LOCOMOTOR CONTROL: FROM SPRING-LIKE REACTIONS

OF MUSCLES TO NEURAL PREDICTION

In: AThe Somatosensory System: Deciphering the Brain's Own Body Image@

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By Arthur Prochazka and Sergiy Yakovenko

Centre for Neuroscience
507 HMRC
University of Alberta,
Edmonton AB, T6G 2S2
Fax 1 780 492 1617
Ph   1 780 492 3783

arthur.prochazka@ualberta.ca
http://www.ualberta.ca/~aprochaz/hpage.html

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ABSTRACT

The sensory control of mammalian locomotion has been studied for around 150 years. Many systems are involved: skeletomuscular actuators, spinal reflex and pattern generating networks, propriospinal and brainstem networks, the vestibular apparatus, cerebellum, deep brain nuclei and the cerebral cortex. All of these systems are directly or indirectly affected by mechanical or sensory input related to the locomotor movements they help control. In this chapter we will argue that since locomotor movements vary tremendously according to task, terrain and context, sensory input is crucial in controlling them. Experimental results as well as control systems simulations will be used to show that sensory input is crucial for determining the timing of phase transitions and thus the cadence (cyclic frequency) of locomotion, as well as the relative scaling of muscle activation and thus the amplitude of locomotor movements. We will argue that stretch reflexes play a relatively minor role in this scheme, basically augmenting the load compensation that occurs by virtue of the intrinsic compliance characteristics of skeletal muscle. With the help of biomechanical models, we will show that in quadrupeds, a carefully constructed pattern of muscle activations can produce sustained locomotion over flat ground in the absence of sensory input. However, small variations in terrain, initial conditions, or biomechanical parameters can disrupt locomotor stability. The situation is more critical in bipedal locomotion, where sensory input is vital for stable step cycles. The main function of the huge flow of multimodal sensory information from limb mechanoreceptors to the CNS is therefore continuously to adapt the locomotor pattern to variations in terrain and posture and to mediate higher level prediction of requirements in upcoming step cycles. Sensory systems must therefore be considered as integral parts of the semi-autonomous locomotor pattern generator. Taking the broad view, at least five levels of locomotor control can therefore be identified: load compensation due to skeletomuscular properties, load compensation due to stretch reflexes, bodily motion resulting from cyclical pattern generation and adaptive and predictive control in relation to terrain and to behavioural goals and contexts.

ACKNOWLEDGMENT

INTRODUCTION

Dr. P.R. Burgess organised a Society for Neuroscience symposium in 1992 to discuss his contention that AYou can only control what you sense.@ The question is, what is being controlled in locomotion and which of the many sensory inputs to the CNS are the main players? There are numerous ways of answering this, each implying a different level of control and different neural systems. For example, at one level, that which is controlled is support and movement of the body with respect to uneven terrain. The control problem at this level is to cope with support surfaces of variable orientation, consistency, stability, friction and compliance. At another level, that which is controlled is movement of the body with respect to a moving target (e.g. as in the hunting of prey). At this level the problem is to anticipate future positions of the target and to control and adapt one=s own trajectory accordingly, taking into account obstacles and hazards in the way.

CELLS VERSUS SYSTEMS

Stuart *et al.* (2001) recently pointed out that sensorimotor control has been studied either Ainside-out,@ from cellular and molecular mechanisms within small neuronal networks (the cellular level) or Aoutside-in,@ from complex behaviours to reflexes (the systems level). Although these two approaches often remain far apart, more and more laboratories are tackling specific problems from each end (Rossignol 1996; Jordan 1998; Kiehn and Kjaerulff 1998; O'Donovan *et al.* 1998; Grillner *et al.* 2001).

Historical development

The outside-in approach started centuries ago, when it was suggested that complex behaviours including locomotion comprised chains or assemblies of simple behaviours or reflexes (Descartes 1664; Mettrie 1745; Spencer 1855; Sechenov 1863). These ideas gained credibility with early experimental work that showed that after removal of the cerebrum in birds, frogs and quadruped mammals, the brainstem and spinal cord could still generate complex movements such as righting reflexes and locomotion (Flourens 1823; Goltz 1869; Freusberg 1874; Goltz 1892; Brown 1911) .

      The inside-out approach gained momentum with the neuroanatomical studies of Ramon y Cajal (Cajal 1894) and the technical breakthrough of electronic recordings of single-neuron activity (Adrian and Zotterman 1926). Within years the glass microelectrode had allowed intracellular potentials to be measured and the scene was set for the detailed study of the ionic mechanisms of the action potential, the synaptic actions of sensory axons on motoneurons and interneurons (Eccles *et al.* 1957a; Eccles *et al.* 1957b), the role of neurotransmitters in simple reflex behaviour (Eccles *et al.* 1954; Jankowska *et al.* 1967; Jankowska *et al.* 2000) and the neuronal analysis of reflexes elicited in anesthetised or mid-collicular decerebrated animals (Chen and Poppele 1978; Terzuolo *et al.* 1982). In the 1970s patch-clamping and molecular techniques allowed the functioning of membrane channels and their associated intracellular mechanisms to be studied in detail (Neher and B. 1976).

      In the 1960s, it was shown by the Moscow group of Shik, Orlovsky and their colleagues that locomotion in decerebrate and spinal animals provided an excellent basis for electrophysiological studies at both cellular and systems levels (Shik *et al.* 1969). This in-between approach has provided much useful insight and, combined with pharmacological and molecular techniques, has begun to allow the first comprehensive analyses of locomotor control ranging from ions to behaviour (Grillner *et al.* 2000).

      To return to the main theme of this chapter, deafferentation studies, modelling and lessons learnt from designing walking robots all show that it is important to have sensory information throughout the step cycle about the terrain and obstacles ahead, ground reaction forces and displacements, internal forces and displacements and relative velocities of the body segments. Numerous reviews have been written in the last

few years on one or more of these topics (Pearson 1995; Horak and MacPherson 1996; Prochazka 1996b; Rossignol 1996; Buschges and Manira 1998; Marder and Pearson 1998; Pearson *et al.* 1998; Duysens *et al.* 2000).   We will focus mainly on control mediated by mechanoreceptors, but key aspects of the visual control of locomotion will be included toward the end of the chapter.

THE EFFECT ON LOCOMOTION OF THE LOSS OF SENSATION

It has long been assumed that one=s sense of movement derives from internal sensory signals generated in the moving tissues. (Bell 1834) discussed Amuscle sense@ in detail both in relation to movement control and as a conscious sensation. He spoke of the pleasure of muscle sense during vigorous exercise. In a particularly striking passage he described a woman afflicted with the loss of muscle sense, who could not hold her child safely without constant conscious effort. Since then, literally hundreds of deafferentation studies in animals and humans have underscored this dramatic loss of motor control in the absence of input from muscle receptors. One of us recently reviewed the deafferentation literature (Prochazka 1996b) and summarised the main points as follows:

1) The basic ability to produce voluntary force and move limbs is preserved after deafferentation. However movements are generally uncoordinated and inaccurate, especially when visual guidance is absent .

2) coordination of the different segments of the primate hand in precision tasks is particularly impaired. The accuracy of spatial orientation, fractionated movements and anticipatory pre-shaping of the hand is reduced, and writing may be severely affected.

3) Gait is possible after deafferentation, but again it tends to be irregular and uncoordinated. This holds true in vertebrates and invertebrates alike. In humans who have lost limb proprioception, gait is severely impaired and requires conscious attention. If neck proprioception is also lost, gait becomes virtually impossible.

4) Control of tasks involving simultaneous changes in several variables, coordination of several limb segments or adaptation to changes in the external environment is impaired. Thus fastening buttons, or holding a cup, are difficult and sometimes impossible without visual guidance.

Regarding locomotion in particular, the effects of deafferentation have not always been clear-cut, because under certain restricted circumstances the nerve or muscle activation patterns or the locomotor movements themselves can appear to be reasonably normal (Grillner and Zangger 1975). For example, though deafferented animals and human subjects with somatosensory loss have great difficulty in walking at first, in time they can learn to use residual sensory cues from the limbs and trunk and other sensory inputs such as vision to control their locomotion quite successfully. Hulliger has identified some of the pitfalls in interpreting deafferentation studies in a recent review (Allum and Honegger 1998). He concludes that complete deafferentation of the limbs and trunk results in a massive deficit in the coordination of locomotor movements, though some of the deficits may be overcome through adaptation and intensive training.

RECEPTORS INVOLVED IN THE CONTROL OF LOCOMOTION

Mechanoreceptors (Sherrington 1906) elaborated on muscle sense, and defined proprioceptors as receptors mediating the conscious sensation of the body=s own movements. He assumed proprioception to

be mediated by receptors in muscles, joints and ligaments (Sherrington 1906; Sherrington 1947). From the 1930s to the 1960s, physiologists (but not clinicians) came to believe that muscle receptor activity and therefore proprioception did *not* involve conscious sensation, but this view had to be reversed again when it was shown that tendon vibration, which fairly selectively excites muscle spindles, produced clear illusions of movement (Goodwin *et al.* 1972).

Skin receptors were originally assumed to respond mainly to external forces impinging on the body and so were classified by Sherrington as exteroceptors, along with visual, auditory and olfactory receptors. However, skin receptors also respond to the stretching of skin that occurs during most limb movements and under these circumstances they contribute to kinaesthesia (Moberg 1983; Collins and Prochazka 1996), so this would seem to qualify skin receptors as proprioceptors too. By the same token, it is now clear that muscle receptors can respond very sensitively to stimuli applied to the body. The classification of mechanoreceptors as Aproprioceptors@ or Aexteroceptors@ has thus become rather confusing and of dubious usefulness.

In 1926 the first electrical recordings from single sensory axons were obtained (Adrian and Zotterman 1926) and for the next 50 or more years, the response properties of different types of sensory mechanoreceptor have been studied in great detail in many species. In mammals, muscle spindle and tendon organ endings have been characterised and modelled mathematically. Various types of skin receptor have been identified and their responses to skin indentation of different amplitudes and frequencies have been elucidated in detail (Birder and Perl 1994).

Vision and hearing

The other senses that have a profound influence on the control of locomotion are vision, vestibular input and to a lesser extent, hearing. Though locomotion can be generated by all animals in the absence of vision, in most cases if the terrain is unpredictable, or if there are obstacles in the way, the control of locomotion is degraded. As we shall see, vision is crucial for the higher levels of locomotor control, in which the external context of locomotion must be taken into account in the predictive and adaptive aspects of control (Schubert *et al.* 1999). Sensory input from the vestibular apparatus also has a powerful effect on the control of posture, balance and locomotion (Horak and MacPherson 1996; Zelenin *et al.* 2000). The contribution of hearing to locomotor control has rarely been studied and is assumed to be of lesser importance. However under certain circumstances auditory input produces rapid orienting responses and can affect postural adjustments (Valls-Sole *et al.* 1999).

STRUCTURE AND RESPONSE PROPERTIES OF PROPRIOCEPTORS

There are several reviews in the literature on the morphology and response properties of mechanoreceptors that signal locomotor movements (vertebrates: (Granit 1970; Matthews 1972; Hulliger 1984; Prochazka 1989; Johansson *et al.* 1991; Jami 1992; Prochazka 1996b; Prochazka and Gorassini 1998a; Prochazka 1999); invertebrates: (Bassler 1983; French 1988; Burrows 1992; Bassler and Buschges 1998). In the following we will concentrate mainly on mammalian proprioceptors, muscle spindles and tendon organs.

