

CHAPTER 16

The neuromechanical tuning hypothesis

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Abstract: Simulations performed with neuromechanical models are providing insight into the neural control of locomotion that would be hard if not impossible to obtain in any other way. We first discuss the known properties of the neural mechanisms controlling locomotion, with a focus on mammalian systems. The rhythm-generating properties of central pattern generators (CPGs) are discussed in light of results indicating that cycle characteristics may be preset by tonic drive to spinal interneuronal networks. We then describe neuromechanical simulations that have revealed some basic rules of interaction between CPGs, sensory-mediated switching mechanisms and the biomechanics of locomotor movements. We posit that the spinal CPG timer and the sensory-mediated switch operate in parallel, the former being driven primarily by descending inputs and the latter by the kinematics. The CPG timer produces extensor and flexor phase durations, which covary along specific lines in a plot of phase- versus cycle-duration. We coined the term “phase-duration characteristics” to describe such plots. Descending input from higher centers adjusts the operating points on the phase-duration characteristics according to anticipated biomechanical requirements. In well-predicted movements, CPG-generated phase durations closely match those required by the kinematics, minimizing the corrections in phase duration required of the sensory switching mechanism. We propose the term “neuromechanical tuning” to describe this process of matching the CPG to the kinematics.

Keywords: neural control of locomotion; central pattern generators; sensory control of locomotion

Introduction: historical development and overview

The control of animal locomotion was among the first mechanisms of nervous systems to be analyzed in detail (Freusberg, 1874; Magnus, 1909a, b; Sherrington, 1910, 1914). A key contradiction soon arose. It had been shown that in spinally transected dogs, a locomotor rhythm could be initiated in pendent limbs by dropping one of the limbs from a flexed position (Freusberg, 1874).

Sherrington found that the rhythm could be halted by holding a limb in mid-cycle (Sherrington, 1910, 1914). He concluded that stepping and walking resulted from a chain of proprioceptive reflexes, the end of one phase triggering the onset of the next. Sensory input was of course crucial to this scheme. The problem was that locomotor-like rhythms were also observed in spinal cats even after sensory input was abolished by extensive deafferentation (Brown, 1911). Brown proposed the existence of what he called the intrinsic factor, located in the spinal cord and capable of producing the locomotor rhythm autonomously, without

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1 sensory input or descending control from the
 3 brain. Over 60 years later Sten Grillner renamed
 this mechanism the central pattern generator
 (CPG) (Grillner and Zangger, 1975).

5 It is now clear that sensory input interacts with
 the CPG in at least three ways. It can trigger step
 7 cycle phase transitions in a discontinuous, switch-
 like manner; it can lengthen or shorten phase
 9 durations in a more continuous manner and it can
 provide continuous, proportional control of muscle
 11 activation through short reflex pathways
 (Rossignol et al., 2006).

13 All of the building blocks of locomotor systems
 have been separately studied, from the molecular
 15 to systems levels. The biomechanical properties of
 the musculoskeletal actuators and body segments
 17 have been determined and modeled (Brown and
 Loeb, 2000; Zajac, 2002; Zajac et al., 2003). The
 19 transducing properties of sensory afferents (Pro-
 chazka and Gorassini, 1998b; Prochazka, 1999;
 21 Mileusnic and Loeb, 2006; Mileusnic et al., 2006)
 and their reflex effects on load compensation and
 23 locomotor phase transitions have been character-
 ized (Frigon and Rossignol, 2006; Rossignol et al.,
 25 2006). The behavior of isolated CPGs in a variety
 of motor systems has been investigated and net-
 27 work models have been proposed (Selverston,
 1993; Arshavsky et al., 1997; Grillner et al.,
 2000; McCrimmon et al., 2000; Zelenin et al.,
 29 2000; Kiehn, 2006; Rybak et al., 2006a, b). In
 mammals, brainstem, cerebellar, and cortical in-
 31 volvement in adaptive locomotor responses has
 been explored (Arshavsky et al., 1986; Beloozer-
 33 ova and Sirota, 1998; Orlovsky et al., 1999; Drew
 et al., 2004). The picture that has emerged from all
 35 of this work is that of a multilevel control system
 (Fig. 1). At the lowest level, the muscles act like
 37 damped springs, providing automatic length feed-
 39 back control of bodily movement. The term “pre-
 flex” has been coined to describe this mechanism
 (Loeb et al., 1999). The second level, which we
 41 will call the output level, comprises motoneurons
 (MNs) that activate muscles. Interneurons that
 43 mediate sensory and recurrent feedback, argu-
 ably are also included (e.g., Renshaw cells and Ia
 45 and Ib interneurons). The third, hypothetical, level
 47 comprises neuronal networks that generate indi-
 vidual muscle activation profiles, also without

