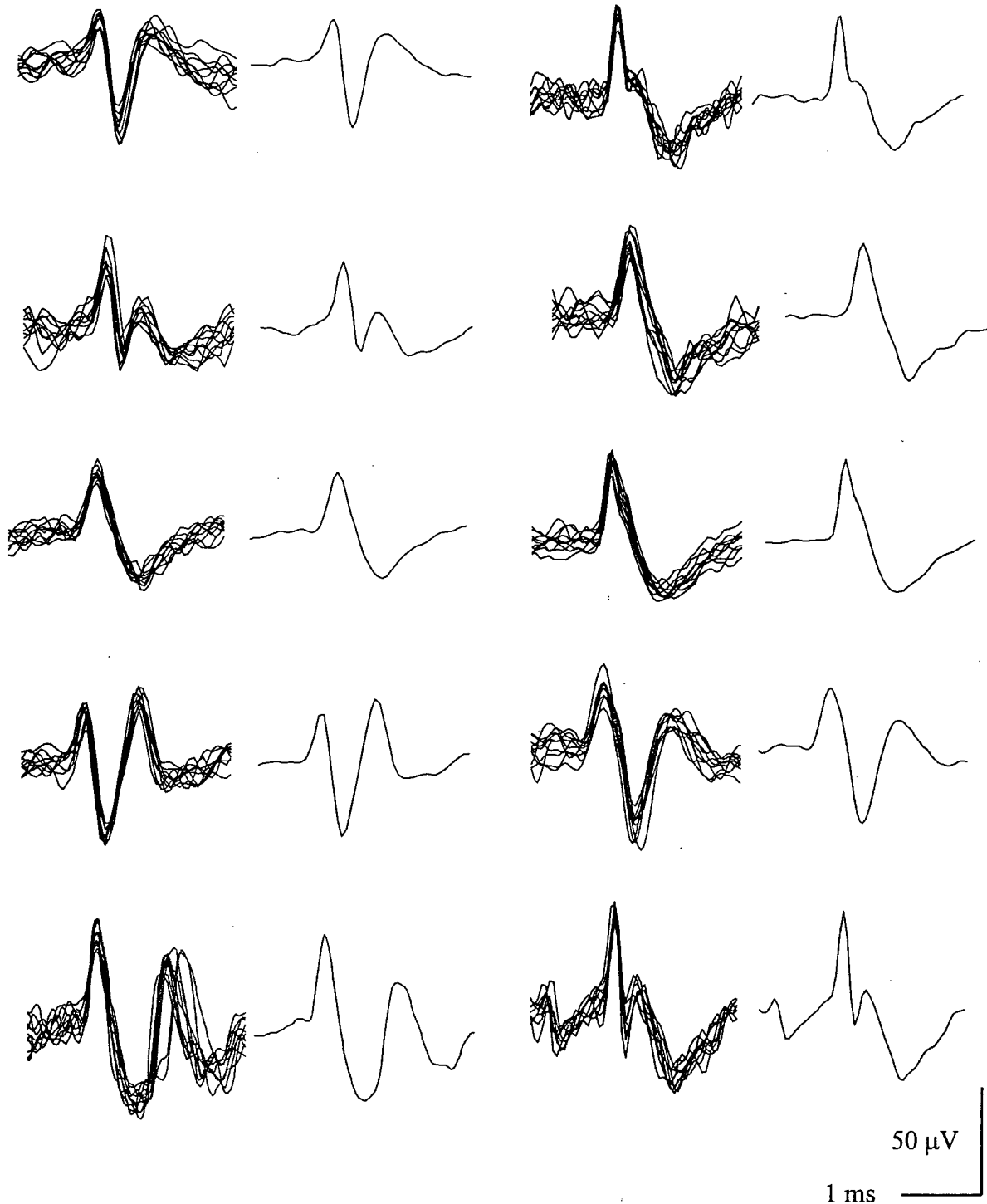
Figure 3 Single Unit Waveform Analysis

Ten consecutive unit recordings were overlaid and aligned according to peak amplitude. A mean unit potential was calculated and illustrated to the right of the sample. The ability to consistently record the same unit potential supports the theory that single unit recording is obtainable with this technique and achieved in this study.

sensations. Following the experiment, some individuals experienced mild discomfort at the site of the needle insertions and within two days there were in some cases minor muscle soreness in the calf. These sensations subsided within a period of seven days.

Of the 126 consecutively recorded units, 106 were from cutaneous mechanoreceptors with 31 slowly adapting and 75 fast adapting units. The remaining 20 units were recorded from presumed muscle receptors (muscle spindles and GTO's). The subdivisions of cutaneous receptors according to adaptation properties was apparent, however the further subdivisions into group I and II was more difficult. The conclusions in this report are dependent upon an effective classification of afferents into appropriate groups. Assessing vibration sensitivity was effective in dissociating between FAI and FAII units. The presence of a background discharge could not be used to dissociate between SA types, as there was no apparent background activity in any of the SAII units. The slow adapting behaviour was a more appropriate criterion as SAI's demonstrated irregular discharge and SAII units were more regular in their firing patterns. Based on this classification scheme for cutaneous afferents the results yielded 15 SAI's (14%), 16 SAII's (15%), 60 FAI's (57%), and 15 FAII's (14%) (see table 1.0 on page 53). The threshold levels for both SA and FA afferents were higher in the glabrous skin of the foot sole in comparison with the hand (Johansson et al. 1980). However the relative distribution of threshold levels between receptors was similar. That is, the SAII units had the highest median thresholds (115 mN) and FAII units had the lowest (5 mN). In figure 4 on page 54, the location of the receptors and the thresholds of the population are illustrated. This figure also depicts how adaptation properties were used to distinguish between receptor types.

Type	No.	% of Total	Mean Threshold (mN)	Median Threshold (mN)	Area (mm^2)		
					Mean	Median	Range
SAI	15	14	96.64	35.61	98.37	70.93	11.81-277.46
SAII	16	15	431.10	115.26	146.73	127.42	43.99-296.16
FAI	60	57	36.66	11.79	50.49	38.38	5.83-333.58
FAII	15	14	265.50	5.39	413.73	284.19	41.74-1248.00
Total	106	100	--	--	--	--	--

Table 1.0 - Single Unit Sample of Cutaneous Afferents in the Lower Limb
The characteristics of the cutaneous receptors in the lower limb are listed in this table. The total number of units for each population, the threshold levels as estimated with calibrated nylon monofilaments, and the receptive field properties were calculated.
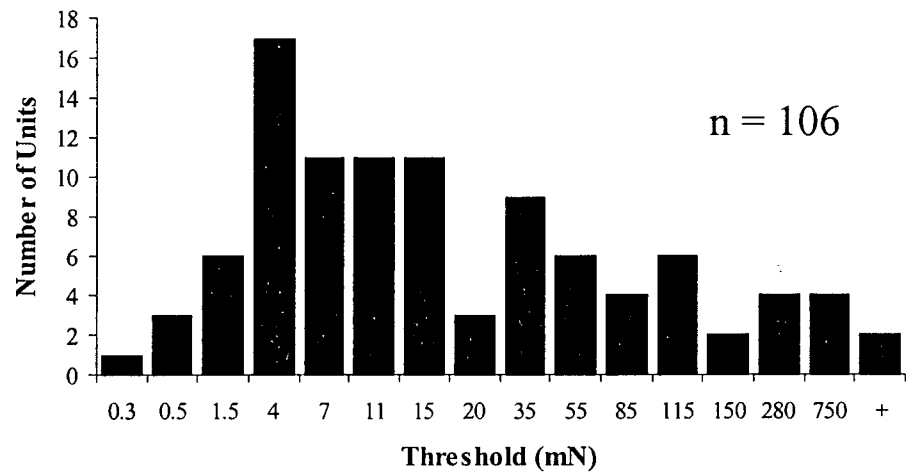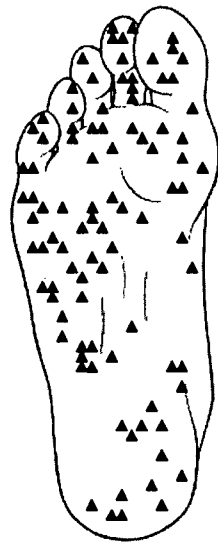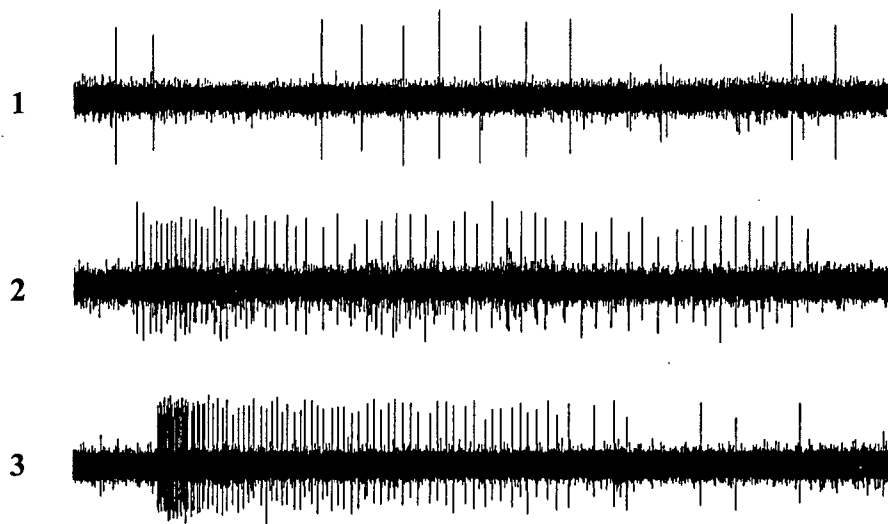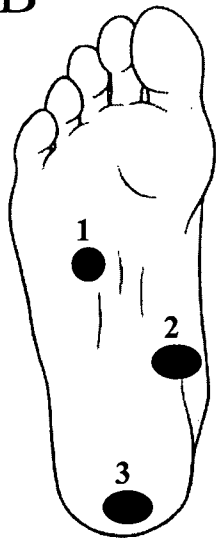
Figure 4 Identifying Cutaneous Mechanoreceptors in the Foot Sole

(A) Of the 106 single unit recordings, the location of the receptors on the glabrous skin of the foot sole are indicated ▲ in the schematic illustration. Once this has been achieved the receptive field and its accompanying adaptive properties can be investigated. In (B), the receptive fields of three receptor types (1-FAI, 2-SAII, 3-SAI) and their adaptation properties are represented.

3.3 RECEPTIVE FIELD DISTRIBUTIONS AND CHARACTERISTICS:

The receptive fields of the FAI, SAI, and SAII units shared some defining characteristics. These units were typically round to oval in shape with the point of lowest sensitivity located on the lateral aspect of the field. This region of low sensitivity is often referred to as the receptor's hot spot. A number of these units exhibited a pattern in which the lateral borders of the field were distinctly marked by the flexure lines in the skin. The median RF sizes for FAI, SAI, and SAII units were 38, 71, and 127 mm^2 respectively (mean values were 51, 98, 147 mm^2). In comparison, the FAII units were rather large and obscure in dimensions with no obvious positioning of the hot spot. Two of the FAII units covered the entire foot sole and extended their RFs onto the hairy skin of the calf. From the measurable FAII units, the median RF size was estimated at 284 mm^2 (mean 414 mm^2).

Receptors were found within the distribution of both the medial and lateral plantar branches of the tibial nerve. For the most part receptors could be isolated as deriving from one branch or the other by observing the position of the hot spot and the previously recorded multiunit activity. There were two observations that were made with regards to the distributions of the receptors. First, there appeared to be a clustering of units within certain regions of the foot sole (see figure 5 on page 56). The SA units demonstrated a medial to lateral gradient as SAI's were primarily located along the lateral border of the foot and SAII's were observed towards the medial edge. The FAII units also demonstrated a distribution shift by clustering around the distal edge of the foot sole. The FAI's exhibited no such pattern in the glabrous skin as they constituted almost two-thirds of the present sample. Second, the RF is a function of the initial threshold of the receptor. There
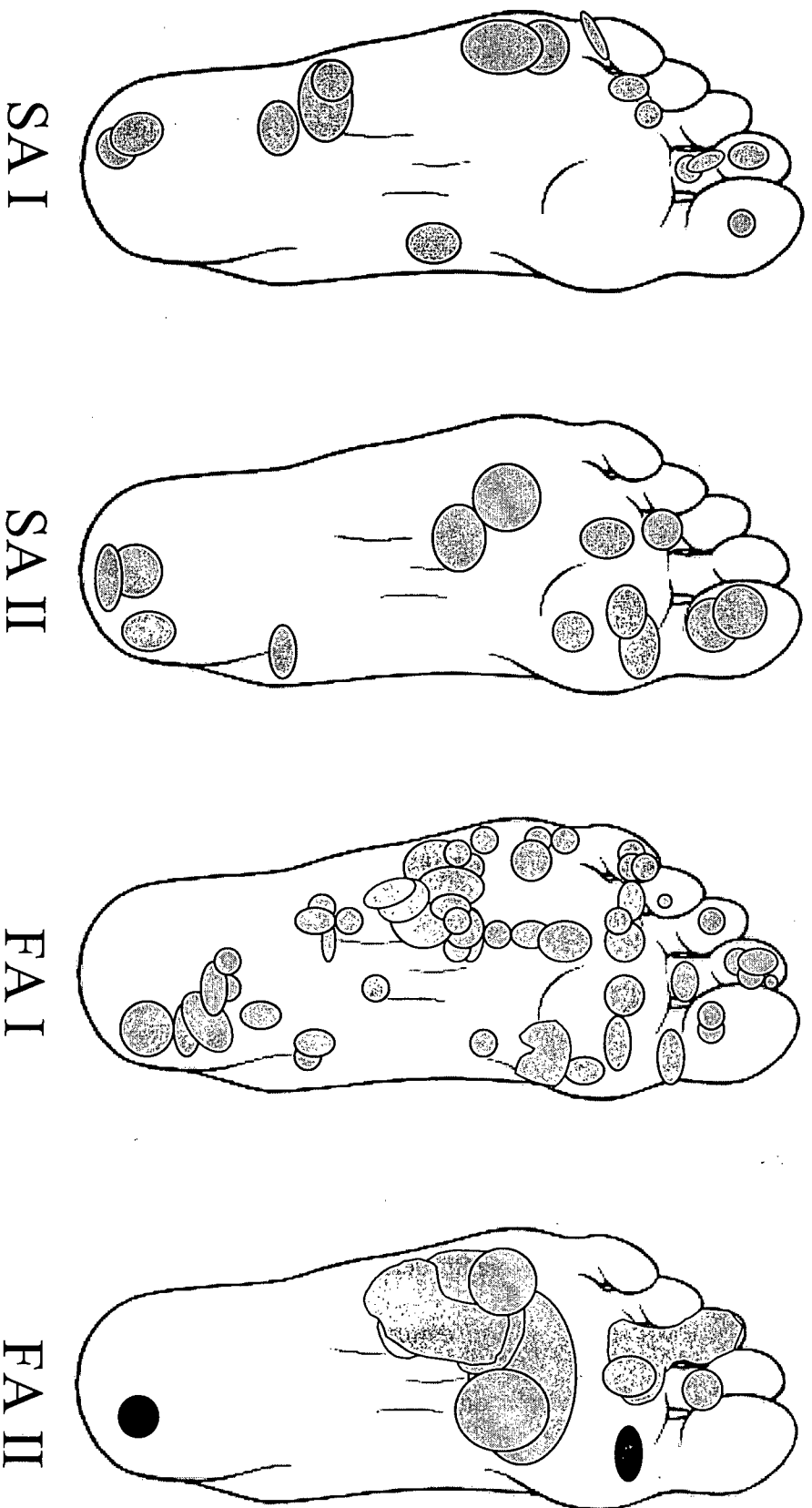
Figure 5 Receptive Field Profiles

The receptive field for each unit on the foot sole is illustrated above. The black outline on the FAII profile indicates the zone of maximal sensitivity. For this region, the receptive field cannot be represented as these units covered the entire foot sole and extended onto the lower calf.

