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Experiments and models of sensorimotor interactions during locomotion

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Abstract During locomotion sensory information from cutaneous and muscle receptors is continuously integrated with the locomotor central pattern generator (CPG) to generate an appropriate motor output to meet the demands of the environment. Sensory signals from peripheral receptors can strongly impact the timing and amplitude of locomotor activity. This sensory information is gated centrally depending on the state of the system (i.e., rest vs. locomotion) but is also modulated according to the phase of a given task. Consequently, if one is to devise biologically relevant walking models it is imperative that these sensorimotor interactions at the spinal level be incorporated into the control system.

Keywords Locomotion · Sensorimotor interactions · Model · Central pattern generator · Spinal cord

1 Introduction

Locomotion is a complex task requiring interactions at various levels of the nervous system, and as such it proffers several challenges for the design of computer simulations and/or robots emulating walking biological systems. There are obviously several ways by which complex robots or even simple toys can "walk" from one point to another. One can design machines that may use completely different principles, and in some cases more efficient, than those that have evolved in biology. However, if one is to design an accurate and adaptable robot based on models of locomotion that incorporate available biomechanical and physiological data, then several sensorimotor interactions must be considered. Such an approach is undoubtedly more complex and more costly, but it would probably benefit both neuroscientists and robot engineers and provide a useful common theoretical framework. Therefore, we will aim here at describing some essential components of the sensorimotor interactions that take place during locomotion and extract some principles that may be useful in designing walking machines. Some of these ideas are briefly explored in a recent review (Pearson et al. 2006).

At the heart of sensorimotor interactions is the spinal cord where the central pattern generator (CPG) for locomotion is located. The CPG provides the basic locomotor rhythm and basic locomotor synergies integrating powerful commands from various sources that serve to initiate or modulate its output to meet the requirements of the environment (Fig. 1). It is thought that the CPG elegantly controls muscle activation and hence movement of the mechanical system during walking by adjusting its output in response to a plethora of sensory inputs. Signals from supraspinal, spinal, and peripheral structures are continuously integrated by the CPG for the proper expression and short-term adaptation of locomotion. The present review will firstly focus on experimentally derived sensorimotor interactions between sensory afferents from the periphery and the CPG within the spinal cord. A detailed review of these sensorimotor interactions was recently published (Rossignol et al. 2006) and only some highlights will be reported here. For instance, proprioceptors may exert

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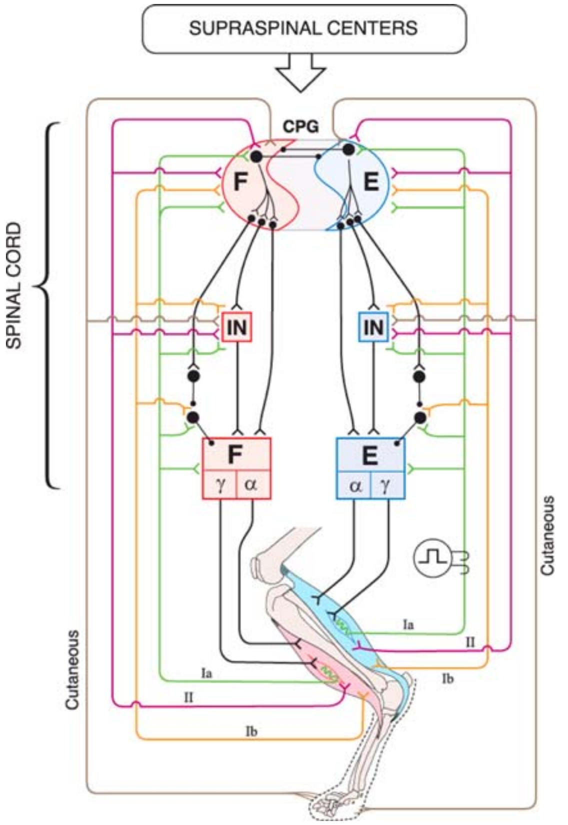

Fig. 1 General scheme of sensory pathways from the cat hindlimb on spinal locomotor control. This scheme is subdivided into three parts. The supraspinal level includes various descending pathways from the telencephalon and brain stem involved in activating, stopping, or modulating characteristics of the spinal locomotor CPG as well as the excitability of transmission in reflex pathways at motoneuronal or premotoneuronal (presynaptic and/or interneuronal) levels. The large *arrow* from the supraspinal level includes all these functions and is not discussed further. The spinal cord level includes the CPG illustrated as reciprocally inhibited flexor (F) and extensor (E) networks. These two antagonist phases of the CPG are separated to indicate that each part may exert an influence on other spinal mechanisms (represented by three output neurons emerging from each part of the CPG) as well as interact between each other (inhibitory connections between F and E). Interneurons (IN) for F (*pink*) and E (*blue*) receive input from several CPG and spinal afferents and project to F and E motoneurons, respectively. Other more specific inhibitory interneurons (*black*) represent disynaptic inhibitory pathways (such as Ib inhibitory interneurons), which can also be inhibited by other interneurons in certain tasks such as locomotion. Motoneuron pools include both α- and γ-motoneurons projecting to extrafusal and intrafusal muscle fibers, respectively. In the periphery, an ankle flexor (*pink*) and extensor (*blue*) muscle are shown each with a muscle spindle. Group Ia and II axons respectively represent sensory fibers from primary and secondary muscle spindles and signal rate and amount of muscle stretch. The stimulation symbol on the Ia fiber from the extensor illustrates direct stimulation of Ia afferents as performed during H-reflex studies. Ib fibers originated from GTOs, which measure the force output of the muscle. Cutaneous afferents from the paw are included and relay information relating touch, pressure, and vibration. Connectivity of the various afferents is partial and largely based on established work and is reviewed extensively elsewhere (Rossignol et al. 2006)

control over the rhythmic pattern being selected, the pattern frequency (speed of walking), the duration of component subphases, as well as the amplitude of muscle bursts and the force generated. Cutaneous inputs on the other hand can trigger various specific rhythmic patterns with some similarities to locomotion (scratching, fast paw shake), control foot positioning during locomotion, and can serve to step over obstacles that may occur in different phases of the locomotor cycle and in different modes of locomotion (i.e., forward or backward walking). These are but a few examples of how sensory inputs can adapt the locomotor pattern to the real world, and undoubtedly some of the principles and mechanisms uncovered in these regulatory sensory pathways would be useful in the design of versatile walking machines to cope with real environments.

The second part of the article reviews how some of these principles have been incorporated in models of locomotion developed in recent years and how other elements could be implemented to create more efficient and realistic walking machines. Computer simulations have been performed to simulate locomotion for several animals including salamanders (Bem et al. 2003; Ijspeert 2001; Ijspeert et al. 2005), snakes (Jayne 1988), fish (Ekeberg 1993; Kuo and Eliasmith 2005), lampreys (Ekeberg and Grillner 1999; Ekeberg et al. 1995), insects (Cruse et al. 1995, 1998; Ekeberg et al. 2004), cats (Wadden and Ekeberg 1998; Ivashko et al. 2003; Yakovenko et al. 2004; Ekeberg and Pearson 2005), and humans (Taga 1995a, b, 1998; Taga et al. 1991; McFadyen et al. 1994; Paul et al. 2005). The present review will focus mainly on conceptual models of cat locomotion since much is known about sensorimotor interactions of these animals during locomotion (for reviews see Rossignol et al. 2006) but models of human walking will also be discussed. Several aspects of locomotor control in cats and humans have been investigated using computer simulations including rhythm generation (Yakovenko et al. 2002; Ivashko et al. 2003; Rybak et al. 2006a), reflex function (Yakovenko et al. 2004; Rybak et al. 2006b), stance-to-swing transitions (Ekeberg and Pearson 2005), and obstacle avoidance (McFadyen et al. 1994; Taga 1998). Insights provided by these models should enable us to further our understanding of locomotion.

Therefore, Sect. 2 describes various sensorimotor interactions occurring during locomotion based on experimental evidence derived primarily from cats and underscores how these interactions should be implemented in theoretical models of locomotion to generate more effective and functional walking systems. The third section reviews some of the theoretical models that have been developed to conceptualize cat and human locomotion, particularly how sensory inputs are integrated and transformed, highlighting key findings and limitations of these models.

2 Sensory interactions with the spinal CPG during locomotion

In recent years, major reviews (Zehr and Stein 1999; Duysens et al. 2000; Pearson 2000; Rossignol et al. 2006) and a book (Orlovsky et al. 1999) have covered extensively the topic of sensorimotor interactions during locomotion, and therefore the present review will only summarize some key aspects. First, it should be recalled that real locomotor movements can still be expressed after removing sensory afferents through complete or partial dorsal rhizotomies, which remove all or some sensory afferent information (Grillner and Zangger 1984; Wetzel et al. 1976; Goldberger 1977, 1983; Giuliani and Smith 1987; Mott and Sherrington 1895; Twitchell 1954; Taub and Berman 1968; Taub 1976), or pyridoxine intoxication, which destroys large caliber afferents but supposedly leaves smaller afferents intact (Pearson et al. 2003). Moreover, after neurochemical blockade, which prevents all movements and therefore all phasic locomotor-related afferent feedback, a detailed rhythmic pattern called "fictive locomotion" can be recorded from muscle nerves (Grillner and Zangger 1979; Pearson and Rossignol 1991). As such, rhythmic sensory feedback is not necessary for generating the basic locomotor output in quadrupeds due to the presence of a spinal CPG for locomotion (Grillner 1981). However, this does raise questions as to the roles played by sensory afferent feedback in controlling the CPG.