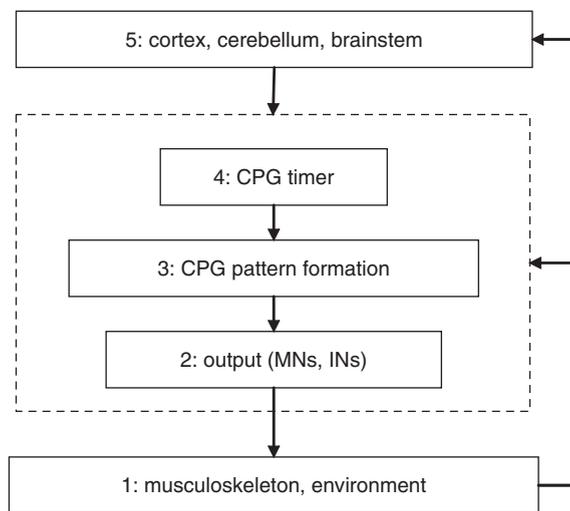


Fig. 1. Hypothesized CNS levels of locomotor control.

affecting the basic rhythm (Perret and Cabelguen,
 1980; Perret, 1983; Lafreniere-Roula and McCrea,
 2005). This level was recently called the pattern
 21 formation layer (Rybak et al., 2006a). The fourth
 23 level comprises the CPG rhythm generator or os-
 25 cillator, whose activity is adjusted or reset by sen-
 27 sory input, as well as by input descending from the
 29 fifth and highest level, which comprises the brain-
 stem (Shik et al., 1966; Takakusaki et al., 2004),
 31 cerebellum (Arshavsky et al., 1986), and motor
 cortex (Beloozerova and Sirota, 1993; Drew, 1993;
 33 Widajewicz et al., 1994). These higher centers in-
 35 tegrate a wide variety of inputs, including motiva-
 tional (Jordan, 1998), exteroceptive (Drew, 1991;
 37 Rossignol, 1996; Patla et al., 1999), and prop-
 39 rioceptive inputs, to define state and intention and
 41 to predict upcoming motor requirements.

There have been several excellent reviews of the
 43 above mechanisms over the last few years (Pear-
 45 son, 2004; Frigon and Rossignol, 2006; Rossignol
 et al., 2006). Yet in spite of all the neurophysio-
 47 logical knowledge, there has been relatively little
 progress in understanding precisely how the neu-
 43 ronal mechanisms combine with the biomechanics
 to produce the stability, adaptability and grace of
 45 animal movement. Neuromechanical simulations
 are becoming increasingly useful in this regard
 (Taga et al., 1991; Taga, 1995; Yakovenko et al.,
 2004; Ekeberg and Pearson, 2005; Pearson et al.,

2006). In what follows, we will concentrate on the properties of mammalian locomotor systems that are relevant for computational approaches. We will then present the results of recent neuromechanical simulations, followed by some general propositions about locomotor control.

Sensory inputs in mammals

The vast majority of mechanoreceptors are cutaneous or hair follicle receptors. Most of these are only sporadically active during the step cycle, for example upon ground contact in the case of foot-pad receptors, or during surface airflow for hair follicle receptors (Prochazka, 1996). Although cutaneous afferents have demonstrable reflex actions on MNs and as event detectors, can elicit specific motor programs such as the stumble reaction, most of the *continuous* reflex control during stepping must be attributed to the proprioceptive afferents, muscle spindles and tendon organs. This is not to deny a role for cutaneous input to provide kinesthetic information (Collins and Prochazka, 1996) and affect muscle activation and the timing of locomotor phase transitions (Rossignol et al., 2006). Indeed event-related multiunit activity of cutaneous afferents recorded from nerve cuffs has been used to trigger bursts of functional electrical stimulation (Haugland and Sinkjaer, 1999).