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was a greater degree of calluses in certain areas of the foot (i.e. heel vs. arch). If the skin mechanics bias the initial threshold value, then the RF is being inflated because of skin quality and not receptor sensitivity. The resultant would be an overestimation of RF size in callused regions. In comparing the mean RF thresholds, this did not prove to be a significant factor. The interpretation of these results is therefore, that the RF sizes were an accurate reflection of the sensitivity of receptor regardless of the varying skin mechanics across the different regions of the human foot sole.

3.4 SLOWLY ADAPTING RECEPTORS:

Slow adapting receptors were assessed primarily on their response to a sustained indentation. These units accounted for approximately one-third of the total population, a number that is significantly less than that previously reported in the glabrous skin of the hand (Johansson and Vallbo 1979). The dissociation between receptor types was based on certain cited criteria such as the presence of a background discharge. This was not appropriate in this study as it was apparent that none of the SA cutaneous receptors had any background activity. Furthermore, during certain recordings it was difficult to recognize the difference between the boundaries of the SA RFs. That is, despite the fact that SAII RFs were slightly larger than the fields of SAI units, the regions were rather well defined which made it difficult to dissociate between the two receptor types. To expedite the classification of receptors, units were temporarily assigned a classification based on the number of hot spots. Once the location of the receptor was identified, a sustained indentation was maintained for approximately ten seconds and the discharge pattern was examined. The number of action potentials generated by a stimulus can be expressed in

the form of impulses per second, or by their instantaneous frequency. Instantaneous frequency displays are calculated by plotting the inverse of the time interval between an impulse and the previous action potential. During a sustained indentation of the skin, Type I units exhibited an irregular discharge whereas type II units were more regular in behaviour. This provided a positive measure for classifying these recordings in the foot sole (see figure 6 on page 59). These discharge characteristics were observed in stimulus histograms, which plots the time between impulses, or the interspike interval. With an irregular discharge, there is a random pattern between the interspike interval so the histogram will be rather diffuse. In comparison, a regular discharge will be reflected by a histogram that has a rather tight distribution. During this adaptation period, the recorded units responded in a vibrant and varied manner. At the onset of indentation, an initial dynamic firing period was followed by a prolonged static discharge for the duration of the stimulus. The dynamic sensitivity was present in all SA afferents (20-100 imp/s in SAI's and 50-115 imp/s in SAII's) as this initial burst reflected the velocity and intensity of the stimulus. When the dynamic response gave way to the static discharge, the SAI units fired at a mean discharge level around 5-10 imp/s (mean 7 imp/s). The SAII units fired at a higher frequency that was approximately 5-20 imp/s (mean imp/s).

3.5 FAST ADAPTING RECEPTORS:

If a unit could not respond to the constant mechanical pressure demonstrating bursts only at the onset and removal of the stimulus, it was classified as a fast adapting receptor. The majority of these units had small, well-defined RFs and as a result they were classified as FAI units. The total population responded with exquisite sensitivity to edge

(A) Instantaneous Frequency

60

Hz

0

Stimulus

Stimulus

Histogram

Skewed Distribution

Number of Bins

0 0.02 0.04 0.07 0.09 0.11 0.13 0.15 0.18 0.2 0.22 0.24 0.26 0.29

Interspike Interval (s)

(B) Instantaneous Frequency

75

Hz

0

Stimulus

Stimulus

Histogram

Tight Distribution

Number of Bins

0 0.02 0.04 0.07 0.09 0.11 0.13 0.15 0.18 0.2 0.22 0.24 0.26 0.29

Interspike Interval (s)
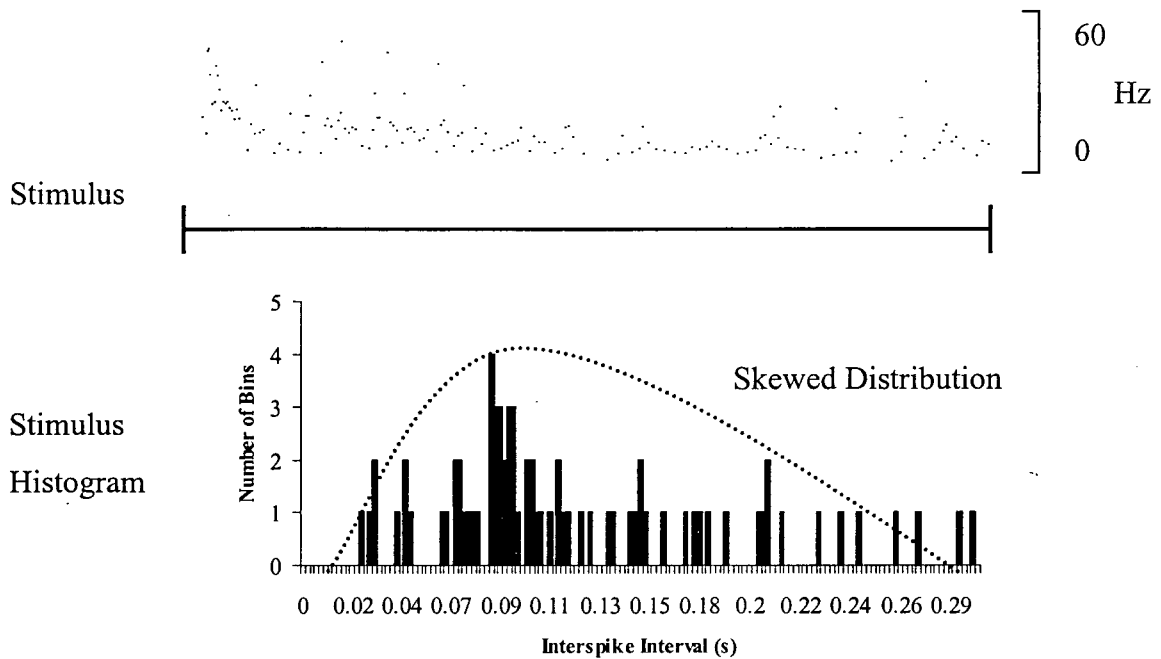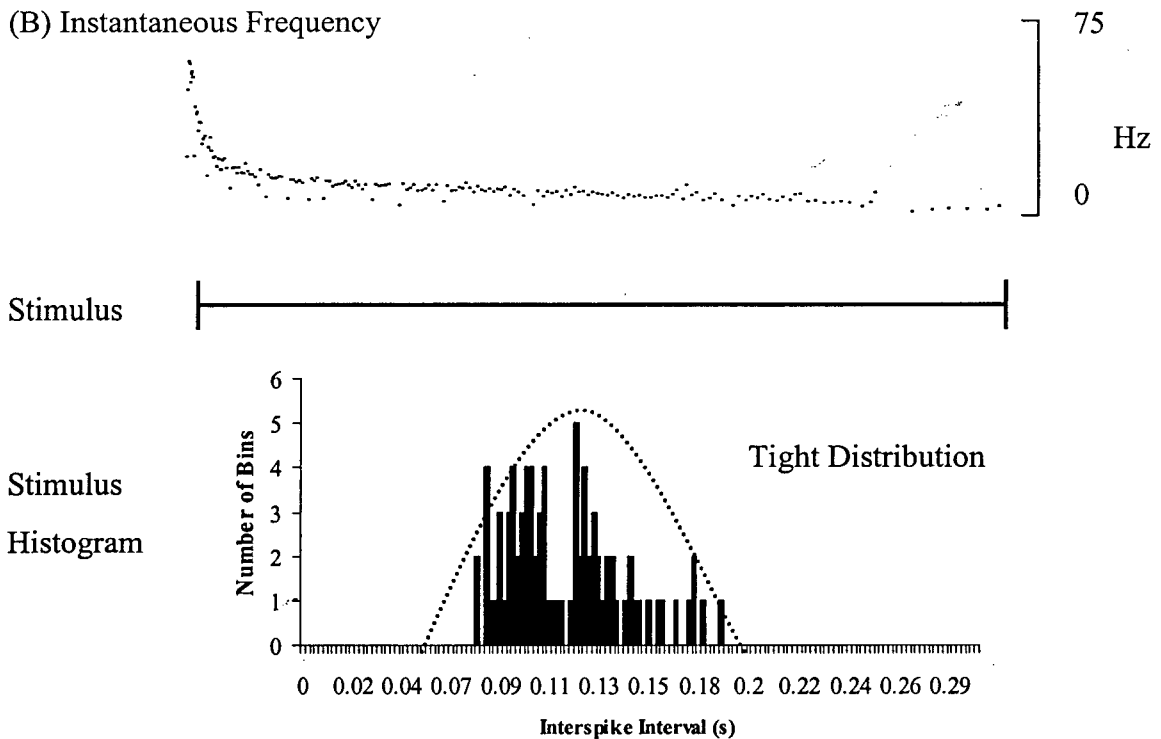
Figure 6 Adaptation Properties of Slow Adapting Receptors

One manner in which to distinguish between SA types is to examine the discharge properties during a prolonged indentation. (A) SAI units fire in an irregular pattern demonstrated in the random pattern between action potentials illustrated in the stimulus histogram. (B) SAII units have a regular discharge pattern as exhibited by the small tight distribution between impulses.   Page 59

contours passing through the RF with distinct on- and off-discharge bursts (see figure 7 on page 61). The interspike intervals of the bursting patterns reflected the velocity of the movement as well as the duration of the stimulus. The faster the movement, the shorter the interspike interval and the greater the number of impulses. Type I units showed minor responses to vibration however this elicited a more effective response in FAII units. Vibration sensitivity was used to assess the position of the hot spot in low threshold, high sensitivity FAII's. When the vibrator was placed over the hot spot, the unit responded and became entrained, firing approximately at the frequency of the stimulator (see figure 8 on page 62). Type II units were extremely sensitive to mechanical transients (i.e. acceleration) in the skin associated with tapping. This remote sensitivity was displayed in one unit in which the receptor terminal, located near the base of the big toe, could detect remote transients half way up the calf (i.e. tapping the leg with a pen).

3.6 STIMULUS-RESPONSE PROFILES:

During perpendicular indentation of the skin, SA receptors faithfully code the contact of the probe with the skin. The initial burst of impulses details the intensity and the velocity at which the stimulus is applied. The specific stimulus to evoke the response is the stretch of the skin. Movement around a joint not only deforms the skin overlying that particular joint, but also in the surrounding regions. Four FAI afferents were located at the base of the proximal phalange. Movement of the toes in either flexion or extension that was significant enough to cause a deformation of the RF elicited a response from the

(A) Neurogram

Stimulus

(B) Instantaneous Frequency

250

Hz

0

Neurogram

Stimulus

50 μV

1 s
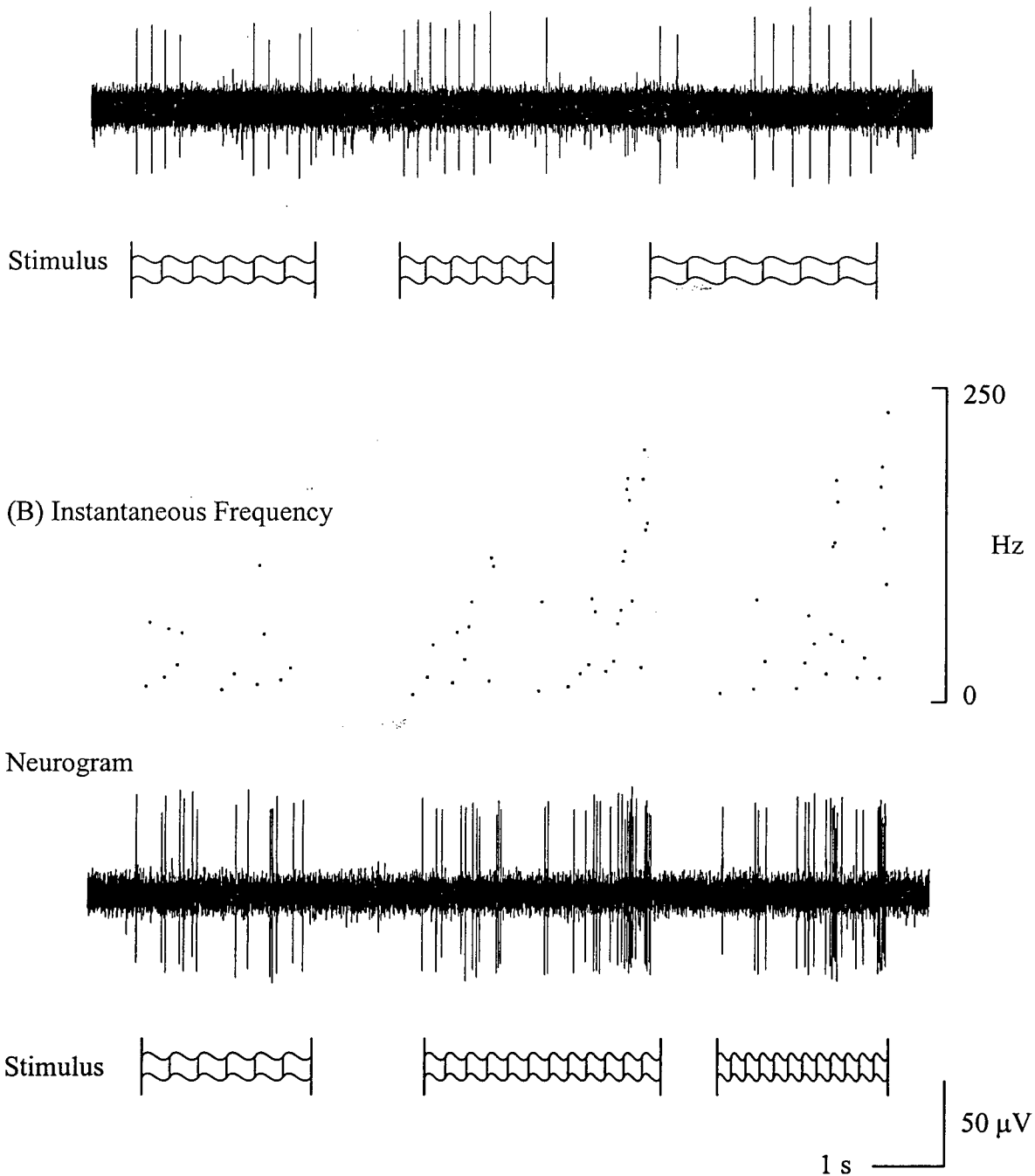
Figure 7 Stimulus Response of FAI's to Edge Contours