Essentially, sensory feedback adapts the output of the CPG in the real world. In other words, specific sensory inputs can have a global influence so that some rhythmic patterns are selected, permitted, and/or abolished, thus acting like switches that trigger certain patterns or set their range of operation. Once the movements themselves have been triggered, sensory afferents can set the pattern frequency, regulate the structure and transition of subphases, modify the amplitude of the electromyographic activity underlying the locomotor pattern, strongly assist foot positioning on irregular terrains, and also correct the pattern when obstacles appear in the path of progression. Such short-term adaptation not only provides great versatility to the pattern but also affords a great deal of flexibility within the multitude of spinal and supraspinal circuits carrying sensory information that interact dynamically with the CPG. It will be shown that dynamic interactions between afferent inputs and the CPG vary according to the task (task dependence) but also in relation to the phases of the task (phase dependence). Thus afferent signals exert context-dependent effects, indicating that a multiplicity of spinal and supraspinal pathways as well as numerous mechanisms are involved in the selection and/or modulation of the excitability of these various pathways.

2.1 Proprioceptive inputs

Muscle afferents appear to play three major roles during locomotion.

Firstly, locomotor movements can be initiated or blocked by some proprioceptive afferent inputs. For example, stimulating hip joint proprioceptors by extending the hindlimbs can initiate air stepping in spinal cats (Sherrington 1910b). In chronic spinal cats capable of walking on a treadmill, flexion of one hip joint abolishes the ability to step on that side whereas the other side can continue to walk. When extending the hip approximately to the angle normally attained at the end of stance the held limb resumes stepping provided the other hindlimb is in a phase where it can accept the weight of the animal (Grillner and Rossignol 1978). Similar to the hindlimb, a maintained protraction of the shoulder on one side of a decorticate walking cat can altogether abolish forelimb locomotion whereas a tonic retraction of the shoulder can increase the vigor of locomotion, especially in ipsilateral flexors and contralateral extensors (Rossignol et al. 1993; Saltiel and Rossignol 2004a). In "fictive locomotion," we also showed that the degree of hip extension greatly influences the locomotor pattern (Pearson and Rossignol 1991). Thus proprioceptive information from a proximal joint (hip, shoulder) exerts strong influences on the spinal locomotor CPG. Another powerful signal to the locomotor CPG originates in the ankle extensors. For instance, it was shown that loading the ankle extensors during decerebrate walking in cats markedly increased the extensor bursts while diminishing the flexor bursts (Duysens and Pearson 1980). As such, it was concluded that load signals from ankle extensor muscles inhibit flexor components of the locomotor pattern and that unloading of ankle extensors is essential to initiate swing. In this model, force seems to play a larger role than actual muscle length (Donelan and Pearson 2004a, b).

Secondly, proprioceptive afferents may participate in adapting walking speed, in determining overall cycle duration, and in regulating the structure of the step cycle's subphases (i.e., swing, stance), which is required for speed adaptation and interlimb coupling. For example, increasing speed on a treadmill shortens the stance phase while the swing phase remains relatively constant across a wide range of walking speeds in both normal and spinal cats (Grillner 1981; Halbertsma 1983; Forssberg et al. 1980a; Barbeau and Rossignol 1987). Moreover, when the hindlimbs of a spinal cat are walking at two different speeds (split treadmill) each hindlimb adapts the structure of its step cycle to match its respective speed (Forssberg et al. 1980b). It is thought that proprioceptors from moving legs provide the main inputs responsible for adapting the speed of each hindlimb. Indeed, the fictive locomotor rhythm recorded from cut peripheral muscle nerves can be powerfully entrained by sinusoidal movements of the hip joint at different frequencies (Andersson and Grillner 1983; Kriellaars et al. 1994).

There is evidence that both positive and negative feedbacks arising from hip afferents influence muscle timing. In one study of fictive locomotion, when ramp movements of the hip were applied early during ankle flexor nerve activity (tibialis anterior, TA) there was an increase in the amplitude of TA (positive feedback) but a decrease in its duration (Andersson and Grillner 1981). When the same flexion was applied at a slightly later time, both the amplitude and duration of TA increased, but if it was imposed during late extension, then the extensors were turned off and the next swing phase was generated earlier (i.e., it was phase-shifted). In another study, during fictive forelimb locomotion, perturbations in the direction of the expected movements in a given phase shortened that phase and the converse occurred in the opposite phase (Rossignol et al. 1993; Saltiel and Rossignol 2004b). Such negative feedback was seen with specific stretches of hip muscles in decerebrate walking cats (Lam and Pearson 2001). For instance, during swing, hip protraction shortened the flexion phase, whereas resistance to hip flexion increased the amplitude and duration of bursts in Iliopsoas (Ip) and Sartorius (Srt). It was also shown that repetitive stretches of flexor muscles (usually in combination) could entrain the walking rhythm (Hiebert et al. 1996), just as sinusoidal stretches of extensors in spinal paralyzed cats injected with DOPA entrain the fictive locomotor rhythm (Conway et al. 1987).

The role of afferents in structuring the step cycle is seen not only in experiments where afferents entrain the rhythm but also in experiments where stimulating afferents actually resets the step cycle (see Rossignol et al. 2006 for a review including experiments in humans and animals). For example, in experiments designed to identify afferents responsible for the effects exerted by the hip, an electrical stimulus at a strength of 1.6 T and higher of a hip flexor nerve (Srt) can reset the cycle in walking decerebrate cats, suggesting that Srt actions on the rhythm generator is mediated by group Ia and Ib (polysynaptic) pathways (Lam and Pearson 2002). In addition, stimulating group Ia (Hiebert et al. 1996) as well as group II afferents (Schomburg et al. 1998) of the ankle flexor EDL during the extension phase can reset the rhythm to flexion in walking decerebrate cats and during fictive locomotion, respectively. Stimulation of specific muscle afferents [Golgi tendon organs (GTOs) of extensors] can also reset the locomotor cycle in the spinal cat (Conway et al. 1987) (see also Fig. 1).

Thirdly, proprioceptive afferents are involved in setting the level of muscle activity through various reflex pathways (Donelan and Pearson 2004a, b). The simplest pathways are undoubtedly activated by stretch (groups Ia, II). Thus, when extensor muscles are stretched during stance these pathways, via their simple connections, can increase synaptic inputs to extensor motoneurons (Fig. 1). The importance of the activation of these receptors can be shown in cats in which the limb is unloaded as in “foot-in-the hole” experiments where intact cats make one step through a trap (Gorassini et al. 1994) or walk on a peg lower than expected (Donelan and Pearson 2004b). When the sensory feedback is decreased from ankle extensors (ankle extensors are stretched much less or not at all) the activity in these muscles is reduced. In humans, unloading using a harness, which can support the whole body during walking, produces a major reduction in burst discharge amplitude of antigravity muscles (Dietz and Colombo 1998; Dietz and Duysens 2000; Harkema et al. 1997; Sinkjaer et al. 2000). Similarly, if ankle extensors are unloaded during stance by mechanically extending the ankle using an external ankle brace there is a 50% decrease in the EMG amplitude of ankle extensor muscles. Although stretch receptors might be the most obvious source of excitatory feedback to motoneurons, it turns out that afferent feedback from load receptors (Ib from GTOs) also provides an excitatory feedback to motoneurons during locomotion. This represents a clear case of a dynamic state-dependent modification in sensory transmission where the usual autogenic inhibition from group Ib afferents observed at rest is changed to a disynaptic excitation during locomotion by activating specific spinal pathways (Gossard and Hultborn 1991; Gossard et al. 1994; Quevedo et al. 2000; Angel et al. 1996; McCrea et al. 1995). This is represented in Fig. 1, where inputs from Ib afferents can be switched to excitatory or inhibitory interneurons, and this concept of state-dependent reversal from autogenic inhibition to excitation from GTOs is clearly presented in a recent review (Hultborn 2006).

Another example of proprioceptive feedback modulation occurs when responses to afferent stimulation change in a phase-dependent manner. A prime example is the cyclical modulation of monosynaptic reflexes (H-reflexes in humans) throughout the step cycle.

