# Predictive and reactive tuning of the locomotor CPG

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**Synopsis** The neural control of locomotion involves a constant interplay between the actions of a central pattern generator (CPG) and sensory input elicited by bodily movement. With respect to the CPG, recent analysis of fictive locomotion has shown that durations of flexion and extension tend to covary along specific lines in plots of phase duration versus cycle duration. The slopes of these lines evidently depend on internal states that vary among preparations, but, within a preparation, remain rather steady from one sequence to the next. These relationships can be reproduced in a simple oscillator model having two pairs of preset parameters, suggesting that steady internal drives to flexor and extensor half-centers determine how phase durations covary. Regarding the role of sensory inputs, previous experiments have revealed state-dependent rules that govern phase-switching independently of the CPG rhythm. In addition, sensory input is known to modulate motoneuronal activation through stretch reflexes. To explore how sensory input combines with the locomotor CPG, we used a neuromechanical model with muscle actuators, proprioceptive feedback, sensory phase-switching rules, and a CPG. Interestingly, sequences of stable locomotion were always associated with phase durations that conformed to an extensor-dominated phase-duration characteristic (where extension durations vary more than flexion durations). This is the characteristic seen in normal animals, but not necessarily in fictive locomotion, where movement and associated sensory input are absent. This suggests that to produce the biomechanical events required for stability, an extensor-dominated phase-duration characteristic is required. In the model, when the preset CPG phase durations were well matched to coincide the biomechanical requirements, CPG-mediated phase switching produced stable cycles. When CPG phase durations were too short, phases switched prematurely and the model soon fell. When CPG phase durations were too long, sensory rules fired and overrode the CPG, maintaining stability. We posit that under normal circumstances, descending input from higher centers continually adjusts the operating point of the CPG on the preset phase-duration characteristic according to anticipated biomechanical requirements. When the predictions are good, CPG-generated phase durations closely match those required by the kinetics and kinematics, and little or no sensory adjustment occurs. We propose the term "neuromechanical tuning" to describe this process of matching the CPG to the biomechanical requirements.

## Introduction

The neurophysiological mechanisms controlling locomotion have been studied for over a century. There is a similarly long history of biomechanical studies of locomotion. Only recently have there been any serious attempts to bring these two streams together.

Even within the neurophysiological studies there has been a separation between work on central neural oscillators and peripheral reflexive mechanisms. Recent models of the mammalian central pattern generator (CPG) have begun to include the effects of sensory input (Rybak et al. 2006b), but there have been few attempts to also include the biomechanical components of the overall system.

At the opposite extreme, sensory phase-switching rules have been proposed that take into account the kinematics and kinetics, but ignore the CPG (Cruse 1990; Prochazka 1993; Ekeberg and Pearson 2005).

The present article briefly reviews some of the recent attempts to bring the various streams together and discusses some neuromechanical simulations of locomotion that show the importance of mechanical events in shaping the basic rhythm of the CPG.

## Components of locomotor systems

The main components of locomotor systems have been studied in great detail. Musculoskeletal actuators and body segments have been characterized and modeled (Brown and Loeb 2000; Zajac 2002;

Zajac et al. 2003), as have sensory afferents (Prochazka and Gorassini 1998b; Prochazka 1999; Mileusnic et al. 2006; Mileusnic and Loeb 2006) and their reflex actions (Frigon and Rossignol 2006; Rossignol et al. 2006). CPGs have been studied in isolation and modeled in a variety of animals (Selverston 1993; Arshavsky et al. 1997; Grillner et al. 2000; McCrimmon et al. 2000; Zelenin et al. 2000; Kiehn 2006; Rybak et al. 2006a, 2006b).