Due to the rapid adaptation of FAI units, the typical response pattern does not reflect the sustained pressure of the stimulus. (A) FAI's respond to movement of an edge through the receptive field. (B) Furthermore, this response pattern also reflects the speed at which the object moves through the receptive field as indicated by a higher instantaneous firing frequency.
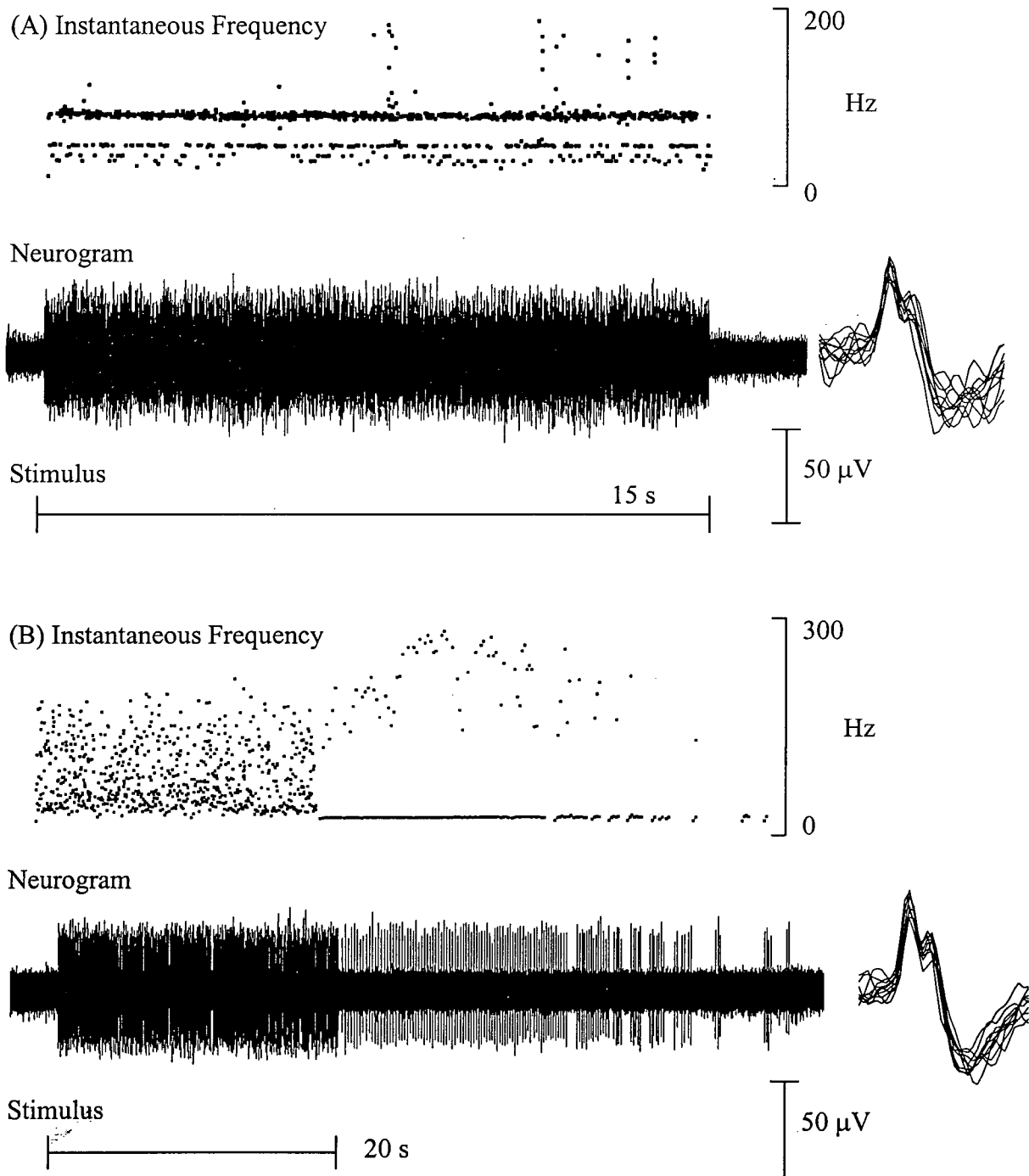
Figure 8 Stimulus Response Profile to Vibration

The response of two different Fast Adapting Type II (FAII's) to vibration in which the receptor fires at the frequency of the stimulus. In the lower example (B), the receptor continues to fire once the stimulus has been removed demonstrating a post-stimulus discharge.

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receptor. In addition, 5 SAI and 2 SAII units were located near the proximal border of the toes. Movements that were significant enough to stretch the skin in the RFs evoked a response in all seven of these units. The velocity of the movements was reflected in the dynamic index. Similar to the firing frequency of FA units, there is an increase in the number of impulses with a decrease in the interval between these potentials (figure 9A on page 64). Some of these units demonstrated a preferentially firing pattern to either flexion or extension depending on the degree of skin stretch evoked by the movement. Directional sensitivity of SA units, specifically type II units has been well documented (Edin and Abbs 1991, Johansson and Vallbo 1983). This response was clearly demonstrated in a single-unit recording of an SAII unit recording that lasted over 30 minutes. If the RF was displayed as a clock, skin stretch in the twelve o'clock direction produced a significant response. For the same relative amount and duration of skin stretch in the six o'clock direction, only a limited number of action potentials were generated. As the direction of applied stretch approaches the preferred bearing, a higher number of signals are generated for the corresponding interval (figure 9B on page 64).

A completely unique response was observed in two FAII units, each located in the distal portion of the foot, from two different experimental sessions. Following a period of vibration (varied between 100-200 Hz) there was a silent neural period followed by a harmonic-bursting pattern in the absence of any further stimulation. This post-stimulus discharge (< 10 imp/s) contained a series of synchronous time-locked doublets that were not present during the vibratory response (see figure 10 on page 65). The amplitude of the doublet and the time between the doublet potentials varied between the pairs although there did not appear to be any pattern in this distribution. The duration of the neural

(A) Instantaneous Frequency

Stimulus

Neurogram

80 µV

3 s

(B) Instantaneous Frequency

Stimulus (Direction of Stretch)

Neurogram

75 µV

5 s
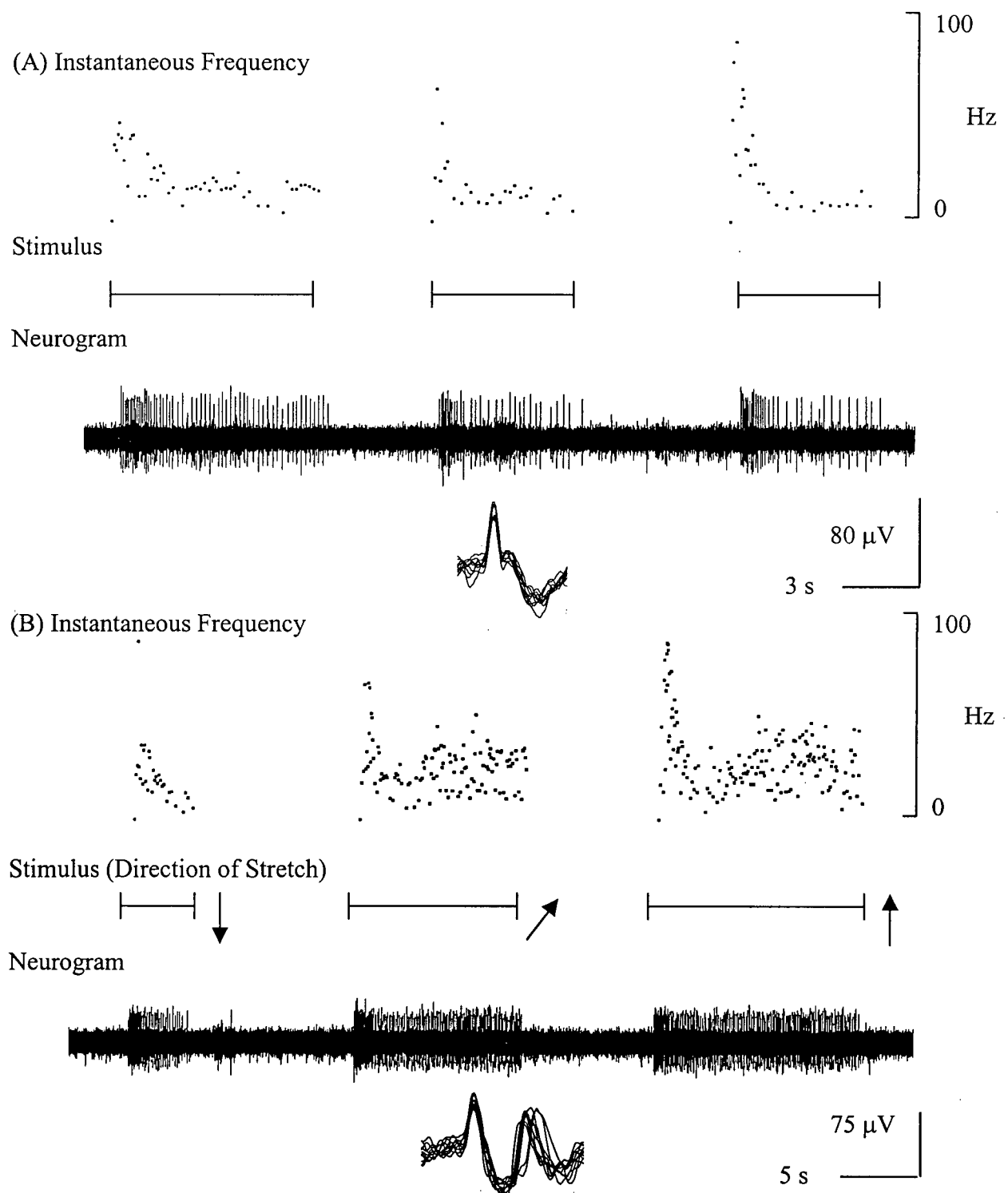
Figure 9 Stimulus Response Coding of Slow Adapting Receptors

This example illustrates the specificity in coding that is inherent to SAII's. (A) This receptor is able to code for the velocity of stimulus as indicated by the initial burst of impulses. (B) This is an example of directional sensitivity. For the same approximate degree of skin stretch, this unit is maximally excited when the stretch is towards the toes, and minimally activated when the stretch is in the opposite direction.

Instantaneous Frequency

300

Hz

0

Neurogram

Vibration   Post-Stimulus Discharge

80 µV

5 s

Stimulus   Neural Silence   Doublet Discharge

2 s   1.5 s   3 s
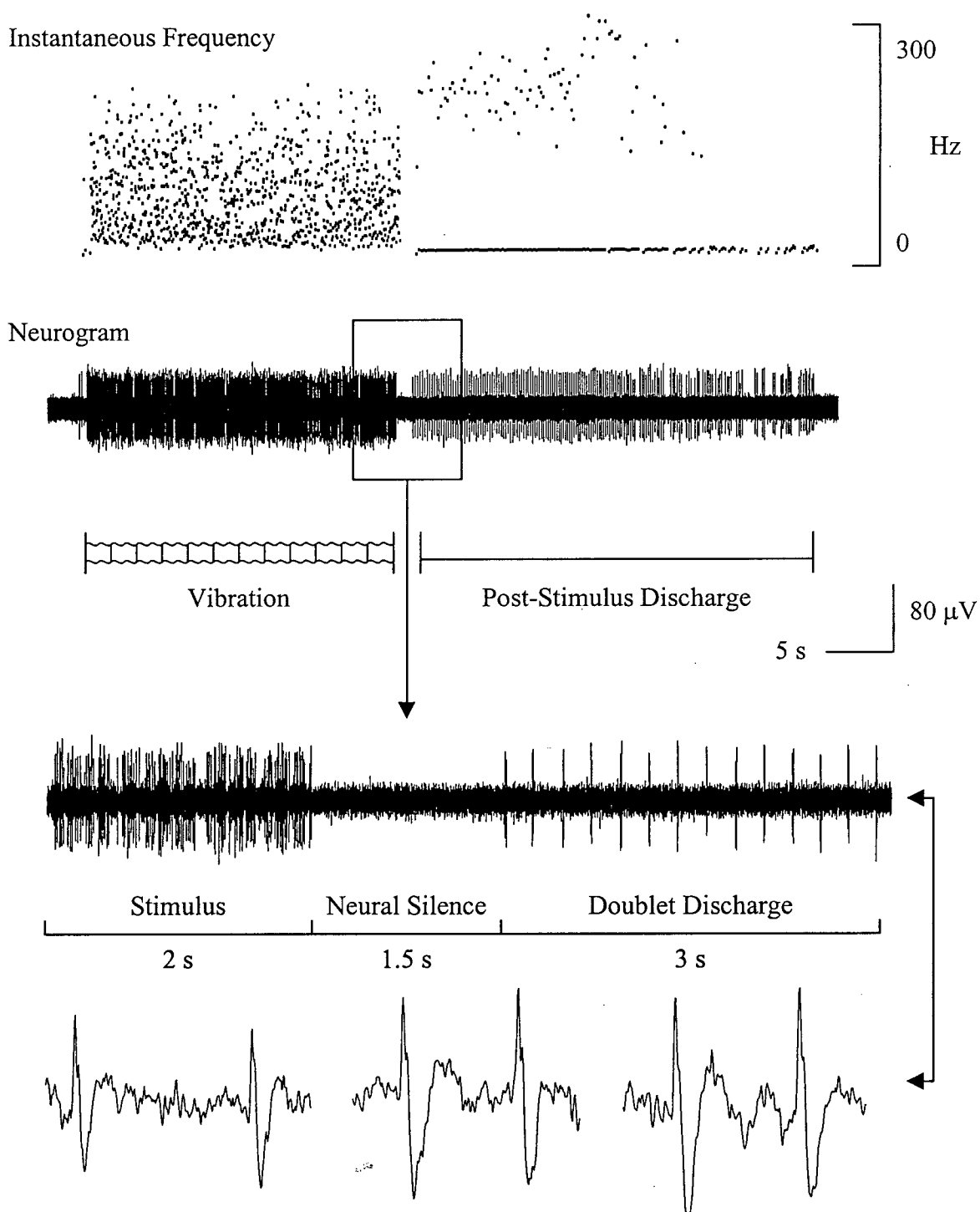
Figure 10 Post-Stimulus Discharge in FAII Units

Following a period of vibration, a post-stimulus discharge was observed in two FAII units. After the stimulus was removed, there was a period of neural silence in which the unit did not fire. This time was related to the length of the stimulus. Following this, a post-stimulus discharge was observed in which the units fired in doublets that varied slightly in amplitude.