There is much detailed information on the transducing properties of proprioceptors. To a first approximation, tendon organs signal muscle force and muscle spindles signal muscle length and velocity. Models have been developed that predict their responses reasonably accurately. It is of course debatable as to the level of accuracy that is required for biomechanical modeling. Because stretch reflexes probably account for no more than 30% of muscle activation during locomotion (see below), models that account for 80% or more of the variance in afferent ensemble firing rate would introduce 6% or less error in predicted muscle activation.

Models are available that predict the responses of tendon organ ensembles with >80% accuracy (i.e., $r^2 > 0.8$ in linear regressions of predicted versus actual firing rate) (Prochazka, 1996; Mileusnic

and Loeb, 2006). Muscle spindles are more problematic, because their responses are modulated by fusimotor action emanating from the CNS. If this action fluctuates substantially, predictions of spindle responses based only on length variations are bound to be inaccurate. Models of varying complexity have been developed and compared with ensemble spindle responses recorded from dorsal roots in freely walking cats (Prochazka and Gorassini, 1998a, b). In some muscles, more than 80% of the variance was accounted for by quite simple models, presumably because fusimotor action does not fluctuate very much in these muscles during walking. In other muscles, for example the ankle extensors, modeling was less satisfactory, even after presumed fusimotor action was added. Recently, a model has been developed that includes not only fusimotor action, but also tendon compliance, muscle pennation and other nonlinear features (Mileusnic and Loeb, 2006; Mileusnic et al., 2006). The main problem here is that fusimotor fluctuations during gait in normal animals have never been established with certainty. They have been inferred from recordings in walking decerebrate cats (Taylor et al., 2000a, b, 2006; Ellaway et al., 2002; Durbaba et al., 2003) but there are discrepancies between the normal and decerebrate data. Because fusimotor activation profiles remain uncertain, the improvement in accuracy the new complex model offers is also uncertain.

Locomotor stretch reflexes

Muscle spindles reflexly excite MNs that innervate their parent muscles, resisting deflecting forces. This reflex action is equivalent to negative length and velocity feedback. During locomotion, tendon organ afferents respond to increments in muscle force by exciting homonymous MNs to produce even more force. This is equivalent to *positive* force feedback, the loop gain of which is evidently less than unity in normal gait, but may transiently exceed unity in bouncing gait (Prochazka et al., 1997; Geyer et al., 2003; Donelan and Pearson, 2004). We have estimated that at most 30% of the activation of extensors in the stance phase of the cat step cycle is attributable to proprioceptive stretch

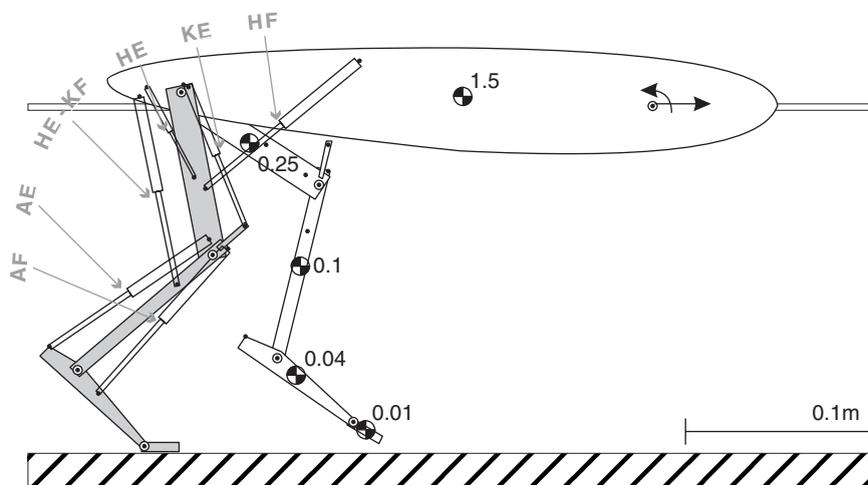


Fig. 2. Neuromechanical model used in locomotor simulations.

reflexes (Prochazka et al., 2002). Furthermore, there is a surprisingly long delay (20–40 ms) before the EMG response to ground contact manifests itself (Gorassini et al., 1994; Gritsenko et al., 2001). Given the modest and delayed contribution of stretch reflexes to muscle activation and the relatively normal locomotion of cats deprived of proprioceptive afferents (Pearson et al., 2003) the importance of stretch reflexes in load compensation came into question (Prochazka and Yakovenko, 2002; Prochazka et al., 2002).