Moreover, studies on ankle stretch during walking in humans (Yang et al. 1991; Andersen and Sinkjaer 1999) suggest that responses to stretch are twice as large during stance compared to swing and that 30 – 60% of soleus muscle activity might result from the activation of its stretch receptors during stance (Stephens and Yang 1999; Stein et al. 2000). Since stretch velocity of ankle extensors is maximal during swing (e.g., just after toe-off) it would have been expected that monosynaptic reflexes would reach their peak amplitude in this phase, but instead these reflexes are profoundly inhibited during this period probably as a result of antagonist reciprocal inhibition and/or presynaptic inhibition. Reflex enhancement during stance is thought to stem from increased fusimotor drive (Prochazka et al. 1985; Prochazka 1989).

In conclusion, proprioceptive pathways can modulate the locomotor pattern and cycle duration via various pathways such as monosynaptic to motoneurons, excitatory disynaptic pathways open during locomotion, and polysynaptic excitatory pathways acting through the CPG (see Hultborn 2006 for a recent historical review of these various pathways). In turn, the transmission in these reflex pathways is controlled by the CPG so that sensory afferents and the CPG are in constant dynamic interaction. The reader is referred to a more complete description of such complex interactions in a previous review (Rossignol et al. 2006).

2.2 Cutaneous inputs

The role of cutaneous inputs to locomotion has often been neglected, but recent work on denervation of the foot pads in the cat has shed some light on putative functions (Bouyer and Rossignol 2003a, b). After denervating all cutaneous nerves, which supply the hindpaws of cats with intact spinal cords, normal walking on a treadmill returned, but precision walking on a ladder was abolished for several weeks. After spinalization at T13, however, the same cats that had recovered a normal locomotion permanently lost the ability to place the foot correctly on the plantar surface, the paw dragged during swing, and the steps were much shorter. In chronic spinal cats with intact cutaneous innervation, these deficits are only observed transiently in the early stages of spinal locomotion (Bélanger et al. 1996; Rossignol et al. 2000).This illustrates that intact cats can use alternate inputs to compensate for the loss of cutaneous inputs but that in spinal cats cutaneous inputs are critically important for locomotion because the brain cannot select other sources of cues.

As is the case for proprioceptive inputs, some cutaneous inputs also have major effects in triggering or halting locomotion. For example, perineal stimulation can facilitate the expression of spinal locomotion (Rossignol et al. 2000; Sherrington 1910a). Stimulation of some specific skin areas can also evoke rhythmic patterns such as fast paw shake (Barbeau and Rossignol 1987; Pearson and Rossignol 1991; Langlet et al. 2005). Tonically stimulating the skin of the back, for instance, can also inhibit real or fictive locomotion (Vial and Buser 1974; Viala et al. 1978).

Probably the most obvious role for cutaneous inputs was demonstrated by electrical and/or mechanical stimulation of the skin of the foot during walking. These experiments showed that cutaneous inputs during locomotion could generate corrective responses that were appropriate to the locus as well as the phase of stimulation. Early studies performed on chronic spinal cats (Forssberg et al. 1975, 1976, 1977) and intact cats (Forssberg 1979) showed that contacting the dorsum of the foot during swing triggered a prominent knee flexion that withdrew the foot away from the impact followed by a flexion of the ankle and hip to step over the obstacle. The same contact during stance did not evoke flexion but an extension or a short latency inhibition of extensors. A similar mechanical stimulus applied to the dorsum of the foot during backward walking in intact cats (Buford and Smith 1993) evoked a different type of response that was nonetheless appropriate to remove the foot. Thus, different spinal reflex pathways appear to be selected during forward and backward walking.

Electrically stimulating the skin or cutaneous nerves during the swing phase generates a short latency excitatory response (P1, ∼10 ms) in the knee flexor/hip extensor Semitendinosus (Duysens and Loeb 1980), and very often a second excitatory response (P2, ∼25 ms) appears in chronic spinal and intact cats (Forssberg 1979) (see also Fig. 2). Often these two responses are independently modulated in amplitude (Abraham et al. 1985; Forssberg 1979; Duysens and Loeb 1980), as also seen in Fig. 2. The period of reflex responsiveness of a muscle does not necessarily correspond to its period of activity, and indeed sometimes it can be completely out of phase with its duty cycle (Drew and Rossignol 1987). Also, during fictive locomotion (LaBella et al. 1992) the amplitude of short latency reflexes exhibited phase-dependent modulation, suggesting that the phase dependency was not related solely to interactions between afferents but to central mechanisms as well. Recent papers by McCrea and colleagues (1995) and Quevedo et al. (2005a,b) have shed new light on the pathways implicated in stumbling corrections by recording such responses in conditions of fictive locomotion. Indeed, the detailed timing of functional stumbling responses can be recorded during MLR-evoked fictive locomotion.

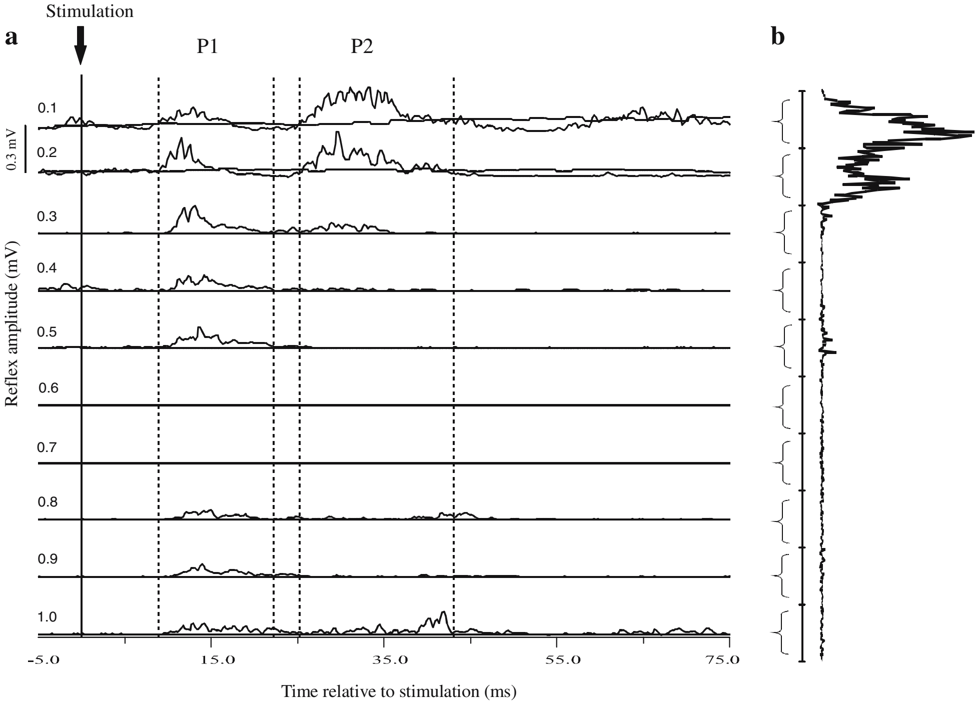

Fig. 2 Phase-dependent modulation of cutaneous reflexes during locomotion. (**a**) Stimulation of the tibial nerve innervating the plantar surface of the foot and reflexes recorded in the semitendinosus (St) during different phases of the step cycle. During a recording session about 120 stimulations are given at varying latencies in relation to the onset of activity of a given muscle to evoke responses during different phases of the cycle. The locomotor cycle is then divided into ten phases and approximately ten responses are grouped and averaged in each phase according to the time they were evoked in the step cycle. In St we see that both P1 (~10 ms) and P2 (~25 ms) are modulated throughout the step cycle varying in magnitude. Responses are typically higher when the muscle is active (i.e., first two traces) but can also be evoked despite quiescence in the muscle (i.e., bottom three traces). The activity of St during the step cycle is given in (**b**)

Cutaneous nerve stimulation applied during the fictive flexor phase evoked responses in flexors, whereas during the fictive extensor phase it evoked excitatory responses in ongoing extensor muscle nerves, consistent with the notion that cutaneous afferents also have short latency connections to ankle extensors (LaBella et al. 1992). Work by others has also clearly established that for a given cutaneous input reaching two different synergistic muscles active during fictive locomotion in the same phase, the responses in the two muscles can vary because the same input is redirected through different interneuronal routes within the spinal cord (Fleshman et al. 1984; Schmidt et al. 1988; Moschovakis et al. 1991, 1992; Burke 1999; Burke et al. 2001; Degtyarenko et al. 1996).

In man, nonnociceptive electrical stimulation during walking also yields phase-dependent responses that induce withdrawal responses during swing and stabilizing responses during stance (Zehr et al. 1997). Tibial nerve stimulation, which mimics a stimulation of the plantar surface of the foot, evokes an ankle flexion at the stance-to-swing transition to remove the foot, whereas it produces an ankle extension in late swing to accelerate foot placement on the ground (Zehr et al. 1997; Duysens et al. 1992). Therefore, cutaneous inputs are greatly involved in the overall expression of locomotion (start, stop) but also in foot placement during normal or obstructed locomotion.