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silence and the after effect appeared to be directly linked to the length of the vibratory stimulus. This behaviour attributed to Pacinian corpuscle afferent has not been previously discussed in the literature. It was difficult to draw any conclusions due to the confined recording time and limited response of only two afferents.

3.7 MEASUREMENT OF THE GLABROUS SKIN REGIONS:

The area of the glabrous skin in the foot sole ranged from 131.3 cm^2 to 173.5 cm^2 in the five subjects whose feet were measured. The size of the glabrous skin as measured with the grid technique was plotted against the product of the length and width of the foot (see figure 11A on page 67). These distances were used to maximize the product. The length was measured from the tip of second toe to the distal edge of the heel. The width was measured at the greatest point between the metatarsal bones. The value of the correlation coefficient ($r = 0.957$) indicates that the glabrous skin size may be estimated with reasonable accuracy from two simple measurements using the following equation (Johansson and Vallbo 1979):

$$Y = 0.7483 \times (L \times W) - 3.154$$

To calculate the relative densities for the unit populations the mean glabrous skin area, 150.72 cm^2, was used. The total glabrous skin area of the foot was divided into nine regions separating the foot sole along the natural flexure lines. The toes were not separated, as it was difficult to isolate the skin of the proximal phalange from the distal border. In the schematic drawing of the foot in figure 11B on page 67, the number inside the individual blocks indicates the percentage of the total glabrous skin area for that region. The relative unit densities were calculated for the plantar surface of the foot using the mean size of each region (see table 2.0 on page 68). These calculations were derived

A.

y = 0.7483x - 3.154

B.

1.9   2.8   3.4   4.6   8.8

27.9   13.8   19.0

17.8
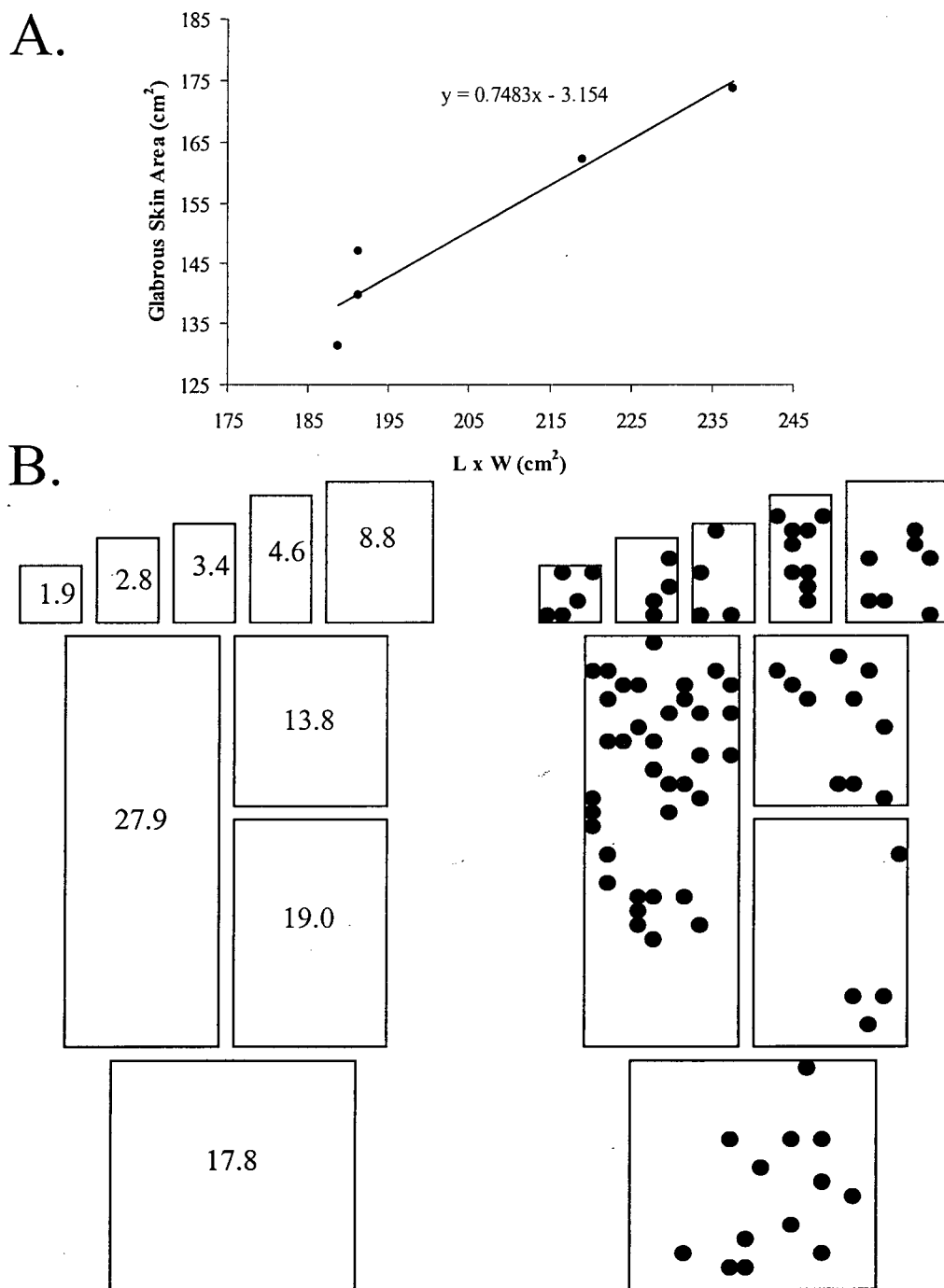
Figure 11 Measurement of the Glabrous Skin Area

(A) A regression equation was calculated by comparing skin size plots and length/width products. (B) The foot sole was divided into nine regions and the percentage of total skin area is marked within each section. The location of the receptors are illustrated in each region.

Region	Heel	Lat. Foot	Toes	Front Foot	Arch
SAI	0.075	0.173	0.219	0	0.024
FAI	0.261	0.864	0.564	0.194	0.071
SAII	0.149	0.173	0.125	0.145	0
FAII	0.037	0.173	0.094	0.145	0
Total	0.522	1.383	1.002	0.484	0.095

Table 2.0 - Calculation of Relative Density of Cutaneous Mechanoreceptors
The relative unit density was calculated by dividing the number of units sampled in per cm^2 of skin. The relative densities are displayed for both the total population and the individual receptor types.

from the number of units sampled per cm^2 of skin area and are illustrated in figure 12 on page 70. Starting at the heel, the total unit density increased along the lateral aspect of the foot in the distal direction. With a slight decrease in the number of units in the toes, the unit density continued to decrease along the medial aspect in the proximal direction. There was a considerable increase in the FAI unit density in the distal direction. The FAI units primarily accounted for the differences in total unit density.

3.8 MUSCLE RECEPTOR RECORDINGS:

Muscle receptor recordings were not specifically analyzed during the recording sessions and subsequently will not be addressed in the discussion. Of the 20 units that were not cutaneous mechanoreceptors, a background discharge was present during the majority of the recordings. This finding in conjunction with the lack of background activity in SA receptors was further used in the classification of muscle afferents. It was concluded that these were muscle afferents after a positive response to movement particularly during voluntary activation, and an adaptation of the discharge during gradations of forceful pressure was present. The classification of muscle afferents is based on a scheme that incorporates eight discriminating tests (Edin and Vallbo 1990). The receptor is categorized based on its responses and a likelihood function is established. This categorizes the afferent as a primary or secondary muscle spindle, or a Golgi tendon organ. As this was not performed in this study, the broad categorization of muscle receptor was used.

Relative Unit Density

□ SAI □ FAI ■ SAII □ FAII

Relative Density (units/cm²)

Skin Region

Heel | Lat. Foot | Toes | Front Foot | Arch
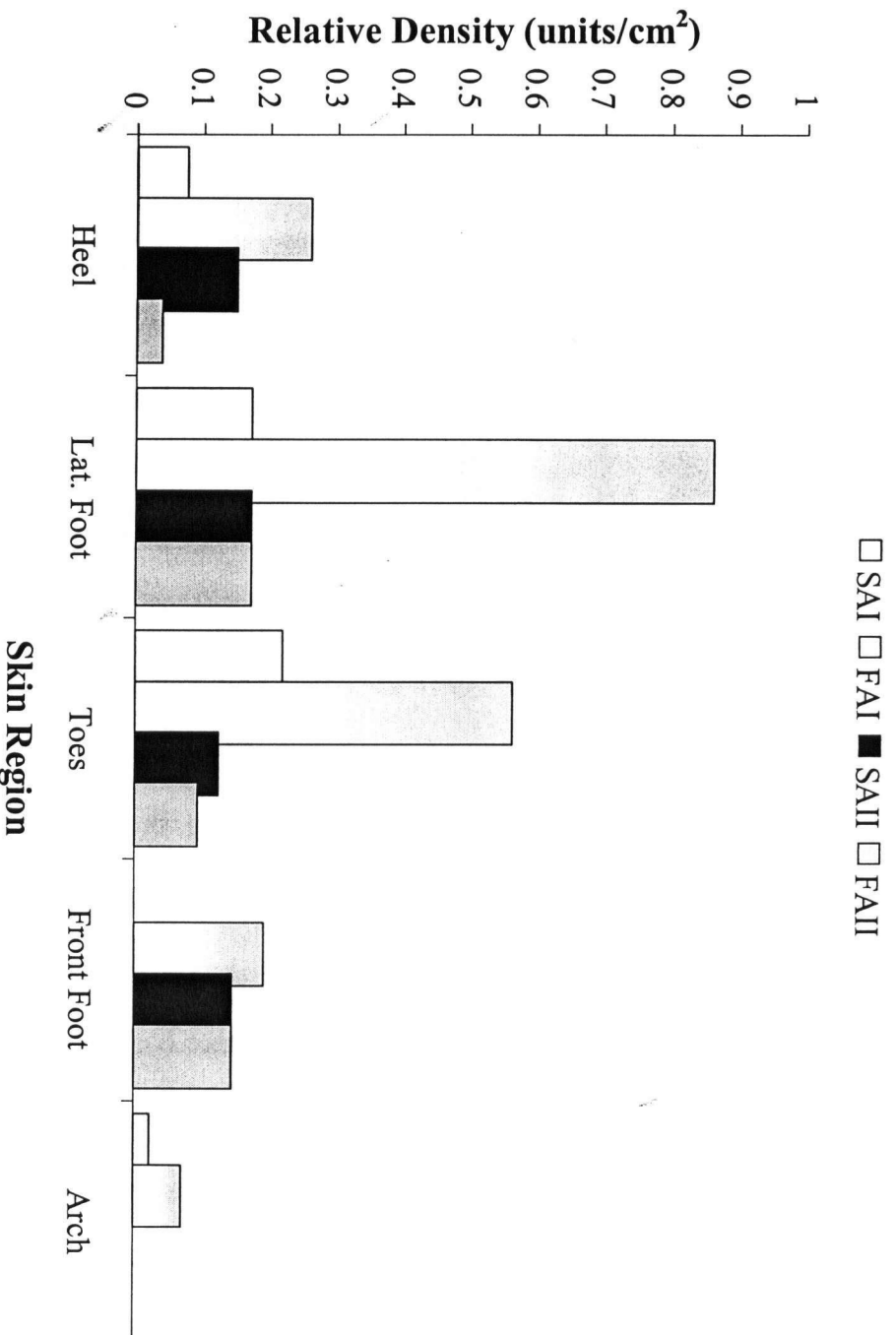
Figure 12 - Relative Density of Cutaneous Mechanoreceptors in the Foot Sole

The relative density for each specific type of cutaneous receptor is illustrated above. The number of units for each region divided by the size of the glabrous skin region was used to calculate the relative density for that unit.

Chapter Four
Discussion

DISCUSSION:

CUTANEOUS MECHANORECEPTORS IN THE GLABROUS SKIN:

The present study provides a qualitative description of the cutaneous mechanoreceptors in the lower limb. Of the 106 single unit recordings from cutaneous afferents, an overwhelming majority of these receptors were recorded from the glabrous skin of the foot sole (104/106 - 98%). The remaining two units that were isolated to the calf were both FA units, a type II receptor and a type I. However two FAII units had receptive fields that extended onto the hairy skin of the calf. These recordings proved to be quite stable with the average recording lasting over 10 minutes allowing for small movements at the toes and ankle.

The distributions of cutaneous mechanoreceptors in the glabrous skin were as follows: FAI 57%, SAII 15%, SAI 14%, and FAII 14%. These numbers could be compared to another study in which the sensory properties of mammalian cutaneous receptors were investigated in the foot in the rat. The distribution of receptor types in the plantar nerves from this study was FAI 35.2%, SAI 30.5%, SAII 23.9%, and FAII 7.5% (Leem, Willis, and Chung 1993). The rat model demonstrated a higher static sensitivity in the foot sole in comparison with the present data. To determine why there was a higher dynamic sensitivity reported in the human foot sole methodological considerations such as a tendency to bias certain receptor types must be brought into consideration. If there were a discrepancy between the diameter of the myelinated fibers innervating the receptor terminals, it would be more feasible for the electrode to make contact with the larger fibers. Examining the conduction velocities of the axons for all four receptor types, there is some variation in recording time but this is minimal (Mackel 1988). It was concluded

that since conduction velocity is a function of diameter, cutaneous afferents cannot be separated on the basis of their axonal conduction properties and therefore have similar nerve diameters. The high preponderance of fast adapting activity in this study consequently cannot be resolved according to a receptor selection bias.

To further minimize a selection bias, the experimenter must carefully listen to the quality of the audio signal when searching for single unit activity. This is because signals in neighbouring units can be evoked during global skin stimulation. Both sustained indentation and rapid tapping actions were adopted to eliminate the preferential excitement of either fast or slow adapting receptors. Even in the multi-unit activity, the fast adapting responses were more prominent which made it easier to isolate the FA units. The small discrete receptive fields of these afferents would provide localized information about transient stimulation. As a population, these receptors have the capacity to provide information regarding the direction and the velocity of pressure exerted as the foot makes contact with the ground. This information might be used in the moment-to-moment examination of the position of the forces in the foot sole.

