Analysis of Human Locomotion via Entrainment to Mechanical Perturbations to the Ankle during both Treadmill and Overground Walking

by

Julieth Ochoa

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Abstract

Rehabilitation of human motor function is an issue of utmost significance affecting millions of Americans. Robot-aided therapy emerged as a promising method to meet the increasing demand for effective rehabilitation services. While robot-aided therapy for upper-extremity provides clinically-proven, efficient rehabilitation, human-interactive robots for lower-extremity therapy have been substantially less successful. Given the labor-intensive nature of conventional, human-administered walking therapy, effective robot-aided assistance is urgently needed. The use of robots and treadmills that may inadvertently suppress the expression of the natural oscillatory dynamics of walking is addressed in this thesis as a possible explanation for the ineffectiveness of robotic walking therapy.

To further investigate the natural oscillatory dynamics of walking, the existence and provenance (spinal or central) of a neuro-mechanical oscillator underlying human locomotion was assessed. This oscillator was studied via gait entrainment to periodic mechanical perturbations at the ankle in both treadmill and overground environments. Experiments with unimpaired human subjects provided direct behavioral evidence of the non-negligible contribution to human walking made by a limit-cycle oscillator in the spinal neuro-mechanical periphery. *Entrainment* was always accompanied by *phase-locking* so that plantar-flexion perturbations assisted propulsion during ankle 'push-off' while dorsi-flexion perturbations assisted toe-clearance during 'initial swing'. The observed behavior seemed to require a neural adaptation that could not easily be ascribed to biomechanics, suggesting a hierarchical organization between the supra-spinal nervous system and the spinal neuro-mechanical periphery: *episodic supervisory control*.

Thesis Supervisor: Neville Hogan
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Chapter 1

Introduction

The study of locomotor control has been dominated by the perspective that the supra-spinal nervous system dictates the different elements of movement, which are then executed by the neuro-mechanical periphery. Neuroscience studies have been dedicated to investigating how the activity of the supra-spinal nervous system causes body movements. Conversely, biomechanics studies have aimed to understand how the dynamics of the neuro-mechanical periphery respond to neural inputs. While convincing evidence has been presented from both ends, there is no conclusive principle yet identifying the specific cause and effect of body movement that is generated by the interaction between the supra-spinal nervous system, the neuro-mechanical periphery, and the environment.

Neuroscience studies of animal locomotion have identified rhythm-generating networks in the nervous systems as the main controllers of rhythmic movement. These rhythm-generating networks are called central pattern generators (CPGs) [1–3]. While a CPG may be capable of generating rhythmic movement, the specific interaction between a CPG and additional sensory inputs (e.g. the environment) may play an essential role in execution of stable locomotion [4–6]. In that case, locomotion (i.e. the motor output) emerges as the result of the dynamic interaction between the supra-spinal nervous system, the neuro-mechanical periphery, and the environment.

Biomechanics studies of human locomotion have investigated mainly the dynamic properties of the neuro-mechanical periphery, using forward and inverse dynamics methods. The forward dynamics methods have facilitated the mathematical simulation of locomotion using neural inputs [7]. Instead, inverse dynamics methods have used mathematical models of the body and human movement to study forces and moment patterns [8,9]. Together, these conceptually different studies have offered insightful information about the relation between the activation of the neuro-mechanical periphery and the execution of movement. However, the specific link between the dynamics of the supra-spinal nervous system and the dynamics of the neuro-mechanical periphery remain unclear, and are essential to fully understand the generation and control of human locomotion.

An integrative principle linking the interaction between the supra-spinal nervous system, the neuro-mechanical periphery, and the unknown environment to generate stable and flexible locomotion was proposed by Taga and colleagues: "global entrainment" [10]. Such new principle suggested that human locomotion is achieved as a "global limit-cycle generated by a global entrainment" between the rhythmic behaviors of both the neural oscillators in the nervous system and the neuro-mechanical periphery (including the environment).

> *The study presented in this thesis was directed towards gaining understanding of locomotor control by further investigating the neuro-mechanical oscillator postulated to underlie human locomotion via gait entrainment to periodic mechanical perturbations at the ankle joint in treadmill and overground environments.*

1.1 Robotic Walking Therapy and its Limitations

1.1.1 The Problem

Rehabilitation of human motor function is an issue of utmost significance as the demand for effective rehabilitation service continues to grow with the graying of the population and the rise of age-related disorders. Robot-aided therapy has emerged as a promising method to meet the increasing demand for effective rehabilitation services. Robots are not only capable of supporting the labor-intensive tasks performed by therapists but can also provide therapeutic services more frequently. Additionally, therapeutic robotic devices can quantitatively measure patients' performance and assess improvements made over time, which is essential for systematic training. Yet the inclusion of robotic systems in physical therapy has not been as efficient as originally envisioned. While upper-extremity robot-aided rehabilitation has proven effective [11–14] and is recommended by the American Heart Association and US Veteran's Administration, lower-extremity robotic therapy has proven to be inferior to conventional therapy [15,16] and declared "still in its infancy" [17]. Given the labor-intensive nature of human-administered walking therapy, effective robot-aided assistance to locomotor recovery is urgently needed.

1.1.2 Critical Barrier to Progress

A plausible explanation for the ineffectiveness of robotic walking therapy is that human-interactive robots may inadvertently suppress the expression of the natural oscillatory dynamics of walking. Most current therapeutic robots for walking emphasize the nominal kinematics of normal lower-limb motion [18–20], discouraging (often preventing) voluntary participation of patients. This approach is based on the premise that repeated exposure results in recovery of motor function. By emphasizing nominal kinematics without sensitivity to the patient's performance, this approach does not encourage voluntary participation of the patients—an essential element of successful neuro-restoration [21–23].

Another problem with current therapeutic robots, such as the Lokomat (Hocoma), Lokohelp Gait Trainer (Lokohelp group), Haptic Walker [24], and GEO System (Reha Technologies), is that these tend to confine their assistance to the sagittal plane of motion. A major problem with this limited assistance is that joint torque and motion in the frontal plane—constrained in the aforementioned therapeutic robots—are significant elements of normal human locomotion [25]. A particular task during human walking for which frontal motion is, indeed, critical is maintaining balance. Hence, technologies for robot-aided recovery of locomotor function should definitely incorporate natural and voluntary frontal plane motion.

Unlike robotic walking therapy, the most effective form of upper-limb robot-aided therapy was carefully designed to be *permissive* [11, 12, 26]: it allows the nervous system to express whatever action it can, and reinforces appropriate action as needed. Either by inappropriate design or ineffective control strategies, robotic walking therapy has not yet been permissive. Given the critical role of foot-ground interactions in walking, therapeutic robots should allow patients to re-learn how to take advantage of the natural oscillatory dynamics resulting from their foot-ground interactions. Yet most current robots for walking therapy, such as Lokohelp Gait Trainer, Haptic Walker, and GEO System, neglect this criterion by emphasizing nominal kinematics of normal lower-limb motion [18–20].

Neurologically-impaired subjects typically do not have intact neural control. To provide an effective rehabilitation strategy for this population and overcome the limitations of present robotic locomotor therapy, it is essential to examine the minimal 'mechanical components' that contribute to robust stable human walking. Energy dissipation and compensation through foot-ground interactions not only contributes to robust stability of human locomotion, but may also reduce the burden on higher centers of the brain. The fact that muscles do more positive than negative mechanical work during locomotion [27] suggests that the supra-spinal nervous system takes advantage of interaction within the neuro-mechanical periphery to guarantee stable walking. *An effective strategy needs to allow the impaired patients to re-learn how to take advantage of the natural oscillatory dynamics that result from their foot-ground interactions*.

1.2 Dynamics of Human Locomotion

The center of mass of the human body extends past the base of support during most of the normal gait cycle; thus, from a mechanical point of view, the human body could be regarded as fundamentally unstable. In fact, the overall dynamic stability of the entire body is compromised due to the presence of unpowered degrees of freedom since torques cannot be exerted specifically at the center of pressure (COP) of the ground reaction forces [28].