The picture that emerges from all this work may be summarized as follows. Muscle actuators provide propulsive force and load compensation through spring-like properties termed "preflexes" (Loeb et al. 1999). Motoneurons (MNs) activate the muscles and receive synaptic input from sensory afferents and spinal interneurons. Some of these interneurons (termed the pattern formation layer) select and coordinate MNs (Perret and Cabelguen 1980; Perret 1983; Lafreniere-Roula and McCrea 2005). Other interneurons within the network collectively called the CPG, act as timing elements in a rhythm generator. The CPG receives sensory input and descending drive from the brainstem and other higher centers including the brainstem (Shik et al. 1966; Takakusaki et al. 2004), cerebellum (Arshavsky et al. 1986; Mori et al. 1998), basal ganglia (Jordan 1998), and motor cortex (Beloozerova and Sirota 1993; Widajewicz et al. 1994; Drew et al. 2004). These higher centers integrate motivational (Jordan 1998), exteroceptive (Drew 1991; Rossignol 1996; Patla et al. 1999), and proprioceptive (Rossignol et al. 2006) inputs.

Locomotor control studies have tended to concentrate either on neurophysiological mechanisms or on biomechanical mechanisms but rarely on the two combined (Feldman 1966; Bernstein 1967; Dickinson et al. 2000; Biewener 2006; Frigon and Rossignol 2006; Rossignol et al. 2006). Douglas Stuart and his colleagues were among the first to begin bridging the gap in the early 1970s (Goslow et al. 1973a, 1973b). Taga and co-workers provided the first comprehensive models of mammalian locomotor control in their analysis of human locomotion (Taga et al. 1991; Taga 1995a, 1995b, 1998). With the advent of user-friendly modeling software, it has become easier to construct neuromechanical models and run simulations (Yakovenko et al. 2004; Ekeberg and Pearson 2005; Pearson et al. 2006). This article will present further aspects of this type of modeling.

## The locomotor CPG

In normal locomotion in cats and humans, step-cycle duration is controlled mainly through variations in the duration of the stance (extension) phase (Goslow et al. 1973a; Halbertsma 1983; Yang et al. 2004). Extensor phase durations are also dominant in alligators, chicks, dogs, salamanders, and turtles (Earhart and Stein 2000). Furthermore, flexion and extension phase durations covary along a specific pair of lines in plots of phase duration versus cycle duration. In the following this pair of lines is called the phase-duration characteristic. Because the extension phase duration varies more, its line has the steeper slope. The reverse, however, was recently observed in sequences of fictive locomotion in decerebrate cats elicited by stimulation of the midbrain locomotor region (MLR). In that study, the durations of the flexor phases varied more than did those of the extensor phases in a small majority of cases (Yakovenko et al. 2005), i.e., the flexion phase-duration lines had the steeper slopes. In a given preparation, the phase-duration characteristic was similar from one sequence to the next, suggesting that the outcome of decerebration and MLR stimulation in a particular animal produced a specific combination of descending signals that determined the phase-duration characteristic. This showed that the CPG was not inherently extensor-dominant. Flexor-dominant patterns have been reported in rhythmical scratching in the cat (Berkinblit et al. 1978) and turtle (Earhart and Stein 2000) and in air-stepping in the cat (Smith et al. 1986).

We wondered whether the two-line phase-duration characteristic might be a general constraint of any asymmetrical oscillator with controllable cycle duration. A simple oscillator model implemented in Matlab Simulink confirmed this suspicion (Yakovenko et al. 2005). Any of the phase-duration characteristics obtained experimentally could be fitted remarkably well by adjusting just two pairs of parameters corresponding to "bias" and "gain" of the oscillator's timing elements. This suggested that in real CPGs, set levels of drive to timing elements in the CPG determine the phase-duration characteristic. In the model, cycle duration was controlled by one and the same time-varying command to each half-center. The half-center with the lower background drive responded to variations in command with the larger variations in phase duration. Regarding the actual phase switching mechanism, Yakovenko et al. (2005) speculated that the interneuronal networks that determine phase durations do so by integrating descending and sensory inputs and upon reaching threshold, terminate the current phase and initiate the next phase. The reverse is also possible: the timing networks might integrate inhibitory input

and thereby "fatigue," as originally suggested in the half-center hypothesis (Brown 1911). Paul Stein's recordings of "ON" and "OFF" interneurons are arguably the first step in recording from putative locomotor timing interneurons in vertebrates (Stein and Daniels-McQueen 2003).