Muscle spindles: Structure. There are 25,000 - 30,000 muscle spindles in the human body, including about 4,000 in each arm and 7,000 in each leg (Voss 1971; Hulliger 1984). The average number of spindles in a mammalian muscle is roughly 38*(cube root of mass in grams) (Banks and Stacey 1988; Prochazka 1996b). Thus a 64 gram muscle contains about 152 spindles. On average a single limb muscle in the cat contains 50 to 200 spindles, each ranging from 2mm to 6mm in length (Voss 1971; Boyd and Gladden 1985). A muscle spindle consists of a dozen or so intrafusal muscle fibers (Latin Afusus@ = spindle) attached at each end to the surrounding extrafusal muscle fibre, with a central region innervated by sensory endings

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encased in a capsule (Boyd and Gladden 1985). The spindle lengthens and shortens along with the extrafusal muscle fibers to which it is attached. The typical spindle in cats, monkeys and humans contains three types of intrafusal muscle fibre: a dynamic bag_1 (DB1 or b_1), a static bag_2 (SB2 or b_2) and 2 - 11 chain (c) fibers. These intrafusal fibers receive motor input from 10 to 12 ?-fusimotor axons and sometimes from a ß-skeletofusimotor axon, which also innervates neighboring extrafusal muscle fibers (Emonet-Denand *et al.* 1975; Hulliger 1984; Banks 1994).   The central encapsulated region of the spindle contains 1 primary and up to 5 secondary sensory endings spiraled around the non-contractile portions of the intrafusal fibers (Boyd and Gladden 1985). The primary endings are those of group Ia afferents (conduction velocity 72 - 120 m/s in cats) and the secondary endings are those of group II afferents (20- 72 m/s) (Matthews 1972).

Passive response properties of spindle afferents.

Spindle primary and secondary endings respond to muscle length variations similarly in cats, monkeys and humans (for detailed comparisons and a discussion of scaling for different muscle lengths see (Prochazka 1981; Prochazka and Hulliger 1983)). In the absence of fusimotor action group Ia and II afferents respond to muscle length changes dynamically, Ia afferents being more sensitive to muscle velocity and acceleration (e.g. they respond to ramp stretches with larger jumps in firing rate and they show more phase advance in response to sinusoidal inputs). There is a continuum from the smallest diameter group II afferents with low velocity sensitivity, to the largest diameter Ia afferents with high velocity- and acceleration-sensitivity. Group Ia and II afferents both have non-linear aspects of response: e.g. stretch sensitivity that depends on amplitude and offset, after-effects of muscle and fusimotor contraction and non-linear velocity scaling (Hulliger 1984; Prochazka 1996b).

Fusimotor action

The b_1 fibre and its associated Ia sensory spirals are selectively activated by dynamic fusimotor ($?_d$) or $ß_d$ skeletofusimotor axons (Boyd and Gladden 1985; Boyd *et al.* 1985; Banks 1994). The b_2 and chain fibers are activated by static fusimotor or skeletofusimotor ($?_s$ or $ß_s$) axons and rarely by $?_d$ or $ß_d$ axons (Banks *et al.* 1998). Up to 30% of hindlimb spindles lack b_1 fibers and their group Ia afferents are then called b_2c afferents (Boyd and Gladden 1985; Taylor *et al.* 1992; Taylor *et al.* 1998; Taylor *et al.* 1999).
          The main fusimotor actions can be summarized as follows. When muscle length changes are small (< 0.5% rest length), pure $?_d$ action, mediated by b_1 fibers, increases the background firing rate (bias), decreases the stretch-sensitivity (gain) and reduces the phase advance of group Ia afferents (Emonet-Denand *et al.* 1977). For larger-amplitude length changes, $?_d$ action increases group Ia stretch-sensitivity up to 5-fold (Boyd *et al.* 1985) and either increases or decreases Ia phase advance slightly (Hulliger *et al.* 1977; Chen and Poppele 1978). Type b_2c Ia afferents do not exhibit dynamic fusimotor effects, the b_1 intrafusal fibers being absent . $?_s$ action strongly increases the bias of both group Ia and II sensory endings and reduces group Ia stretch-sensitivity (gain) by 50% or more for all amplitudes of length change (Cussons *et al.* 1977; Chen and Poppele 1978). Paradoxically, <u>weak</u> $?_s$ action can <u>increase</u> Ia gain (Hulliger *et al.* 1985). In either case, phase is little changed. Of the 6 to 9 $?_s$ axons acting on a group II ending, each produces some bias, most attenuate its sensitivity to small stretches (< 1% rest length) but one or two of the $?_s$ axons substantially <u>increase</u> group II sensitivity to stretches, presumably by activating b_2 intrafusal fibers (Jami and Petit 1978). The sensitizing action of these $?_s$ fibers on group II endings is similar to the action of $?_d$ fibers on Ia endings. The terms <u>dynamic</u> and <u>static</u> fusimotor action are in fact misleading, in that both types alter mainly the <u>gain</u> and <u>offset</u> rather than the <u>dynamics</u> of group Ia and II responses to stretch (Prochazka 1996b).
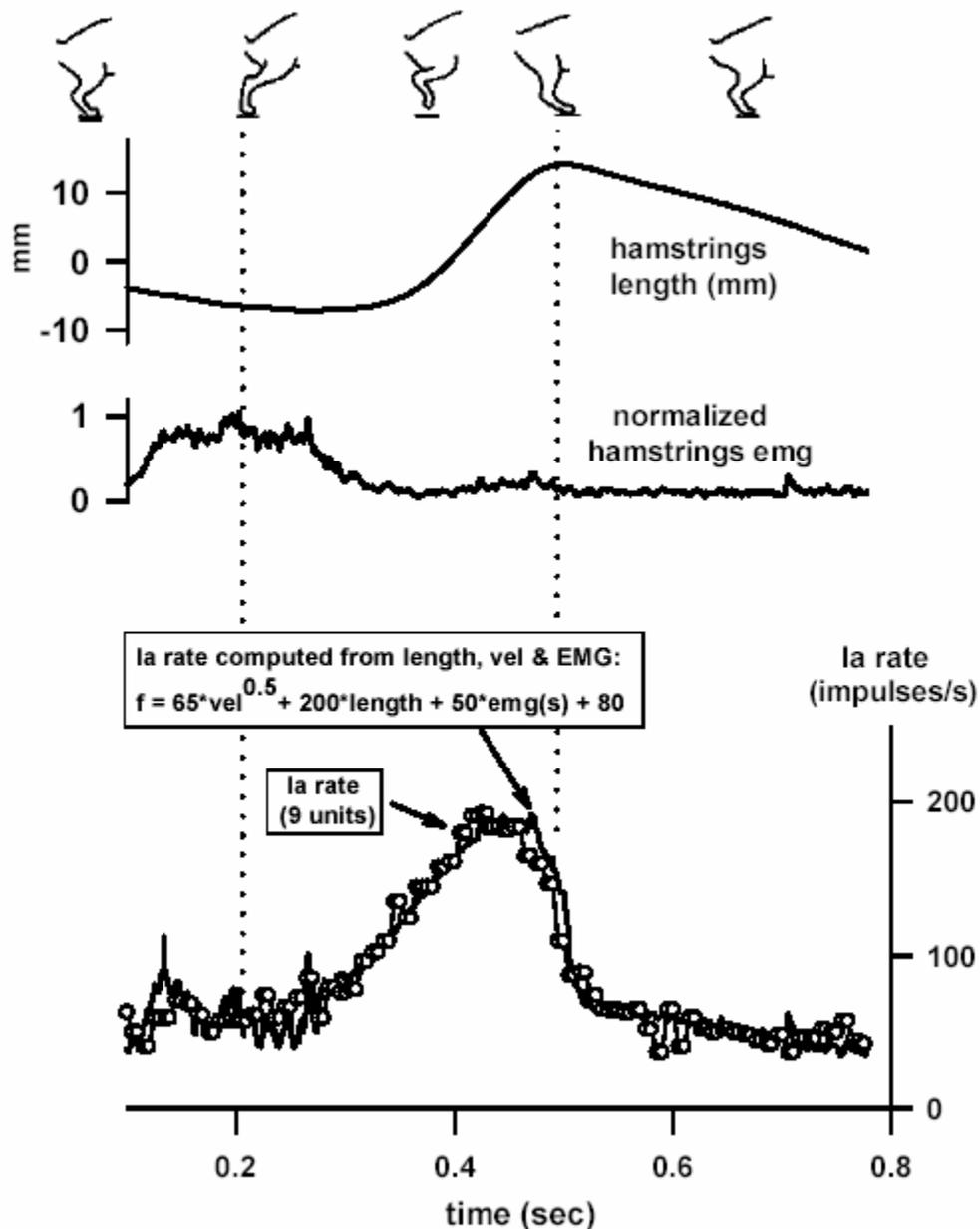
Figure 1. Ensemble firing profile of 9 hamstrings spindle primary (group Ia) afferents recorded during overground locomotion in normal cats. Top: muscle length, middle: electromyogram (EMG), bottom: firing rate profile with superimposed predicted rate derived from the length and EMG signals (adapted from (Prochazka 1999).

Spindle models.

Mathematical models of spindle response characteristics were originally developed from results obtained in acute experiments (Matthews and Stein 1969; Poppele and Bowman 1970; Poppele and Kennedy 1974; Chen and Poppele 1978; Poppele 1981). These models have recently been tested and compared in

ensembles of group Ia and II afferent activity recorded in freely moving cats (Prochazka and Gorassini 1998a; Prochazka and Gorassini 1998b). Because all of the Ia models have a velocity-sensitive term and this tends to dominate the response to the relatively fast changes in muscle length that occur in locomotion, most of the models were reasonably successful in predicting the group Ia responses from the muscle length and EMG activity profiles, as exemplified in the ensemble firing profile of hamstrings Ia afferents shown in Fig. 1. In this example, the small EMG term was added to provide a small amount of alpha-linked biasing of the Ia firing rate, to represent alpha-gamma linkage. In both the group Ia and II models fusimotor action is usually represented as a single gain parameter though recently a more comprehensive model has been developed that incorporates some of the nonlinear features of fusimotor action (Schaafsma *et al.* 1991; Otten *et al.* 1995). Modelling has provided some crucial insights into locomotor control in recent years and the mathematical models of spindle and tendon organ responses have played an important role in this.

Tendon organs: **Structure and response properties**.

Tendon organs are encapsulated structures 0.2-1mm long, usually located at musculo-tendinous junctions (Barker 1974). Generally speaking, there are about 80% as many tendon organs in a typical limb muscle as spindles. Their sensory endings, which become group Ib afferent axons, are entwined amongst the tendinous strands of 10-20 motor units, a given motor unit affecting 1-6 tendon organs (Proske 1981; Jami 1992). In passive muscle, it has long been held that most tendon organs have a high threshold to imposed stretch, but they respond sensitively to force actively generated by the motor units with which they are associated (Houk and Henneman 1967; Stephens *et al.* 1975). This passive/active difference has always been something of a puzzle, as tendon organs are located in fascicles at the ends of muscle fibers, and so might be expected to respond to muscle force regardless of how it is produced.

Tendon organ models.