Fundamentally, human locomotion is a 'hybrid' process that couples continuous rhythmic dynamics (swing of legs and arms) with discrete dynamics (foot-ground contact). Specifically, bipedal walking is characterized by oscillatory dynamics that are caused by the effects of gravity and inertia. Generally, the motion of the entire body during locomotion can be regarded as the motion of an inverted pendulum; i.e. locomotion can be described in terms of the displacement of the body's center of gravity (COG) with respect to its COP. On the other hand, the motion of the swinging leg can be described as the motion of a coupled pendulum. Walking is reasonably approximated as periodic motion. The robust stability of this periodic motion requires both energy dissipation and compensation, for which the role of the foot-ground interaction is essential. Foot-ground interaction dissipates kinetic energy, which requires muscles to do more positive than negative mechanical work. Studies have revealed that, in fact, muscles do more positive than negative mechanical work during locomotion, even at constant preferred speeds on level ground [27]. Moreover, work by Kuo and colleagues has established that the most significant source of energy dissipation—responsible for 60-70% of the net metabolic cost of human locomotion at preferred speed—are step-to-step transitions due to foot-ground interaction [29].

Various studies have demonstrated that the resonant frequency of the entire body system is a key element determining the spontaneous locomotion [30–32]. During steady-state locomotion, various joints exhibit complex rotational movement patterns that are constantly shifting. Indeed, the three major lower-limb joints—ankle, knee, and hip—rarely rotate simultaneously in the same direction; i.e. while some of these joints flex, the others extend, and vice versa [33]. Muscles have their own specific pattern of activity during the different phases of the gait cycle [8], yet the precise mechanisms responsible for generating such patterned signals—capable of maintaining stability—remain unclear.

The generation of animal locomotion is believed to involve spinal CPGs, which regulate single joint activity [2]. For instance, the ankle, knee, and hip joints in quadrupeds move in phase, while the flexor and extensor muscles activate during the swing and stance phase of the gait cycle [34]. These patterns in humans, however, are much more complex. Innate neural networks for stepping have been postulated to exist in the human spinal cord since newborn infants have been shown to exhibit step-like movements when held upright [35]. The plausible development of such neural networks to generate the mature locomotor patterns observed in adults, however, is still uncertain [34,36].

1.3 The Ankle-Foot Complex

Normal walking may involve the modulation of mechanical impedance. A flagship example is found in the ankle-foot complex: the ankle provides propulsion during terminal stance and absorbs energy during heel strike. During normal locomotion, the ankle produces the largest amount of work compared to other joints [37]. Specifically, ankle actuation is the most significant source of propulsive torque [25] and provides more than half of the energy input (53%) required during human walking [38]. Mechanically, the ankle-foot complex is a distal actuator controlling the interaction between the body and the ground. Neurologically, the ankle-foot complex contains receptors for afferent signals that have been identified to be critical in the regulation of the locomotor pattern [39–42].

The ankle-foot complex represents an essential component in regulating the rhythmic pattern of normal human locomotion since it controls both loading and unloading responses through foot-ground interaction during the gait cycle [39, 40]. The ankle-foot complex includes muscles and mechanoreceptors that provide critical proprioceptive inputs that arise from load-related afferent information. Previous studies have suggested that these load-related afferent signals may be integrated in the spinal reflex pathway and may help adapt the automated gait to the actual ground conditions [40]. Additional evidence also suggests that the regulation of locomotion may be influenced by cutaneous reflexes arising from foot-ground contact [25, 41]. Taken together, all these load-related afferent signals are postulated to modulate the rhythmic pattern of normal locomotion while reinforcing muscle activity as well [40].

In the spectrum of neurological disorders affecting the lower-extremity, ankle impairments following stroke have been shown to reduce ankle work while increasing metabolic cost by at least 20% [43]. Regardless of intervention [44–46], these ankle function deficits are comparable to walking 20% faster [47] or carrying an extra 15 kg load [48]. Given the major propulsive and energy-supply role the ankle joint plays in human locomotion, it is plausible that normal ankle function may be restored by directly powering the joint—a technique that has already shown promise [49–51] and will be further investigated in this experimental study.

1.4 Limit-Cycle Oscillators in Human Locomotion and Entrainment

Studies over decades have provided convincing evidence of the predominance of kinematics in reaching movement [52–55]. Thus, it is highly probable that the success of upper-extremity robot-aided therapy depends on the implementation of rehabilitation strategies focused on desired kinematic patterns. In contrast to reaching, walking is a rhythmic process that combines continuous and discrete dynamics [56–58]. To date, the dominant control scheme of human locomotion remains unclear.

For instance, the concept of a CPG as a fundamental movement primitive has found support in animal locomotion, suggesting its plausible existence in the human spinal cord [59–64]. However, the potential contribution of a spinal CPG to human locomotion remains unclear. Recent studies reported that electromagnetic stimulation applied to unimpaired human vertebrae induced involuntary locomotor-like movement patterns [64]. On the other hand, robotic experiments and theoretical studies have demonstrated that simple limit-cycle oscillators can exhibit stable human-like walking [10,32,65–72].

Stable limit-cycles are isolated closed trajectories forming a complete orbit that must attract[1] all neighboring trajectories, which are strictly not closed. Linear systems may exhibit closed-orbits, but these will not be isolated, and thus, will not be considered limit-cycles. Robustly sustained oscillations, such as heartbeats, vibrations in bridges, and human locomotion, can only emerge from a nonlinear[2] oscillator with a limit-cycle attractor. In fact, competent mathematical models of rhythmic locomotion have been developed specifically using nonlinear[3] limit-cycle oscillators, such as the van der Pol oscillator or the half-center Matsuoka oscillator [10,65–69]. Various modeling studies have demonstrated that a combination of the inertial and gravitational mechanics of the legs and intermittent foot-ground interactions with energy dissipation can generate a stable limit-cycle [32,70–72]. For example, passive dynamic walkers can remarkably mimic human-like bipedal walking on a slope with no control and/or actuation [70,71]. These modeling and experimental results suggest that the mechanics of the human periphery and gravity may play an important role in the control of human walking.

Taken together, various studies suggest the critical role of dynamic oscillators in locomotor control, either originating from mechanical interactions, neural circuits, or a combination of both. If any form of these oscillators plays a key role in human locomotor control, then current approaches of most therapeutic

[1] Specifically, the complete orbit *must* be *attracting*, but segments of the trajectory need not be.

[2] A linear system cannot exhibit self-sustained oscillation (refer to Appendix A).

[3] A linear system would be an overly simplified model of locomotion.

robots may inadvertently interfere with the natural oscillating dynamics of walking by focusing only on nominal kinematic patterns. To determine the plausible existence of a nonlinear neuro-mechanical oscillator with a limit-cycle in human walking, we could investigate whether human locomotion is sensitive to the same manipulations as nonlinear limit-cycle oscillators. For instance, one characteristic of nonlinear limit cycles is dynamic entrainment to external perturbation: they synchronize their period of oscillation to that of an imposed rhythmic perturbation. In contrast to linear systems[4], nonlinear systems only exhibit entrainment when the perturbation frequency is sufficiently close to their frequency of oscillations; i.e. they exhibit a *finite basin of entrainment*. If a nonlinear limit-cycle attractor underlies human locomotion, then dynamic entrainment of human walking to external perturbations is plausible.

1.5 Treadmill vs. Overground Walking

Treadmills have long been associated with experimental gait studies and lower-extremity therapy given the undeniable advantages they offer. In treadmill gait analysis, physical space requirements are reduced and environmental factors are easily controlled. Since treadmill gait experiments or training sessions can be performed in a small area, a large volume of successive strides can effectively be documented. Importantly, supplementary equipment needed to measure oxygen intake and/or electromyographic activity, which must be attached to the subject, are not required to be completely mobile which facilitates their use.