From a physiological perspective, the cutaneous mechanoreceptors are widely distributed in the foot sole. The dispersion congregates along the heel, lateral border of the foot, arching medially throughout the toes and in the front footpad. This pattern imitates the transitional shift of the CoP during the normal gait cycle (Horak and Macpherson 1996). The anatomical maps illustrating the position of these receptors, created from this study, indicates that these receptors are ideally located to signal the position of the CoP, the position of the overall ground reaction forces. This is supported by the fact that pressure changes in the foot sole are mainly perpendicular to the plantar surface (Wu and

Chiang 1996). This perpendicular movement through the receptive fields was an effective stimulus that evoked a response from the entire population of single unit recordings in this experiment.

SKIN MECHANICS OF THE FOOT SOLE:

When the skin on the foot sole is exposed to strong frictional forces, it becomes hard and thick resulting in the formation of a callus. Calluses have a tendency to form on the heel, along the distal footpad, and the toes. The degree of callusing varies between foot regions as well as between individuals. The skin mechanics of the foot sole may have biased the classification of receptors in regions where calluses were present. Indenting the skin with nylon monofilaments identified the thresholds of cutaneous afferents. Each monofilament was calibrated to exert a predetermined amount of force, which was used to outline the location of the receptor. Although the velocity and the application of force are difficult to control without some form of visual feedback the variation does not seem to be that large. Consequently, the use of nylon monofilaments for documenting cutaneous mechanoreceptors appears to be an accurate and effective method (Johansson, Vallbo and Westling 1980). However the stiffness of the skin may modify the amount of force required to produce a certain amplitude or gradient of skin displacement (Johansson, Vallbo and Westling 1980). Furthermore, the amount of indentation required to produce a response might also be a function of the skin properties. There is evidence that a decrease in the compliance of the skin may not be an important factor in the responsiveness of type I receptors (Hamann 1996). Both FAI's and SAI's are located very superficially in the dermis and are very sensitive to local skin stimulations. Skin mechanics can be

augmented, in which vitamin A deficiency increases and chronic treatment with neomycin decreases the compliance of the skin (Hamann 1996). In both of these instances, the reduction in type I activity was attributed to the degeneration of the actual receptors and not the change in skin compliance.

The quality of the skin mechanics of the foot sole does not appear to be a confounding variable in this experiment. Upon evaluating the receptor subgroups, there were no apparent discrepancies between the various regions. That is, in comparing the FAI receptors, those units recorded in the heel did not consistently have a higher threshold than those receptors found in a less callused region such as the lateral border of the foot. This was similar for the other receptor subgroups. The random distribution of threshold levels according to type and region affirmed the notion that the estimated threshold was a function of the receptor. It was concluded that the threshold for a given unit was a reflection of the depth of the receptor terminal although skin tissue composition may have had some effect in determining the threshold. Cutaneous mechanoceptors in the foot sole, in contrast with other documented skin regions, have a higher initial threshold. This may be a function of the high level forces that these receptors are constantly exposed to by the body's weight.

DYNAMIC SENSITIVITY IN THE FOOT SOLE:

The distribution of receptor types suggests that there is a high dynamic sensitivity in the glabrous skin of the foot (75/106 ~ 71%). The FAI units were the most sensitive to mechanical indentation (median threshold 11.79 mN) with small discrete receptive fields scattered about the foot sole. From the anatomical map of this receptor group, there was a

high density of receptors in the heel, lateral and medial border of the foot with considerable overlap amongst these fields. Many units responded with a burst of impulses as a finger or probe was moved through the receptive field. The burst of impulses, with distinct on- and off- responses, could reflect the velocity of the movement through the field (Knibestol 1973). When the foot is in contact with the ground, the change in pressure as the position of the CoP is shifted, could possibly be encoded by the population of FA units in the foot sole. These afferents would display a whole range of relative responses each being determined by the relative position of the corresponding receptor in the skin (Lamb 1983). As the pressure shifts are transferred from the proximal-medial portion of the foot, to the distal-lateral aspect of the foot, overlapping and adjacent units would start to fire as their region was stimulated. This would appear as if each receptor is almost passing the signal along. The relative firing of a group of FAI units that would vary in terms of intensity and frequency could therefore approximately determine the position of the CoP.

This concept of population coding in FA receptors has been demonstrated to be of functional significance for the coding of other surface features. A population of FA units can apparently code the composition or roughness of a surface (Johansson and Westling 1984). Many of these afferents produce more than one impulse upon placing a dot in the receptive area. The behaviour of these responses increases as the addition of more dots is placed in the same field. The simultaneous decrease in the interspike interval between a population of FA units could be used as an estimation of the overall roughness of a given surface that the foot is in contact with (Lamb 1983).

Information about the amount of skin in contact with the ground is not only important for measuring stability but a decrease in the area of contact may signal slip

caused by an external perturbation. Rapidly adapting units, FAI's in particular, demonstrate pronounced responses to localized slip of the contact surface with the skin (Johansson and Westling 1987). The detection of slip must be based on the spatiotemporal events occurring on the skin within the region of contact (Srinivasan, Whitehouse, LaMotte 1990). The successive activation of adjacent FA's along the path of slip would provide such a spatiotemporal code for the motion. A wide distribution of FAI units in the foot sole would place these receptors in an ideal position to signal the initial slip at any part of the foot. Contributing to the identification of slip, FAII units may play a supportive role detecting the remote transients in the skin. The FAII's are extremely sensitive to vibratory stimuli transmitted through waves of propagation that would occur as the foot deviated from its stable position with the contact surface.

Documenting FAII's in microneurography is very difficult, as these receptors typically comprise only 10-15% of the total population. These units were not hard to classify, as they were remarkably sensitive to remote transients in the skin. In one example, the receptive field was confined to the distal median aspect of the foot although the remote sensitivity was demonstrated as far as the distal calf. In the glabrous skin of the hand, the area of sensitivity ranged from 40 to 440 mm^2 for the FAII receptors (Knibestol and Vallbo 1970). In comparison, the receptive fields in the foot sole had a greater variability with receptive fields measuring as high as 1250 mm^2. The FAII's have a tendency to cluster within nerve fibers, expressed as adjacent overlapping receptive fields (Wu et al. 1998). This was apparent in this study as the majority of the FAII receptive fields were found in the distal portion of the foot with a high degree of overlap in the receptive area. These FAII units were rather large with obscure borders. It has been

postulated that there is an inherent bias in recording FAII units with tungsten recording electrodes. It is believed that these large receptive fields are a function of two units being classified simultaneously as one. This is not believed to be the case in this example as template matching revealed only one action potential during the recording sessions indicating that the receptive field was outlined by the response of one receptor. This remote sensitivity, at times, made it difficult to identify the location of the receptor. Applying a small vibratory to the foot sole accelerated this process.

FAII units are notably sensitive to vibration with the most pronounced signal being evoked from the apparent position of the receptor terminal. Vibration sensitivity of FAII units in the glabrous skin of the foot has been previously investigated. A recording electrode was inserted into the common peroneal nerve, which innervated the skin along the lateral border of the leg, including the glabrous skin on the lateral edge of the foot. The FAII receptors were particularly sensitive to mechanical vibrations, firing in a one-to-one manner until approximately 200 Hz at which point the locking disappeared (Ribot-Cisar, Vedel, and Roll 1989). In our study, only 2 of the 15 recorded FAII units (~ 13%), a post-stimulus discharge was produced following a period of vibration. Because this behaviour was only elicited in a small percentage of these receptors this post-stimulus activity was not attributed as a characteristic of the population. The behaviour may have been a function of the FAII population since this behaviour was not observed in any of the other three receptor types. Unfortunately because of the recording time, and the limited occurrence of this behaviour it is difficult to speculate on the underlying mechanisms attributed to the post-stimulus discharge in FAII units. It should be noted that this post-adaptation discharge has never been reported in the literature prior to this experiment.

LOW STATIC SENSITIVITY IN THE GLABROUS SKIN:

The numbers of SAII units discussed in microneurography reports are typically low varying between 10-20% of the total population. From concentric electrode recordings a higher proportion of SAII receptors was recorded during a single recording session (Wu, Ekedahl, and Hallin 1998). This does not suggest that tungsten electrodes selectively bias against these receptor's fibers. It merely indicates that these receptors cluster in the peripheral nervous system of humans. This peripheral organization may sometimes (not always) be expressed by a grouping in receptive field location. Despite this clustering, the number of SAII receptors recorded with the concentric design was not substantially greater than those reported in this study. This clustering was evident in this study upon examining the distribution of the SAII units in the foot sole. The majority of these units (11/16 ~ 70%) were confined to areas in the skin with other SAII units. Seven units were isolated in the distal median portion of the foot while another four were confined to a small region in the heel.

There is also evidence that SAI units are clustered within nerve fascicles (Wu, Ekedahl, and Hallin 1998). This overlap in receptive fields was not as prominent as the type II units although more than half of the receptors (10/15 ~ 66%) were located along the lateral border of the foot. The reported distribution of SAI receptors, on the other hand, was a surprise. The SAI receptors demonstrate an initial dynamic response to the onset of mechanical stimulation that is similar to those exhibited by FAI units. In addition these receptors had comparable initial threshold levels. It may be conceivable that a small number of SAI receptors may have been misclassified as FAI units, but not enough to skew the distribution of receptor types. Receptor identification was based on a thorough

classification scheme, which included prolonged stimulation to verify that units belonged to the FA and SA categories.

The placement of the SA units are primarily along the medial and lateral borders of the foot with very few receptors located in the middle of the foot. This situates these units in an ideal position to detail slip or shear forces exerted against the plantar surface of the foot. It may not be necessary to incorporate too many SA receptors in the glabrous skin. Presuppose that the lack of static activity in the glabrous skin is of functional significance. The continuous static activity of SA receptors provides a signal that could be referred to as noise (Clark, Horch, Bach, and Larson 1979). This may suggest that SA receptors are important in signaling the foot's contact with the ground. The response to loading would excite the population of SA receptors that would be signaled by the global noise. The lifting of the foot off the ground would be signaled by the removal of the noise. This would be considered a crude stimulus that does not require specificity – only that the faithful coding that the foot is still in contact with the ground. An abundance of SA receptors may be considered redundant information and consequently may not be necessary.

CUTANEOUS RECEPTORS AND POSTURAL CONTROL:

The normal range of sway about the ankle joint is approximately 10° in the sagittal plane that causes variation in the foot pressure in a proximal-distal manner (Tanaka et al. 1996). The use of cutaneous information may alter the characteristics of sway by stabilizing upright stance by integrating these sensory signals with motor commands that act to counterbalance this movement (Wu and Zhao 1997). The result of this sensory

feedback would be to reduce the movement and isolate the sway to a more defined area. The identification and localization of this pressure distribution is critical in controlling not only sway, but also the initiation of movement. Prior to lifting the foot, the body's weight must be shifted to the stance leg. The force output would be characterized by a decrease in force in the swing leg prior to lift-off and an increase in force adjusted to the support leg to maintain stability (Gordon et al. 1991). Force adjustments are not only pre-planned, but must also respond to postural perturbations. The adaptation of the force between the body and the ground must be adaptable to the frictional coefficients of the surface to prevent slip. The balance or coordination between the magnitudes of the contact and load forces may be critical (Johansson and Westling 1991). Too much force would generate fatigue while too little force would cause instability.

Mechanoreceptors in the glabrous skin are remarkably sensitive to the edges of stimuli. The SA receptors respond to the amount and rate of change in curvature of the skin while the FA units respond to the rate of change (LaMotte et al. 1987). Using only information from the glabrous skin, humans can differentiate between a range of flat and sharply curved surfaces (Goodwin, John, and Marceglia 1991). The primary function of the glabrous skin in the foot may be to determine the characteristics of the skin-surface interface. The role of skin in movement control may be secondary. Only 11 units were found on the actual crease separating the toes from the foot. In the palmar surface of the hand, cutaneous afferents had a tendency to be clustered in the fingers, particularly around joints (Johansson and Vallbo 1979). It was concluded that the high density of receptors around joints was crucial in signaling the finger's position (Edin and Abbs 1991). However around simple joints such as the toes, a lower number of receptors may be all that

is required to resolve the joint configuration (Edin 1992). There are reasons to assume that the receptors in the hairy skin play a more important role than the receptors in the glabrous skin in providing information on joint configuration and movements (Edin 1992). The hairy skin lacks the tight connections to subcutaneous tissues that are present in the glabrous skin and can therefore be both translated and stretched with little resistance in response to movements at nearby joints. It was difficult to assess the sensitivity of the glabrous skin to joint sensitivity. The receptors found near joints often had small RFs that were located underneath the prominent footpad of the toes. To isolate the receptor, the surrounding toes had to be moved which often pre-stretched the skin of the actual receptor. Often, grabbing the toe itself stretched the skin, which deformed the receptive field generating a response. Consequently it was possible to establish skin sensitivity to joint movement, although it was difficult to quantify this activity. These signals strongly suggest that cutaneous receptors potentially have a kinesthetic function in the lower limb.

There are some issues that must be raised in drawing conclusions from the relative responses to artificial stimuli to the natural firing patterns of sensory afferents in postural control. In aging and disease, where there is a documented loss of peripheral nerve constituents, diminished proprioceptive capacity in the toes, impaired cutaneous sensation, and reduced strength at the ankle have been correlated to a decrease in postural stability (Gandevia 1996). It is therefore tempting to transfer the abnormal responses observed in cutaneous afferents in clinical populations in the upper limb to that of the lower limb (Mackel 1989, Mackel et al. 1994). Individuals with peripheral neuropathy demonstrated poor postural stability in quiet stance positions. If the relevant kinesthetic information is transmitted through these peripheral nerves, then a corresponding decrease in activity

should be observed in these afferents. Investigating a potential change in cutaneous information with disease is a potential area for future research involving microneurography.

COMPARISON BETWEEN CUTANEOUS RECEPTORS IN THE UPPER AND LOWER LIMB:

Microneurography has been used to document the properties of cutaneous afferents in a number of body areas. The results from extensive investigations in the upper limb have been translated in discussions to the lower limb. The similarities between the two regions make this attractive to do so. Apart from the anatomical similarities each region includes both the glabrous skin on the inferior aspect and the hairy skin on the superior surface. Briefly, the hairy skin of the hand contains low threshold receptors (between 0.5 to 5 mN) with a greater degree of static activity (Edin and Abbs 1991). The FA units had a tendency to be grouped around joints whereas the SA units were more evenly distributed. The cutaneous receptors in the hairy skin seem to be intimately involved in signaling skin stretch that accompanies movement of the hand. It would be interesting to see if this is also true of the hairy skin in the foot and around the ankle joint.