All these biological observations aver that models for walking (theoretical or robots) should incorporate not only afferent feedback but also the rules that govern them during locomotion such as state- and phase-dependent modulation. Afferent signals can be involved in selecting the appropriate rhythmic pattern (walking, scratching, paw shake, struggling) and can also adjust and limit the operating range of these patterns (limits of joint motions). Once in operation, afferent feedback can participate in setting the overall frequency of the pattern, thus adjusting the different subphases of the pattern. This is particularly important for interlimb coupling when turning or walking at two different speeds. Afferent feedback may also be used to adjust discharge magnitude and hence contraction strength of several muscles in various phases. To accomplish this a sophisticated apparatus is required to change the excitability of afferents in different phases (fusimotor drive, presynaptic inhibition). Afferent feedback can participate in the correct placement of the foot and in responding to obstacles presented in various phases of walking and in different modes of walking (forward, backward). This again requires sophisticated mechanisms of interneuronal selection to redirect sensory inputs to appropriate pathways in order to generate corrective responses that are congruent with the ongoing phase of the movement.

3 Modeling sensorimotor interactions during locomotion

Before we discuss models of locomotion and how sensory inputs can be integrated, a brief overview of models of the actuators moving the limbs during movement and receptors signaling changes in muscle length or force is provided since these are necessary for effectively and realistically simulating locomotor control.

Movement is produced by moving linked (joints) segments (bones) by actuators (muscles) driven by command signals (neural impulses). Muscles pose a major design problem since they are not linear force generators whereby an increase in neural drive corresponds to a linear increase in muscle force. Both muscle length and shortening velocity greatly influence force generation, and as such these relationships must be considered when simulating movement to closely mimic normal motor control. Keeping these relationships in mind, several models have been devised to mimic mammalian muscle properties (Brown et al. 1996, 1999; Brown and Loeb 2000; McMahon 1984; Hill 1938; Zajac 1989; Zajac et al. 2003). The design of mathematical models of muscles is discussed at length in other articles of this special issue and will not be described here. However, we will mention that incorporation of muscle actuators derived from some of these models has already been implemented in simulations of locomotion, and, as described below, these simulated muscles can generate realistic limb movements during walking. Moreover, several muscles cross more than one joint and can have multiple functions such as knee flexion/hip extension (e.g., semitendinosus) during locomotion. Bifunctional muscles pose a special problem in designing the control system because they can receive both flexor and extensor commands, which is thought to be governed by phasic afferent inflow during the step cycle (Perret and Cabelguen 1976, 1980). Therefore, if models are to realistically simulate locomotion, then an accurate anatomical linkage with mono- and biarticular limb muscles governed by a biologically accurate central drive must be included. As the complexity of locomotor simulations increases these various components will undoubtedly be incorporated.

Another major hurdle in designing realistic computer models of locomotion is to determine how command signals are generated and modified. In other words, how is sensory information from supraspinal centres and/or the periphery integrated within the CPG to generate an appropriate motor output? Since the present review focuses primarily on interactions from sensory receptors originating in the hindlimbs with the spinal CPG, we will now describe some models of limb proprioceptors that convey information related to muscle velocity, length, and force and, later on, how they can modify ongoing movement.

3.1 Models of sensory receptors in the hindlimbs

3.1.1 Muscle spindles

As discussed in Sect. 2, limb proprioceptors can greatly influence locomotion, and as such accurate physiological models of these receptors that can readily be incorporated into computer simulations of walking are required. In muscle spindles, the central sensory region transmits changes in muscle velocity and length via group Ia or II afferents and contractile fibers can alter the sensitivity of this central region by receiving different types of gamma innervation (Hunt 1990). These various elements provide the spindle with a range of firing properties, and therefore it is important to appropriately conceptualize these regions. Several models of muscle spindles have been developed over the last few decades to capture the range of responses exhibited by these receptors under various conditions (Matthews and Stein 1969; Schafer 1974; Chen and Poppele 1978; Hasan 1983; Houk et al. 1981; Mileusnic et al. 2006). Although an exhaustive review of muscle spindle models is outside the scope of this paper, we will describe the basic properties of a recent model (Mileusnic et al. 2006) to highlight the functioning of these receptors. We will then discuss how some of the previous models compared to biological data recorded during locomotion (Prochazka and Gorassini 1998b).

The mathematical model we will describe was based on feline muscles and attempted to mimic the structure and physiology of primary and secondary muscle spindles (Mileusnic et al. 2006). The basic structure of the spindle is similar to a previous model (McMahon 1984) and consists of a sensory (transduction) region with afferent endings intertwined around it and a polar (contractile) region. The sensory region is modeled as a spring whose stretch is proportional to afferent firing. Once a threshold length is reached, the sensory region discharges, and above this value afferent firing is scaled linearly with stretch magnitude. The polar region is composed of a passive spring in parallel with a contractile element, which can be influenced by fusimotor activation (see also Fig. 1). Thus, the polar region can modify the sensitivity of the sensory region and, hence, afferent firing, as is the case in physiological spindles.

Different intrafusal fibers and gamma-innervations are incorporated into the model. For instance, the spindle is comprised of efferent and afferent connections to and from, respectively, the three different types (bag_1, bag_2, and chain fibers) of known intrafusal fibers. Each type of intrafusal fiber responds to changes in fascicle length and can be influenced by fusimotor drive (dynamic or static depending on fiber type). The model generates two outputs: primary (group Ia) afferents respond to input from all three types of intrafusal fibers while secondary (group II) afferents receive input only from bag_2 and chain fibers. The model accounted for distinct activation dynamics of bag_2 and chain fibers by providing these two types of fibers with different fusimotor saturation points and temporal properties. In addition, the model captured well secondary afferent behavior by using static fusimotor drive to bag_2 and chain fibers. Overall the model faithfully reproduced known physiological data under various kinematic and fusimotor conditions.

Muscle spindle activity during locomotion is complex since it can be influenced by static and dynamic fusimotor activity, which can be tonic and/or phasic and can vary from one muscle to another [see Rossignol et al. (2006) and Taylor et al. (2004) for reviews that extensively review this topic]. Due to the complexity of spindle activity during locomotion no models have yet incorporated this important component of locomotor control. Instead of implementing muscle spindle activity into models of locomotion, what has been done is to compare predicted primary spindle activity of previous models (Matthews and Stein 1969; Chen and Poppele 1978; Hasan 1983; Houk et al. 1981) with firing profiles of primary spindle afferents of hamstring (Prochazka and Gorassini 1998b) and triceps surae (Prochazka and Gorassini 1998a) muscles recorded in cats during overground locomotion to elucidate the critical variables influencing spindle output. It was shown, comparing modeled and actual data, that during locomotion muscle velocity is the key variable modulating primary afferent activity in hamstring muscles and that it mostly precludes contributions from other variables such as muscle length, phasic fusimotor drive, tendon strain, and intramuscular mechanical effects (Prochazka and Gorassini 1998b). Despite fundamental differences in the design of these models, all, except for one (Matthews and Stein 1969), gave a good prediction of hamstring Ia firing during the step cycle at different velocities. In particular, the model by Chen and Poppele (1978), as well as the two modified by the authors, provided the best fits. Phasic modulation of fusimotor activity did not improve the accuracy of the models in predicting hamstring Ia afferent activity, although a static contribution was required since recorded primary afferent firing was quite high and was never completely silenced during the step cycle. This indicates that a tonic static fusimotor drive participates throughout the step cycle, as demonstrated recently (Durbaba et al. 2003). Moreover, similar to the experimental observation that dynamic fusimotor activity in extensors may be phasically active during stance (Taylor et al. 2004), the addition of phasic fusimotor activity more closely approximates simulated Ia afferent firing in triceps surae muscles (Prochazka and Gorassini 1998a). That dynamic and static fusimotor activity respectively prevail in triceps surae and hamstring muscles has been suggested based on experimental data (Bessou et al. 1989).

In the case of secondary afferents, better fits are obtained when the dynamic component is altogether removed (Prochazka and Gorassini 1998a). In other words, unlike primary Ia afferents, which almost exclusively respond to the velocity of muscle stretch, the discharge rate of secondary afferents is determined almost entirely by muscle length. Furthermore, similar to primary afferents, adding tonic static fusimotor activity and a phasic fusimotor effect improves secondary afferent model fit in triceps surae but not hamstring muscles.

Therefore, if one is to study the neural control of locomotion using “in silico” preparations, then accurate models of muscle spindles with appropriate fusimotor activity tested rigorously against experimental data are required to reproduce the powerful signals and wide range of responses generated by these receptors under a variety of conditions.

3.1.2 Golgi tendon organs

Afferent input from muscle spindles is not the only proprioceptive signal capable of influencing locomotion. Input from GTOs via Ib afferents (Fig. 1), which transmit information related to force-generated tension (Jami 1992), as described in Sect. 2, strongly impact locomotor control (Duysens et al. 2000). A few models of GTOs are currently available and attempt to explain the complex behavior of these receptors during simple contractions (Anderson 1974; Houk and Simon 1967; Grillner 1981; Mileusnic and Loeb 2006). Only the most recent model (Mileusnic and Loeb 2006), which was based on the cat *medial gastrocnemius (MG)* muscle, will be described to illustrate the complexity of these receptors and the signals they provide during ongoing movement.