In the spectrum of lower-extremity physical therapy, treadmills also offer great advantage since the patient is slightly elevated and stationary, which eases the positioning of the therapist when providing assistance and monitoring physical activity. Additionally, gait analysis often requires the use of cameras for motion tracking purposes; treadmill environments considerably reduce the number of cameras needed since locomotion is permitted within a small area for a continued

[4] Stable linear systems—not necessarily oscillatory—will *entrain* to inputs of all frequencies.

period of time. For accurate comparison of kinematic and kinetic patterns between several experimental or training sessions, it is important to control steady-state locomotion speeds. In treadmill ambulation, speed constraints are selectable and well-controlled. In fact, force-sensing and instrumented treadmills have been developed to measure ground reaction forces and quantify kinetic aspects of locomotion, respectively.

While treadmills seem to offer many advantages in the analysis of human locomotion, they certainly have been a source of much discrepancy. Specifically, there is concern regarding the equivalence of treadmill and overground locomotion. In relation to recovery of locomotor function, the goal is for patients not just to be able to walk on a treadmill but actually overground in their daily lives. Hence, it is critical that the locomotor control strategies employed in treadmill and overground ambulation be fundamentally similar in order to facilitate transferability of possible treadmill training improvements. The discrepancies reported in the literature regarding the approximation of treadmill and overground ambulation give rise to many pressing questions that need to be addressed:

- *Does the movement of the treadmill itself represent the natural properties of locomotion overground?*
- *Does the intrinsic pattern of human locomotion change upon treadmill use?*
- *Does treadmill training obstruct the functional outcomes of walking therapy?*
- *Or essentially, are the experimental results of human gait research involving treadmills transferable to all modes of ambulation and walking environments, or at least to normal overground locomotion?*

1.5.1 Reported Discrepancies

Evidence for or against the two modes of locomotion—treadmill vs. overground—being equivalent is ultimately inconclusive. While some studies have concluded that treadmill walking can be reasonably approximated to overground walking in the sagittal plane [73,74], others have reported significant step-width increase during treadmill locomotion in comparison to overground [75]. Small differences have been reported regarding the fundamental gait patterns exhibited during treadmill vs. overground walking [76–79]; however, such differences have been said to vanish after a certain accommodation period [80]. Furthermore, in studies specifically with the elderly population, evidence has been presented regarding significant difficulty accommodating to treadmill locomotion [81].

van Ingen Schenau demonstrated analytically that the physics of treadmill and overground locomotion were identical provided the treadmill belt speed was kept constant [82]. Indeed, significant alterations in gait mechanics have been reported as a result of intra-stride variations in treadmill belt speed; these variations were determined to be highly dependent on the particular treadmill used and the type of locomotion it is used for (walking or running) [83]. Moreover, a study comparing vertical ground reaction forces during overground and treadmill walking with 24 healthy subjects reported that treadmill belt speed fluctuations as small as $\pm 4\%$ appeared to have a significant effect on peak forces related to ankle 'push-off' during late stance [84]. Such reduced peak forces during treadmill walking were 5-6% less than those recorded during overground locomotion. Lack of peak forces during late stance can affect propulsion and lead to reduced limb extension, which may in turn elicit shorter stride length during treadmill locomotion. Additionally, at comparable speeds, the oxygen intake [85] and the magnitude and timing of the electromyographic patterns of the lower-limb muscles in treadmill and overground locomotion do not seem to differ significantly [86,87].

On the other hand, different knee [78,88] and hip [88] joint kinematic patterns in the sagittal plane have been reported in treadmill compared to overground walking, and temporal differences have also been observed [78]. Indeed, statistically significant reduction of peak hip [74] and knee flexion [74,78–80] and extension have been documented for treadmill gait of healthy subjects. The reduced range of motion in knee angle during treadmill walking was reported to vanish after 4-6 minutes of adaptation in [78–80], whereas it was observed to persist over three sessions in [74]. Particularly regarding the lower-extremity joints—ankle, knee, and hip—the ankle has been reported to exhibit the largest differences in terms its angular values in overground vs. treadmill walking [89]. Moreover, different reaction force patterns have been found in treadmill vs. overground walking [84].

Dissimilarities have also been documented regarding step/stride length (SL), width (SW), time (ST), and cadence, as well as stance, swing, and double-limb support periods during treadmill vs. overground walking at preferred, slower, and faster speeds. A trend has been reported across several studies regarding shorter SL [79, 90] and greater SW [91], as well as shorter swing phases accompanied by longer double-limb support periods [79, 92] during treadmill compared to overground locomotion. Specifically, SW was 15% greater across all steps during treadmill walking in [91], yet SW variability was 23% smaller. The reports on ST, however, have been inconclusive. In [79] the observed shorter SL and faster cadence during treadmill walking required a concomitant decrease in ST. Conversely, treadmill walking was associated with 7% longer ST across all steps in [91].

1.5.2 Perceived Single-Limb Instability during Treadmill Walking

Several studies have reported faster cadence during treadmill walking, characterized by shorter swing phases and considerably longer stance periods—specifically double-limb support [79, 92, 93]. During treadmill walking, there is always a potential or perceived risk of accidentally stepping off the continuously moving treadmill belt. In virtue of certain anxiety or difficulty to maintain proper balance when walking on a relatively narrow surface—the treadmill belt—with different visual cues given the stationary surroundings, subjects may turn to different control strategies to increase stability. Indeed, longer double-limb support as reported in [79, 92, 93] indicates a plausible attempt to minimize the duration of 'unsteady' single-limb support over the moving treadmill belt. In that case, the reported faster cadence and shorter SL during treadmill locomotion may stem from a sense of urgency to place the swinging foot onto the treadmill surface, especially when the single-supportive limb is being driven past the upper-body by the moving belt. Nevertheless, it is possible that these particular gait parameters arise due to the limited length of the treadmill surface along with the constant speed of the moving belt. Additionally, the reported greater SW [91] during treadmill walking could emerge as a further attempt to increase lateral stability on the narrow treadmill surface by actively controlling foot placement. In that sense, the reported smaller step width variability during treadmill locomotion [91] also evidences increased precision of foot-placement control, which is significantly different from the locomotor control strategy overground.

1.5.3 Significance to Robot-Aided Therapy for Walking

A possible explanation for the diminished effectiveness of robotic therapy for walking might be a misapplication of robotic 'high-tech'. Such misuse is evidenced in the design of human-interactive robots that are constrained to environments (e.g. treadmills), which may suppress the expressiveness of the natural oscillatory dynamics of walking.

Most of the experiments in robotic gait rehabilitation are conducted using treadmills that subtly interfere with natural movement control, which could possibly be why the 're-learned' gait patterns frequently do not transfer to overground walking [94–97]. In fact, even without a robot involved, recent research revealed that locomotor training on a treadmill, assisted by multiple human therapists, was no better than a home exercise program that did not involve locomotor experience [94, 95].

Evidence from various studies suggests that further investigation of the dynamic and mechanical differences between treadmill and overground walking is of critical importance. For instance, walking on a standard motorized treadmill imposes a nominally constant speed constraint that may interfere with the natural oscillatory characteristics of human locomotion. Likewise, the foot-ground interactions between these two walking environments are also mechanically different. To design effective technology for lower-limb therapy, it is essential to investigate the expression of the oscillatory dynamics of locomotor control in these two notably different environments: treadmill vs. overground.

1.6 Overview of Thesis Outline by Chapters

This introductory chapter has presented the overarching limitations of current lower-extremity robotic rehabilitation and explained the urgent need for effective robot-aided recovery of locomotor function. At this point, it should be clear that the immaturity of robotic walking therapy is mainly due to: **(1)** the use of fundamentally flawed approaches—emphasizing the nominal kinematics of lower-limb motion—and **(2)** the use of robots that constrain therapeutic training to environments that subtly interfere with natural movement control—motorized treadmills. Hence, a shift of approach to robot-aided walking therapy is crucial. Further investigation of the natural oscillating dynamics of human locomotion in different walking environments is very much needed and will be addressed in the scope of this thesis.