The issue was tackled with a neuromechanical model (Yakovenko et al., 2004) a torso supported at the front by a frictionless horizontal rail and at the back by a pair of hindlimbs (Fig. 2). Each hindlimb comprised four rigid-body segments (thigh, shank, foot, and toes), which were driven by six musculo-tendon actuators. The model was implemented with Matlab and Working Model software. Each actuator had Hill-type muscle properties driven by a CPG that generated muscle activation patterns derived from the literature. Spindle and tendon organ models added reflex components to muscle activations, contributing on average 30% of total activation. The stability of locomotor simulations with and without reflexes was assessed by randomly varying actuator gains and computing the size of stable regions in parametric space.

In the absence of stretch reflexes the CPG, acting through the intrinsic biomechanical properties of the model, could produce stable gait over a surprising range of muscle activation levels. When the activation levels were deliberately set too low to support stable gait (Fig. 3, left panels), stretch reflexes adding 30% to the muscle activation profiles helped “rescue” stability. This is shown by the fact that when the reflexes were suddenly withdrawn, the model fell within two-step cycles. When the CPG activation profiles were set to levels that produced stable gait (Fig. 3, right panels), the addition of stretch reflexes made the kinematics slightly more vigorous and slightly increased the stable range of activation in parametric space. In some cases when CPG activation was high, the addition of stretch reflexes resulted in a fall after a few steps (not shown in Fig. 3). We concluded that stretch reflexes could rescue locomotion when CPG activation levels were low and improve overall stability by a modest amount (Yakovenko et al., 2004).

Phase switching with If-Then sensory rules increases stability

Some years ago it was suggested that although stretch reflexes may contribute to load compensation at the output level defined in Fig. 1, the