Because it is impossible to monitor the net force produced by the particular group of motor units Asampled@ by a tendon organ, it is difficult to determine precise input/output characteristics for the receptor. Nonetheless, frequency analyses have been performed by applying feedback-controlled force signals to whole muscle (Houk and Simon 1967; Anderson 1974; Stephens *et al.* 1975). These showed that tendon organs had transfer functions comparable to those of spindle group II endings (Alnaes 1967). Like group II afferents, tendon organ group Ib afferents fire fairly regularly, except at low levels of active force, when unfused twitch contractions of newly recruited motor units cause bursts of group Ib firing (Jami *et al.* 1985). Various types of non-linearity in tendon organ transduction have been described. For example, a given Ib ending may be unloaded by contractions of muscle fibers not inserting into the receptor capsule (Houk and Henneman 1967; Stuart *et al.* 1972). As group Ib afferents sample from a restricted subset of motor units, they do not necessarily signal whole muscle force linearly (Jami *et al.* 1985). The transfer function models describing the relationship between whole muscle force and Ib firing rate (Houk and Simon 1967; Anderson 1974) have recently been tested on firing profiles of small ensembles of Ib afferents recorded during locomotion in normal cats. The EMG activity from the receptor-bearing muscles was used in lieu of muscle force. In spite of this substitution, and in spite of concomitant length changes which would have modulated force somewhat due to inherent force-length properties of the muscles, the tendon organ firing rate profiles were surprisingly well predicted (Fig. 2).
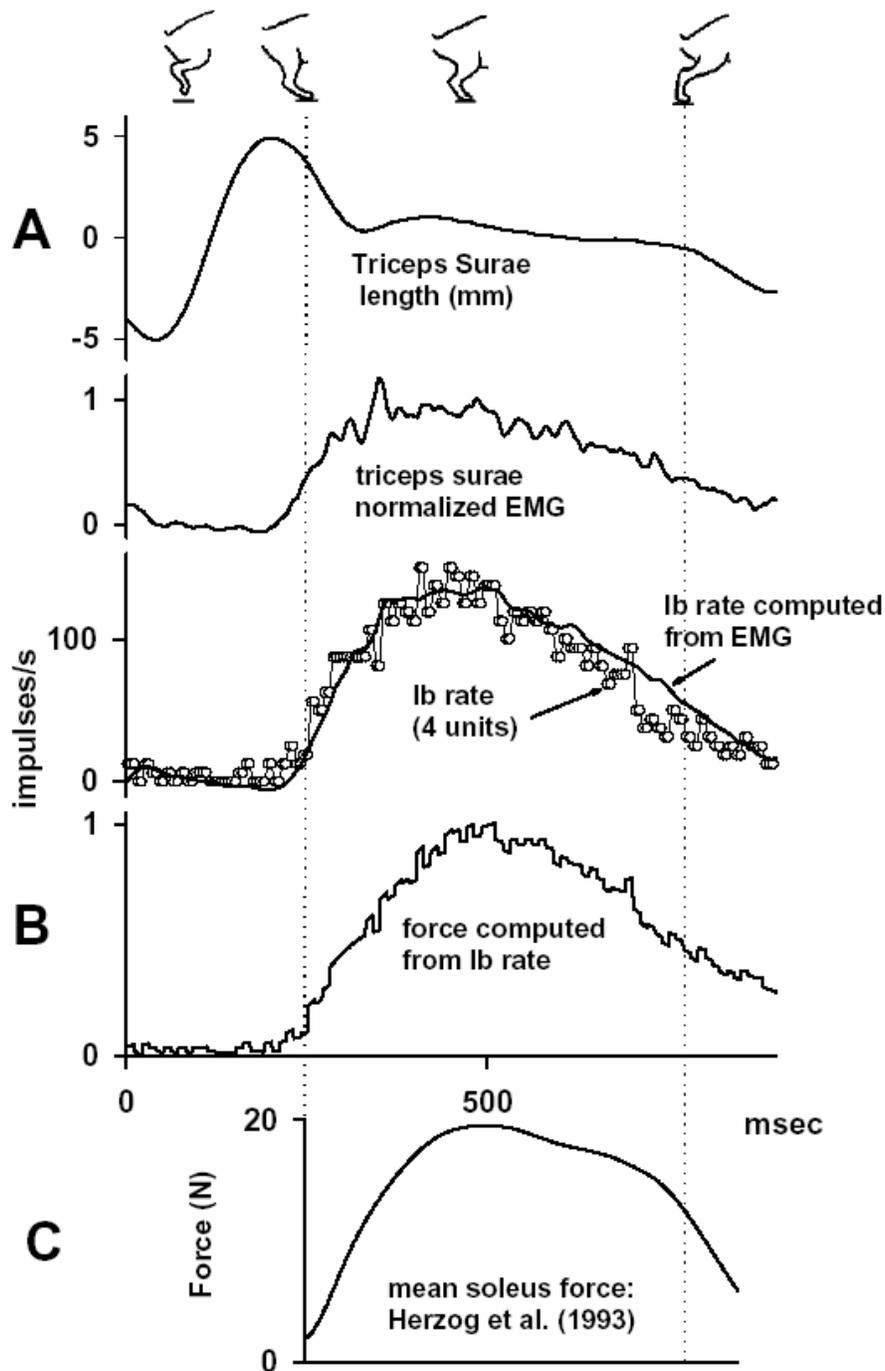
Figure 2. Ensemble firing profile of 4 triceps surae tendon organ (group Ib) afferents recorded during overground locomotion in normal cats. Top: muscle length, second panel: electromyogram (EMG), third panel: ensemble Ib firing rate profile with superimposed predicted rate derived from the EMG signal, B: muscle force as predicted from the firing rate, C: mean force in soleus obtained in separate experiments in another laboratory (Herzog *et al.* 1993). Adapted from: (Prochazka 1999).
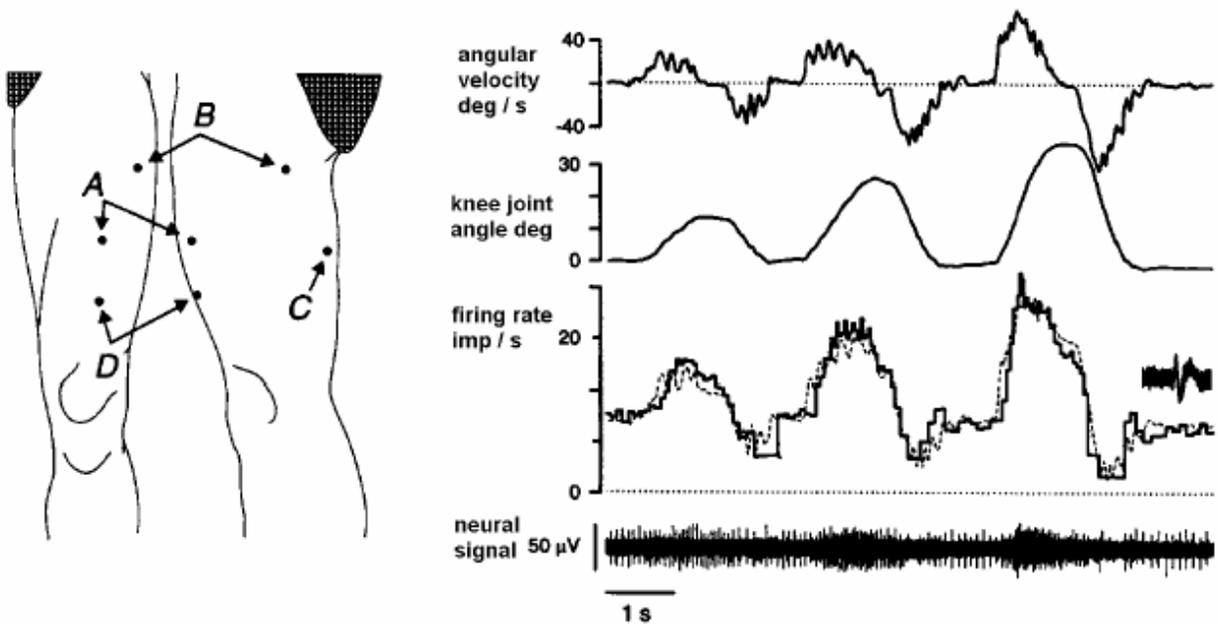
Figure 3. Firing rate profile of a slowly adapting type III cutaneous receptor located at ▮D@ in the left panel recorded in a human subject with microneurography (letters A, B and C refer to other afferents recorded in this subject). The afferent responded to knee joint displacement. The third trace on the right shows superimposed the instantaneous firing rate (bold) and the predicted rate derived from the joint angular velocity and joint angle signals in the two top traces. The bottom trace shows the raw action potentials of this unit (reproduced with permission from (Edin 2001).

Mechanoreceptors in joints, ligaments and skin

Mechanoreceptors in joint capsules, joint ligaments and skin are strategically placed to provide proprioceptive feedback, but proving this role has been difficult. Until the late 1960s, joint receptors were assumed to signal joint position over the full range of motion (Boyd and Roberts 1953). However, it was then reported that most joint receptors in the cat knee and wrist only fired at the extremes of the range (Burgess and Clark 1969; Tracey 1979). Subsequently several groups reported full-range signaling (Godwin-Austen 1969; Zalkind 1971; Carli *et al.* 1979; Ferrell 1980; Lund and Matthews 1981) though some of the full-range afferents in the cat knee joint may have been either muscle spindle or tendon organ afferents (McIntyre *et al.* 1978). Loading of the joint capsule by muscle contraction sensitizes joint receptors, in some cases enough to confer mid-range responsiveness on them (Grigg and Greenspan 1977).

On balance, it seems that joint capsular and ligamentous afferents are capable of signaling limb position and movement at the extremes of motion and in some joints over the full range of motion. Single-unit discharges are detectable in recordings from whole joint nerves (Ferrell 1980), so the total number of joint receptors signaling mid-range movement is probably low compared to the number of muscle and skin receptors responding to the same movement. Joint afferents have conduction velocities mainly in the group II range (Burgess and Clark 1969) and their segmental reflex connections with a-motoneurons are less direct than those of muscle spindles (Johansson *et al.* 1991; Jankowska 1992). It has been suggested that they have a special role in reflexly inhibiting motoneurons of muscles near joints that are damaged (Iles *et al.* 1990).

Cutaneous receptors overlying joints and muscle respond phasically as well as tonically to movement (Edin and Abbs 1991; Edin 1992; Edin and Johansson 1995; Edin 2001) and it has been argued

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that they probably contribute to the sense of position and motion of the extremities. There are massive numbers of skin receptors in the limbs. For example it has been estimated that there are about 17,000 skin mechanoreceptors with myelinated afferent fibers on the surface of the human hand (Johansson and Vallbo 1979), compared to about 4,000 muscle spindles, 2,500 tendon organs and a few hundred mid-range joint receptors in the whole arm (Voss 1971; Hulliger 1984). Type I skin receptors and hair follicle receptors are responsive to rapidly varying skin stimuli. Slowly-adapting type II and III receptors respond sensitively to stretching of the skin and continue to signal maintained stretch (Horch *et al.* 1977). In two recent studies, it was shown that stretching of the skin overlying finger joints produced illusions of movement of the fingers, reinforcing the idea of a proprioceptive role for skin receptors (Edin and Johansson 1995; Collins and Prochazka 1996). Fig. 3 shows the firing rate of a slowly adapting type III cutaneous receptor located at AD@ in the left panel recorded in a human subject with microneurography. The afferent clearly provided information about knee joint displacement and velocity. Its firing profile was extremely well fitted with a first order transfer function similar to that used in the simpler models of group Ia transduction.

Overview of proprioceptive firing during locomotion.

Fig. 4 summarizes the current knowledge regarding the firing rate profiles of ensembles of group Ia, Ib and II muscle afferents during medium-speed stepping in cats. The data were quantified or estimated from numerous single-unit recordings obtained with microwire electrodes implanted in dorsal root ganglia of free-to-move cats (Prochazka *et al.* 1976; Loeb and Duysens 1979; Loeb 1981; Loeb 1984; Prochazka and Gorassini 1998a). If we assume a mean firing rate per receptor of about 75 impulses/s during locomotion (Fig. 4), at any given moment the net input to the spinal cord from the 10,000 or so muscle afferents in each leg is between 0.5 and 1 million impulses/sec. Fig. 4 also shows that the firing rates of muscle afferents are deeply modulated during stepping, and so in principle this would provide highly detailed information to the CNS for locomotor control.

SIMPLE LOCOMOTOR REFLEXES

The neurophysiological significance of the age-old observation that decapitated animals can display coordinated locomotion had been recognized and documented by the mid-18th century (Mettrie 1745). Clearly the neuronal machinery in the spinal cord was capable of controlling quite complex activities without descending input from the brain. The notion that all movements were simply chains of reflexes developed a century later (Spencer 1855). In the late 19th and early 20th century the elementary movements involved in locomotion began to be studied in detail, particularly in spinalized or decerebrated dogs and cats (Freusberg 1874; Sherrington 1910; Brown 1911). Sherrington=s (1910) study was a tour de force of careful experimentation and highly detailed description and remains a definitive reference work to this day. In it, he described the biomechanical actions of most of the muscles of the cat hindlimb, how these muscles were activated or fell silent in flexion and extension reflexes, and how they participated in what he termed Areflex stepping@ (now referred to as air-stepping) in spinal cats and Areflex walking,@ i.e. weight-bearing gait, in decerebrate cats.