Chapter 2 outlines the criteria for investigating and exploiting the natural oscillatory characteristics of human walking through gait entrainment to periodic mechanical perturbation at the ankle joint using a wearable therapeutic robot. Previous work is presented identifying the existence of a nonlinear neuro-mechanical oscillator with a limit-cycle attractor in human locomotion. The motivation to lay the foundations for the implementation of effective, permissive locomotor therapy is detailed. Chapter 2 also explains the goals for this experimental study to identify the effects of different walking environments on locomotor control and gait entrainment to ankle mechanical stimuli. Since this project involves the use of a specific therapeutic ankle robot—the Anklebot—an overview of the design criteria of this wearable device is presented.

Chapter 3 presents experimental work with unimpaired human subjects to address the feasibility of gait entrainment to periodic mechanical plantar-flexion perturbation at the ankle joint. The assessment of gait entrainment and gait phase convergence implemented in this particular project is further explained in detail. A direct comparison of the rate of gait phase convergence in treadmill versus overground walking is presented. In addition, the effects of the imposed plantar-flexion perturbations in subjects' walking cadence during and after removal of mechanical stimuli are also discussed. Overall, the experimental data presented in Chapter 3 revealed clear evidence of gait entrainment to plantar-flexion perturbation, phase-locking, and persistence of the entrained gait periods, as well as significant differences in treadmill and overground walking.

Chapter 4 presents experimental work with unimpaired human subjects to address the feasibility of gait entrainment to periodic mechanical dorsi-flexion perturbation at the ankle joint. A direct comparison of the rate of gait phase convergence in treadmill versus overground walking is presented. In addition, the effects of the imposed dorsi-flexion perturbations in subjects' walking cadence during and after removal of mechanical stimuli are also discussed. Overall, the experimental data presented in Chapter 4 revealed clear evidence of gait entrainment to dorsi-flexion perturbation and phase-locking, as well as significant differences in treadmill and overground walking.

Lastly, Chapter 5 provides a summary of the accomplishments of this study and the implications of the experimental findings presented in this these. Directions are suggested for future implementation of novel approaches for robot-aided locomotor therapy, which are *permissive, minimally-encumbering, and capable of exploiting the natural oscillating dynamics of human walking—providing assistance only as needed*.

Chapter 2

Entrainment to Ankle Mechanical Perturbation using a Wearable Therapeutic Robot

2.1 Previous Work

Based on previous evidence suggesting the existence of a nonlinear oscillator with a limit-cycle attractor in human locomotion, Ahn and Hogan proposed to test the role of such oscillator via dynamic entrainment of human walking to mechanical perturbations [98]. Specifically, they demonstrated that, indeed, subjects' gaits synchronized with the periodic plantar-flexion perturbations at the ankle joint. Such entrainment, however, was only observed when the period of the imposed perturbation was sufficiently close to the subjects' preferred walking period; i.e. a finite basin of entrainment was observed. Interestingly, it appeared that subjects' gaits synchronized with the plantar-flexion torque pulse at 'push-off', suggesting that the perturbations assisted propulsion. While this experimental work was the first to reveal clear, behavioral evidence of an underlying neuro-mechanical oscillator with a limit-cycle in human walking, it only assessed such behavior during treadmill locomotion. Given the fundamental differences between treadmill and overground ambulatio—previously presented in Chapter 1—it is essential to further investigate whether those gait entrainment observations are also evidenced during treadmill waking.

Ahn and Hogan also developed a highly simplified state-determined walking model without an intrinsic self-sustaining oscillator or supra-spinal control that was capable of reproducing their previous gait entrainment observations [99]. Their one-degree-of-freedom model encapsulated several of the fundamental features of human bipedal locomotion that are indicative of an underlying nonlinear limit-cycle oscillator:

(1) periodic gait that is asymptotically stable,

(2) dynamic entrainment with a finite basin of attraction when exposed to periodic mechanical perturbations, and

(3) phase-locking to locate the perturbation at ankle 'push-off'—the end of double stance.

It is important to emphasize that this simplified mathematical model was only capable of reproducing gait entrainment to perturbation periods that were "faster" than the model's unperturbed period, but not to those that were "slower".

2.2 Motivation and Goals

Despite advances in robotic technology and state-of-the-art humanoid robotic bipeds, robotic walking therapy has shown clear immaturity mainly due to **(1)** the inappropriate design of robots that constrain important motions during walking, and **(2)** the absence of a proper control strategy that reckons with the essential mechanisms of human walking. The goal of this study is to set the stage for effective robot-aided walking therapy to be pioneered by first providing essential insight about the overarching control architecture of human locomotion. To pioneer effective robot-aided recovery of locomotor function, it is critical to operate suitably designed robots with appropriate control that exploits essential but hitherto-neglected mechanisms of human walking: its *natural oscillatory dynamics*.

As a first step in the complex study of robot-aided walking rehabilitation, this experimental work aims further to evaluate the previously identified nonlinear limit-cycle oscillator postulated to underlie human locomotion [98]. The previously reported behavioral evidence of such oscillator only evaluated treadmill walking. Given that treadmill and overground walking are fundamentally different, this study analyzed how the differences in walking environments affect entrainment of the nonlinear limit-cycle oscillator postulated to underlie normal human locomotion.

The goals of this study were to: **(1)** *understand the role of the ankle in unimpaired human walking*; **(2)** *quantify the response of treadmill and overground human locomotion to different types of mechanical perturbations at the ankle*; **(3)** *demonstrate the presence of a nonlinear limit-cycle oscillator in human walking and assess its provenance—central vs. spinal*; and ultimately, **(4)** *characterize the overarching architecture of human locomotor control*.

The human locomotor control insight gained from this study may not only have implications for exoskeleton design and legged locomotion research, but could also suggest new avenues to engineer better robot-aided therapy to recover locomotion after injury.

2.3 Overview of the Wearable Robot: the Anklebot

The wearable robot featured in this study—the Anklebot—was the first device designed to enable *multi-variable* mechanical interaction with the ankle in *both sagittal and frontal planes* (detailed in [100]). The compact design of this wearable therapeutic device enables its application to both treadmill and overground walking. The Anklebot consists of two highly back-drivable linear actuators attached to the leg via a knee brace and a customized shoe, allowing normal range of motion in all degrees of freedom of the ankle (Figure 2-1). In fact, these actuators have low intrinsic static friction (less than 1 N·m) opposing ankle motion. High-precision[1] optical encoders monitor the motion of these actuators. The assistance provided by the Anklebot allows the natural dynamics of walking since it does not confine any degree of freedom as most current therapeutic robotic devices do. Motion can be assisted in sagittal and frontal planes. Specifically, actively controllable torques can be generated simultaneously in two degrees of freedom: dorsi-/plantar-flexion and inversion/eversion. The third degree of freedom (tibial rotation) is passively movable with extremely low friction. Overall, the Anklebot provides on-board measurement of knee angle in the sagittal plane (using a potentiometer embedded in the knee brace) and ankle angle in dorsi-/plantar-flexion and inversion/eversion, as well as control (with reasonable/good accuracy) of ankle torque.