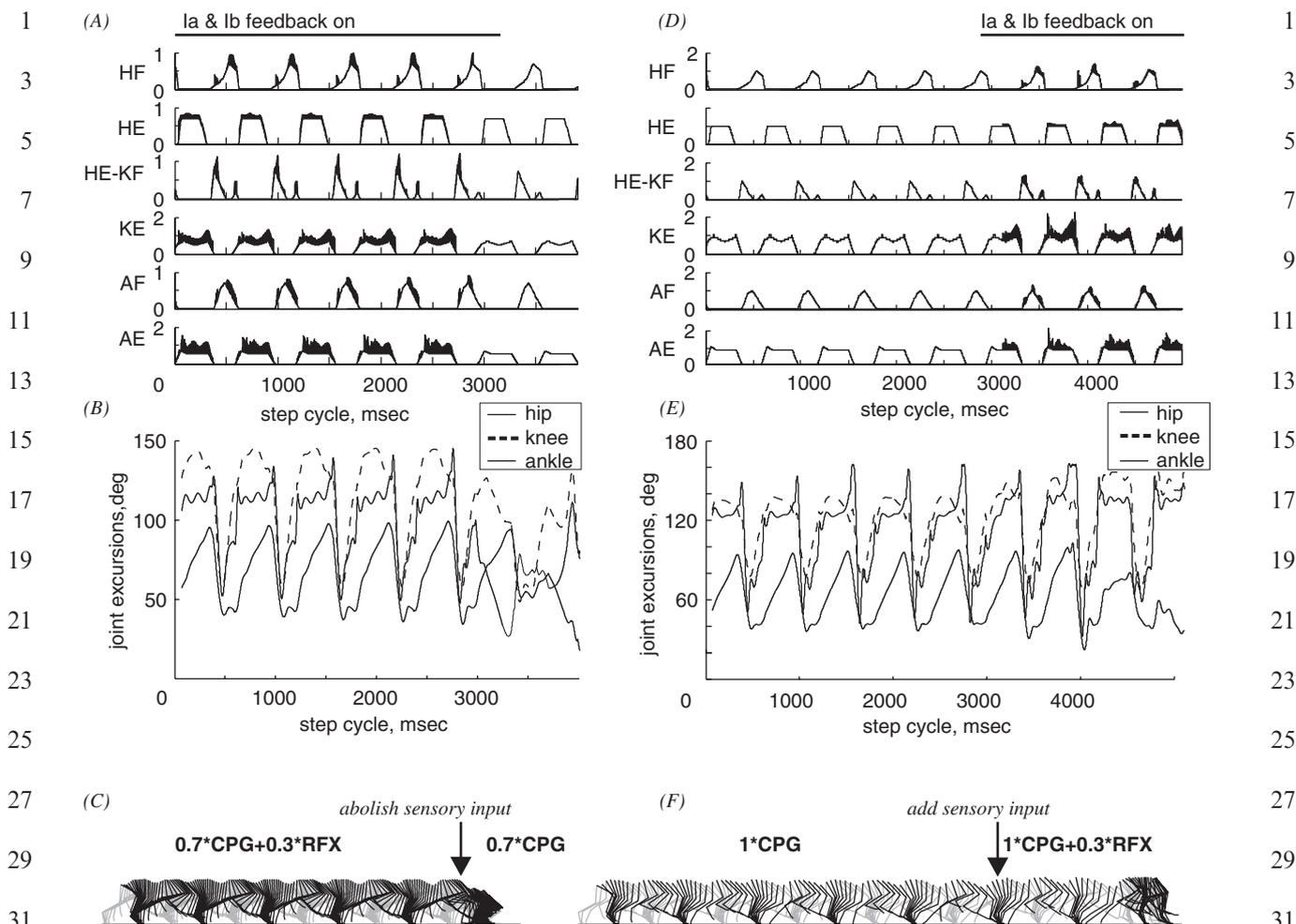


Fig. 3. Contribution of stretch reflexes during modeled locomotion. Left panels: centrally generated levels of muscle activation were insufficient of themselves to support stable locomotion. Stretch reflex contributions comprising 30% of the total activation (black portions of the activation profiles) were initially added and then suddenly removed. This caused a rapid collapse (stick figures). Right panels: centrally generated muscle activation levels were sufficient to support locomotion. Initially stretch reflexes were absent and then suddenly added. The only effect was a slight increase in gait velocity and a more vigorous gait. Adapted with permission from Yakovenko et al. (2004).

sensory control of cycle duration was mediated by some other mechanism, most likely through the timing and patterning elements of the CPG at the third or fourth levels. By analogy with robotic systems, it was proposed that finite state (“If-Then”) sensory rules underlay this higher-level interaction (Cruse, 1990; Prochazka, 1993). In our modeling study we therefore also explored the effect on stability of this form of control

(Yakovenko et al., 2004). The sensory rules were of the type:

1. Stance to swing transition: IF stance AND ipsilateral hip is extended AND contralateral leg is loaded THEN swing;
2. Swing to stance transition: IF swing AND ipsilateral hip is flexed AND ipsilateral knee is extended THEN stance.

AU:1

A large number of simulations were performed with and without these If-Then rules. Analysis showed that the rules provided dramatic improvements in flexibility and stability of level over-ground locomotion in our model. The key to the improvement was that each step cycle was adjusted to the prevailing kinematic state. Similar conclusions were reached in a later neuromechanical study in which locomotion was generated entirely by If-Then rules, in the absence of a modulated CPG pattern (Ekeberg and Pearson, 2005).

Control of locomotor phase durations within the CPG

In the next sections we will discuss new findings that indicate that CPG oscillators are “set” to generate phase durations best suited for the biomechanics of locomotion. In normal locomotion in most animals, cycle duration varies mainly as a result of changes in extensor phase duration (Halbertsma, 1983; Fig. 4C). However, recently it was found that in fictive locomotion in decerebrate cats elicited by stimulation of the midbrain locomotor region (MLR), in which the locomotor rhythm is generated almost exclusively by the CPG, flexor phase durations varied more than extensor phase durations in over half of the sequences observed (Fig. 4A). The phase (flexion or extension)