## Sensory input

Sensory input interacts with the CPG in several ways. It can trigger phase transitions in a switch-like manner; it can change phase durations in a graded way and it can contribute to load compensation through stretch reflexes (Rossignol et al. 2006). Cutaneous receptors form the majority of mechanoreceptors. They have short-latency reflex actions on MNs and they can trigger coordinated responses such as the stumble corrective reaction. Many cutaneous receptors, however, only fire at step-cycle transitions, for example upon ground contact, or at foot-lift (Loeb 1981). Although there is evidence in humans that cutaneous receptors may fire continuously and contribute to conscious proprioception (Collins and Prochazka 1996; Edin 2001), abolishing cutaneous input from the footpads does not lead to aberrant locomotion in normal cats (Engberg 1964; Rossignol et al. 2006). Continuous control of locomotor reflexes and phase transitions is therefore *mainly* attributable to muscle spindles, which to a first approximation signal muscle length and velocity, and tendon organs, which signal force. Simple models have been developed that predict the ensemble firing rates of proprioceptors from muscle length and force, accounting for 80% or more of the variance (Prochazka and Gorassini 1998a, 1998b; Prochazka 1999). A more complex muscle-spindle model has recently appeared that includes not only fusimotor action, but also tendon compliance, muscle pennation and other nonlinear features (Mileusnic et al. 2006). With the right choice of parameters and with accurate fusimotor drive profiles, this model would probably provide more accurate predictions but it has not yet been used in locomotor simulations to our knowledge.

## Stretch reflexes

Steadily activated muscles resist length perturbations through inherent spring-like mechanical properties. These "preflexes" are equivalent to negative length-feedback control. Afferent activity in Group I and Group II afferents innervating muscle spindles reflexly excite homonymous MNs, and thus augment the length feedback of the preflexes (He et al. 1991).
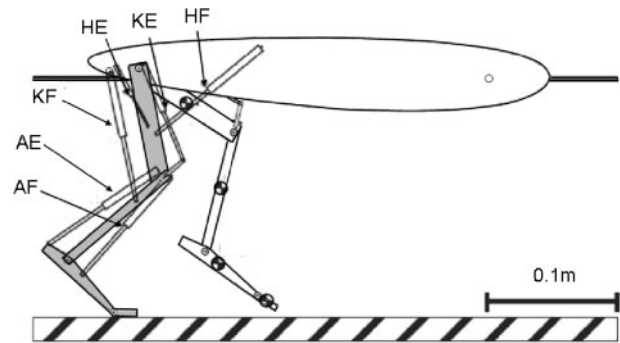


Fig. 1 Neuromechanical model used in locomotor simulations. Each leg had six muscle actuators endowed with muscle-like properties. Front of body was supported on a frictionless railing. Simulations were performed with Working Model 2D (WM2D) linked to Matlab v.6.5 software. The model included sensory feedback from each actuator, based on the response properties of muscle spindles and tendon organ afferents. Abbreviations: AE = ankle extensors, AF = ankle flexors, HE = hip extensors, HF = hip flewors, KE = knee extensors, KF = knee flexors.

Tendon organ afferents respond to increases in muscle force and during gait they reflexly excite homonymous MNs to produce even more force (Conway et al. 1987). This is equivalent to *positive* force feedback, the loop gain of which is less than unity except perhaps in bouncing gait (Prochazka et al. 1997; Geyer et al. 2003). Up to 30% of the neural activation of extensors in the stance phase of the cat step cycle is attributable to proprioceptive stretch reflexes (Prochazka et al. 2002). There is a significant delay (up to 40 ms) after ground contact, however, before the reflex component of electrical activation appears (Gorassini et al. 1994; Gritsenko et al. 2001). Given this modest and delayed contribution of reflexes and the fact that after training, de-afferented cats generate rather normal stance phases (Pearson et al. 2003), the importance of stretch reflexes in load compensation came into question (Prochazka et al. 2002).