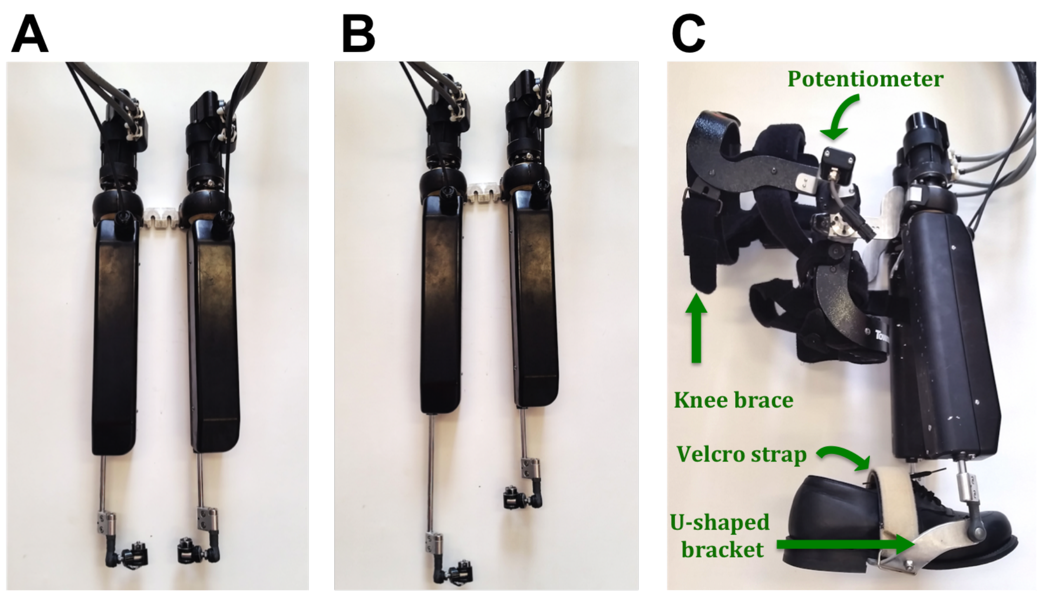

Figure 2-1: The Anklebot—a wearable ankle robot. **(A)** Anklebot's linear actuators. **(B)** Anklebot's linear actuators displaced in opposite directions, so as to achieve motion in the inversion/eversion direction. **(C)** Anklebot connected to the knee brace and the custom designed shoe; the shoes included a U-shaped bracket for the end effectors to connect to and a wide Velcro strap to secure the tightly fastened shoelaces and prevent foot slippage inside the shoe.

[1]Rotary encoders, which are mounted coaxial with the motors, have a resolution of $8.78 \times 10^{-3}\,^{\circ}$. Linear incremental encoders, which are mounted on the traction drive, have a resolution of 5×10^{-6} m.

Most of the robot's weight (3.6 kg) is concentrated at the knee and borne by the thigh, leaving the shank or foot free to move and minimizing the end-effector inertia during locomotion. For safety, subjects who participate in experiments with the Anklebot are always asked to wear a harness in order to distribute the robot's weight over the upper body. Previous studies have shown that unilateral loading with one Anklebot had minimal influence on gait parameters [100, 101], suggesting that the intrinsic impedance of the Anklebot does not have a significant effect on human locomotion.

Although the Anklebot can provide a wide range of ankle torques, it has limitations. The assistance is confined to the ankle, and the continuous torque is upper-bounded by 23 N·m in the sagittal plane for dorsi-/plantar-flexion and 15 N·m in the frontal plane for inversion/eversion, which is not sufficient to assist non-ambulatory patients. However, the scope of this particular project does not extend beyond unimpaired human subjects, in which case this torque limitation is not a concern.

Chapter 3

Rhythmic Plantar-flexion Perturbations to the Ankle Joint

This chapter characterizes the entrainment of human locomotion to rhythmic plantar-flexion perturbations applied to the ankle joint during treadmill and overground walking. Such characterization is demonstrated via experimental work involving the voluntary participation of 14 healthy subjects and the use of a wearable ankle robot to deliver the imposed mechanical perturbations. Additionally, this chapter discusses the implication of the experimental results on characterizing the architecture of human locomotor control, which remains a pressing problem in neuromotor science.

3.1 Introduction

The control of human locomotion is incompletely understood. Despite a vast and growing literature, a comprehensive understanding of the relative importance of low-level spinal circuits and their fundamental interaction with limb biomechanics, high-level perceptual and planning processes, and feedback control has not been established.

Rhythmicity is a hallmark of locomotion. In neurophysiology, numerous observations demonstrate neural sources of rhythm generation. For instance, fictive locomotion in non-human vertebrates provides unequivocal evidence that neural circuits generating sustained rhythmic activity exist in the spinal cord isolated from it periphery, although sensory feedback is known to play a key role [60–63,102–104]. Importantly, rhythmic output is sustained by sparse input from higher centers. Studies have demonstrated that, in humans, both continuous leg muscle vibration and electromagnetic stimulation applied to the spinal cord are capable of inducing locomotor-like movements, which suggests the existence of a rhythmic pattern generator that may contribute to locomotor activity [64,105].

Sensory feedback related to limb loading, hip extension or foot contact also play important roles in locomotor control [40,61,106]. Unlike in normal human walking, the locomotor-like movements evoked by continuous leg muscle vibration and electromagnetic stimulation were observed in gravity-neutral position, rendering it difficult to assess how those results would apply to upright locomotion [64,105]. Neurophysiological detail during functional human locomotion can be difficult to assess, hence the importance to adopt a more theory-driven behavioral approach to advance our understanding.

Stable rhythm generation is also the heart of a line of research in robotic legged locomotion—Dynamic Walking. Since McGeer's pivotal work demonstrated that strictly passive mechanisms—with *no* computation, control, sensing or even actuation—exhibited stable walking on a slope, numerous subsequent studies have extended this insightful work [32,70]. Indeed, some display astonishingly human-like locomotion, at least under certain conditions [71,107]. The central idea of this engineering approach is to use interaction between the robot's mechanics, control system and gravito-inertial environment to comprise a nonlinear oscillatory dynamical system. With suitably-configured interactions and/or feedback control, stable rhythmic locomotion is an emergent property of this dynamical system; hence, tools of dynamical systems analysis and control may be applied [108,109]. The approach presented in this chapter to understand the control of human locomotion—*dynamic entrainment of human gait to rhythmic ankle perturbations*—follows the footsteps of this line of research.

Fundamentally, if a peripheral neuro-mechanical system is governed by a semi-autonomous nonlinear dynamical system, human walking should exhibit entrainment to periodic perturbations—a distinctive behavior of nonlinear oscillators. Indeed, direct evidence of a nonlinear oscillator that makes a non-negligible contribution to normal upright human treadmill walking, was previously presented by Ahn and Hogan [98]. However, a limitation of the results presented in [98] is that, because the treadmill's speed was constant—at the subject's preferred speed—the amplitude and cadence of the locomotor cycle were artificially constrained. Consequently, the shortening of stride period required a concomitant shortening of stride length (and vice versa) to avoid falling off the treadmill. Overground walking—the overarching focus of this thesis—may be significantly different.

In the experimental study presented in this chapter, unimpaired subjects were asked to walk both on a treadmill and overground while the Anklebot exerted periodic plantar-flexion torque pulses to the ankle joint. Gait entrainment and phase-locking were quantitatively evaluated to assess the sensitivity of the nonlinear oscillator to different walking environments and characterize the subtlety and adaptability of human walking. In the following sections, the experimental protocols and results are described in detail.

Importantly, the experimental study presented in this chapter not only tests the feasibility of gait entrainment during overground walking but also addresses the fundamental problem of human locomotor control. Indeed, the assessment of gait entrainment to mechanical perturbations in different walking environments may characterize the ultimate role of limit-cycle oscillators in human locomotion. Essentially, dynamic entrainment to mechanical perturbations may not be observed in these different walking environments should human locomotion be *dominantly* controlled by a supra-spinal kinematic pattern instead of a *semi-autonomous* spinal neuro-mechanical periphery. In that case, entrainment of human walking would evidence a steadily growing error—actual vs. commanded kinematic pattern—that the supra-spinal controller would need to correct.

Instead, if dynamic entrainment to mechanical perturbations is observed in these different environments, then it would serve as direct behavioral evidence of the non-negligible contribution to human locomotor control made by a nonlinear limit-cycle oscillator in the spinal neuro-mechanical periphery.