showing the larger variation was termed the “dominant” phase (Yakovenko et al., 2005). In a given animal, phase-duration plots were similar from one sequence to the next, suggesting that in a given preparation MLR stimulation produced specific descending signals that determined the phase-duration characteristics. We concluded that the locomotor CPG is not inherently extensor- or flexor-dominant, but depending on the balance of descending drives, it can show a continuum between the two. All three phase-duration plots in Fig. 4 were fitted remarkably well with a simple oscillator model (Fig. 5) by adjusting just two pairs of parameters that corresponded to “bias” and “gain” of the oscillator’s timing elements. This suggested that in real CPGs the phase-duration characteristics could be the consequence of particular set levels of drive to neural timing elements in the CPG. The half-center receiving the lower set level would respond to additional drive with the larger variation in phase duration. On this view, the set level, or background drive, would determine which half-center was dominant.

Interestingly, it is known that neurons in which persistent inward currents (PICs) have been activated show an inverse relationship between PIC level and sensitivity to synaptic inputs (Lee et al., 2003; Li et al., 2004). This raises the intriguing possibility that interneurons in the extensor timing element may receive less PIC-generating input and

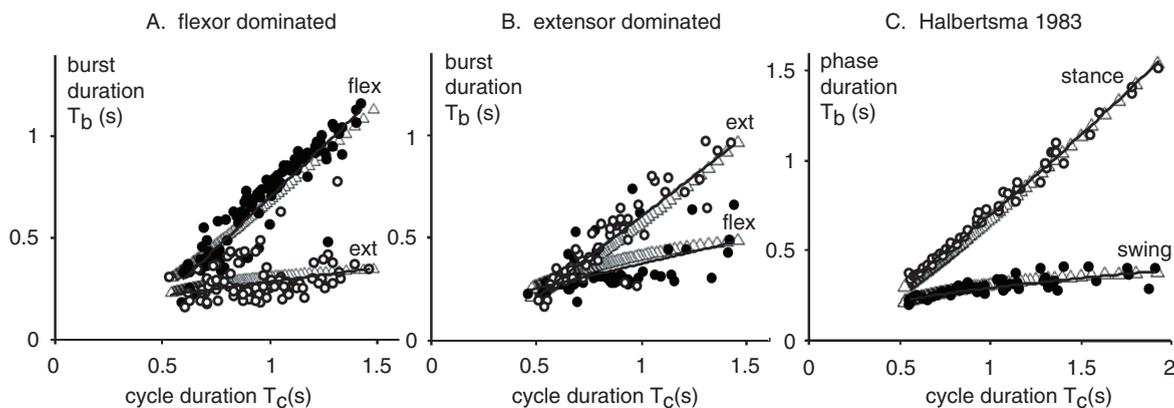


Fig. 4. Phase-duration versus cycle-duration plots in cat fictive locomotion (A and B) and normal cats (C). Filled circles: flexor phase (swing) durations, open circles: extensor phase (stance) durations. Triangles show the phase durations obtained from a simple oscillator model (Fig. 4), having adjusted the gain and offset parameters to fit the start and endpoints of the regression lines (solid) fitted to the data points.