The mathematical GTO model used by Mileusnic and Loeb (2006) consisted of several muscle fibers originating from different motor unit (MU) types and was structured with bypassing (attached to muscle fibers inserted into receptors but not intertwined with afferent endings) and innervated collagen (loosely- and densely-packed), which were interconnected with two common collagen networks. Each common collagen network comprised a spring in parallel with a damper (rearranges collagen following stretch) connected in series with another spring, delineating the sensory region (impulse-generating site). Ib afferent firing depended on the stretch of this sensory region and on the flower-shaped cross-sectional area of collagen in the common collagen network. The two independent generating sites were in competition whereby the stronger output site completely suppressed activity in the other (complete occlusion). Thus only the dominant common collagen network provided output activity for the GTO. Although the model made several assumptions in design such as the flower-shaped cross-sectional area, complete occlusion, and the existence of multiple generating sites, thanks to these properties the model was able to capture several phenomena observed empirically. For example, self- and cross-adaptation, whereby previous activation of the GTO decreases its responsiveness to subsequent changes in tension generated by the same MU or a different MU, respectively (Gregory and Proske 1979; Gregory et al. 1985), was shown. Moreover, nonlinear summation, which is an Ib response smaller than the linear sum of two separate MU inputs (Gregory and Proske 1979), was also demonstrated. The model was also able to show the dynamic and static responses of Ib firing. Thus the response properties of this model resembled those of physiological GTOs.

To the best of our knowledge only one model (Houk and Simon 1967) has been tested to predict the firing rate of GTOs during locomotion (Prochazka and Gorassini 1998b). Using the inverse of the Houk and Simon transfer function it was shown that the predicted force from triceps surae Ib afferents closely resembled the actual measured muscle force. This strongly implies that GTOs can faithfully signal whole muscle force during locomotion. However, the contribution of GTOs to locomotor control has not been modeled as of yet, although, as discussed later on, Ib input has been incorporated into some simulations.

Therefore, realistic models of GTOs are now available, and implementing these principles will undoubtedly ameliorate the simulation of movement by providing accurate force signals to the CPG or neural controller.

3.1.3 Cutaneous receptors

Another important receptor for the control of locomotion lies embedded in the skin. As discussed in Sect. 2, cutaneous receptors can influence rhythmicity in various ways, but during locomotion they are especially important in correcting limb trajectory and foot positioning. Although models of cutaneous receptors are available (Wu et al. 2004), there have been no attempts to incorporate them in the context of locomotor control. Instead, most locomotor models incorporate cutaneous information simply as a foot contact sensor (Wadden and Ekeberg 1998; Ivashko et al. 2003) or as a force (load) transducer (Paul et al. 2005) without taking into account the diverse effects of these receptors on locomotion. Due to the wide range of deficits incurred by modifying or abolishing cutaneous information during locomotion (Bouyer and Rossignol 2003a, b), it is imperative that more accurate models incorporate these receptors to provide the control system with this critical input.

3.1.4 Summary

Models of muscle or skin receptors can provide the nervous system with information regarding muscle length, velocity, force, *and* touch, but exactly how this input is collated into a sense of limb position and/or locomotor movement is largely unknown. What we do know is that this sensory information can shape the locomotor pattern. As we saw in Sect. 2, a given sensory input can influence motor output in different ways depending on the phase and state of the system. Thus, not only must accurate models of limb receptors form an integral part of any physiologically accurate locomotor control system, but it is also critical that the CPG be capable of integrating this sensory information in an appropriate and dynamic manner through various pathways, as suggested in Fig. 1, for the flawless and context-dependent execution of locomotion.

3.2 Models of locomotion

Now that we have reviewed sensorimotor interactions occurring during locomotion and models of limb receptors that give rise to sensory information, we will describe some models of locomotion that have attempted to implement some of these principles in their control system. Although simulating locomotion in mammals is still in its infancy, the last decade or so has seen the number and complexity of different models increase considerably. Conceptual models of mammalian locomotion have been devised using principles derived from some of the simulations described above and based on the abundance of biological evidence obtained primarily in the cat. As stated in the introduction, numerous facets of locomotor control using the cat as a model have been investigated using computer simulations (Ivashko et al. 2003; Yakovenko et al. 2002, 2004; Rybak et al. 2006a, b; Wadden and Ekeberg 1998; Ekeberg and Pearson 2005). To closely approximate locomotor control it is imperative that models include a system analogous to the CPG that can receive feedback from simple reflex pathways originating from muscle and/or cutaneous receptors. Using this minimal system as the basic framework for simulating locomotor control more complex biomechanical and neurophysiological features of locomotion can then gradually be integrated.

3.2.1 The control of phase transitions

Before we discuss interactions between the CPG and sensory events from the periphery we will describe how phase transitions are governed during overground locomotion. For simplicity, experimenters generally break down the step cycle of the cat into different phases with each phase characterized by the activation of a different set of muscles (e.g., muscle synergies). However, as we saw in Sect. 2, how the switch is made from one phase to another can be complex. As such, an instrumental concept in the design of locomotor models has been the development of finite-state or conditional rules to control phase transitions based on data recorded in animals (Prochazka 1996). For example, the rule for switching from stance to swing is: IF stance AND ipsilateral leg is unloaded AND ipsilateral hip is extended, THEN initiate swing (Granat et al. 1993; Prochazka 1993, 1996; Cruse 1990). Moreover, the rule for the swing to stance transition is: IF swing AND ipsilateral hip is flexed AND ipsilateral knee is extended, THEN initiate stance. More rules can be applied to include the contralateral leg such as: IF stance AND contralateral swing THEN delay flexion and prolong stance. This ensures that ipsilateral flexion does not occur while the contralateral leg is still in swing, which would cause the animal to collapse. Several more rules can be assigned to generate a myriad of phenomena observed during locomotion, such as phase-dependent reflex reversal, gallop, backward walking, stumble corrective response, properly coordinating all four limbs, etc. (Prochazka 1996). In a biological system, as stated in Sect. 2, these rules are likely mediated by sensory receptors, which interact with the CPG to govern phase transitions. Evidently, regulating phase transitions is a crucial part of any realistic locomotor modeling effort.

To better understand how phase transitions are achieved during locomotion, models can be developed to systematically investigate the contribution of various sensory inputs in governing these finite-state rules. In Sect. 2 we outlined that two important sensory mechanisms regulate the transition from stance to swing in the cat hindlimb during locomotion. Stretch-sensitive afferents in hip flexors and force-sensitive afferents in ankle extensors influence the activity of hindlimb flexors and thus are thought to control the transition from stance to swing. The relative role of these two mechanisms was recently investigated by simulating the cat hindlimbs during locomotion using either of these mechanisms in isolation or by combining the two (Ekeberg and Pearson 2005).

The three-dimensional model developed by Ekeberg and Pearson (2005) consisted of two hindlimbs, governed by separate finite-state controllers that could be coupled (i.e., mutual inhibition) or uncoupled, and two stiff front legs working as frictionless struts. Several muscles actuated each of the three-segment hindlimbs, which produced a force linearly proportional to the activation level provided by the controller. The hindlimbs progressed repeatedly through a sequence that included liftoff, swing, touchdown, and stance. The transition between these four states was accomplished using sensory signals from the legs, which activated different muscle synergies in each state. Different rules were applied based on joint angles and muscle activity to determine the transition from one state to another. For example, liftoff (stance-to-swing transition) was initiated when the ankle extensor force was low enough (unloading rule) and hip extension reached an arbitrary value (hip extension rule), which simultaneously activated muscles involved in liftoff. A linear combination of these two factors could initiate liftoff at high ankle extensor force provided hip extension was sufficiently large enough, or vice versa. The model also tested either the unloading or hip extension rules in isolation to determine if liftoff could be generated by either of these mechanisms alone. Transition between the other states is described in detail in the original paper and is not reiterated here. The simulation was first made using the combined rules, and then, when walking had stabilized, a bilateral switch to one of the two rules was performed. Switching to the unloading rule did not alter coordinated stepping in the two legs, but a switch to the hip extension rule generated an unstable gait and the model eventually tripped or fell. This instability with the hip extension rule was attributed to a progressive shift in the reciprocal coordination of the two legs away from 0.5. If the controllers were coupled, as is the case in normal animals, the unloading rule generated results identical to those obtained with uncoupled controllers, and although the hip extension rule was now capable of producing a stable gait, the reciprocal coordination between the hindlegs remained abnormal.