ANKLE

Triceps surae

stance | swing | stance

e.m.g.

length

Ia (11)

II (2)

Ib (5)

Plantaris

stance | swing | stance

e.m.g.

length

Ia (3)

II (1)

Ib (4)

Flexor Dig. Long.

stance | swing | stance

e.m.g.

length

Ia (1) — 200 / 100 / 0

II (1) ? — 200 / 100 / 0 impulses/s

Ib (2) — 200 / 100 / 0

Tibialis Anterior

stance | swing | stance

e.m.g.

length

Ia (2)

Ext. Dig. Longus

stance | swing | stance

e.m.g.

length

(2)

Peroneus Longus

stance | swing | stance

e.m.g.

length

(2) — 200 / 100 / 0 impulses/s

HIP/KNEE

Vasti.

stance | swing | stance

e.m.g.

length

Ia

II ?

Ib ?

Sartorius

stance | swing | stance

e.m.g.

length

Ia

II

Ib ?

Post. hamstrings

stance | swing | stance

e.m.g.

length

Ia (9) — 200 / 100 / 0

II (1) — 200 / 100 / 0 impulses/s

Ib (2) — 200 / 100 / 0

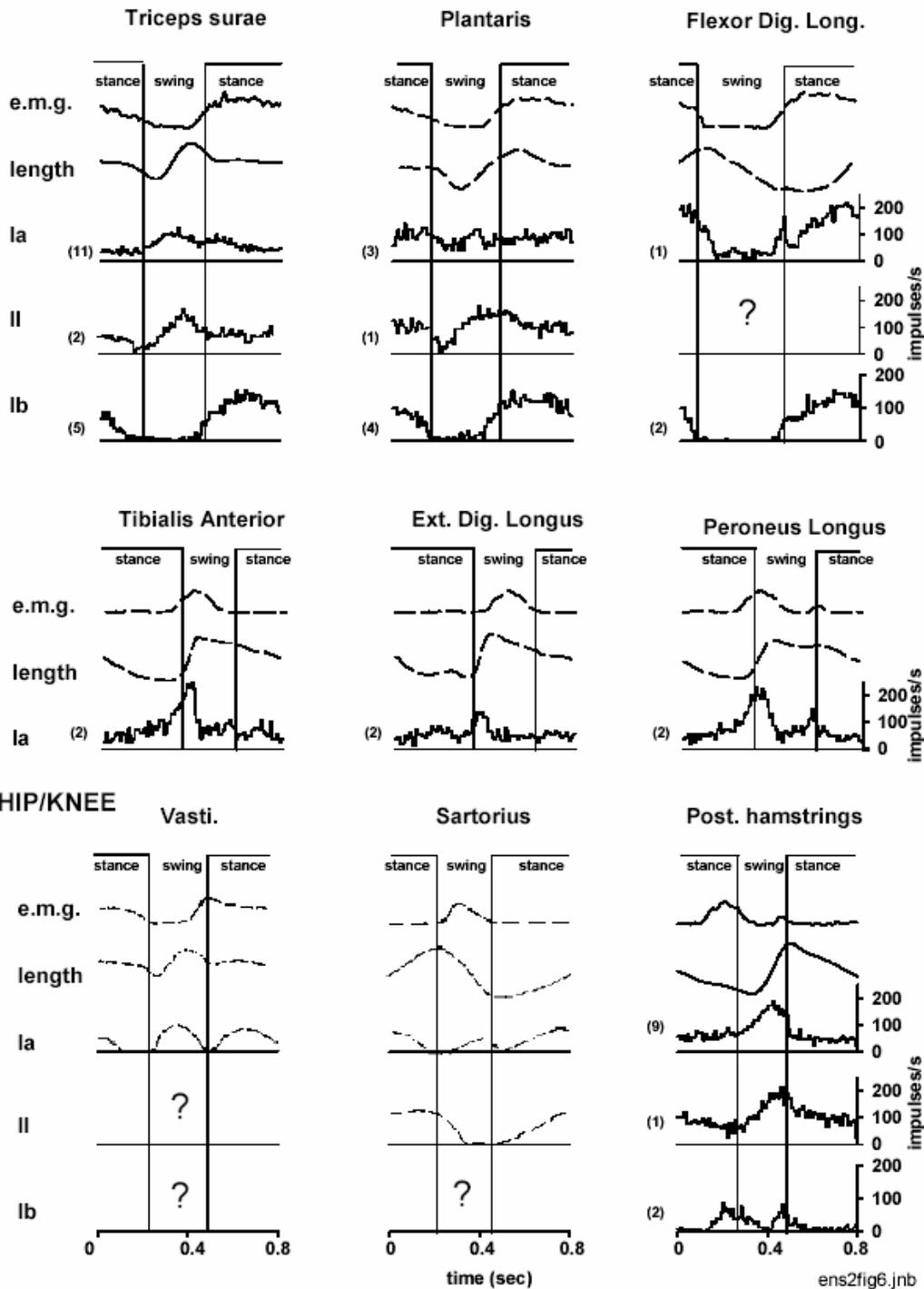0   0.4   0.8

time (sec)

ens2fig6.jnb

Figure 4. Summary figure showing firing rate profiles of ensembles of group Ia, Ib and II muscle afferents during medium-speed stepping in normal cats. The data were compiled from numerous single-unit recordings obtained with implanted dorsal root electrodes (reproduced with permission from (Prochazka and Gorassini 1998a).

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The stretch reflex

The Astretch reflex@ differs in decerebrate and intact animals and since Sherrington's time it has come to be realised that several CNS mechanisms may contribute components of different latency to the stretch reflex response. At the segmental level, muscle spindle Ia afferents activated by muscle lengthening monosynaptically excite homonymous alpha motoneurons which in turn cause the muscle to resist the stretch. In static postures Ib input generally results in homonymous inhibition, but recently it has been shown that this switches to longer-latency homonymous excitation during locomotion (Conway *et al.* 1987), at least in cat extensor muscles (the evidence for Ib homonymous excitation in human locomotion is a matter of controversy: see below). Group II input from muscle spindles has also been implicated in long-latency components of stretch reflexes (Matthews 1991; Sinkjaer *et al.* 2000; Grey *et al.* 2001). Ia homonymous excitation represents negative *displacement* feedback, which augments the intrinsic stiffness of active muscles in the face of length perturbations. Ib homonymous feedback on the other hand represents positive *force* feedback. Positive feedback is synonymous with instability and oscillation in engineering systems, but when muscles are the actuators, their nonlinear length-tension properties turn out to stabilize the positive feedback loop (Prochazka *et al.* 1997a; Prochazka *et al.* 1997b).

Segmental stretch reflexes and their electrically-elicited counterparts, H-reflexes, have been studied intensively for many years, partly because they are modulated in interesting ways, but mainly because it is technically relatively easy to elicit and measure them. Studies of this type have been reviewed many times in recent years (Dietz 1996; Prochazka 1996b; Brooke *et al.* 1997; Dietz 1998; Duysens *et al.* 2000; Schneider *et al.* 2000). Human H-reflexes are smaller during locomotion than during static postures and they show phase-dependent fluctuations (Garrett *et al.* 1981; Garrett and Luckwill 1983; Garrett *et al.* 1984; Capaday and Stein 1986). It is often assumed that H-reflexes represent transmission in the short-latency pathway from Ia afferents to homonymous motoneurons, though an oligosynaptic contribution cannot be ruled out (Burke 1983). There is evidence that the faster the locomotion and the more difficult the terrain, the greater the suppression of H-reflexes (Capaday and Stein 1987; Llewellyn *et al.* 1990). It is vigorously debated whether this modulation is centrally generated (Schneider *et al.* 2000) or due to reafferent signals (Misiaszek *et al.* 1998). Stretch reflexes elicited during locomotion by rapidly stretching individual muscles (Akazawa *et al.* 1982; Hiebert *et al.* 1996) or imposing sudden rotations about joints (Orlovsky and Shik 1965; Sinkjaer 1997; Gritsenko *et al.* 2001) also show phase-dependent modulations, but these are less predictable than H-reflex modulations (Sinkjaer 1997; Christensen *et al.* 2001). This is not too surprising, as stretch reflexes comprise not only the Ia-mediated short latency responses but also longer-latency responses involving group II reflexes, group Ib reflexes and higher-level processing in the CNS (Sinkjaer *et al.* 1999).

Before one delves too deeply into the mechanisms and modulation of stretch reflexes however, one should ask how important they are in the control of locomotion and movement anyway. Would an animal be simply unable to support its weight if it had no stretch reflexes? The answer is no, on both experimental and theoretical grounds. Provided that the alpha motoneurons of load-bearing muscles are activated from *some* source in the nervous system, the muscles develop an intrinsic stiffness that resists stretching and that can in fact be represented as displacement feedback (Partridge 1966). This is easily seen in the stretch reflex model of Appendix Fig. 1, whereby in the inner feedback loops muscle stretch results in reactive forces due to the force-length and force-velocity properties of muscle. Muscle afferent feedback mediated by Ia and Ib pathways in the outer loops of the mode provides a source of input to alpha motoneurons but it is not the only source. There are many descending and propriospinal pathways that also activate motoneurons, represented by just one input in the model of Appendix Fig. 1.
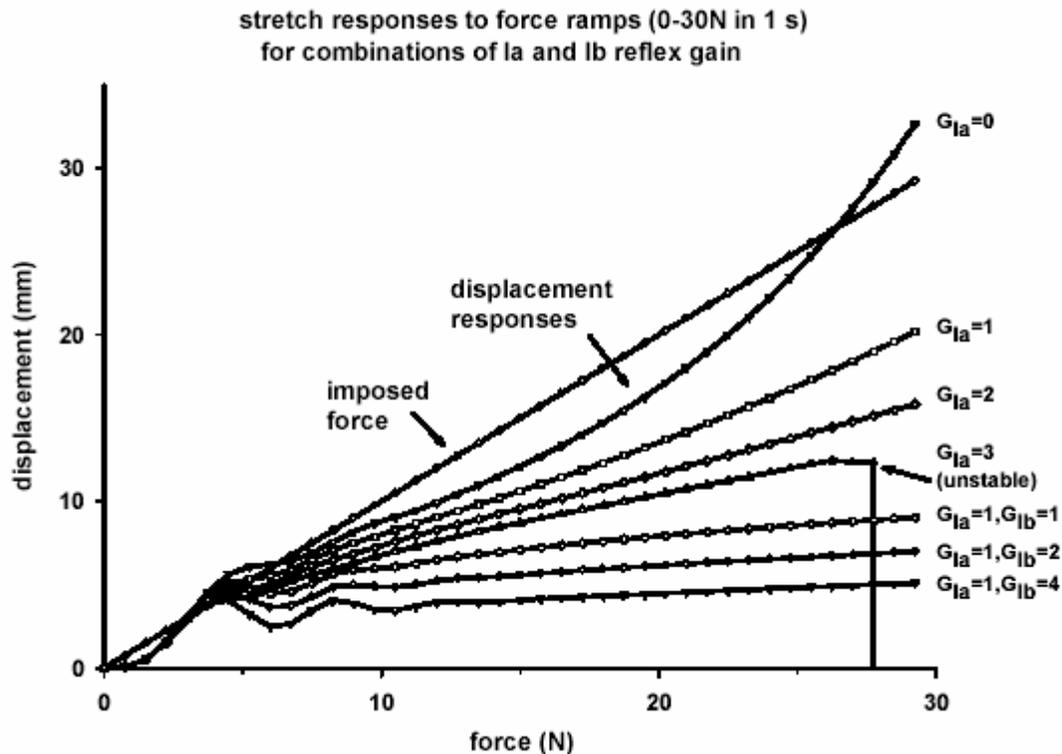
stretch responses to force ramps (0-30N in 1 s)
for combinations of la and lb reflex gain

Figure 5. Responses of stretch reflex model (Appendix Fig. 1) to ramps of force, with 7 different combinations of Ia gain (G_{Ia}) and Ib gain (G_{Ib}), as indicated. The slope of the displacement curve marked $G_{Ia}=0$ corresponds to the intrinsic stiffness of the active muscle alone. As negative feedback Ia gain increases, the stiffness also increases, but for $G_{Ia}=3$, the loop goes unstable at the point indicated by the arrow on the right. The addition of positive Ib feedback to negative Ia feedback greatly increases the stiffness of the system.