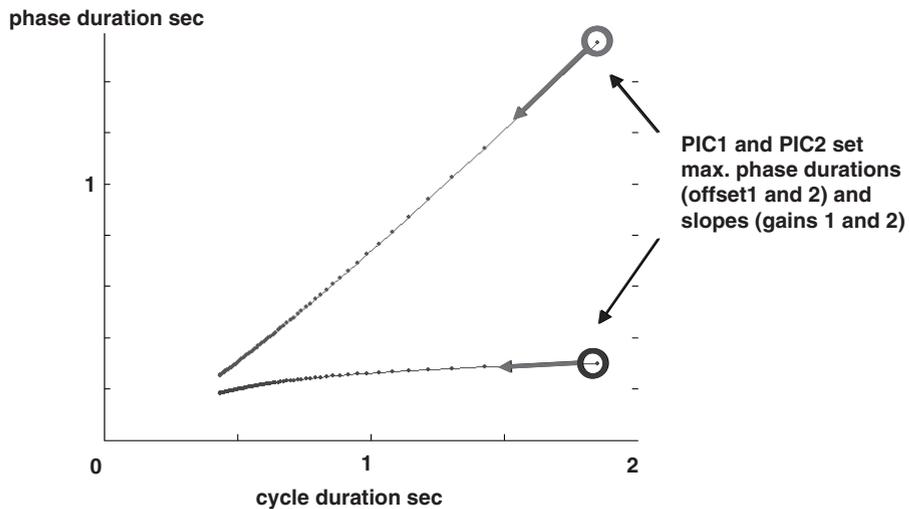
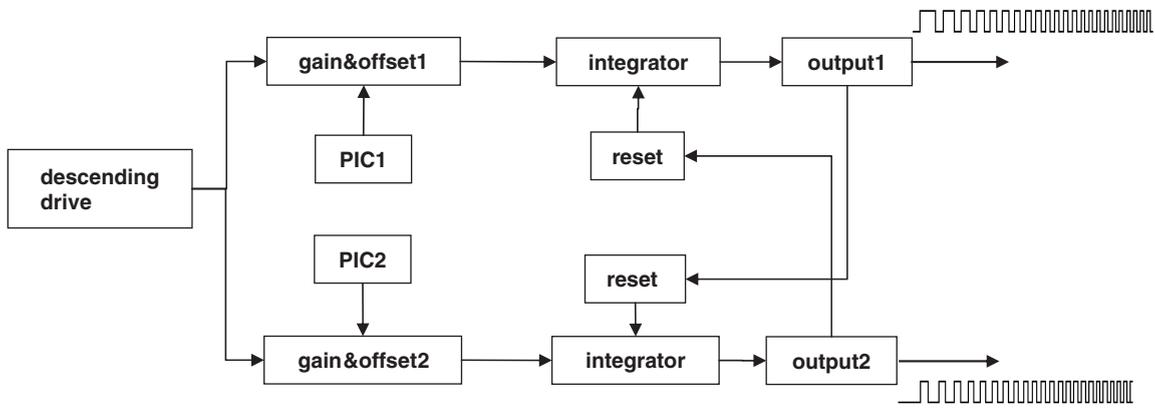


Fig. 5. Top: CPG oscillator model. PIC1 and PIC2 represent hypothesized persistent inward currents that determine the phase-duration characteristics (bottom). Open circles represent phase durations set by PICs when descending drive is zero. As descending drive increases, phase and cycle durations decline according to the sensitivity set by the PIC inputs. Note that the PIC inputs are hypothesized to set both gain and offset.

therefore as a network they are not only set to have longer half-cycle durations, but also to be more sensitive to synaptic commands for higher or lower cycle rates descending from supraspinal areas. The descending control of cadence could then reduce to a single signal driving these flexor and extensor timing interneurons (Fig. 5). As we will see next, in locomotion controlled by finite state rules, extensor-dominant phase-duration characteristics are the most likely to produce stable gait. We speculate that the appropriate drives to the extensor and flexor half-centers to produce these

characteristics are set at birth and are subsequently adjusted during the years of motor learning and body growth.

Sensory control of phase durations during locomotion

The section above discusses phase-duration control in the absence of sensory input. The spinal rhythm generator is effectively blind to the unfolding kinematics, except when supraspinal areas provide descending commands based on

exteroceptive inputs. We saw that in fictive locomotion in decerebrate MLR-stimulated cats the spinal CPG could generate cycles ranging from extensor- to flexor-dominant (Fig. 4A, B), presumably because the balance of descending drives to the half-centers ranged from normal to abnormal.

We wondered whether our neuromechanical model, provided with If-Then rules (see above), would exhibit phase-duration plots such as those in Fig. 4C. If it did, this would suggest that the biomechanics of locomotion require extensor-dominant phase-duration characteristics. It would also suggest that to harmonize with the kinematics and therefore the sensory input, the CPG oscillator should not only have an extensor-dominant phase-duration characteristic, but its operating points on this characteristic should be matched as closely as possible to the upcoming biomechanical requirements.