3.2 Methods

Fourteen healthy subjects participated in an experimental study. All participants gave informed consent in accordance with procedures approved by the Institutional Review Board (IRB) of the Massachusetts Institute of Technology (MIT). The purpose of the study was to compare the subjects' walking performance on a standard treadmill versus overground while exposed to a series of rhythmic plantar-flexion perturbation applied to the ankle joint via a wearable robot.

3.2.1 Equipment and Protocols

Each subject performed 2 trials on a Sole Fitness F80 treadmill (with a 0.84 m $\times$ 1.90 m deck), and 2 other trials walking overground in a large corridor at MIT. For both walking conditions, "slow" and "fast" perturbation periods were delivered. In all trials, subjects performed a cognitive distractor task that consisted of listing countries, cities, animals, etc. in alphabetical order (one category at a time).

The robot used in these experiments was the Anklebot by Interactive Motion Technologies, Inc. (Figure 3-1). This wearable therapeutic robot attached to the leg via a knee brace and a shoe. A potentiometer embedded in the knee brace recorded the subjects' knee angle profile during walking. The Anklebot's highly back-drivable linear actuators were capable of actuating the ankle in dorsi-/plantar-flexion and inversion/eversion. In all trials subjects wore a harness to distribute the weight of the Anklebot over the upper body. The robot was preprogrammed to deliver periodic square torque pulses of magnitude 10 N·m and duration 100 ms in the same fashion as in Ahn and Hogan [98]. In addition to exerting the torque pulses, the robot behaved like a torsional spring-and-damper with 5 N·m/rad stiffness, 1 N·m·sec/rad damping, referenced to a constant equilibrium position measured from the subject's upright posture (see also Ahn and Hogan [98]).

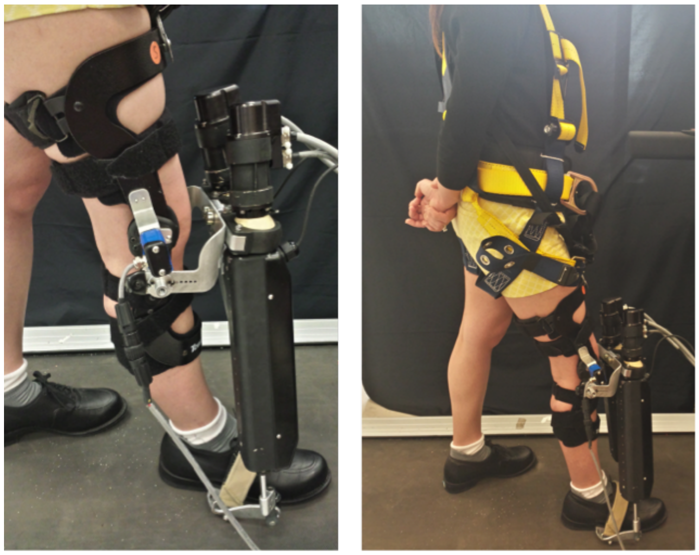

Figure 3-1: An unimpaired human subject wearing the Anklebot, including the knee brace, custom designed shoes, and safety harness.

3.2.2 Treadmill Trials

Subjects were asked to adjust the speed of the treadmill to a comfortable walking speed. The selected speed was recorded and maintained throughout the duration of any one trial. A treadmill trial (TM) began with subjects walking at their preferred speed. Subjects' preferred stride duration (τ_0) was measured as the average duration of 15 consecutive strides. The perturbation period (τ_p) was selected to be 50 ms "slower" (TM-slow) or "faster" (TM-fast) than the subjects' preferred stride duration (τ_0). Each trial was divided into 3 sections: *before*, *during*, and *after*. The *before* section consisted of 15 strides with no perturbation. The *during* section comprised 50 consecutive perturbations. In the *after* section the robot stopped exerting the torque pulses but maintained its spring-damper behavior. Subjects stopped walking and the trial terminated immediately afterwards.

3.2.3 Overground Trials

Overground trials (OG) differed from treadmill trials mainly in that there was no fixed-walking-speed constraint. The overground trials began by asking the subjects to walk at their preferred walking speed. Once comfortable walking speed was achieved, their preferred walking period (τ_0) was measured using the subsequent 15 strides. Overground trials were conducted in the same fashion as treadmill trials, for "slower" (OG-slow) and "faster" (OG-fast) perturbation periods. Throughout all overground trials subjects were followed from a close distance by the experimenters who moved the computer equipment on a rolling cart (see Figure 3-2).

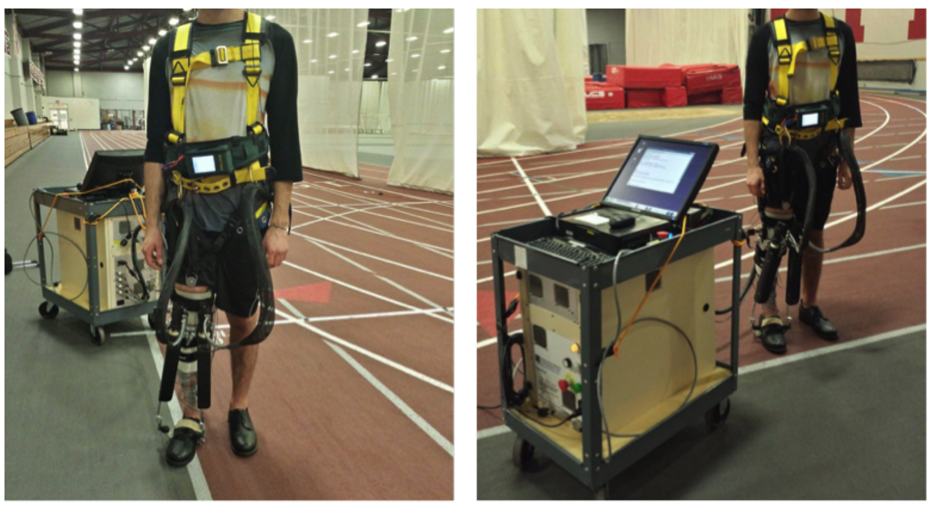

Figure 3-2: Experimental setup for overground trials.

3.3 Data Analysis

The gait cycle was defined based on knee angle measurements recorded by a potentiometer embedded in the Anklebot's knee brace. All data collected from onboard sensors were recorded at a sampling rate of 200 Hz. Subjects' stride durations *before*, *during*, and *after* perturbation were compared to evaluate whether mechanical perturbations sped up or slowed down the subjects' walking cadence. Statistical significance was set at a 5% significant level.

3.3.1 Gait Cycle

The gait cycle is typically estimated in locomotion experiments using pressure sensors to identify heel strike (i.e. the moment of initial loading) as 0%. For the experiments presented in this thesis it was important to simplify the number of additional sensors involved other than the ones included in the Anklebot equipment. Thus, it was decided to use the potentiometer embedded in the Anklebot's knee brace to measure the knee angle of the leg wearing the device in order to identify the duration of each stride instead of placing pressure sensors inside the shoes. This particular strategy had also been successfully implemented by Ahn and Hogan in previous work with the same equipment [98].

The gait cycle was estimated from extrema in the knee angle profile, which was filtered using a 4^{th} order zero-lag low-pass filter with 7 Hz cutoff frequency. Four landmarks were used in subsequent analyses: maximum knee flexion during stance phase, maximum knee extension during terminal stance phase, maximum knee flexion during swing phase, and maximum knee extension during terminal swing phase before heel strike. The knee angle profile was normalized from 0 to 100% to define a gait phase for each stride, with 100% defined as the maximum knee extension adjacent to heel strike (Figure 3-3).

3.3.2 Assessment of Entrainment

The plantar-flexion perturbations were delivered at a constant period throughout each trial; however, the onset of the torque pulses could vary with respect to landmarks in the gait cycle (e.g. the maximum knee flexion) given its 50 ms difference from the preferred stride period. Hence, the phase of the gait cycle at which perturbations occurred would not necessarily be constant. In order to entrain to the applied perturbations, subjects' gaits period must be the same as the period of the imposed torque pulses; entrainment requires each pulse to occur at the same phase of the gait cycle.