   To study this and other questions, we developed a neuromechanical model with 2D Working Model 2D (WM2D) and Matlab v.6.5 software (Yakovenko et al. 2004). The model consisted of a torso supported at the front on a frictionless horizontal rail and at the back by two legs (Fig. 1). Each leg comprised four segments (thigh, shank, foot, and toes) with six actuators mimicking hip, knee and ankle extensors, and flexors. The actuators had Hill-type muscle properties and were driven by muscle-activation patterns derived from EMG studies of cat locomotion. Spindle and tendon organ models were used to add reflex components to the muscle-activation profiles. These models, which included linear and nonlinear dynamic components

of response, were selected from the literature on the basis of their ability to predict firing rates of spindles and tendon organs from signals of length and force (Prochazka and Gorassini 1998b; Prochazka 1999). The outputs of the spindle and tendon organ models were delayed by 35 ms and added to the activation profiles with gain factors set so that they each contributed about 15% to the overall activation profile. The stability of locomotion with, and without, these reflexes was quantified by principal component analysis (for details see Yakovenko et al. 2004).

The CPG pattern alone, acting through the spring-like properties of the muscle actuators, produced stable gait over a surprising range of muscle-activation levels. When these activation levels were set too low to support stable gait, stretch reflexes helped restore stability. When they were set at levels appropriate for stable gait, stretch reflexes caused a more erect and vigorous gait and slightly improved stability. We concluded that stretch reflexes could help stabilize locomotion when CPG activation levels were low, but otherwise their effect was limited to adjusting posture (Yakovenko et al. 2004).

### Phase switching with if-then sensory rules

A mechanism other than stretch reflexes is required to explain sensory-mediated phase switching. Starting with Freusberg (1874), numerous experiments have shown that phase durations can be either lengthened or shortened by combinations of sensory input (Sherrington 1914; Grillner and Rossignol 1978; Hiebert et al. 1994; Bassler and Buschges 1998; Pearson et al. 2006). Some years ago it was recognized that locomotor control in various species seemed to conform to so-called finite state rules (e.g., "If stance and leg extended and extensor force low, switch to swing phase") (Cruse 1990; Prochazka 1993). Misiaszek (2006) recently extended the rule-based concept to the control of postural reactions. It has been suggested that in stick insects, phase control is entirely sensory-mediated, with little evidence of CPG control either within a leg or between legs (Schmitz et al. 2001).

To explore this further, we added If-then rules to our neuromechanical model (Yakovenko et al. 2004). The firing of a rule overrode and reset the read-out of CPG activation profiles. An example of such a rule is as follows: "If leg is in stance and hip flexor length is greater than $x$ and ground reaction force is greater than $y$, shift cycle read-out time to swing onset in ipsilateral leg and stance termination in contralateral leg." Thousands of simulations were
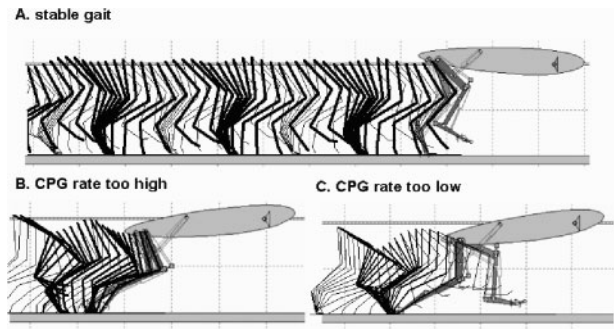


**Fig. 2** Examples of stable and unstable sequences of locomotion. (**A**) Model with stretch reflexes and if-then rules, CPG cycle period set to 0.5 s, which resulted in stable locomotion; (**B**) No if-then rules, cycle period 0.2 s, too short to result in stable locomotion with CPG actuation alone; (**C**) No if-then rules, cycle period 1 s, too long to result in stable locomotion with CPG actuation alone.