Figure 6 shows phase-duration plots computed from 20 simulations, each involving a minimum of five sequential step cycles. In a given simulation,

the amplitudes of CPG activation profiles and durations as well as the trigger levels for If-Then rules were set to a variety of different levels, in order to generate gait of varying velocity and cadence. In two of the simulations, on-off activation profiles were used rather than the modulated EMG profiles obtained from the literature. In spite of all these parametric differences, the phase durations in all stable sequences (five steps or more without falling) were constrained along extensor-dominant phase-duration characteristics.

This result supports the idea that phase-duration characteristics are dictated by biomechanical attributes. The structure of the body (segment lengths and masses), as well as the disposition and force-generating properties of the muscles would be among the important determining factors. In future simulations we will explore the effect of limb segment length, body mass and other factors, including for example physical properties of the support surface. At this stage the results are sufficiently persuasive for us to formulate the conclusions below.

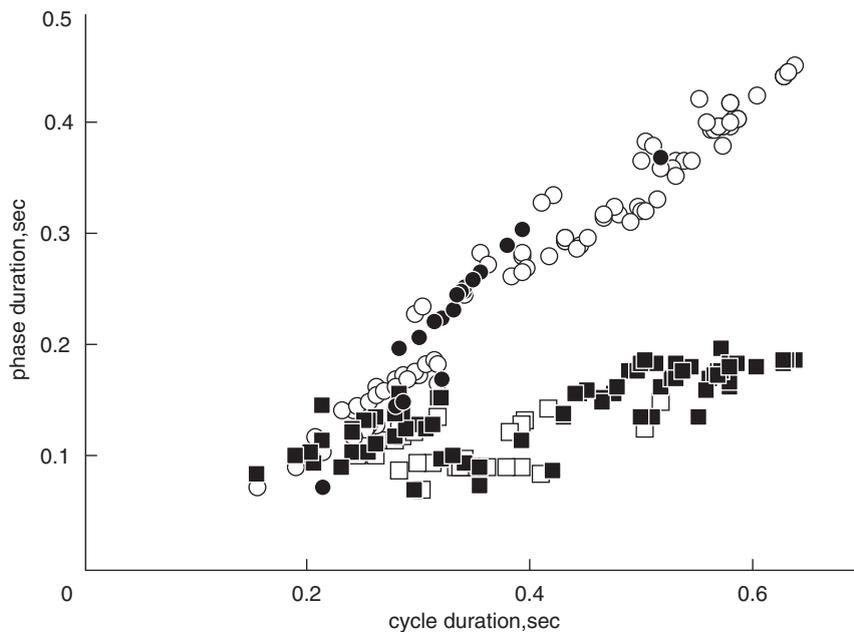


Fig. 6. Phase-duration plots computed from 20 simulations, each involving a minimum of 5 sequential step cycles. Circles: stance phase, squares: swing phase. Filled symbols indicate phases terminated by an If-Then rule, open symbols indicate phases terminated by completion of the CPG profile for that phase.

Conclusions: general propositions

1. For gait to be stable, swing and stance phase durations are constrained to characteristic values, described by two lines in a plot of phase- versus cycle-duration.
2. The phase-duration characteristics were modeled surprisingly well by setting just two pairs of parameters in a simple oscillator. This suggests that a particular phase-duration characteristic is preset by tonic drive to spinal interneuronal networks forming the timing elements of the CPG.
3. Stable gait was also achieved without specific CPG activation profiles, by switching muscles on and off according to sensory-mediated rules. The key new finding is that the phase-duration characteristic in such simulations was similar to the extensor-dominant characteristics in purely CPG-generated rhythms. This suggests that the constraints on phase durations in normal behavior are predetermined by the biomechanics.
4. We posit a spinal CPG timer and a sensory-mediated switch that operate in parallel, the former being driven primarily by descending inputs and the latter by the kinematics. We suggest that the system works best when the CPG timer is preset to produce an extensor-dominant phase-duration characteristic. Descending input from higher centers then adjusts the operating point on this preset phase-duration characteristic according to anticipated biomechanical requirements. In well-predicted movements, CPG-generated phase durations closely match those required by the kinematics. Residual errors are corrected by the sensory switching mechanism. We propose the term “neuromechanical tuning” to describe this process.

Epilogue

It is always humbling to discover that conclusions derived from complicated mathematical analyses were anticipated many years ago. Here is an extract from T. Graham 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.

Acknowledgments

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