Although the model suggested that unloading of the ankle extensors was more important for phase transitions than hip angle, it did not attempt to show how these sensory signals interacted with a locomotor CPG. Instead, the rhythmic activation of muscles was controlled by sensory signals from the legs, as was proposed early in the 20th century by Sherrington (Sherrington 1910a). Biologically relevant views of locomotor control assert that locomotion is not produced by chains of reflexes but by a CPG, which sets the basic locomotor rhythm, although its output can be modified by sensory signals. It is more likely that the two mechanisms (hip extension and unloading rule) act in concert during normal locomotion and that their relative contributions vary according to the task or its context. For example, during rhythmic behaviors where loading of the ankles provides a strong signal, such as level stepping, it would be anticipated that the weight of this cue would be important for phase transitions. However, if ankle extensor loading is low, such as during swimming, scratching, or air stepping as extreme examples, then signals from hip afferents would become increasingly critical for phase transitions. It is also known that below-knee amputees can walk despite a complete lack of feedback from ankle extensors. In addition, since locomotion can be achieved when all sensory feedback is abolished (Goldberger 1987) or when large-caliber afferents from the limbs have been destroyed (Pearson et al. 2003), it is unlikely that sensory input is essential for phase transitions. Thus the CPG can generate phase transitions without sensory feedback, but it is evident that sensory input can shape and strongly influence the pattern. Therefore, what is clear is that phase transitions can be accomplished without unloading of the ankle extensors (or sensory input). In addition, the notion that one mechanism is more important for all forms of rhythmic behavior or even all modes of overground walking is highly improbable based on the available data. As discussed next, to closely mimic normal control and to elucidate sensorimotor interactions during locomotion a CPG is required.

3.2.2 *Motoneuron activation and the basic locomotor pattern*

It should be noted that a CPG is not essential to generate a walking system since models and robots lacking a CPG can still produce stable locomotion, as exemplified by the Ekeberg and Pearson model (Ekeberg and Pearson 2005). However, if one is to accurately model locomotion and to understand how sensorimotor interactions are performed, then a CPG should be a sine qua non element of such a control system. The CPG is thought to turn muscles on and off, thereby generating a rhythmic pattern, but the general organization of this system has been the source of debate for decades. Some argue that the CPG consists of half-centers (Jankowska et al. 1967; Lundberg 1981), whereas others view it as a system composed of multiple, coupled, unit burst generators (Grillner 1981). Another theory indicates that the CPG, because of recorded phenomena such as deletions or resetting (Lafreniere-Roula and McCrea 2005), possesses two layers composed of a rhythm generator that provides the basic locomotor rhythm and a pattern-formation network that distributes and coordinates the activity of motoneuron pools (Rybak et al. 2006a; Perret and Cabelguen 1980; Cabelguen et al. 1981; Koshland and Smith 1989; Kriellaars et al. 1994; Burke et al. 2001). However, with current techniques, identifying large ensembles of neurons involved in rhythm and/or pattern generation is impossible (Kiehn 2006).

Thus, theories abound as to the internal organization of the CPG. To circumvent this problem we can model the CPG in varying forms using computer simulations to draw some general principles and insights from available data. One of the first steps that should be undertaken in such an effort is to gain an understanding of the complexity of motoneuron activation during the locomotor step cycle. Recent studies, although they do not provide a working CPG model, elegantly have accomplished this by showing the spatiotemporal activation of motoneuron pools during locomotion in the cat (Yakovenko et al. 2002) and in humans (Ivanenko et al. 2006).

In the cat (Yakovenko et al. 2002), this was done by combining known distributions of motoneuron pools innervating numerous hindlimb muscles within the spinal gray matter (Vanderhorst and Holstege 1997) with previously recorded EMG activity profiles of these muscles during locomotion (Rossignol 1996; Abraham et al. 1985; Bélanger et al. 1988; Buford and Smith 1990; Carrier et al. 1997; Engberg and Lundberg 1969; Hasan 1983; Pratt et al. 1991; Wand et al. 1980). It was shown that the pattern of activity within the spinal cord proceeded in a rostrocaudal direction during the step cycle. During stance the caudal half of the enlargement was active before abruptly switching to the rostral half during liftoff and swing. Thus, unlike the lamprey where activity progresses rostrocaudally as a traveling wave (Orlovsky et al. 1999; Wallen and Williams 1984), this suggests that in cats discrete CPGs are involved and activate muscles more like light switches, thus providing a clue as to the organization of the mammalian CPG. The authors also indicated that extensor-flexor antagonist motoneuron pools were widely spaced from one another and that connectivity would require long and overlapping propriospinal neurons.

In a similar vein Ivanenko and colleagues (2006) recorded EMG activity from several muscles of the limbs and trunk on the right side of the body during human walking and combined these profiles with known cervical to sacral segmental organization of motoneuron pools (Kendall et al. 1993; Sharrard 1964). They showed that during the step cycle the pattern of activity shifted twice from rostral to caudal segments on the right side of the body. For example, just before and during foot contact activity is seen in the upper lumbar segments and then shifts caudally at mid-stance. At the transition from stance to swing activity shifts rostrally before jumping caudally at the end of swing. These results are also consistent with discrete pattern generators whereby different spinal segments control specific phases of the step cycle.

Although these spinal maps in cats and humans accounted well for the location and segmental distribution of motoneuron pools activated during locomotion they provided few insights as to the general organization, loci, or number of CPGs. Moreover, what is lacking is any information on the multitude of interactions and connections between different "modules" (Schouenborg 2002; Stein and Daniels-McQueen 2002; Bizzi et al. 1995) or "unit burst generators" (Grillner 1981) that control discrete muscles or synergies during different phases of the step cycle. However, if one is to model the CPG with the complexity that is thought to exist within biological systems, this then becomes an increasingly daunting task. Instead, studies have implemented simplified CPG circuitry within their locomotor models to generate the basic rhythm, and to study sensorimotor interactions, very simple reflex pathways have been integrated.

3.2.3 The CPG and sensorimotor interactions

To evaluate sensorimotor interactions during locomotion studies have modeled relatively rudimentary CPGs with simple reflex pathways. For example, Wadden and Ekeberg (1998) modeled a single leg of a cat controlled by a CPG (they termed this neural phase generator or NPG) that received sensory information from the periphery and a "supraspinal" command that served to initiate and select the movements akin to the MLR described in cats (Shik et al. 1966). The NPG consisted of four interconnected modules each one controlling a separate phase (stance, liftoff, swing, and touchdown) of the step cycle with each module consisting of three neurons. The hold (H) neuron keeps the stepping generator in a specific phase and has excitatory connections with the quash (Q) and transfer (T) neurons. Whereas Q inhibits all other phases T activates H of the next phase and inhibits Q of its own phase. The smooth sequence of locomotor events is ensured because the excitatory connection from H to T has a longer time constant than H to Q and because T only excites the H of the next phase. Sensory feedback related to hip position and ground contact is also provided to the network. The sensory neuron signaling hip extension activates the T neuron of the stance phase and motoneurons of liftoff thus promoting a switch from stance to swing. Conversely, the sensory neuron activated by hip flexion excites the T neuron of the swing phase and motoneurons of touchdown therefore signaling the transition from swing to stance. In addition, the neuron that senses ground contact indirectly inhibits and excites motoneurons responsible for swing and stance, respectively, thus assuring that swing is not initiated while the leg is still in contact with the ground. Stretch reflexes to hip and knee extensors were also incorporated into the system to increase stiffness at these joints during touchdown but the functioning of these pathways was not based on physiological parameters. The model produced stable rhythmic locomotor patterns by changing the active elements during different phases and stepping velocity could be altered by modifying the strength of the supraspinal command. Although this system was relatively rudimentary, it did show that interconnecting elements of a distributed network could effectively control muscle activation and phase transitions in one leg, thus providing a good first step in approximating a CPG for mammalian locomotion.

More recently, a model of cat locomotion consisting of two coupled CPGs driving muscle activity in several muscles for each hindlimb, which received proprioceptive reflex feedback from the hindlegs, was devised (Ivashko et al. 2003). Each hindlimb comprised three rigid segments connected to the pelvis, which was fixed to the trunk. The spinal cord circuitry consisted of separate modules with each module including an alpha-motoneuron controlling one muscle, a Renshaw cell, and Ia and Ib interneurons. Each module was driven by its respective CPG and by reflex feedback. Two types of CPG neurons were included in the model. "Principal" CPG neurons activated alpha-motoneurons in a given module during a specific phase of the step cycle. For example, some CPG neurons activated alpha-motoneurons for muscles active during stance, while others controlled muscles active during three different stages of the swing phase. "Switching" CPG neurons, on the other hand, controlled phase transitions by turning off principal CPG neurons. Activation of these switching elements was controlled by proprioceptive feedback from both hindlimbs and from touch sensors that signaled

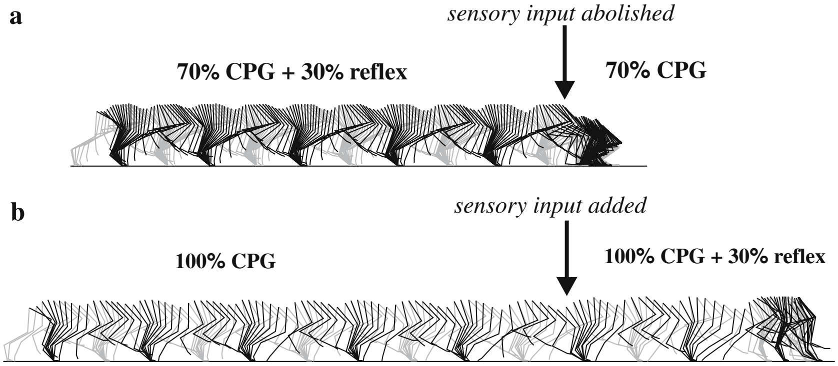

Fig. 3 Contribution of stretch reflexes to simulated hindlimb locomotion in the cat. Simulation of hindlimb walking with muscle activity being generated by combined inputs of 70% CPG and 30% group I reflexes (**a**) or solely by the CPG (**b**). **a** If motor output during walking is generated by a combination of CPG and sensory input to motoneurons, then the abolishment of sensory input causes the model to immediately collapse. **b** If, however, the motor output is being supplied entirely by the CPG, then the addition of sensory input does not cause the muscle to collapse, but some anomalies in locomotion do occur a few step cycles later (reprinted and modified with permission)

foot contact. Several established features were incorporated into the model such as Ia-mediated reciprocal inhibition of antagonists and reversal of inhibition to excitation from group Ib afferents during locomotion.