Analysis of responses to loading with this model showed that simple stretch reflexes mediated by spindle Ia afferents for example can at most triple the prevailing muscle stiffness without causing instability (Prochazka *et al.* 1997a). This is illustrated in Fig. 5, where Ia gains of 1 and 2 reduced the muscle stretch caused by applied force by factors of about 2 and 3 respectively; the loop became unstable when the gain in the Ia-mediated pathway was set to 3. Though there are several simplifying assumptions in models of this type, their predictions have been shown to be fairly accurate in hybrid experiments in which actual muscles were stretched and Areflexly@ activated by electrical stimulation modulated by a signal obtained by filtering the displacement signal with a spindle Ia transfer function (Bennett *et al.* 1994).

Fig. 5 also illustrates another aspect of proprioceptive reflexes that was quite unexpected from a control theoretical point of view, and that has only recently been understood analytically: positive force feedback. To the surprise of many in the field, it was discovered in 1987 that signals from Ib afferents, which normally inhibit homonymous and synergistic alpha motoneurons (MNs) in the absence of locomotion, switched to *exciting* these motoneurons *during* fictive locomotion in the acute spinal cat (Conway *et al.* 1987). This has been confirmed in the cat by several other groups since (Pearson and Collins 1993; Guertin *et al.* 1995; Angel *et al.* 1996), though the evidence for this switch in humans is equivocal (Dietz 1998; Stephens and Yang 1999; Capaday 2000; Misiaszek *et al.* 2000; Pang and Yang 2000). MN excitation causes muscles to generate more force, further increasing Ib firing, which in turn would produce yet more excitation, i.e. positive feedback. Would this not result in an explosive increase to

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maximal force? The surprising answer is that because the response of muscles to increments in activation declines as the muscle gets shorter, an equilibrium length is reached at which the force-related excitation does not cause further muscle shortening. Thus in Fig. 5, for three different levels of positive force-feedback gain the Amuscle@ resisted stretching with a much higher stiffness than could be achieved with spindle Ia feedback. Not only is this scheme remarkably stable, but as the large increase in stiffness in this example shows, positive force feedback is potentially more effective in load compensation than spindle-mediated feedback. Evolution was evidently not constrained by conventional control systems theory! Since the publication of the analytical work in 1997, positive force feedback has been implemented in a cockroach robot with muscle-like actuators, and has been found to be effective and useful in load compensation (Nelson and Quinn 1999).

Thus stretch reflexes should be seen as adding a controlled level of stiffness to the underlying intrinsic muscle stiffness. Mammals, including humans, with large-fibre sensory loss and absent tendon jerks, though severely incapacitated and uncoordinated, can regain full weight-support and can walk if supported laterally. It has been confirmed in such experiments that there has been no recovery in sensory input (Allum *et al.* 1998). This shows that the intrinsic stiffness of muscles activated through non-reflexive pathways can generate enough force to bear the weight of the body and propel it forward. We will support this position with further modelling below.

If stretch reflexes are not the primary mechanism of load compensation in locomotion, does this mean that sensory input from the limbs only plays a minor role in locomotor control? Again we will argue that in general the answer is no: sensory input does play a vital role, but through mechanisms other than the stretch reflex.

Flexion and extension responses, Areflex stepping@ and Areflex walking.@

As mentioned above, the neural basis of flexion and extension reflexes was first studied in spinal and decerebrate dogs and cats in the late 19th century. These reflexes were elicited by aversive stimuli applied to the skin or cutaneous nerves of the ipsilateral or contralateral limb. The movement synergies thus evoked were similar, though not identical, to those in the flexion and extension phases of locomotion. AReflex stepping@ was studied in decapitated dogs by Freusberg (Freusberg 1874) and then in decerebrate and spinal cats by Sherrington and Brown (Sherrington 1910; Brown 1911). An hour or so after spinalization, locomotor movements could be triggered by lifting the animal and dropping one hindlimb from a semi-flexed starting position. An important observation of both Sherrington and Brown was that position and loading of the limbs were crucial in triggering and maintaining reflex stepping. If the downward motion of the hindlimb were again stopped in semi-flexion, stepping movements ceased in this limb as well as in the other, free limb, as well. These results have been verified in numerous experiments since (Rossignol 1996; Orlovsky *et al.* 1999).

Reflex stepping could also be elicited by kneading, squeezing or continuous electrical stimulation of the skin of the tail, perineum, back, neck or pinna. It could also be elicited by continuous electrical stimulation applied to the transected spinal cord at cervical level. Sherrington struggled to explain how these remote, continuous stimuli applied to Aexteroceptive@ sensory receptors interacted with phasic sensory signals from the limb (which he argued were mainly proprioceptive) to produce cyclical movement. He suggested a scheme whereby the remote stimuli evoked a Aprimary reflex@ (causing either extension or flexion, depending on the site of stimulation), which evoked proprioceptive stimuli in the moving limb. These elicited a secondary reflex which alternated with or Ainterrupted@ the primary reflex to produce cyclical activity. One flaw in this argument was preliminary evidence that deafferentation did not necessarily abolish the rhythm. Sherrington wondered whether the central rebound effect described a few years earlier by Magnus and von Uexkuell (AUmkehr,@) could be contributing. A year later Sherrington presented a paper to the Royal Society by his student Graham Brown (Brown 1911), confirming the

deafferentation results in decerebrated and spinalized cats. After a low thoracic transection, the deafferented lumbosacral spinal cord could still generate rhythmical movements in an isolated pair of hindlimb muscles in the absence of descending input or sensory input from either hind limb. Graham Brown dubbed the underlying mechanism the "intrinsic factor", a term that has now been superceded by the more specific term ACentral Pattern Generator (CPG)@ (Grillner and Zangger 1975).

CENTRAL PATTERN GENERATORS AND SENSORY FEEDBACK

Cyclical motor patterns generated without sensory input. Literally hundreds of studies in which sensory input has been reduced or abolished by deafferentation have since demonstrated beyond doubt that isolated neuronal networks in the CNS can generate the basic rhythmical motor patterns involved not only in walking but also in the activities of breathing, chewing, swimming, flying, scratching, paw-shaking and autonomic functions such as micturition and sexual Areflexes@ (Grillner 1975; Prochazka 1996b; Kiehn *et al.* 1998; Orlovsky *et al.* 1999).

There has been much discussion about the ability of CPGs, in the absence of sensory input, to generate complex coordinated patterns of muscle activity such as those required for overground locomotion. After deafferentation in the cat many subtle features of normal activation sequences can still be seen (e.g. the small burst of activity in knee flexor muscles at the end of the swing phase in cat locomotion (Grillner and Zangger 1975). However the locomotor rhythm is generally more labile (Grillner and Zangger 1975; Wetzel *et al.* 1976; Goldberger and Murray 1980; Grillner and Zangger 1984; Giuliani and Smith 1987; Koshland and Smith 1989) and above all, there is an inability to compensate for the changes in loading or terrain (Allum *et al.* 1998).

This latter defect is more serious than it may sound. If information on joint angles, body posture, loading and displacement of the extremities are all unavailable to the central controller, the amplitude and timing of the cyclical motor output can only be set to some default level and cannot be matched to the varying requirements. To quote Brown (1911):

> *A purely central mechanism of progression ungraded by proprioceptive stimuli would clearly be inefficient in determining the passage of an animal through an uneven environment. Across a plain of perfect evenness the central mechanism of itself might drive an animal with precision. Or it might be efficient for instance in the case of an elephant charging over ground of moderate unevenness But it alone would make impossible the fine stalking of a cat over rough ground. In such a case each step may be somewhat different to all others, and each must be graded to its conditions if the whole progression of the animal is to be efficient The hind limb which at one time is somewhat more extended in its posture as it is in contact with the ground, in another step may be more flexed. But the forward thrust it gives as its contribution to the passage of the animal must be of a comparatively uniform degree in each consecutive step. It may only be so if it is graded by the posture of the limb when in contact with the ground, and by the duration of its contact with the ground. This grading can only be brought about by peripheral stimuli. Of these we must regard the proprioceptive stimuli from the muscles themselves as the most important, and the part which they play is essentially the regulative -- not the causative.*

The loss of proprioceptive input in humans is more devastating than in quadrupeds: without vision and/or external supports, people with large-fibre sensory loss find it difficult to take more than a step or two without stumbling and falling, even on a flat floor (Lajoie *et al.* 1996). Though evidence has been adduced for the existence of a locomotor CPG in the human lumbosacral spinal cord in people with spinal cord

injury, the types of rhythmical movement observed were weak and inadequate for weight-bearing locomotion (Calancie *et al.* 1994; Dimitrijevic *et al.* 1998) and because the legs were suspended and sensory input was intact, it is possible that they could have resulted from reciprocating stretch reflexes. In a recent study in normal subjects, steady vibration of the legs resulted in cyclical air-stepping (Gurfinkel *et al.* 1998). It was suggested that the steady sensory input activated Athe central structures responsible for stepping generation.@ However, vibration of phasically contracting muscles is known to produce phasic firing of muscle spindles (Matthews and Watson 1981; Prochazka and Trend 1988), so the development of pendular reciprocating motion in the suspended legs cannot be ruled out here either.

In certain cases, it has been claimed that accurate, goal-directed movements in a normal animal can only be attributed to central programming, because the moment-to-moment participation of sensory input can be ruled out. For example, in cockroaches, it has been shown that sensory feedback in fast walking is too delayed to have a reflex effect within a given cycle, the duration of which is 40 ms or less (Zill 1985; Delcomyn 1991a; Delcomyn 1991b). In the most rapid ballistic movements in humans, sensory feedback is also too slow to modify the movements once they are underway (Desmedt and Godaux 1979).

Does this mean that in very rapid movements sensory input is unimportant? If a very rapid movement is considered in isolation it is true that the sensory input related *to that movement* may come too late to contribute to its control. But that movement, like all others, was preceded by sensory input that provided the CNS with information on the overall biomechanical state of the limbs and the rest of the body in the immediately preceding period. In locusts it has been shown that sensory input influences the wing-beat cycle <u>following</u> the one in which it was elicited (Wolf and Pearson 1988). Similarly, it has been suggested that in the example of cockroach locomotion given above, the sensory input from one step cycle provides postural information for the control of *ensuing* step cycles (Prochazka 1985). This could either be viewed as delayed feedback or as prediction, depending on the way the signals are handled. We would argue that in the generation of ballistic movements that accurately reach their target, the CNS has taken into account the biomechanical initial conditions and the relative position of the target, which is only possible with prior sensory input. The only movements that might be controlled entirely open-loop (without any significant involvement of sensory input) would be escape behaviours in which the animal propels itself forward as rapidly as possible without regard for stability or the likelihood of a fall.

Interaction between CPGs and sensory feedback.

In the mid-1960s it was found that cats decerebrated rostral to the superior colliculus were more likely to walk than those with a mid-collicular decerebration, particularly with steady electrical stimulation of a region that has since become known as the midbrain locomotor region (MLR) (Shik *et al.* 1966; Shik *et al.* 1969). This allowed the spinal mechanisms of locomotion to be studied with microelectrodes, pharmacological interventions and lesioning experiments. Some of the early observations of Sherrington, Brown and their predecessors on the effect of limb position on locomotor-like reactions were soon confirmed and extended to stable treadmill locomotion. In one such experiment, both hindlimbs were de-efferented, leaving sensory input to the spinal cord intact (Orlovsky and Feldman 1972). MLR-evoked locomotor rhythms recorded electrically in S1 ventral root filaments were then found to be entrained by cyclical imposed movements of one of the limbs. The rhythm could be halted by moving the limb into extreme flexion or extension. After partial deafferentation, the rhythm could also be halted by arresting locomotor movements of one of the limbs in mid-cycle, just as Sherrington had described. In a more sophisticated version of this experiment a few years later, it was found that the hindlimbs of chronic spinal kittens walking on a split-belt treadmill could adapt their cadence to each belt separately, i.e. the sensory input to each limb was entraining that limb individually (Forssberg *et al.* 1980).