The glabrous skin of the foot sole was actually one of the first regions investigated in the very first microneurography experiment in human subjects (Vallbo and Hagbarth 1968). Since then, the majority of investigations have focused their attention on the skin of the upper limb. It was initially reported that as much as three quarters of the total sample was composed of slow adapting receptors (Knibestol and Vallbo 1970). This is in comparison with a later study, which suggested that there was an overestimation in the SA

component. This study recorded over 300 single units derived from skin in the following proportions; FAI (42.8%), SAI (25.1%), SAII (19.2%) and FAII (12.9%) (Johansson and Vallbo 1979). This is arguably the most extensive microneurography investigation to date examining over three times more receptors than the previous study. This raises the issue of sampling in microneurography. It was estimated that there are approximately 17,000 mechanoreceptive units in the glabrous skin of the hand (Johansson and Vallbo 1981). Although there is no such estimate for the units in the foot sole, the question still remains at what point does the sample population reflect the total population? Unlike conventional research techniques, it is not possible to perform power calculations to determine the necessary number of sampled afferents. With approximately 71% of the total population of the receptors in the foot sole being rapidly adapting, one must be open to the possibility that these proportions would be different in a larger sample. Nevertheless, the discrepancy between the distributions with the hand and foot are not dramatic. Both demonstrate a high preponderance of FAI units as well as a low distribution of type II units. The surprising finding was the reduced numbers of SAI units in the foot sole. At this point, assuming that these distributions are a reflection of the total population of cutaneous receptor, the high dynamic sensitivity in the foot sole would be a function of the underlying role of that region.

In determining the size of a unit's receptive field, the protocol has remained standardized between experiments in order to facilitate comparisons. The reported area for SAI units has ranged from 5 to 350 mm^2 (Knibestol and Vallbo 1970). The average field size for these units is remarkable similar in the glabrous skin of the hand and face at 11 mm^2 and 7 mm^2 respectively (Vallbo, Olausson, Wessberg, and Kakuda 1995). The units

in the foot sole are substantially larger than both these regions with the mean area calculated at almost 100 mm^2 (median 71 mm^2). This is similar for the other receptors in which there was a not only a greater mean area but also a greater range between receptive field sizes (5 mm^2 to 1250 mm^2).

Despite these differences, there are some similarities between the receptors in the upper and lower limb. In absolute terms, the receptors in the foot sole have a higher initial threshold. Relatively speaking, FA units were the most sensitive receptors in the hand with thresholds less than 1 mN (Johansson, Vallbo, and Westling 1980). In the glabrous skin of the foot, skin mechanics may have biased the thresholds of receptors in more callused regions. It is therefore more appropriate to compare the median as opposed to the mean values, which could be skewed by extreme calculations. From this perspective, both FA receptor types had the lowest threshold in the foot sole. The SAII units in both the hand and foot were the least sensitive types of receptors.

MICRONEUROGRAPHIC RECORDINGS IN THE LOWER LIMB:

There is a technical bias inherent in the recording procedure involving conventional tungsten microelectrodes to preferentially discriminate myelinated fiber activity (Hallin, Ekedahl, and Frank 1991). This was not an issue as the objective was to isolate these large myelinated fibers which innervated the skin of the lower limb. Once a single unit was isolated, the receptors were manually outlined by using nylon monofilaments. This method was brought into question by comparing it with that of an electronic scanner which outline marked regions on the skin. In comparison with the use monofilaments it was concluded that the scanning approach is only better suited to map the detailed geography of

afferents in hairy skin where the fields are larger than in glabrous skin (Vallbo, Olausson, Wessberg, Kakuda 1995). The majority of the receptive fields in the foot sole were relatively small with the exception of the FAII units. The configuration of the 3-dimensional recording surface of tungsten electrodes might simultanesouly record impulses from adjacent nodes of Ranvier belonging to separate fibers supplying more than one FAII unit with neighbouring receptive fields (Ekedahl, Frank, Hallin 1998b). The possibility that some FAII units with exceptionally large receptive fields reported in previous studies using tungsten electrodes might have reflected overlapping recordings (Ekedahl, Frank, Hallin 1998b).

A fundamental problem of electrophysiological work within the nervous system relates to the identification of single unit activity (Wu, Hallin, and Ekedahl 1998b). This is brought to the forefront in microneurography in which many receptors are activated by an applied stimulus. Single unit identification is essential in correlating the response of the unit with a specific action. There are a number of arguments, which insinuate that both multi-unit and single unit activity are derived from extracellular sources (Wu, Hallin, and Ekedahl 1996). This could potentially place the recording surface of the electrode in close proximity to several sensory axons. If these fascicles innervated adjacent or overlapping areas in the skin, then defined stroking or taping of the foot sole would generate several impulses that could be simultaneously recorded. In fact on two separate occasions, simultaneous recordings of sufficient sound quality and a high SNR for classification were recorded. The observations from these recordings indicate that action potentials derived from different even adjacent receptors exhibit waveforms that vary in shape. The potentials may share similar features but vary in terms of duration and amplitude. It is

possible to distinguish between action potentials by creating templates within the commercial software (Spike2) that will then catalogue the two units and code them on the computer screen according to colour or a label. From the examples in this study, one multiple recording included a cutaneous mechanoreceptor from the heel and a presumed muscle receptor from the distal portion of the foot. The second example was comprised of two FAI units, one from the medial aspect of the heel and the other just prior to the crease line of the big toe. Fortunately considerable regions of skin separated both these examples. Since none of the receptors were receptive to remote transients in the skin, it was quite feasible to evoke a response in one receptor without generating impulses in the second. Both units within a recording varied according to shape. Furthermore, with respect to FAII units, while outlining the receptive fields, the shape of the action potentials were monitored on-line with an oscilloscope. Template matching off-line confirmed that the recorded files consisted of single waveshape within a train of action potentials. It was therefore concluded that at no point did the simultaneous recording of a second unit compromise a single unit recording.

OTHER CONSIDERATIONS:

Some important characteristics of peripheral nerves have been identified with the use of a concentric recording electrode. Proponents of this needle design feel that in comparison with tungsten electrodes, this restricted and unidimensional-recording area enables the researcher to study specific aspects within a nerve. In addition, the electrical and mechanical properties are more stable with a concentric electrode. Despite this, the greatest technical limitation of tungsten recording electrodes is the single recording site at

the tip of the electrode. The number of recording surfaces can be altered on a concentric needle enabling multi-channel recordings. This has proven to be critical for documenting the previously undetected peripheral nerve fiber arrangements (Ekedahl, Frank, and Hallin 1998b). Since the purpose of this study was to document the distribution pattern of cutaneous mechanoreceptors in the foot sole, the consequence of using a tungsten-recording electrode with a single recording site may have limited the yield in a given area of skin during a particular recording session. Based on the total number of single unit recordings, this does not appear to be a significant factor and therefore the use of a tungsten electrode was sufficient for this experiment.

Besides assessing the properties of cutaneous afferents in the lower limb, microneurography could be applied to other endeavours. Stimulating a region of skin and measuring the time in which it takes the action potential to reach the electrode can assess the conduction properties of an axon. In this case microneurography could be used as a sensitive means for assessing the impact of neural disorders on neural impulse transmission (Brink and Mackel 1993). The results could be used in comparison with normal counterparts to evaluate the impact of disease on action potential generation and propagation. This could provide important information in a clinical environment about the progression and impact these disorders have on normal sensory function in the lower limb.

Chapter Five
Summary and Implications

<u>SUMMARY AND IMPLICATIONS</u>:

The tibial nerve is comprised of plantar branches of cutaneous fascicles that innervate regions of the glabrous skin of the foot sole. For this reason, the tibial nerve was chosen for this study. Due to the superficial position of the nerve in the popliteal fossa, the electrode was inserted and positioned with minimal discomfort to the subject. During an attempt to access the tibial nerve four centimeters below the posterior knee crease proved to be unsuitable as mechanical irritation from the tip of the needle induced intense discomfort to the subject. Single unit recordings proved to be quite stable from the original site. Although the criticism has been raised with respect to the origin of these signals, for the purpose of this study, it is irrelevant where single unit activity was recorded. Upon stimulating a particular region of skin, it was ensured that the activity was recorded from a single unit. This was achieved either on-line by monitoring the shape of the potential with an oscilloscope, or off-line through matching the impulses with a template and averaging consecutive action potentials.

With respect to the original objectives a number of conclusions have been derived from the results of this study:

(1) Single unit recordings with a relatively high SNR were sustained for an average of 13.5 minutes (despite the fact that the experimenter artificially terminated several recordings). This afforded ample opportunity to classify the unit and perform a variety of functional tests while maintaining the size and shape of the waveform. The subject was able to perform small movements in toes and at the ankle while maintaining the

recording. The stability of these recordings indicates that it may not only be possible but also relatively comfortable to obtain these recordings in a standing position.

(2) Recordings from all four receptor types were used to create an anatomical map including the location of the receptor and its receptive field. There is considerable variation between receptors in terms of initial thresholds and receptive field sizes which may make it difficult to establish a baseline calculated from mean values. As a result, when discussing these receptors it may be more appropriate to refer to the median values expressed along side of the overall range.

(3) It appears that cutaneous afferents in the foot sole could potentially be involved in movement control. Receptors in the toes responded to movement that generated stretch of the skin. This movement sensitivity in conjunction with the lack of a background discharge could provide valuable sensory input during the gait cycle including the coding of the foot's contact with the ground.

(4) With respect to postural control, the high density of FA receptors and their exquisite sensitivity to force indicate that these receptors would be ideal for signaling the position of the CoP.

This study has documented the distribution and characteristics of the cutaneous receptors in the glabrous skin of the foot sole in a young, healthy population. The responses to skin stimulation have revealed a number of attributes that differ from the

glabrous skin of the hand. Consequently, it may not be appropriate to translate conclusions based on the upper limb to the lower limb. With only a few studies in the literature examining cutaneous afferents in the lower limb, potential studies could venture in a number of directions. Based on the conclusions of this investigation, the dynamic sensitivity of the foot could be used to calculate the position of the CoP. To evaluate this, a paradigm could be employed in which the CoP is measured with a force plate while simultaneously recording from the skin of the foot sole. This would clarify if cutaneous receptors were sensitive to pressure shifts in the foot. This would also fulfill a secondary purpose by loading the receptors. The apparent lack of a background discharge in the SAII units was attributed to the functional significance of signaling the foot's position in the air. Loading the receptors would elucidate if a predominance of static activity would be present and thus carry out this task. Subsequent experiments could investigate the role of the glabrous skin in the assessment of surface features including overall contact force, frictional force, and the detection of slip.

Cutaneous afferents from the lower limb convey impulses that vary in the number of active units, as well as the temporal, spatial and modal patterning (Wu 1996). Because the insertion point of the electrode was similar between subjects, a very defined region of the tibial nerve was examined. Altering the insertion point and attacking the nerve from different angles might allow researchers to sample from different, possibly deeper fascicles. This will provide more information about the type of fibers and their functional distribution in this nerve. These results, in conjunction with data from other lower limb nerves that innervate the hairy skin of the foot and leg could provide a more complete picture of the role of skin in the lower limb.

It was originally postulated that cutaneous afferents played a subsidiary or facilatory role in kinesthesis (Burke, Gandevia, and Macefield 1988). This would appear to underestimate the contribution of cutaneous input. In clinical populations, such as diabetic neuropathy or Guillain-Barre Syndrome patients, where there is a degeneration of the myelin of peripheral nerves there is a reduction in postural stability. These individuals exhibited abnormal responses in both fast and slow adapting receptors to indentations of skin in the upper limb (Mackel 1989, Mackel et al. 1994). The present study contains a large sample of cutaneous receptors in the lower limb. This data could be used to establish a baseline in which the mean and median values for receptor thresholds, receptive field sizes, and firing rates could be established. Microneurography could be used to record the response of cutaneous afferents from these clinical populations, which would then be compared to the normal subjects. These values may be used to assess the effect of normal aging and disease on cutaneous afferents in the lower limb. Alterations in the firing frequencies of cutaneous afferents expressed as reductions in overall stability may be the definitive testament of the role of cutaneous information in standing balance.

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APPENDIX ONE – EXPERIMENTAL DATA TABLES:

TABLE 3.1 – SUBJECT PROFILES

Subject Initials	Sex	Age	Nerve Time (hr)	# of Trials
PK	M	24	2.5	5
BI	F	34	1.5	1
TI	M	38	2.0	4
MG	M	29	2.0	1
CW	F	28	2.0	3
GS	M	34	2.0	2
CS	F	27	2.0	1
BN	M	25	2.5	6
AH	F	22	2.25	1
LB	F	25	2.0	3
SW	M	26	2.0	2
JM	F	23	2.0	1
JF	M	50	1.5	1

TABLE 3.2 – RECORDING PROFILES

Unit Number	Type	Impedance	Length (min)	Nerve Depth
1	SAI	110	30	20
2	SAI	110	25	20
3	SAI	100	10	22
4	FAI	100	10	37
5	FAI	95	18	35
6	FAI	100	9	23
7	FAII	100	30	23
8	FAI	80	13	15
9	SAII	110	30	25
10	FAI	50	10	29
11	FAI	100	15	35
12	SAI	100	10	36
13	FAI	100	12	35
14	FAI	110	10	35
15	FAI	110	15	33
16	FAI	50	8	35
17	FAI	50	11	35
18	SAII	50	10	33
19	FAI	50	12	35
20	FAI	50	10	25
21	SAII	50	10	28
22	SAI	50		27
23	FAII	110	25	
24	SAII	120	9	22

25	FAI	120	10	23
26	FAI	120	10	23
27	SAI	120	10	20
28	SAII	120	8	18
29	SAII	120	10	18
30	FAI	60	10	20
31	SAII	60	28	21
32	FAI	60	7	22
33	FAI	60	8	18
34	FAI	60	6	18
35	FAII	85	22	23
36	FAI	120	10	18
37	FAI	120	15	17
38	FAI	120	9	19
39	FAI	120	20	19
40	FAI	120	10	18
41	FAI	120	7	30
42	FAI	120	10	32
43	FAI	120	7	29
44	SAI	120	6	27
45	FAI	320	10	28
46	SAI	320	7	29
47	FAI	320	6	
48	FAI	330	23	28
49	FAI	330	7	32
50	SAI	180	20	20
51	SAII	180	10	20
52	SAII	180	13	20
53	FAI	180		22
54	FAI	180	11	21
55	FAII	130	20	
56	FAII	100	15	32
57	FAI	100	10	33
58	FAII	100	9	33
59	FAI	100	10	33
60	FAII	140	20	20
61	FAI	140	15	24
62	SAI	220	15	18
63	FAI	140	11	22
64	SAII	200	5	30
65	FAII	200	5	30
66	FAI	200	10	32
67	FAI	200		32
68	SAI	170		20
69	FAI	170		19
70	FAI	170		19

71	FAI	170		19
72	SAI	400	15	28
73	FAI	360	15	28
74	FAI	360	25	30
75	FAI	140	15	31
76	FAI	140	10	31
77	FAII	140	20	
78	FAI	140	20	31
79	SAII	140	20	30
80	FAI	140	18	30
81	FAI	140	36	31
82	FAI	140	5	31
83	SAI	200	20	29
84	FAII	200	14	30
85	FAI	200	5	30
86	FAI	200	5	30
87	FAI	200	8	31
88	FAI	200	7	28
89	FAI	100	10	
90	FAI	100	15	
91	FAII	100	10	29
92	SAI	100	5	30
93	FAI	180	10	21
94	FAI	180	10	20
95	FAII	300		25
96	FAI	300		23
97	SAII	300	20	22
98	FAII	300	15	22
Mean		149.9	13.5	26.1
Median		120	10	27.5
S.D.		8.11	0.71	0.61
Range		350	31	22
Maximum		400	36	37
Minimum		50	5	15

TABLE 3.3 – UNIT PROFILES					
Location	SAI	FAI	SAII	FAII	TOTAL
Big Toe	1	3	2	1	7
2nd Toe	2	6		1	9
3rd Toe	2	3	1	1	7
4th Toe	1	2	1		4
5th Toe	1	4	5		10
Front Foot		4	3	3	10
Lateral Foot	5	25		5	35
Arch	1	3			4
Heel	2	7	4	1	*14*
Med. Heel		2		2	*4*
Calf		1		1	*2*
Total	*15*	*60*	*16*	*15*	*106*

TABLE 3.4 – RECEPTOR THRESHOLDS	
T (mN)	Number of Units
0.3	1
0.5	3
1.5	6
4	17
7	11
11	11
15	11
20	3
35	9
55	6
85	4
115	6
150	2
280	4
750	4
2000+	2

T (g) – THRESHOLD MEASURED IN GRAMS, RF (g) – RECEPTIVE FIELD MEASURED IN GRAMS, T (N) – THRESHOLD MEASURED IN NEWTONS, RF (N) RECEPTIVE FIELD MEASURED IN NEWTONS, P/D – PROXIMAL-DISTAL BORDER OF RF MEASURED IN mm, M/L – MEDIAL-LATER BORDER OF RF MEASURED IN mm, LxW – LENGTH x WIDTH PRODUCT MEASURING AREA OF RECEPTIVE FIELD, AREA – SIZE OF RF AS MEASURED BY REGRESSION EQUATION.