run with and without the set of finite state rules. We found that rule-based switching significantly improved stability. On many occasions, step cycles that would have ended in a fall if the CPG profile had been allowed to run its course, were rescued by early phase switching forced by the firing of one of the rules (Fig. 2). A recent modeling study of quadruped gait, in which phase switching was controlled entirely by if-then rules, showed that stability could be achieved even when the coupling between legs was weakened or abolished (Ekeberg and Pearson 2005).

As stated earlier, the spinal CPG is not inherently extensor-dominant or flexor-dominant. We posited that under normal conditions, descending and local drive to the half centers set up an extensor-dominant characteristic. We wondered whether our neuromechanical model, when provided with wide-ranging sets of parameters producing gait of different velocities and cadence, would also exhibit an extensor-dominant phase-duration characteristic, or for that matter, whether it would conform to an orderly phase-duration relationship at all. The Matlab component of the software had an interface that allowed easy adjustment and setting of the following: (1) individual shapes of the six CPG muscle-activation profiles (including ON/OFF profiles); (2) maximal activation level of each muscle; (3) percentage contribution of stretch reflexes; (4) cycle duration (achieved by setting the read-out rate of the activation profiles); (5) trigger levels for if-then rules. The WM2D software allowed quick re-setting of initial velocity, as well as physical parameters such as body mass, ground friction, elasticity and initial posture.
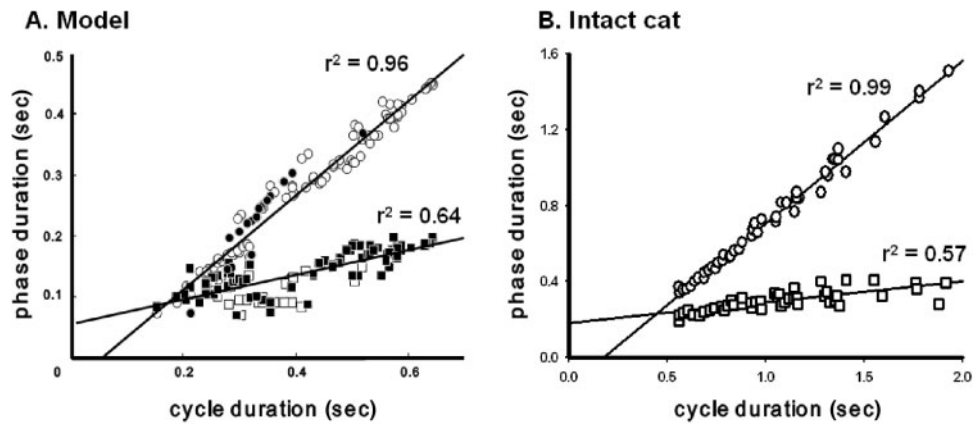
**Fig. 3** (**A**) Phase-duration plots computed from 20 simulations, each involving a minimum of 5 sequential step cycles. Circles: stance phase, squares: swing phase. Open symbols indicate phases terminated by an if-then rule, filled symbols indicate phases terminated by completion of the CPG profile for that phase. (**B**) Phase duration plots in an intact cat (Halbertsma, 1983) for comparison. Note the similar regression coefficients and relationships between flexion and extension phase durations in A and B. Note too the difference in overall range of cycle durations in A and B (see text).

Approximately 150 simulations were performed, of which 20 turned out to be stable. A stable sequence was defined as one in which there were five or more step cycles without a fall or obvious deficiencies such as foot-drag or laterally asymmetric gait. Figure 2 shows examples of stable and unstable sequences, the latter caused by CPG cycle periods that were too short (B) or too long (C). Each simulation required 1–4 min of computer time to run, depending on whether it turned out to be stable or not. 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 (the Supplementary Material movie clip bm2006.avi shows a simulation in which cadence, velocity and stride length varied widely within one stepping sequence). In two of the simulations, ON–OFF activation profiles were used rather than the normal modulated EMG profiles.