Entrainment and override of the locomotor rhythm by sensory input from a limb has been confirmed and studied in detail in dozens of experiments since the early 1970s in the high decerebrate MLR

cat, in chronic spinal cats and in acute spinal cats treated with clonidine (rev: (Rossignol 1996)). By the mid-1980s, two separate sensory variables had been identified as being capable of entraining or overriding the locomotor rhythm: hip position (Andersson and Grillner 1983; Kriellaars *et al.* 1994) and extensor force (Duysens and Pearson 1980). In a recent review of these findings, it was realised that the same two variables had been implicated in triggering the switch from stance to swing in species as widely separated as cats, crayfish and locusts (Prochazka 1996b). In simple terms the sensory rule that seemed to prevail in all these animals could be stated as follows: IF the leg has become very extended *and* extensor force has become very low, THEN initiate swing. This same rule had been quite independently Adiscovered@ in the technological control of above-knee prostheses as well as in the control of functional electrical stimulation in human gait.

It is clear from all of the above that the basic locomotor pattern can be generated by the CNS without sensory input, but sensory input can promote, delay, or even block the switching between stance and swing phases and thereby completely determine step cycle frequency. The question of the relative importance that should be placed on central versus sensory control has been quite bothersome to neurophysiologists over the years, some taking the view that sensory input is only important when the CPG-generated pattern fails to produce the required movements (the centralist view), while others suggest that the CPG rhythm is a default pattern that is only manifested when sensory input is withdrawn (the peripheralist view).

The paradox can be partly understood by considering the family of electronic circuits called multivibrators (also known as flip-flops). These consist of a pair of switchable elements such as transistors, interconnected such that when one is active, it suppresses the other by applying an Aoff@ signal to its gate. In a free-running (Aastable@) flip-flop, the Aoff@ signal discharges through a capacitor from the moment it is applied. Consequently, halfway through the cycle the suppressed partner is Areleased,@ turns Aon@ and becomes the Aoppressor@ for the next half-cycle. The frequency can be modulated by controlling the rate of discharge or decay of the Aoff@ signals by varying passive circuit components or by applying external inputs to the gates. These can override the oscillation completely and hold the circuit in one or other half-cycle indefinitely. Thus although the core circuit can generate a default rhythm, the additional circuit components promote, delay, or block phase switching and are therefore integral parts of the system as a whole. The flip-flop analogy was recognised in the late 1970s (Miller and Scott 1977) and forms the basis of some CPG models to this day (Orlovsky *et al.* 1999).

The usual compromise position between centralists and peripheralists is that the CPG generates the basic locomotor pattern, but this is Asculpted@ or Afine-tuned@ by sensory input. However, given the fact that sensory input can entrain and halt the rhythm, and given the extreme disability in human bipedal gait caused by even partial deafferentation (Lajoie *et al.* 1996), Asculpting@ and Afine-tuning@ seem to understate the case.

Human Locomotion

A puzzle remains about the role of local reflexes mediated by muscle receptors in *human* locomotion. As already mentioned, large-fibre deafferentation (which can eliminate input from muscle spindle primary and tendon organ afferents from the legs and trunk) can have a devastating effect on human locomotion (Lajoie *et al.* 1996). Yet when these receptors are excited by test mechanical stimuli applied to muscles during gait, the effects are disappointingly small. For example, bursts of powerful vibration of the lower leg muscles, which most likely entrain the firing of many spindle group Ia spindle afferents and probably numerous group Ib afferents too, have virtually no effect on the trajectory of locomotor movements (Ivanenko *et al.* 2000a; Ivanenko *et al.* 2000b). Interestingly, tonic vibration of the upper leg muscles or the subject's neck did have a generalized effect on body tilt and speed of locomotion.

Short-latency EMG responses can certainly be elicited during gait by electrical stimulation of the

large afferents (Garrett *et al.* 1984; Capaday and Stein 1986), by tapping on tendons (Llewellyn *et al.* 1987) or by applying rapid joint rotations via pneumatic orthoses (Sinkjaer *et al.* 1996). But the muscle stretches have to be faster than those occurring in unimpeded locomotion for the EMG responses to be significantly larger than the prevailing levels. Ischaemic block of large afferents had very little effect on short-latency soleus EMG unloading responses elicited by the pneumatic orthosis, though longer-latency responses persisted (Sinkjaer *et al.* 2000). This led to the suggestion that presynaptic inhibition effectively eliminates any significant contribution of Ia signals to homonymous muscle activation during normal locomotion, and it is only in very rapid perturbations that Ia-mediated activation of MNs Abreaks through.@ A significant contribution to EMG activation (up to 50%) was claimed for the longer-latency pathways, though these reactions were delayed enough and of long enough duration to involve more complex central processing rather than simple segmental loops.
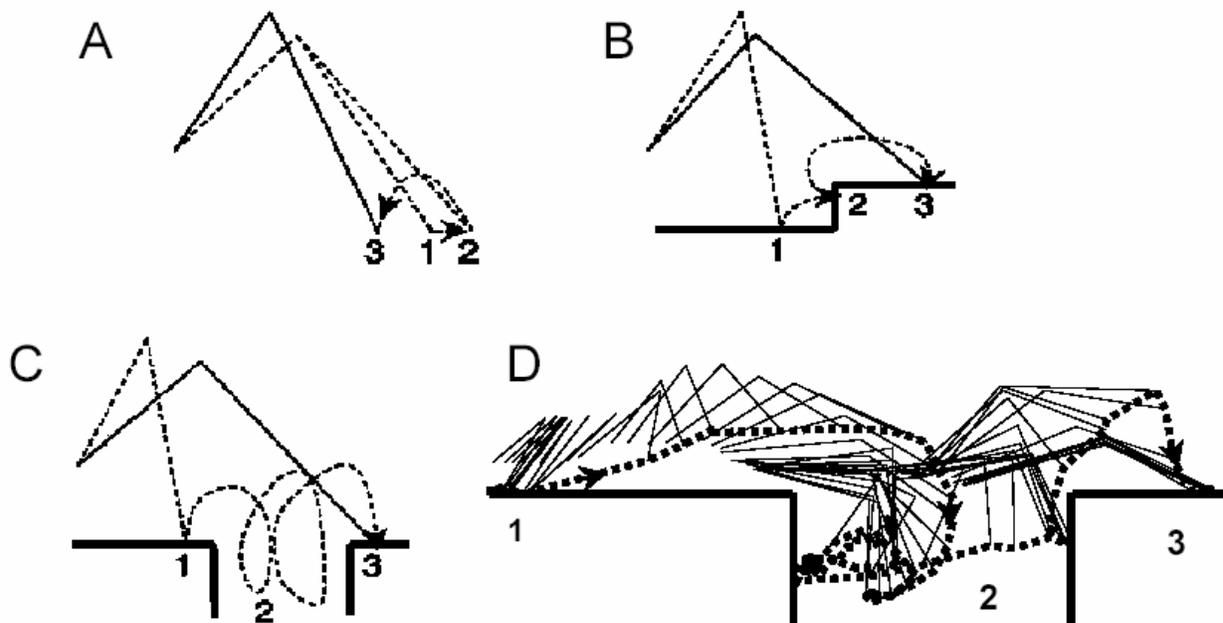

Figure 6. Kinematics of leg movement in a hexapod robot (A,B,C) and a locust (D). A) perturbed stance: imposed movement of the foot from 1 to 2 evokes a corrective reaction with placement at 3. B) tripping reaction: foot contacts obstacle at 2, is lifted and placed beyond the obstacle at 3. C) Afoot-in-hole:@ foot enters hole, which triggers searching movements at 2 and eventually a placing reaction at 3. D) locust Afoot-in-hole. Stick figures traced from frames of a movie. Leading limb enters a hole at 2, searches, and is eventually placed at 3. (A, B and C reproduced with permission from (Quinn and Ritzmann 1998).

Robots.

Recently there have been two interesting developments in technology that may provide insight into these issues. The first is the design of walking robots. Some of the most advanced work in this area is of a corporate nature (e.g. the humanoid robots developed by the Honda company), and the information available on the control strategies used tends to be sketchy. Nonetheless, it is quite clear that the most versatile robots, including the extraordinary Honda Asimo P4, rely heavily on sensory input to generate locomotion over uneven terrain. The robot designers carefully reviewed the essential aspects of biological

locomotor control in insects, quadruped mammals and humans and then implemented the most promising aspects in their machines. The instructive thing here is to consider which control strategies turned out to be effective. Two hexapod robots, a Astick insect@ and a Acockroach@ developed in Cleveland provide useful information in this regard (Espenschied *et al.* 1996; Nelson and Quinn 1999). In both cases, the robots have six two- or three-segment limbs. Each joint has a passive spring for compliance, an actuator and a position sensor. The actuator is under proportional position feedback control of variable gain, providing a controllable stiffness that adds to the passive Ainherent@ spring stiffness. The stiffness properties of each joint therefore mimic the intrinsic properties of biological muscles under stretch reflex control. Locomotion is achieved by a mixture of processes local to joints and legs, and two governing (Aglobal@) algorithms. The local processes include the active stiffness control just mentioned, as well as IF-THEN control rules based on end-point position for stance-swing and swing-stance transitions, and special rules for adaptive responses to tripping (stumble reaction) and Afoot-in-hole@ (Gorassini *et al.* 1994). Fig. 6 shows the reactions of a leg of the hexapod robot in three situations, perturbed stance, placing reaction and Afoot-in-hole@. For comparison, we have included a panel showing the searching movements of a locust in which the leading limb enters a hole (at 2), searches, and is eventually placed (at 3).

Regarding the two Aglobal@ algorithms, one adjusts leg trajectories to distribute force equally among weight-bearing legs, and to match leg Alengths@ according to the terrain (i.e. to keep the body horizontal in the face of slopes and other unevenness of ground support). Interestingly, leg length (the distance from the end of the paw to the hip joint) has recently been identified as an emergent variable that accounts best for the firing behaviour of dorsal spinocerebellar tract neurons in the cat, even when individual joints are constrained (Bosco and Poppele 2001). These authors suggest that the spinocerebellar system may be viewed as the end-point of processing of proprioceptive sensory information in the spinal cord. The other global algorithm quoted by Aencourages stance legs to lift into their swing phases in a coordinated manner, swing forward, and transition to stance@ (Quinn and Ritzmann 1998).

Like the hexapod robots, the Honda robot also utilizes local active and passive joint compliances, IF-THEN phase transitions, special adaptive reactions similar to the ones just described and a novel global strategy of setting a moving target of ground reaction force as the command for forward or backward locomotion. The actual ground reaction force is continually computed from the sensor signals. The difference between this vector and the target vector is referred to as the Afalling moment.@ This falling moment is minimized by Areflexes@ to the joint actuators, which are presumably synergistically coupled. Notice that in neither of the above robots is it easy to extract the notion of an autonomous CPG from the various global algorithms. Rather, the central controllers respond to external requirements by issuing general commands to move in particular directions (e.g. by proposing a virtual trajectory for the ground reaction force), selecting sensory rule bases appropriate to the task and context and evaluating performance for predictive adjustments. Hazard rules are also computed (e.g. the Honda robot resists lateral imposed forces by stiffness control, but when sway exceeds the imbalance point, it yields and takes a step in the direction of the imposed force).

Virtual animals.