TABLE 4.1 - SLOW ADAPTING TYPE I UNITS

Unit #	Location	T (g)	RF (g)	T (N)	RF (N)	P/D	M/L	LxW	Area
1	2nd Toe	0.407	2.041	0.00399	0.02002	4	5	20	11.812
2	Lat. Foot	0.692	2.041	0.00679	0.02002	9	11	99	70.9277
3	3rd Toe	0.692	3.63	0.00679	0.03561				
4	2nd Toe	1.202	5.495	0.01179	0.05391	11	8	88	62.6964
5	4th Toe	1.479	5.465	0.01451	0.05361	11	6	66	46.2338
6	5th Toe	2.041	11.749	0.02002	0.11526	5	11	55	38.0025
7	Big Toe	3.63	15.136	0.03561	0.14848	6	8	48	32.7644
8	Lat. Foot	3.63	15.36	0.03561	0.15068	7	8	56	45.0588
9	Lat. Foot	5.495	28.84	0.05391	0.28292	15	13	195	142.765
10	Lat. Foot	5.495	28.84	0.05391	0.28292	25	15	375	277.459
11	Heel	8.511	75.858	0.08349	0.74417	11	15	165	120.316
12	Heel	11.749	75.858	0.11526	0.74417	11	10	110	79.159
13	Lat. Foot	11.749	125.892	0.11526	1.235	15	25	375	277.459
14	3rd Toe	15.136	75.858	0.14848	0.74417	11	9	99	70.9277
15	Arch	75.858	281.838	0.74417	2.76483	10	14	140	101.608
Median		3.63	15.36	0.03561	0.15068	11	10.5	99	70.9277
Mean		9.85107	50.2601	0.09664	0.49305	10.7857	11.2857	135.071	98.3705

TABLE 4.2 - FAST ADAPTING TYPE I UNITS

Unit #	Location	T (g)	RF (g)	T (N)	RF (N)	P/D	M/L	LxW	Area
1	Heel	0.068	0.407	0.00067	0.00399	5	5	25	15.5535
2	Lat. Foot	0.068	0.407	0.00067	0.00399	5	6	30	19.295
3	3rd Toe	0.166	0.692	0.00163	0.00679	4	5	20	11.812
4	Big Toe	0.166	0.407	0.00163	0.00399	4	4	20	11.812
5	Big Toe	0.166	0.692	0.00163	0.00679	5	5	25	15.5535
6	Lat. Foot	0.166	0.692	0.00163	0.00679	5	6	30	19.295
7	Lat. Foot	0.166	0.692	0.00163	0.00679	5	7	35	23.0365
8	5th Toe	0.407	2.041	0.00399	0.02002	4	4	16	8.8188
9	5th Toe	0.407	2.041	0.00399	0.02002	5	4	20	11.812
10	3rd Toe	0.407	2.041	0.00399	0.02002	5	6	30	19.295
11	2nd Toe	0.407	2.041	0.00399	0.02002	5	4	20	11.812
12	Lat. Foot	0.407	2.041	0.00399	0.02002	5	8	40	26.778
13	Heel	0.407	2.041	0.00399	0.02002	7	8	56	38.7508
14	Lat. Foot	0.407	2.041	0.00399	0.02002	7	9	63	43.9889
15	2nd Toe	0.407	2.041	0.00399	0.02002	7	10	70	49.227
16	Front Foot	0.407	2.041	0.00399	0.02002	9	6	54	37.2542
17	Lat. Foot	0.407	2.041	0.00399	0.02002	10	8	80	56.71
18	Front Foot	0.407	2.041	0.00399	0.02002	13	15	195	142.765
19	Big Toe	0.407	2.041	0.00399	0.02002				
20	Lat. Foot	0.692	3.63	0.00679	0.03561	4	7	28	17.7984
21	Lat. Foot	0.692	2.041	0.00679	0.02002	7	7	49	33.5127
22	Lat. Foot	0.692	4.56	0.00679	0.04473	8	6	48	32.7644
23	Heel	0.692	3.63	0.00679	0.03561	8	12	96	68.6828
24	Lat. Foot	0.692	2.041	0.00679	0.02002	9	6	54	37.2542
25	Heel	0.692	3.63	0.00679	0.03561	9	7	63	43.9889
26	Heel	0.692	3.63	0.00679	0.03561	9	12	108	77.6624

A2

27	Lat. Foot	0.692	3.63	0.00679	0.03561	11	6	66	46.2338
28	Arch	1.202	5.495	0.01179	0.05391	2.5	6	15	8.0705
29	4th Toe	1.202	5.495	0.01179	0.05391	4	3.5	14	7.3222
30	2nd Toe	1.202	5.495	0.01179	0.05391	3.5	10	35	23.0365
31	5th Toe	1.202	5.495	0.01179	0.05391	5	6	30	19.295
32	Front Foot	1.202	5.495	0.01179	0.05391	7	14	98	70.1794
33	Arch	1.202	5.495	0.01179	0.05391	8	9	72	50.7236
34	Lat. Foot	1.202	5.495	0.01179	0.05391	9	7	63	43.9889
35	Side Heel	1.202	5.495	0.01179	0.05391	9	11	99	70.9277
36	2nd Toe	1.202	5.495	0.01179	0.05391	10	14	140	101.608
37	Lat. Foot	1.479	5.495	0.01451	0.05391	4	9	36	23.7848
38	Lat. Foot	1.479	5.495	0.01451	0.05391	5	6	30	19.295
39	Lat. Foot	1.479	5.495	0.01451	0.05391	5	6	30	19.295
40	Lat. Foot	1.479	5.495	0.01451	0.05391	6	7	42	28.2746
41	3rd Toe	1.479	5.495	0.01451	0.05391	9	9	81	57.4583
42	Lat. Foot	1.479	5.495	0.01451	0.05391	9	14	126	91.1318
43	Lat. Foot	1.479	5.495	0.01451	0.05391	10	7	70	49.227
44	Lat. Foot	1.479	5.495	0.01451	0.05391	10	7	70	49.227
45	Front Foot	1.479	5.495	0.01451	0.05391	12	11	132	95.6216
46	2nd Toe	1.479	5.495	0.01451	0.05391	9			
47	5th Toe	2.041	8.511	0.02002	0.08349	9	7	63	43.9889
48	Lat. Foot	3.63	15.136	0.03561	0.14848	6	6	36	23.7848
49	2nd Toe	3.63	15.136	0.03561	0.14848	6	9	54	37.2542
50	Arch	3.63	15.136	0.03561	0.14848	9	8	72	50.7236
51	4th Toe	3.63	15.136	0.03561	0.14848	10	8	80	56.71
52	Lat. Foot	3.63	15.136	0.03561	0.14848	15	13	195	142.765
53	Side Heel	5.495	28.84	0.05391	0.28292	5	11	55	38.0025
54	Heel	5.495	28.84	0.05391	0.28292	7	12	84	59.7032

55	Lat. Foot	5.495	28.84	0.05391	0.28292	16	11	176	128.547
56	Lat. Foot	8.511	28.8	0.08349	0.28253	15	7	105	75.4175
57	Heel	8.511	28.84	0.08349	0.28292	16	12	192	140.52
58	Lat. Foot	28.84	125.892	0.28292	1.235	4	3	12	5.8256
59	Lat. Foot	28.84	125.892	0.28292	1.235	25	18	450	333.581
60	Calf	75.858	281.838	0.74417	2.76483	10	6	60	41.744
Median		1.202	5.495	0.01179	0.05391	7	7	55.5	38.3767
Mean		3.73717	15.3609	0.03666	0.15069	7.91379	8.05172	71.6897	50.4914

TABLE 4.3 - SLOW ADAPTING TYPE II UNITS

Unit #	Location	T (g)	RF (g)	T (N)	RF (N)	P/D	M/L	LxW	Area
1	Big Toe	3.63	15.136	0.03561	0.14848	13	18	324	239.295
2	Front Foot	5.495	28.84	0.05391	0.28292	12	15	225	165.214
3	Front Foot	8.511	75.858	0.08349	0.74417	14	13	169	123.309
4	Lat. Foot	11.749	75.858	0.11526	0.74417	8	14	112	80.6556
5	Heel	11.749	28.84	0.11526	0.28292	9	7	63	43.9889
6	Big Toe	11.749	28.84	0.11526	0.28292	13	17	289	213.105
7	Front Foot	15.136	75.858	0.14848	0.74417	14	11	121	87.3903
8	Heel	28.84	125.892	0.28292	1.235	8	15	120	86.642
9	Heel	28.84	125.892	0.28292	1.235	14	20	400	296.166
10	Lat. Foot	75.858	446.683	0.74417	4.38196	15	12	180	131.54
11	Heel	281.838		2.76483					
12	4th Toe								
13	3rd Toe								
14	Lat. Foot								
15	Lat. Foot								
16	Lat. Foot								

	T (g)	RF (g)	T (N)	RF (N)	P/D	M/L	LxW	Area
Median	11.749	75.858	0.11526	0.74417	13	14.5	174.5	127.424
Mean	43.945	102.77	0.4311	1.00817	12	14.2	200.3	146.73

TABLE 4.4 - FAST ADAPTING TYPE II UNITS

Unit #	Location	T (g)	RF (g)	T (N)	RF (N)	P/D	M/L	LxW	Area
1	2nd Toe	0.0275	0.166	0.00027	0.00163	10	6	60	41.744
2	Calf/Foot	0.068	0.407	0.00067	0.00399				
3	Lat. Foot	0.166	0.692	0.00163	0.00679	16	20	320	236.302
4	Front Foot	0.407	2.041	0.00399	0.02002	10	7	70	49.227
5	Side Heel	0.407	2.041	0.00399	0.02002	16	24	384	284.193
6	Lat. Foot	0.407	2.041	0.00399	0.02002	35	23	805	599.228
7	Lat. Foot	0.407	2.041	0.00399	0.02002	44	38	1672	1248
8	Lat. Foot	0.407	2.041	0.00399	0.02002	30	40	1200	894.806
9	3rd Toe	0.692	4.56	0.00679	0.04473				
10	Side Heel	1.202	5.495	0.01179	0.05391	9	7	63	43.9889
11	Big Toe	2.041	8.511	0.02002	0.08349				
12	Calf	3.63	15.136	0.03561	0.14848				
13	Front Foot	11.749	75.858	0.11526	0.74417	20	22	440	326.098
14	Heel	75.858	281.838	0.74417	2.76483				
15	Lat. Foot	281.838		2.76483					
Median		0.5495	2.041	0.00539	0.02002	16	22	384	284.193
Mean		27.0643	30.8328	0.2655	0.30247	21.1111	20.7778	557.111	413.732

TABLE 4.5 – REGIONAL MEAN VALUES

Location	T (g)	RF (g)	T (mN)	RF (mN)	P/D	M/L	LxW	Area
Big Toe	3.339714	11.05542	32.76259	108.4537	8.4	10.4	141.2	102.505
2nd Toe	1.107055	4.822777	10.86021	47.31145	7.25	8.125	62.125	43.3341
3rd Toe	3.18033	15.5351	31.1990	152.399	6.75	6.75	55	38.0025

Location	T (g)	RF (g)	T (mN)	RF (mN)	P/D	M/L	LxW	Area
4th Toe	2.103666	8.698666	20.63697	85.33392	8.16666	6	53.333	36.7553
5th Toe	1.2196	5.9674	11.96427	58.54019	5.8	6.2	36.8	24.3834
Front Foot	1.3405	5.495	13.15030	53.90595	12	13	132	95.6216
Lateral Foot	5.886722	31.675555	57.74874	310.7372	12.0555	11.5555	204.25	149.861
Arch	20.473	76.991	200.8401	755.2817	7.375	9.25	74.75	52.7814
Heel	47.85157	41.9465	469.4239	352.7101	9.5	11.25	123.5	89.2610
Medial Heel	2.28625	11.22175	22.42811	110.0853	9.75	13.25	150.25	109.278
Calf	43.8035	178.848	429.7123	1754.498	10	6	60	41.744

TABLE 4.6 – REGIONAL MEDIAN VALUES

Location	T (g)	RF (g)	T (mN)	RF (mN)	P/D	M/L	LxW	Area
Big Toe	3.63	15.136	35.6103	148.4841	6	8	48	32.7644
2nd Toe	1.202	5.495	11.79162	53.90595	6.5	7.5	57	39.4991
3rd Toe	0.947	4.5625	9.29007	44.7581	7	7	50.5	34.6351
4th Toe	1.479	5.495	14.50899	53.90595	10	6	66	46.2338
5th Toe	1.202	5.495	11.79162	53.90595	5	5	30	19.295
Front Foot	10.897	47.9914	106.8995	470.7956	12.3333	12.6666	167.111	121.895
Lateral Foot	1.479	5.495	14.50899	53.90595	9	8	68	47.7304
Arch	2.416	10.3155	23.70096	101.1950	8.5	8.5	72	50.7236
Heel	8.511	28.84	83.49291	159.2653	9	12	102	73.1726
Medial Heel	1.6215	7.003	15.90691	68.69943	9	11	81	57.4583
Calf	43.8035	178.848	429.7123	1754.498	10	6	60	41.744