The gait phase of each perturbation was determined as the percentage of the

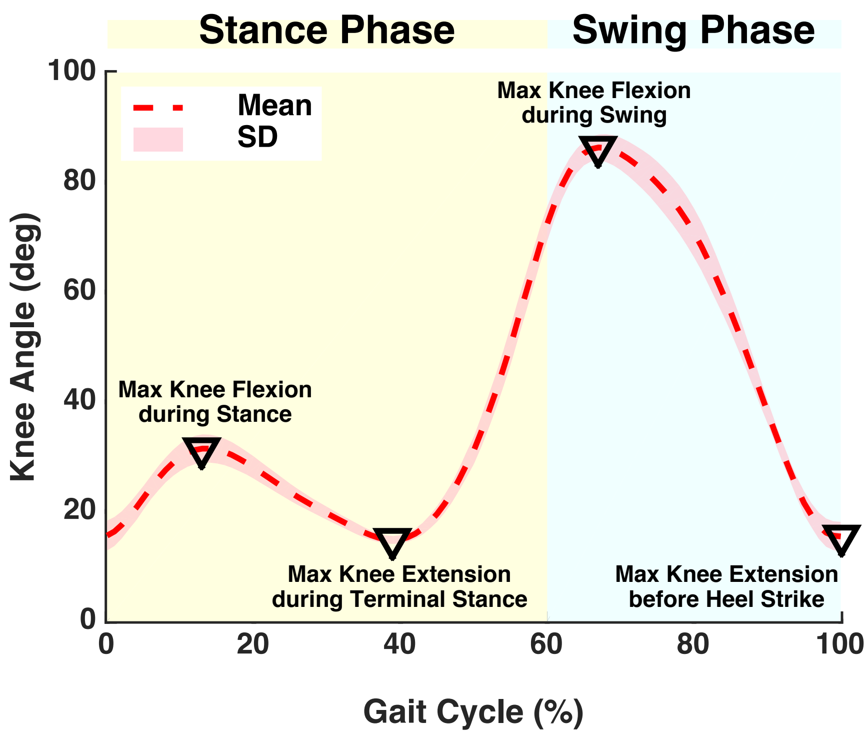

Figure 3-3: Typical knee angle trajectory across the gait cycle (in percent). The trajectory illustrates the four extrema (∇) that defined the gait cycle from 0 to 100%.

gait cycle that coincided with the onset of the torque pulse. The gait phases related to the 50 consecutive perturbations were calculated in reverse order starting from the 50^{th} perturbation. To avoid sudden jumps in the gait phases when the onset of a perturbation crossed the 0 or 100% boundaries, *wrap-arounds* in the gait cycle were allowed (i.e. gait phase values greater than 100% or less than 0%).

A linear regression of gait phase (Y) onto perturbation number (x) should evidence entrainment as a zero-slope segment. This regression ($Y = mx + b$) was applied to the last 10 perturbations in each trial; entrainment was indicated if the 95% confidence interval included zero slope (Figure 3-4). If the null hypothesis was accepted (H_0: $m = 0$), then the gait was considered *entrained*. Trials for which H_0 was rejected were defined as *not entrained* to "slow" perturbations ($m > 0$) or *not entrained* to "fast" perturbations ($m < 0$). Figure 3-5 shows three representative cases of entrained and not entrained trials.

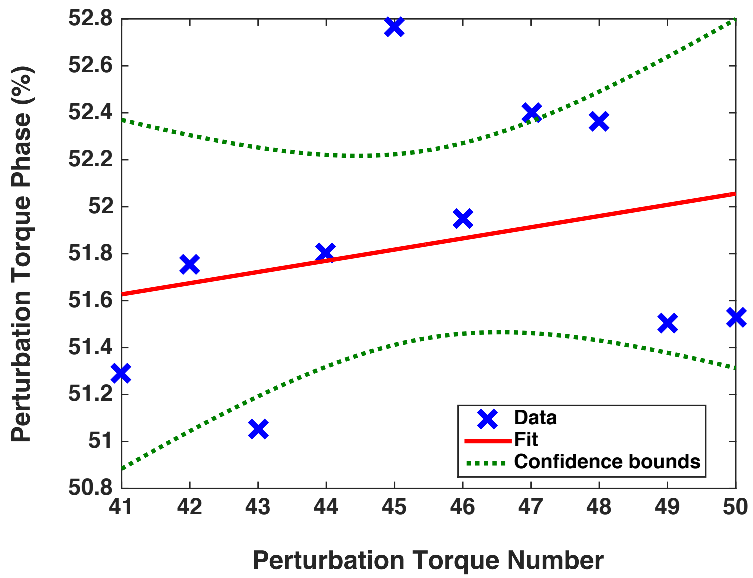

Figure 3-4: Linear regression fit applied to the last 10 consecutive perturbations for a representative trial. The 95% confidence interval for this particular trial identified a near zero slope for the linear fit (m $\sim$ 0.048). Thus, this trial was identified as entrained.

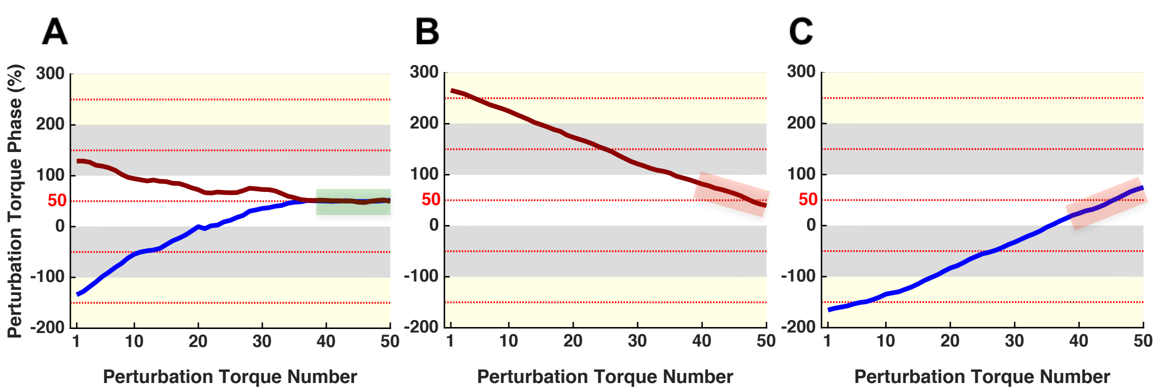

Figure 3-5: Regression of perturbation torque phase vs. perturbation number in the last 10 torque pulses for three representative scenarios. **(A)** Two regression slopes not significantly different from zero, in entrained gaits to "fast" (burgundy, m $\sim$ 0.023) and "slow" (blue, m $\sim$ 0.014) perturbations; **(B)** Significantly negative regression slope in a gait that did not entrain to "fast" perturbations (m $\sim$ -4.59); **(C)** Significantly positive regression slope in a gait that did not entrain to "slow" perturbations (m $\sim$ 5.51). The alternating regions shaded in light gray and yellow correspond to *wrap-arounds* in the gait cycle.

3.3.3 Converged Gait Phase

To evaluate gait phase convergence for each entrained gait, the phase and the onset of phase convergence were determined. To calculate these two measures the standard deviation (σ) of the gait phases at which the last 10 perturbations occurred was determined. The converged gait phase value (φ_{conv}) was determined as the mean gait phase corresponding to the greatest number of consecutive perturbations lying within an interval $\varphi_{\text{conv}} \pm 2\sigma$. When determining φ_{conv}, it was deemed acceptable for up to 3 consecutive perturbations to lie outside the interval, provided the subsequent perturbation re-entered the interval (Figure 3-6). The onset of converged gait phase or phase-locking was determined as the first perturbation to lie within the defined interval. For each subject the torque pulse number of the onset of entrainment was recorded in all 4 trials (except those trials that did not entrain). The dependent measures, gait phase and onset of phase convergence, were submitted to a 2 (TM vs. OG) $\times$ 2 (Slow vs. Fast) ANOVA using SAS JMP® statistical software package [110].