Simulations showed that the modeled circuitry generated stable locomotion of the hindlimbs and that kinematics closely resembled real cat stepping. However, EMG patterns differed somewhat from published data (Rossignol 1996; Yakovenko et al. 2002). For example, modeled flexor (iliopsoas, semitendinosus, tibialis anterior) and extensor muscles (biceps femoris anterior, vastii, gastrocnemii) were inactive prior to swing and stance, respectively, which is not the case during real locomotion. Moreover, rectus femoris (hip flexor/knee extensor) should fire before and after stance, but in the model it only fired from mid to late swing. Biceps femoris posterior (knee flexor/hip extensor) had a short burst of modeled activity prior to stance and swing, whereas in real locomotion this muscle fires before and after lift-off and/or foot contact. The model also showed that soleus (ankle extensor) fired during mid-swing then fell silent before foot contact and before becoming active during stance, while in real locomotion soleus activity is characterized by activity commencing just before stance and continuing through this phase. Furthermore, vertical ground reaction forces predicted by the model were much higher than actual forces. The abnormal patterns of activity in several muscles of the hindlimbs might have contributed to the greater ground reaction forces. The model was also not tested under different circumstances such as incline or decline walking. Thus, although the model was successful in generating rhythmic locomotor activity and incorporated several reflex pathways known to operate during locomotion, further studies are required to refine and test the validity of this approach for modeling central locomotor control in the cat.

Another important aspect of locomotor control, as discussed in Sect. 1, is the interaction of the CPG with reflex pathways from limb receptors. Stretch reflexes are thought to contribute strongly to the force-generating capacity of muscles during the stance phase of locomotion (Yang et al. 1991; Bennett et al. 1996; Stein et al. 2000), even though muscles possess springlike properties capable of accomplishing a similar function. Thus the role of stretch reflexes has been questioned (Prochazka et al. 2002), and the extent to which this sensory input contributes to weight bearing during locomotion was recently addressed (Yakovenko et al. 2004). In this study, the model consisted of two hindlimbs attached to a horizontal torso supported at the front by a frictionless wheel. Hindlimb muscles were driven by a CPG and during activity of a given muscle, reflex feedback from group Ia and Ib afferents contributed to contractile force at a latency of 35 ms, adding 30% to the CPG EMG of that muscle during the step cycle. Finite-state rules, as described above, were used to govern transitions from stance to swing and from swing to stance (Granat et al. 1993; Prochazka 1993). What the model demonstrated was that in instances where CPG output was sufficiently high to generate a stable locomotor pattern the addition of reflex feedback from group I afferents did not improve the quality of locomotion. However, when CPG output and reflex feedback both contributed to locomotion, the sudden loss of group I reflexes then caused the model to collapse almost instantly (Fig. 3). Thus, if CPG output is inadequate for the demands of the task, then reflex contribution becomes critical, but if CPG output is sufficient, then reflexes only participate minimally. The authors further added that stretch reflex latency is not too long to assist in load compensation and augment central drive during stance.

What is unclear at present is whether CPG output is sufficient during normal locomotion in cats. In other words, do stretch reflexes normally supplement CPG output for weight bearing during locomotion? It is probable that stretch reflexes complement CPG output during simple locomotion, thus allowing the system a greater range through which it can operate. Moreover, we can speculate that under certain circumstances the output from the CPG is by itself incapable of meeting the task requirements and that group I feedback from limb proprioceptors then becomes critical, if not essential. It would be interesting to test these hypotheses by simulating locomotion during more difficult tasks such as incline or decline walking using the model. Decline stepping has already been shown to be severely impaired in cats with sensory denervations of triceps surae muscles (Abelew et al. 2000). The loss of sensory information from ankle extensors in these cats did not produce visible deficits in level or incline walking, but considerable disruption of interjoint coordination was seen during decline walking where muscles undergo active lengthening and group I feedback is normally elevated. Therefore, it would seem that CPG output is not necessarily sufficient for all locomotor tasks and that group I feedback normally complements central drive for the execution of flawless locomotion.

3.2.4 Models of fictive locomotion

To highlight the complexity of interneuronal connections and neuronal properties involved in CPG circuitry and rhythm generation, respectively, recent studies (Rybak et al. 2006a, b) designed a bipartite model comprising a half-center rhythm generator (RG) and a pattern formation (PF) network to simulate the motoneuronal activity recorded during fictive locomotion in decerebrate cats. Whereas the RG provided the basic locomotor rhythm by delineating the duration of flexor and extensor bursts, the PF distributed and coordinated motoneuron activity via numerous excitatory and inhibitory interneuronal connections, thus shaping the final output to motoneurons. Through these various interactions, and by receiving input from the RG, only some neuronal populations in the PF were active during specific phases of the step cycle. The two-level CPG organization enabled sensory inputs to directly access either the RG or PF and thus account for observed physiological phenomena such as deletions or resetting of the locomotor rhythm (Lafreniere-Roula and McCrea 2005). Motoneurons were modeled according to a previous study (Booth et al. 1997) and properties such as persistent sodium currents were incorporated to endow excitatory neurons of the RG with rhythmogenic properties as has been modeled for respiratory CPGs (Butera et al. 1999; Rybak et al. 2003). However, whether such endogenous rhythmogenic properties are present in locomotor CPG neurons is currently unknown.

A tonic MLR-like excitatory descending drive initiated locomotion via distributed connections to excitatory neurons of the RG and PF, which were both separated into flexor and extensor half-centers with mutual excitatory and inhibitory connections. The alternating activity of flexors and extensors respectively defined the flexion and extension phases of the locomotor cycle in the absence of sensory input. Whereas the persistent sodium current mediated burst onset the termination was mostly governed by reciprocal inhibition between half-centers. It was shown that the modeled motoneuron discharge rate was similar to that recorded previously during fictive locomotion in the cat (Brownstone et al. 1992).

Separating rhythm generation from pattern formation allowed the model to faithfully reproduce deletions with a phase shift (resetting) or without. In one example of a resetting deletion, increasing and sustaining the MLR drive to the extensor RG severely reduced activity in the flexor RG, which led to a deletion of flexor motoneuron activity. Once the MLR drive was discontinued the flexor rhythm reappeared but was phase-shifted in time compared to before the stimulation. In contrast, altering the excitability at the PF level could produce a deletion without phase-shifting the post-deletion locomotor rhythm since the activity at the RG level remained unchanged. Furthermore, although a bipartite (two layers) CPG accounts for phenomena such as deletions with or without resetting, it is a contentious issue for several reasons since other elements in the pattern generating circuitry (forelimb, contralateral limb, brain stem neurons) could also keep track of the timing.

In another study Rybak and colleagues (Rybak et al. 2006b) investigated the effects of stimulating various sensory afferents on CPG function by adding several interneuronal populations, such as Ia and Ib inhibitory interneurons, Renshaw cells, and interneurons intercalated in cutaneous reflex pathways, to their fictive locomotion model. During locomotion the spinal circuitry was modified and the reflexes reorganized. For example, the nonreciprocal inhibition from extensor group I afferents was suppressed by the MLR descending drive and instead disynaptic excitation of homonymous motoneurons by group I afferents emerged (Fig. 1), as has been described in decerebrate cats (Gossard et al. 1994; McCrea et al. 1995). The model also incorporated presynaptic inhibition of group Ia afferent inputs during locomotion.