TABLE 5.1 - ABSOLUTE SKIN AREA

Subject	1	2	3	4	5	Front Foot	Arch	Lateral Foot	Heel	Total
1	12.25	6.5	5	3.25	2.5	20.75	21.75	32.55	26.75	131.3
2	12.25	6	5.5	5.25	2.5	22.25	40	55	24.75	173.5
3	13.5	7.75	6	4.25	2.75	18.5	30.25	40.25	23.75	147
4	14.5	6.25	3.25	4.5	3	21.25	27.75	48	33.5	162
5	13	7.5	5.25	3.75	3.25	20.5	25	36.25	25.25	139.75
Mean	13.1	6.8	5	4.2	2.8	20.65	28.95	42.41	26.8	150.71
S.D.	0.9453	0.7786	1.0458	0.7582	0.3259	1.3761	6.9403	9.0772	3.8987	17.011

TABLE 5.2 - RELATIVE SKIN AREA

Subject	1	2	3	4	5	Front Foot	Arch	Lateral Foot	Heel
1	9.3	5	3.8	2.5	1.9	15.8	16.6	24.8	20.4
2	7.1	3.5	3.2	3	1.4	12.8	23.1	31.7	14.3
3	9.2	5.2	4	2.8	1.8	12.6	20.6	27.7	16.2
4	9	3.9	2	2.8	1.9	13.1	16.8	29.6	20.1
5	9.3	5.3	3.8	2.7	2.3	14.7	17.9	25.9	18.1
Mean	8.78	4.58	3.36	2.76	1.86	13.8	19	27.94	17.82
S.D.	0.9471	0.8228	0.81731	0.1816	0.3209	1.3910	2.7919	2.7826	2.5955

TABLE 5.3 - SKIN AREA

Subject	L x W	PLOT
1	237.6	173.5
2	219	162
3	188.7	131.3
4	191.4	147
5	191.4	139.8

Regression Equation: $y = 0.7483x - 3.154$ ($r = 0.957$)

TABLE 5.4 – RELATIVE DENSITY (TOTAL POPULATION)

Region	Area (cm2)	Units	Density
Big Toe	13.1	7	0.53435
2nd Toe	6.8	9	1.32353
3rd Toe	5	7	1.4
4th Toe	4.2	4	0.95238
5th Toe	2.8	5	1.78571
Front Foot	20.65	10	0.48426
Lateral Foot	28.95	40	1.38169
Arch	42.41	4	0.09432
Heel	26.8	14	0.52239

TABLE 5.5 – RELATIVE DENSITY (SAI)

Region	Area (cm2)	Units	Density
Big Toe	13.1	1	0.07634
2nd Toe	6.8	2	0.29412
3rd Toe	5	2	0.4
4th Toe	4.2	1	0.2381
5th Toe	2.8	1	0.35714
Front Foot	20.65	0	0
Lateral Foot	28.95	5	0.17271
Arch	42.41	1	0.02358
Heel	26.8	2	0.07463

TABLE 5.6 – RELATIVE DENSITY (FAI)

Region	Area (cm2)	Units	Density
Big Toe	13.1	3	0.22901
2nd Toe	6.8	6	0.88235
3rd Toe	5	3	0.6
4th Toe	4.2	2	0.47619
5th Toe	2.8	4	1.42857

Front Foot	20.65	4	0.1937
Lateral Foot	28.95	25	0.86356
Arch	42.41	3	0.07074
Heel	26.8	7	0.26119

TABLE 5.7 – RELATIVE DENSITY (SAII)

Region	Area (cm2)	Units	Density
Big Toe	13.1	2	0.15267
2nd Toe	6.8	0	0
3rd Toe	5	1	0.2
4th Toe	4.2	1	0.2381
5th Toe	2.8	0	0
Front Foot	20.65	3	0.14528
Lateral Foot	28.95	5	0.17271
Arch	42.41	0	0
Heel	26.8	4	0.14925

TABLE 5.8 – RELATIVE DENSITY (FAII)

Region	Area (cm2)	Units	Density
Big Toe	13.1	1	0.07634
2nd Toe	6.8	1	0.14706
3rd Toe	5	1	0.2
4th Toe	4.2	0	0
5th Toe	2.8	0	0
Front Foot	20.65	3	0.14528
Lateral Foot	28.95	5	0.17271
Arch	42.41	0	0
Heel	26.8	1	0.03731

APPENDIX TWO: ANATOMY OF THE LOWER LIMB

A transverse section of the right knee as viewed from above. Note the position of the tibial nerve with respect to the popliteal artery and vein.

Anterior Surface

Popliteal Vein

Common Peroneal (Lateral Popliteal) Nerve

Popliteal Artery

Tibial (Medial Popliteal) Nerve
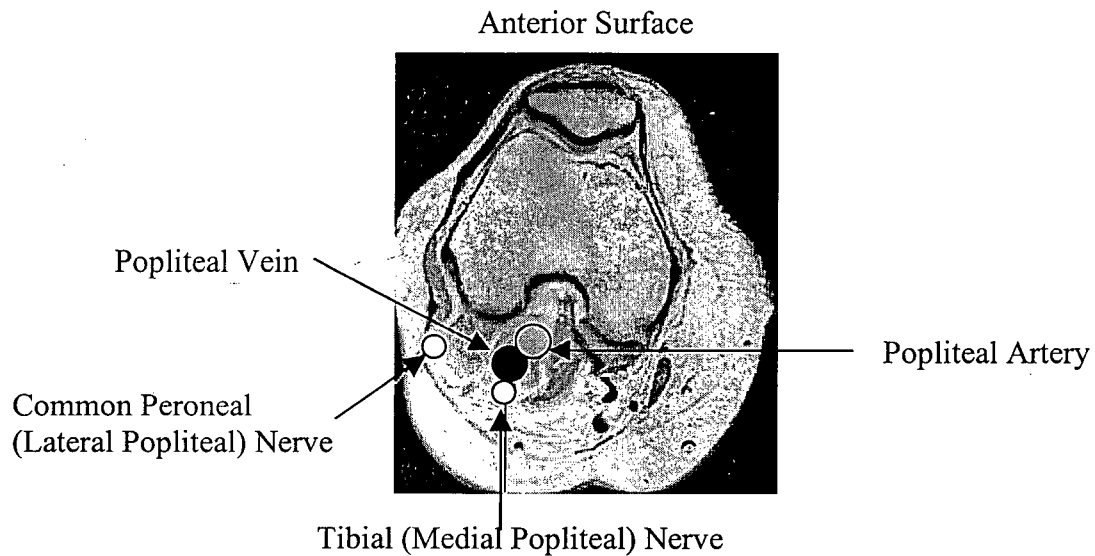
(Below) The anatomy of the popliteal fossa including the muscular, neural, and vascular components is illustrated.

Sciatic Nerve in the Proximal Thigh

Common Peroneal Nerve branching off the Sciatic

Tibal Nerve – Note the superficial position in the popliteal fossa before it descends deeper below the gastrocnemius and soleus muscles.
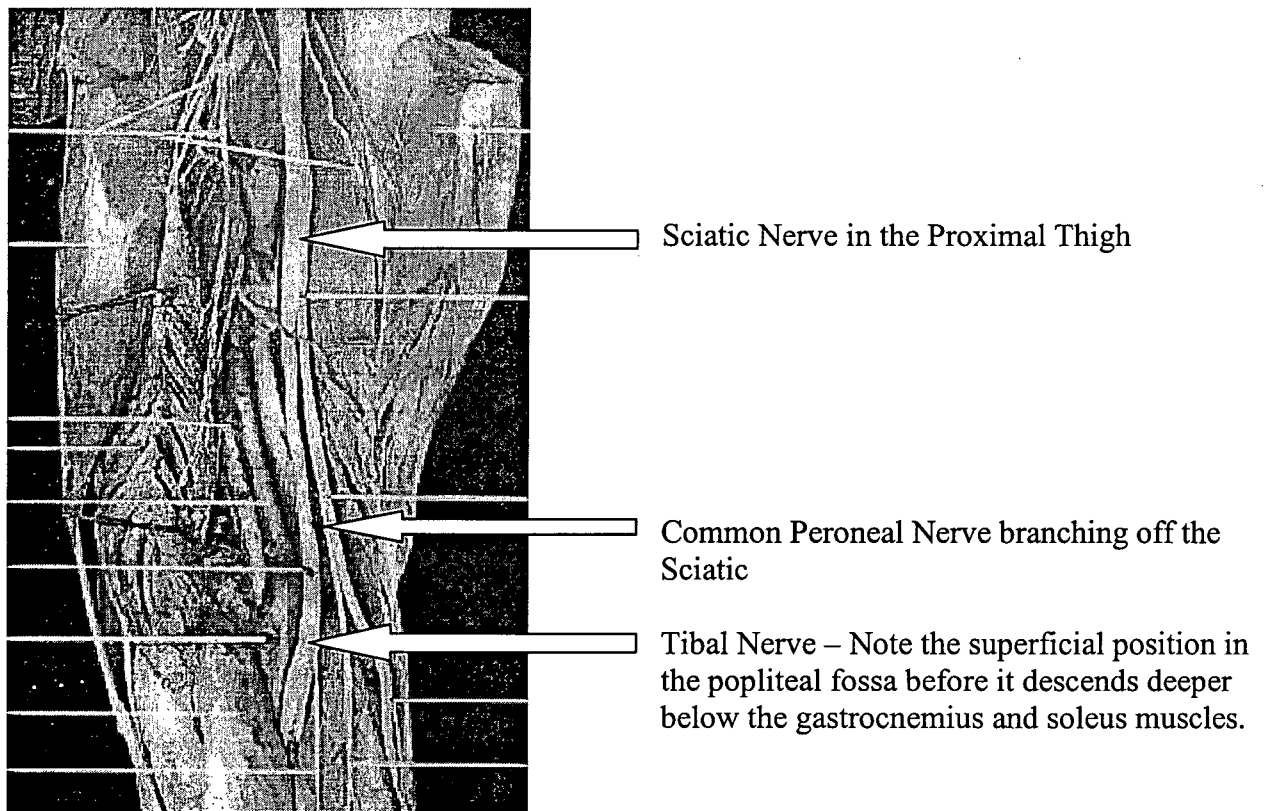
Fascicle Innervation Territories:
The number below each level indicates the distance in millimeters away from joint level.

24   5   ◀ O   JOINT LEVEL ▶

17   40   68   78

(iii) Combined fibres from both plantar nerves.......... +
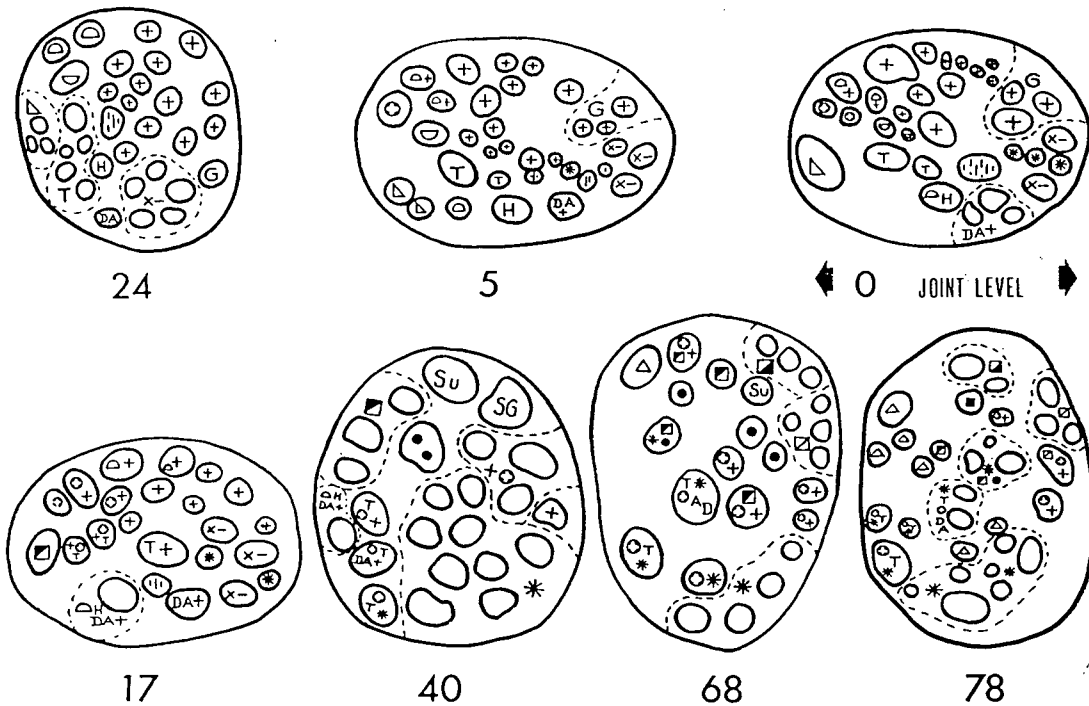
Flexor hallucis longus (distal branch)......................... ✕

Flexor hallucis longus (distal branch) and combined plantar fibres... ✳

Flexor hallucis longus (proximal branch)..................... H

Arterial .... A

Flexor digitorum longus... D

Soleus (distal branch) .... ▽

Soleus (intermediate branch) .... ◠

Soleus: combined fibres from the distal and intermediate branches.. ⊕

Tibialis posterior .... T

Combined fibres from the plantar nerves, the tibialis posterior and the branches to the soleus (distal and intermediate)... ●

Popliteus .... ◺

Lateral head of gastrocnemius .... ◿

Combined fibres from the popliteus and lateral head of gastrocnemius.. ▰

Combined fibres from the soleus (proximal branch) and medial head of gastrocnemius............................... SG

Sural .... SU

Combined fibres from the popliteus, both heads of the gastrocnemius, soleus (proximal branch) and sural ..... ▨

Distal genicular fibres. At and above a level 103 mm above the joint proximal genicular fibres are associated with the sign denoting flexor hallucis longus (distal) and combined plantar fibres but they have not been included in the diagrams. .... G

Proximal genicular fibres...,................................... G′

Combined fibres from all branches excluding the geniculars, medial head of gastrocnemius, proximal soleus, sural and hamstrings .... △

Combined fibres from all branches excluding sural, flexor digitorum longus, arterial and hamstrings................. ▲

Combined fibres from all branches excluding the hamstrings... ⬚

At and above a level 208 mm above the joint:

Adductor magnus .... /////

Semimembranosus .... \\\\\

Long head of biceps and semitendinosus .... |||||

Combined fibres from all three hamstrings, plantars, flexor hallucis longus .... ◼

Combined fires from adductor magnus, semitendinosus, long head of biceps, plantars, flexor hallucis longus ... ◪

Combined fibres from adductor magnus semimembranosus, flexor hallucis longus, plantars .... ◪

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