The other useful advance in technology is the development of powerful biomechanical modelling tools suitable for personal computers. These programs allow one to design quite complex models of Avirtual animals,@ with limbs, joints and muscles whose intrinsic properties can be approximated to those of real animals. Muscle activation profiles based on EMG patterns recorded during locomotion can be used to activate the muscles. The ensuing locomotor performance, which is displayed as a slow-motion movie as the computations proceed, provides similar types of insight to the mechanical robots above, but because changes can be made easily and tested quickly, many different sensorimotor rules and parametric variations can be explored.
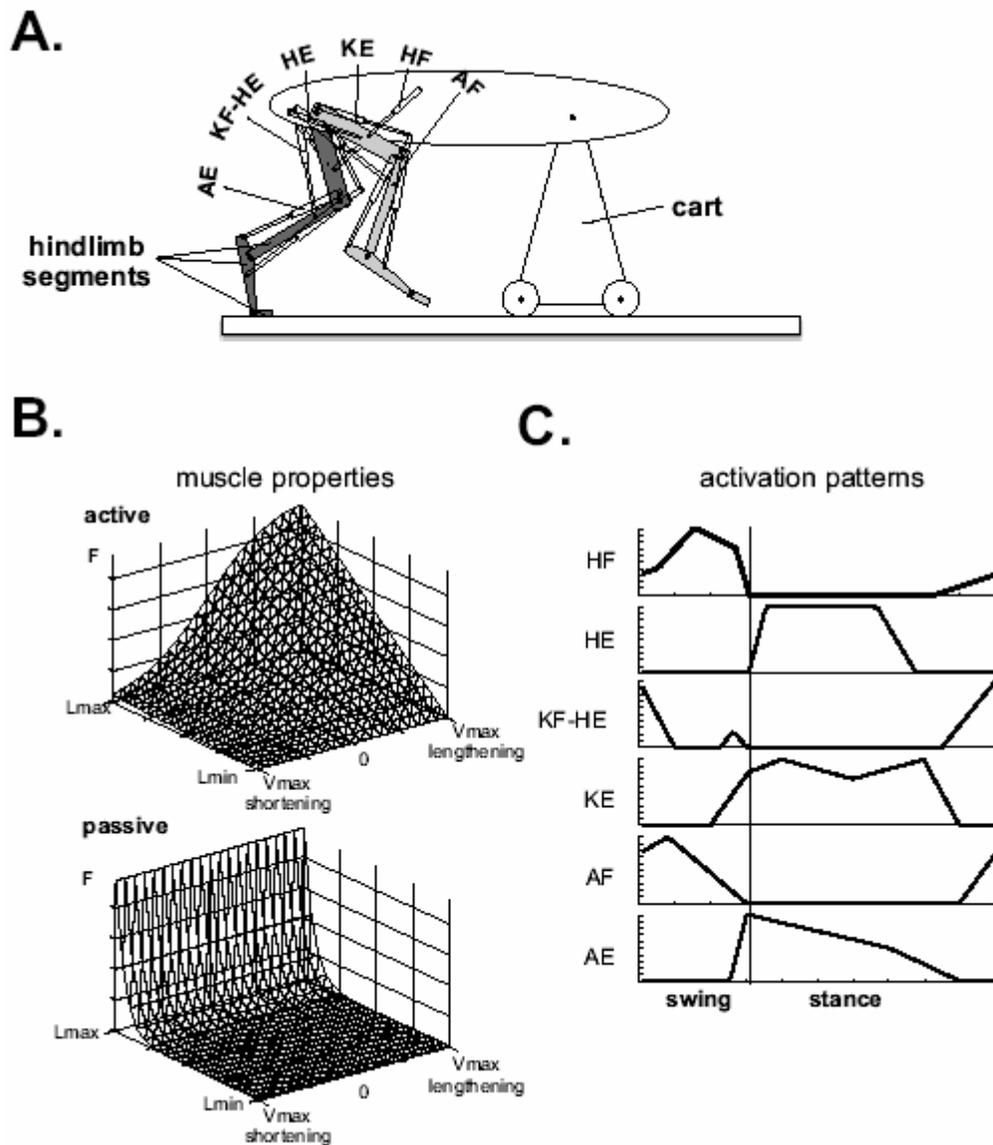
Figure 7. Biomechanical locomotor model based loosely on the cat hindlimb. A) Muscle groups are represented by actuators HF (hip flexors), HE (hip extensors), KF (knee flexors), KE (knee extensors), AF (ankle flexors), AE (ankle extensors). B) Hill-based force-velocity relationship and passive and active force-length curves used in each actuator. C) Step-cycle activation profiles of the actuators.

Fig. 7 shows a biomechanical locomotor model we have been working on for some time. The model is based on the cat hindquarters but it is intentionally not an accurate replica. Many muscles are absent. The origins and insertions of the muscles that are represented do not correspond exactly to those in real cats. The model uses a Hill-based force-velocity relationship and monotonic passive and active force-length curves (Fig. 7B), as our recent results indicated that the static isometric force-length curve with its descending limb is invalid in continuous movements (Gillard *et al.* 2000). Short-range stiffness properties are neglected. The purpose of the model is to test some general hypotheses, not to provide a definitive analysis of gait in any given species.

Once we had "fine-tuned" the "EMG" activation patterns of its various actuators (Fig. 7C), which were based on EMG profiles of cat locomotion (Prochazka *et al.* 1989)), it produced stable locomotion on a flat surface indefinitely, in spite of being "deafferented" (Fig. 8A). Each step was slightly different from the last, which showed that the intrinsic stiffnesses of the muscles provided enough flexibility to make continuous adjustments to compensate for small variations in body speed, height and the relative positions of the limb segments. The deafferented virtual cat could also adapt to modest uphill slopes (Fig. 8A). As mentioned above intrinsic muscle stiffness is equivalent to a length feedback system which resists deviations from some set equilibrium length. Thus locomotion in a deafferented animal is not entirely open-loop.

The stability of the deafferented model was unexpected, because we were aware of the difficulty Gerritsen at al. (Gerritsen *et al.* 1998) had experienced in generating more than three or four steps in a similar model of bipedal human locomotion, though other groups have been able to overcome this by optimizing the EMG patterns with inverse dynamics or neural network learning techniques (Taga *et al.* 1991; Taga 1995a; Taga 1995b; Yamazaki *et al.* 1996; Taga 1998; Neptune *et al.* 2001; Ogihara and Yamazaki 2001). Of course the cart that supports the front of our virtual cat greatly simplifies the problem of maintaining a stable upright posture. It is also a simplification of quadrupedal gait, which requires forelimb-hindlimb coupling for stability. It is very interesting that (Gerritsen and Nagano 1999) recently obtained a far more stable performance when they incorporate some sensory feedback into their bipedal model.

The deafferented virtual cat immediately gets into trouble when the read-out rate of its EMG patterns is increased or decreased, producing a higher or lower gait velocity (Fig. 8b). It does not help just to add stretch reflexes, because these merely augment the muscle intrinsic stiffnesses without affecting step cycle phase-switching. On the other hand, If-Then rules are useful in coping with variations of this type. In Fig. 8b, the If-Then rules governing the transitions from stance to swing and back (see below) allowed the model to adapt to the increased EMG read-out rate and hence increased velocity, though it did not fare so well with the lowered read-out rate.

For the challenging situation of an obstacle impeding the forward swing of one leg, these simple rules were not enough to prevent a fall either. In this case, a separate "hazard" rule was needed, which was invoked when the front of the foot contacted the obstacle (see "tripping reaction" rule below). This initiated an EMG sequence similar to that previously recorded in the tripping reaction of normal cats (Wand *et al.* 1980). The result was a response that looked very true to life (Fig. 8C).

no IF-THEN rules

A.

level

left

right

upward slope

left

right

1 m

B.

no IF-THEN rules   **with IF-THEN rules**   △ stance-swing rule triggered
▽ swing-stance rule triggered

high velocity

left

right

1 m

low velocity

left

right

C.   **tripping (stumble-corrective) reaction**

no IF-THEN rules   **with IF-THEN rules**   ♠ tripping rule triggered
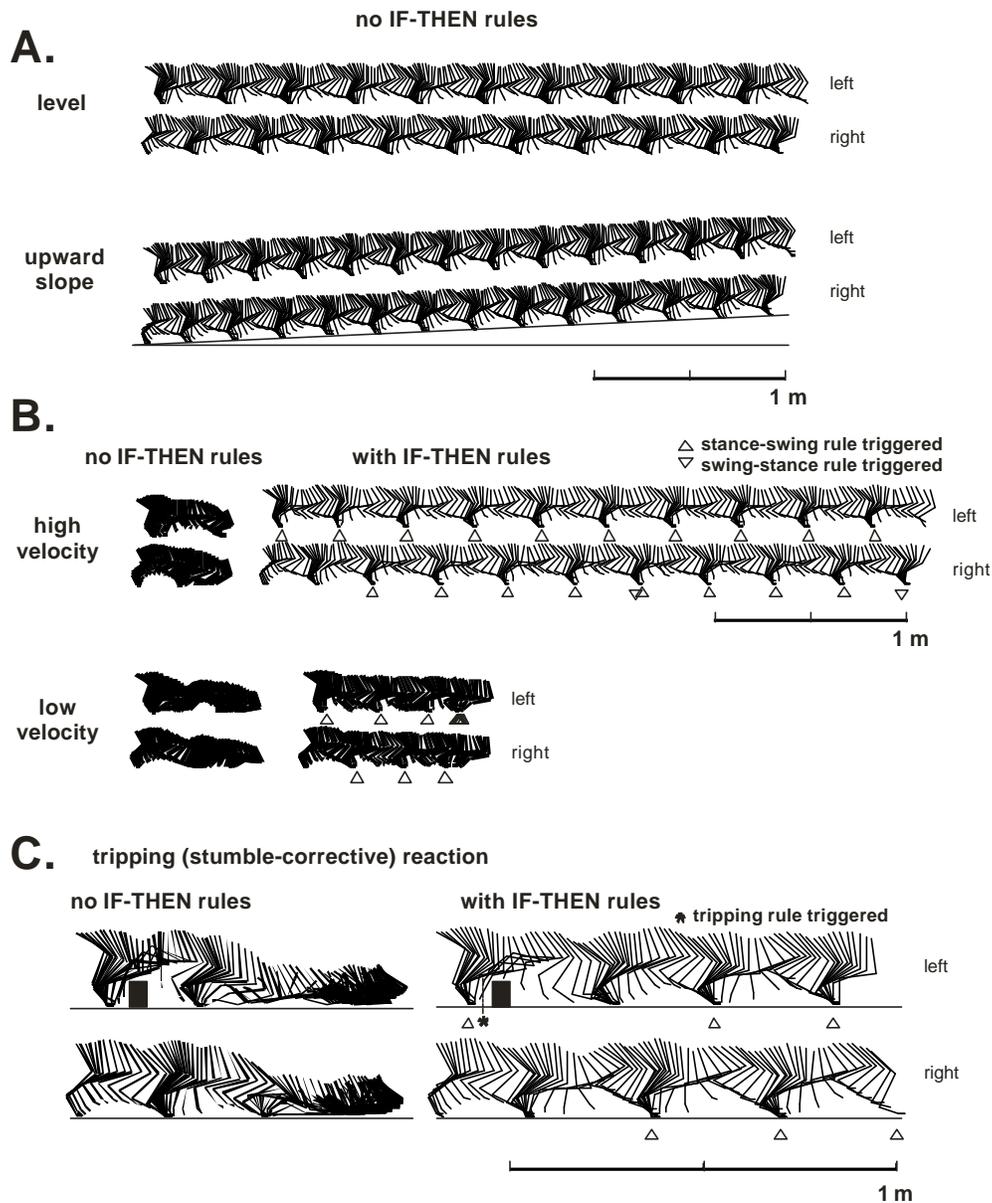
left

right

1 m

Figure 8. Kinematic analysis of behaviour of the model of Fig. 7 in different situations. A) locomotion of the model without feedback rules. The intrinsic stiffnesses of the muscles sufficed to compensate for kinematic and kinetic variations in locomotion over flat surface and up a small slope.   B) Gait velocity increased (top) or decreased (bottom) by ~20%. Locomotion failed in the Ade-afferented case, but improved with If-Then rules (triggering of stance-swing transitions marked with upward triangles; note that contralateral leg was phase-locked to ipsilateral leg, so did not Afire@ its rules except in one case of a swing-to-stance transition marked by downward triangle). C) obstacle impeded forward swing of one leg. The de-afferented model (left) failed to compensate and dragged its foot over obstacle, causing a subsequent fall. Inclusion of a Atripping rule@ (triggered at *) resulted in good reactive compensation with ensuing stable steps.