Remarkably, in spite of the large range of parameters and activation profiles used to generate the various sequences, the phase-duration plot of Fig. 3A shows that extensor phase durations were distributed in an orderly way along a line having a steep slope and flexor phase durations were likewise distributed along a line having a shallow slope. In other words, the model exhibited an extensor-dominant phase-duration characteristic. The regression coefficients in Figs. 3A (model) and Fig. 3B (normal cats, Halbertsma 1983) are similar, indicating similar deviations from the lines of best fit. On the other hand, in unstable sequences, phase durations tended to deviate substantially from the characteristic (not shown in Fig. 3). Note that the

range of cycle durations in Fig. 3A (0.2–0.6 s) was lower than that in Fig. 3B (0.5–2.0 s). It is unusual for cats to exhibit cycle durations greater than 1 s during overground locomotion. On the other hand, the difference may be due to the structure or function of our model. For example the torso mass in our model is 1.5 kg, which is probably only half that of a medium-sized adult cat. This issue is currently being studied.

From the above result, we conclude that for locomotor step cycles to be stable, phase durations generally conform to an extensor-dominant phase characteristic. To put it another way, the phase-duration characteristic is dictated by the biomechanical requirements. This is not to say that it is impossible to generate stable gait without adhering to an extensor-dominant phase characteristic. For example, with conscious effort it is possible to walk at various speeds with identical flexion and extension phase durations. In this type of gait there is no double-support phase. It is an unnatural way of walking and requires adaptive control in order to be maintained.

One final point deserves mention. Actual locomotion in decerebrate animals, as opposed to fictive locomotion, is often more unstable even though sensory input is intact. At first glance this seems to contradict our notion that sensory input is stabilizing. However, the instability in this case is in the form of bursts of vigorous locomotion alternating with slow or absent locomotion. It does not necessarily imply biomechanical instability. If the activation patterns recorded in fictive locomotion could somehow be played into non-paralyzed muscles, it seems very likely from our modeling,

that the biomechanical outcome would nearly always rapidly lead to falls, whereas actual decerebrate locomotion can often be remarkably stable, even adapting to very large changes in treadmill speed (Orlovsky et al. 1999).

## Conclusions

In the earlier sections, we have looked at locomotor phase-switching behavior in free-running CPGs, in controllers that use only sensory rules and in mixtures of the two. Taking all of the evidence together, we propose the following general conclusions:

(1) In stable gait, swing and stance phase durations tend to be constrained to characteristic sets of values that fall along two lines of differing slope in plots of phase duration versus cycle duration.

(2) The phase-duration characteristic can be duplicated precisely in a simple oscillator model having two pairs of control parameters. This suggests that phase-duration characteristics in animals are set by steady, asymmetrical drive to the interneuronal timing elements of the CPG.

(3) The phase-duration characteristic in a simple neuromechanical model of quadruped locomotion was similar to the extensor-dominant characteristic in normal gait. From this we posit that the normal extensor phase-duration characteristic is dictated by biomechanical requirements.

(4) For mammals, we suggest that a spinal CPG timer and a sensory-mediated switch operate in parallel, the timer driven by descending inputs and the switch by kinematic events. The system probably works best if the CPG timer by default produces an extensor-dominant phase-duration characteristic. The higher centers could then adjust the operating point on the phase-duration characteristic according to prevailing and anticipated biomechanical requirements. In good predictions, CPG-generated phase durations would be slightly longer than those required by the kinetics, allowing the sensory switch to make the final small adjustment at the end of each phase. If the predicted duration of the CPG cycle is too short, gait is destabilized for that step cycle and when possible, corrected by the next prediction. We propose the term "neuromechanical tuning" to describe this predictive and adaptive process.

## Supplementary data

Supplementary data are available at ICB Online.

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