Stimulating afferent activity with these modeled connections was in agreement with previously published data (Guertin et al. 1995). For example, stimulating the extensor group I afferents during the flexion phase terminated this phase and initiated extension, but a few cycles later the rhythmic activity occurred at its appropriate place, as if no stimulation had occurred (see Guertin et al. 1995 for corresponding physiological data). Due to the stronger synaptic strength afforded to the PF compared to the RG, the modeled afferent connections can reset PF activity without influencing the basic locomotor rhythm produced by the RG. If extensor group I afferents were stimulated during the extension phase at an intensity where only the PF was acted upon, this enhanced and prolonged the activity of extensor motoneurons. The following flexion phase was delayed and shortened to maintain the timing of rhythmic activity since RG was unaffected. However, if the stimulation was strong enough to influence RG the extension phase was enhanced and prolonged and a reset in the locomotor rhythm occurred. Cutaneous afferents from the tibial nerve were modeled with disynaptic excitatory connections to RG and PF with equal strengths. Thus, stimulating cutaneous afferents during modeled fictive locomotion always reset the rhythm to a new state since the RG was always influenced. The model also incorporated competing influences from group I and II afferents, but this will not be described here.

Although at present the model only includes activity from one pair of antagonist motor pools, it does show that modeled neuronal properties and connections can generate a basic locomotor rhythm of alternating flexor and extensor activity and that sensory input can greatly influence CPG output. The coming years should shed more light as to the general organization of the CPG, the neuronal properties of its constituent elements, and how sensorimotor interactions occur.

3.2.5 Human locomotion

Motion of the entire body during human walking has often been simplified as two coupled pendula with the stance leg acting like an inverted pendulum moving about the stance foot and the swinging limb behaving as a regular pendulum moving at the hip (Kuo et al. 2005; Taga 1995a). Using this analogy several models of varying complexity have been formulated to illustrate some aspects of the kinetic and kinematic patterns of human walking, but relatively few attempts to combine neural control mechanisms such as CPGs and/or sensory feedback from the moving limbs have been made (Kuo et al. 2005; Pand 2001; Pandy 2003; Zajac et al. 2002, 2003). This undoubtedly stems from the fact that, contrary to cat locomotion, many more assumptions with regard to neurophysiological mechanisms must be made and little is known as to the sensorimotor interactions that take place during bipedal human walking.

Despite these limitations and potential pitfalls a few models have been devised using CPGs capable of integrating sensory input (Taga 1995a; Ogihara and Yamazaki 2001, McFadyen et al. 1994; Paul et al. 2005). In a series of papers Taga (Taga 1995a, b, 1998; Taga et al. 1991) investigated the interaction of CPGs with the musculoskeletal system to produce human locomotion and tested the model under various conditions. The model comprised seven neural oscillators, each controlling a single joint, which were regulated by tonic descending input. Each neural oscillator consisted of two paired tonically active neurons with recurrent and reciprocal inhibitory connections. This half-center model (Brown 1914), in which a flexor neuron inhibits its contralateral flexor homolog and its ipsilateral extensor antagonist and vice versa, generated the basic step cycle. The timing of muscle activation by the neural oscillators was determined by specific events within the step cycle and by inhibitory and/or excitatory connections. The step cycle was divided into six separate states and sensory signals relating the current state of the biomechanical system were sent to the ensemble of neural oscillators (e.g., CPG). The “global angle,” which is the orientation of the vector from the center of pressure to the center of gravity in an earth-fixed frame of reference, was computed and informed the CPG about the current state of the system, which then filtered this input according to the phase of the step cycle, thus allowing unwanted information to be ignored in phases where it could produce instabilities (e.g., phase-dependent modulation). Moreover, the model adapted well to different conditions including mechanical perturbations, loading, and terrain alterations (Taga 1995b). However, although the model generated stable walking under varying conditions, it did so within a limited range and without recalibrating the system (e.g., new steady states were produced).

Simulations showed that the model was capable of sensorimotor interactions such as changing walking speed in response to modifying the tonic activity to each neural oscillator and via entrainment of the walking rhythm by imposing signals to hip oscillators. However, unlike the MLR in cats (Shik et al. 1966), whereby velocity increases linearly with stimulation intensity, walking speed as well as stride cycle and stride length “jumped” considerably once tonic activation reached a certain level, despite the lack of corresponding changes in neural activity, muscle torques, and segment displacements. Moreover, entrainment of the walking rhythm could be induced by imposing signals on the hip oscillators but only within a very narrow range above or below the normal rhythm. Thus although the model's CPG integrated sensory information to modify its output, its modus operandi was somewhat limited. This model, however, provided an adequate framework for incorporating more complex and realistic neural control mechanisms. Indeed, in a followup study, a discrete movement generator (DMG), which mimics descending commands from the motor cortex, was implemented to enable the model to avoid obstacles (Taga 1998). The DMG modulated gait by changing the timing and amplitude of specific muscles in response to "visual" information and the current state of the CPG; a similar system is thought to operate in cats (Drew 1988; Drew et al. 1996).

As stated by the author, this model generated stable walking with "characteristics of human gait," although there were some notable anomalies such as a high foot clearance during swing and large ground reaction forces at foot contact. A serious limitation of this approach was the lack of validation against published empirical data of human walking. Thus, we know relatively little as to the similitude of the model's kinetic and kinematic patterns compared to real human walking. Moreover, the model did not attempt to incorporate realistic muscle actuators or limb proprioceptors, which undoubtedly would enhance the overall functioning of the system. This is critical since a given motoneuronal input to a muscle will generate different torques at various joint angles and walking speeds due to the force–length and force–velocity relationships. However, the model did produce a stable bipedal gait and the addition of more components using principles derived from animals could prove useful in testing hypotheses of sensorimotor interactions that occur during human locomotion.

In a more recent study, a model of human locomotion incorporated a CPG with Ia, Ib, and cutaneous reflex pathways (Paul et al. 2005). Like Taga's model (Taga 1995a), the CPG consisted of mutually inhibitory half-center models each controlling one of six joints (hip, knee, and ankle bilaterally), which were each actuated by a flexor and an extensor. Recurrent inhibition produced the rhythmic activity by delineating the amount of time each half-center remained active. The stretch reflex pathway was modeled as a primary muscle spindle with static and dynamic components, but without a corresponding fusimotor drive. Reciprocal inhibition between flexor and extensor antagonists mediated by Ia inhibitory interneurons was also incorporated. The Ib pathway from GTOs was modeled using two separate Ib interneurons, which included an inhibitory and an excitatory connection to motoneurons. This was to highlight the shift from inhibition to excitation that occurs in the Ib pathway during locomotion (Gossard et al. 1994). The inhibitory pathway was active during locomotion only when force exceeded high values. The excitatory Ib interneuron also received input from pressure-sensitive cutaneous receptors from the sole of the foot, thus exciting ipsilateral extensors during the stance phase of the same leg. This neural circuitry actuated flexors and extensors at each joint, which were modeled as described previously (McMahon 1984; Hill 1938) accounting for force–velocity and force-length relationships.

The model could generate stable bipedal walking and was devised as a means to test the relative importance of various sensory pathways in the generation of gait. As such, the gain of the different neural components (e.g., CPG and reflex pathways) could be modulated to test their relative contribution during locomotion. It was shown that completely removing one of the sensory modalities caused the model to collapse during walking, thus indicating that each is critical for normal locomotion. On the other hand, increasing the gain of some these modalities introduced abnormalities in gait. For example, augmenting the gain of muscle spindles caused the muscle to collapse during stance due to strong activation of stretched knee flexors during this phase, whereas increasing the gain of cutaneous receptors deteriorated gait stability, even though speed could be maintained more easily. Increasing the gain of GTOs did not influence locomotion.

Therefore, although the accuracy of reflex pathways was questionable, the model did suggest that sensory pathways are critical for the generation of locomotion. What is curiously omitted in this model is phase dependency whereby some inputs are filtered out in specific phases where they would generate unwanted behaviors. Phase-dependent modulation of sensory input would have prevented the model from collapsing during stance due to excessive activation of knee flexors by canceling out this action during this phase. Moreover, contrary to Taga's model, the pure feedforward nature of this system prevents sensory feedback from entraining or modulating the locomotor rhythm because reflex pathways did not have direct connections with the CPG, which is not the case in biological systems. As we saw earlier, phase transitions critically depend on sensory feedback from limb proprioceptors and this model does not include these important connections.

To summarize, models of human locomotion currently available, although they necessitate some refinement, provide a viable means for testing hypotheses such as the role of sensory feedback in generating a stable bipedal gait. Incorporating accurate sensorimotor interactions from other mammals such as the cat into simulations of human locomotion will undoubtedly ameliorate the robustness and appropriateness of these models. Furthermore, data derived experimentally and tested via computer simulations should elucidate and confirm the multitude of sensorimotor interactions occurring during bipedal human locomotion.

4 Conclusions

The general aim of this review was to suggest that, for the benefit of experimental and theoretical neuroscientists, it would be important to take into consideration as much of the available biological information as possible to increase the realism of current models of mammalian locomotion. As is the case for network simulations, which incorporate several of the membrane properties of individual cells, locomotor networks must incorporate sensory feedback as well as governing rules (i.e., state- and phase-dependent modulation) as key operational elements. Again, this is not necessarily to make better walking robots but to design biologically relevant models that will help clarify the theoretical framework for our understanding of locomotor mechanisms.

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