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If-then rules governing phase switching and the selection of A hazard@ responses

The control of forces in muscles within the flexion or extension phases of locomotion is a smoothly graded process involving continuous proportional feedback, whereas the switching between these phases is usually discontinuous and abrupt. Control systems that switch between well defined states are known as finite-state systems and switching is triggered when certain sensory conditions are met (e.g. IF swing AND hip angle small (flexed) AND extensor force low THEN terminate flexion, initiate extension) (Tomovic and MCGHEE 1966; Tomovic *et al.* 1990). Note that A small@ and A low@ are imprecise terms. This is intentional: the nervous system most likely uses sensory inputs in a probabilistic way rather than setting precise threshold values and requiring each threshold to be met before firing the rule.

A control systems analogy for probabilistic finite-state control is A fuzzy logic,@ in which sensory variables are accorded weighting (A membership@) functions, the sum of the weighted sensory signals determining the motor outcomes. If-then rules are crafted to suit specific behavioural states. More than one rule may be A active@ in a behaviour or a part of a behaviour (e.g. in the stance phase of gait, the stance-swing rule and the foot-in-hole@ rule are both active: see below). The system constantly monitors the A firing strength@ of the rules and retires behaviours and/or recruits new behaviours according to pre-determined thresholds of the firing strengths. A higher level "arbitration mechanism" may decide which behaviours are appropriate for the current global state (Prochazka 1996a).

In such systems, each input effectively A votes@ for a range of possible motor outcomes according to the currently active If-Then rules, the sum of the votes determining what actually happens (Chen *et al.* 1997; Jacobs 1997; Davoodi and Andrews 1999; Jonic *et al.* 1999). Bässler has suggested a similar process in the control of locomotion in stick insects and used the term the A Parliamentary Principle@ as a metaphor for the voting mechanism (Bassler 1993). Fuzzy logic has also been discussed in relation to the changes that occur in forward, sideways and backward treadmill walking in infants (Pang and Yang 2000).

On the understanding that If-Then rules may be used in this probabilistic way, let us now consider some of the rules that might underlie phase switching in biological locomotor control.

Stance phase (forward step)
Rule 1 (stance-swing transition): <u>IF</u> stance <u>AND</u> extensor force low <u>AND</u> hip angle large
      (extended) <u>AND</u> contralateral limb supported, <u>THEN</u> switch to swing.
Rule 2 (A foot-in-hole@ reaction): <u>IF</u> mid-stance (hip angle medium) <u>AND</u> no ground contact <u>AND</u>
      contralateral limb supported, <u>THEN</u> switch to placing reaction.

Swing phase (forward step)
Rule 1 (swing-stance transitions): <u>IF</u> swing <u>AND</u> hip angle small AND knee angle large (knee
      extended) <u>THEN</u> switch to stance.
Rule 2 (A tripping@ reaction): <u>IF</u> swing <u>AND</u> skin stimulus to front of foot <u>THEN</u> switch to placing
      reaction; <u>IF</u> stance <u>AND</u> skin stimulus to front of foot <u>THEN</u> prolong stance.

Stance phase, backward step
Rule 1 (stance-swing transition): <u>IF</u> backward gait <u>AND</u> extensor force low <u>AND</u> hip flexed <u>AND</u>
      contralateral limb supported <u>THEN</u> initiate backward swing.
Swing phase, backward step
Rule 2 (swing-stance transition): <u>IF</u> backward gait <u>AND</u> hip angle large <u>THEN</u> initiate stance

The following rule describes the way the Honda robot invokes the A hopping reaction@ of Magnus (Magnus 1924) when it is pushed in the face:

Static Postural Rule 1 (hopping reaction): <u>IF</u> falling moment is small <u>AND</u> gravity vector is within support surface, activate extensors; IF falling moment is large <u>AND</u> gravity vector is outside support surface, take a step back.

Notes to the rules.

a) The above list of rules describes sensorimotor interactions that occur in locomotion in many animals and that are explicitly programmed in robots, prostheses and bio-mimetic models. Identifying the neural control systems responsible is no trivial matter, just as it remains no trivial matter to identify Brown=s Aintrinsic factor@ (the locomotor CPG) after 100 years of research.

b) Not only is the list far from complete, but the variables chosen are not necessarily the *only* ones that would Awork,@ nor the ones that might be used in biological systems. For example, a possible alternative to Ahip is extended@ is Aleg length is long@ (Bosco and Poppele 2000; Bosco *et al.* 2000; Bosco and Poppele 2001). Likewise, the variables in the postural rule must clearly be derived from several sets of sensors in different parts of the body.

c) As gait speed increases, it is important to phase-advance the switching back and forth between stance and swing to compensate for the delays due to inertia and muscle properties. Rather than invoke more rules using angular velocities, if we assume that muscle spindle signals are used in place of joint angles, their velocity-dependence would automatically provide this phase advance.

PREDICTION AND ADAPTATION

It goes without saying that when animals move they take into account global information on body posture, the environment and the context of the task from visual, auditory and mechanosensory inputs. The greater the motor requirements to maintain stability (e.g. bipedal versus quadrupedal gait), the more crucial are these predictive inputs. The controlling processes are clearly extremely complex, but a start has been made in recording the kinematic and neural correlates of predictive and adaptive responses, e.g.: (Drew *et al.* 1996; McFadyen *et al.* 1999; Rho *et al.* 1999). Some basic concepts regarding prediction and adaptation have been proposed over the years:

1. AEinstellung@ (Aset@). Animals prepare themselves in advance either to initiate movements or to react to impending perturbations (James 1890; Ach 1905; Watt 1905; Gibson 1941). Mental set, orienting, postural set, Bereitschaft (readiness), reflex set and fusimotor set are just some examples (review: Prochazka 1989).

2. ADegrees of Freedom.@ The control of multi-segmented limbs is simplified when the number of degrees of freedom is reduced, either by co-contracting antagonist muscles, or by coordinating the activation of synergists (Bernstein 1967).

3. AEfference copy,@ AInternal models.@ In the 1950s it was posited that the cerebral cortex generates a copy of motor commands from which re-afferent signals are subtracted (von Holst and Mittelstaedt 1950; von Holst 1954). Corrections would only be required if there were differences between the predicted and actual sensory inputs. The same idea was developed independently to overcome delays in industrial control processes (Smith 1959) and it has been rephrased and refined many times since, the most recent example being AInternal Models.@ (Blakemore *et al.* 1998; Bhushan and Shadmehr 1999; Vetter and Wolpert 2000; Wolpert and Ghahramani 2000).

4. **A**Fixed action patterns,**@** Motor Programs,**@ A**Preprogrammed movements,**@ A**Movement Primitives.**@**
Spencer proposed that reflexes were the *atoms of the psyche*, the psyche was an assemblage of reflexes and **A**instincts**@** were reflex assemblies consolidated by repetition and transmitted in an hereditary manner (Spencer 1855) . The idea of stored motor programs or subroutines has been reiterated many times since (review: Prochazka *et al.* 2000). The spinal central pattern generator is essentially an example of this idea. The tripping reaction may be another example.

The cerebellum is thought to be key in nearly all the above operations, in particular generating motor programs, modulating reflex gains and scaling the size of movement sequences (Bloedel and Bracha 1995; Bloedel and Bracha 1998; Mummel *et al.* 1998; Serrien and Wiesendanger 1999). The recent conclusions of Bosco and Poppele on the signaling of derived variables by spinocerebellar tract neurons is therefore of great interest (Bosco and Poppele 2000; Bosco *et al.* 2000; Bosco and Poppele 2001). It has also been suggested that motor cortical activity may be viewed as a summing junction for feedforward signals providing visuospatial information about the environment and feedback signals providing information on the state of the interneuronal pattern generating networks in the spinal cord (Drew *et al.* 1996). In human locomotion, subjects plan foot placement one or two steps ahead and avoid obstacles by anticipatory high-stepping (Patla and Vickers 1997; Patla *et al.* 1999). It is interesting that the reaction of many animals to unpredictable terrain is simply to **A**high-step,**@** a gait modification that can be elicited by injecting a droplet of Lidocaine into the interpositus nucleus of the cerebellum (Gorassini *et al.* 1993).

One of the important conclusions drawn from the modelling work presented above is that the locomotor CPG, even when aided by segmental reflexes and the simplest of the If-Then rules, has a very limited ability to respond to variations in speed, slope, and uneven terrain. The detection of **A**hazard states,**@** and the advance scaling of step cycles to deal with them is clearly a vital predictive and adaptive mechanism (Drew 1991).

SUMMARY POINTS

a) The spinal cord of many vertebrates, possibly including humans, can autonomously generate detailed patterns of muscle activity which form the substrate of locomotion.

b) Deafferentation studies and modelling show that these patterns alone would be of little use in the real world. They are continuously modulated, switched and overridden by control mechanisms that take into account many sensory inputs.

c) If-Then rules can be identified, which describe some of the simpler phase-switching operations as well as some of the higher-level responses to **A**hazards.**@**

d) Predictive and adaptive control, operating though supraspinal centers, are indispensable for locomotion in daily life.

APPENDIX

Stretch Reflex Model

Appendix Figure 1 shows a Matlab Simulink model originally developed to test the effect of excitatory Ib input to homonymous and heteronymous muscles (positive force feedback). In this slightly modified version, we have added a feedback pathway and product element marked by the arrows, to take into account the fact that transmission from group Ia afferents to MNs scales with the number of MNs recruited. The digital version of this model can be downloaded from the authors' website, or obtained upon request.
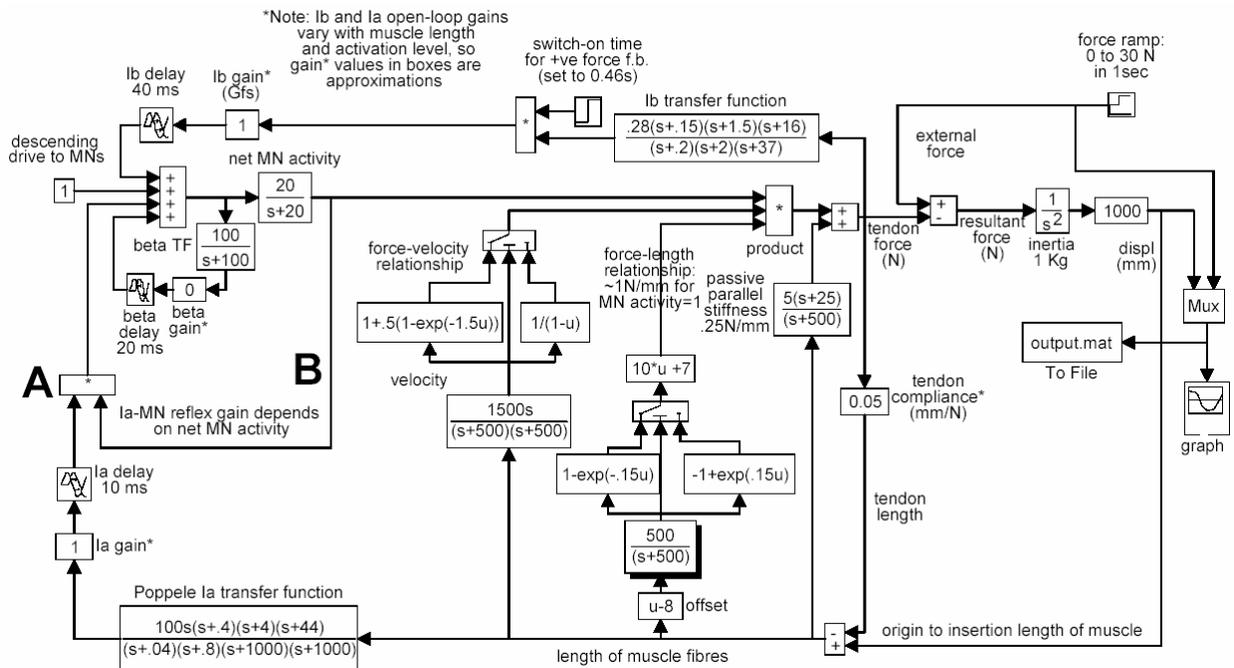
Appendix Figure 1. Matlab Simulink model of stretch reflex used to generate Fig. 5, adapted from (Prochazka *et al.* 1997a). In this slightly modified version of the original model, the feedback pathway and product element marked AA@ and AB@ were added, to take into account the scaling of transmission from group Ia afferents to MNs with the number of MNs recruited.

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