3.3.4 Stride Duration Variability

Both the standard deviation and the coefficient of variation of stride duration can provide a measure of overall fluctuations in gait timing during a set of consecutive strides in the experiments. However, these measures cannot distinguish between large changes from one stride to the next and smaller stride-to-stride variations with more long-term changes, which may arise as a result of the imposed perturbations. To evaluate gait timing independent of local changes, stride variability was assessed as successive stride-to-stride changes; i.e. the difference between the duration of one stride and that of the previous stride. The standard deviation and coefficient of variation (SD/Mean) of the difference in stride-to-stride duration were used to quantify the variability in gait timing throughout the different segments of the experiment.

It was of particular interest to evaluate the immediate effects of the

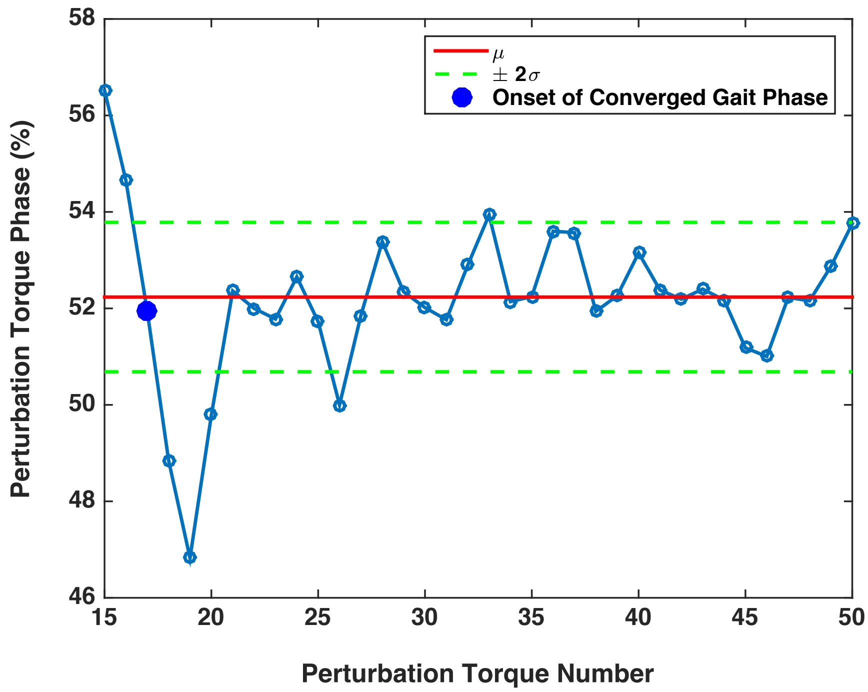

Figure 3-6: Representation of the defined $\pm 2\sigma$ interval used to determine the converged gait phase and the onset of phase convergence for a representative trial. This particular example shows the scenario in which up to three consecutive perturbations were allowed to fall outside the defined interval provided the subsequent perturbation would re-enter the interval.

perturbations in stride duration for each subject and in each of the different types of trials conducted. *Did subjects take longer to react to the applied perturbations in one particular walking environment than the other? Could this affect the rate of entrainment in treadmill vs. overground walking?* To address this questions the analysis of stride-to-stride variability specifically compared the duration of the 15 consecutive strides *before* perturbation and the first 15 consecutive strides *during* perturbation, which were extracted from the continuous time series data. The differences in stride-to-stride duration were obtained for each subject (and each trial) in the two segments of interest in the trials: *before* and *during* perturbation in both overground (OG) and treadmill (TM) walking. The standard deviation and coefficient of variation of such differences were calculated for each subject within the different conditions. The dependent measures, standard deviation and coefficient of variation of stride-to-stride duration, were submitted to a 2 (Before vs. During) $\times$ 2 (TM vs. OG) $\times$ 2 (Slow vs. Fast) ANOVA using SAS JMP® statistical software package [110].

3.3.5 Persistence of the Entrained Gait

The analysis of stride duration described in Section 3.3.4 could provide valuable insight about the immediate effects of the applied perturbations in gait timing within the 15 strides *before* perturbations and the <u>first 15</u> strides *during* perturbation. However, such analysis would not characterize any long-term effects in gait timing that could occur as subjects continued walking after the perturbations were discontinued. Would subjects continue walking at the perturbation period in the case of entrained gaits? Would they instead transition back to walking at their preferred period?

Gaits that entrained to the imposed perturbation could be subjected to persisting changes in stride duration periods even after the torque perturbations had been discontinued. Persistence of the entrained gait was evaluated by comparing the subjects' walking frequency *during* and *after* perturbations. Persistence was present when the periods of the last 15 strides *during* perturbation and the 15 strides immediately *after* perturbation did not differ significantly when evaluated using T-tests with 95% confidence level.

3.4 Results

A total of 56 ankle plantar-flexion perturbation trials were conducted with the fourteen healthy subjects who were recruited to participate in the experiments. Each subject completed 4 consecutive trials (2 TM and 2 OG) in randomized order. None of the subjects requested to opt out of the experiment nor reported pain or significant discomfort during their participation in any of the trials. Table 3.1 indicates each subject's gender, height, preferred treadmill speed, and walking periods *before* perturbation during both treadmill and overground walking. In both treadmill and overground trials subjects were allowed to select their preferred walking speed and these could differ from trial to trial even within the same subject. Remarkably, the mean stride duration (*before* perturbation) for all 14 subjects was significantly lower in overground trials; i.e. subjects always chose a faster cadence during overground walking. Additionally, the standard deviation and coefficient of variation of stride duration (*before* perturbation) was always significantly greater in overground trials (see Table 3.1). These observations are consistent with previous reports of preferred walking speed being significantly lower in treadmill walking based on studies with 10 [91] and 22 unimpaired adults walking on a treadmill and overground [111].

Table 3.1: Subjects' ID, gender, height, preferred treadmill speeds, and walking periods *before* ankle plantar-flexion perturbations. Abbreviations—SD: standard deviation; CV: coefficient of variation (SD/Mean)

Subject ID	**Gender**	**Height (m)**	**Preferred Treadmill Speed (m/s)**	**Preferred TM Stride Period *Before* Perturbation (s)**			**Preferred OG Stride Period *Before* Perturbation (s)**		
				Mean	**SD**	**CV%**	**Mean**	**SD**	**CV%**
S1	Male	1.73	0.80	1.33	0.041	3.08	1.23	0.067	5.45
S2	Female	1.68	0.89	1.32	0.039	2.95	1.20	0.053	4.42
S3	Male	1.91	0.67	1.46	0.024	1.64	1.29	0.043	3.35
S4	Male	1.75	0.72	1.72	0.030	1.75	1.22	0.058	4.75
S5	Female	1.65	0.72	1.50	0.032	2.13	1.29	0.046	3.57
S6	Female	1.73	1.56	1.03	0.014	1.36	0.99	0.046	4.65
S7	Male	1.83	0.76	1.55	0.019	1.23	1.27	0.048	3.78
S8	Female	1.55	0.76	1.45	0.024	1.66	1.04	0.060	5.77
S9	Male	1.88	0.85	1.46	0.051	3.49	1.22	0.074	6.07
S10	Male	1.80	0.98	1.22	0.014	1.15	1.20	0.041	3.42
S11	Male	1.68	0.89	1.27	0.023	1.81	1.22	0.053	4.34
S12	Female	1.60	0.85	1.55	0.019	1.23	1.31	0.045	3.44
S13	Female	1.55	0.89	1.28	0.017	1.33	1.18	0.026	2.20
S14	Male	1.85	0.89	1.36	0.043	3.16	1.26	0.064	5.08
All Subjects	**N/A**	**Mean = 1.73** **SD = 0.12**	**Mean = 0.87** **SD = 0.22**	**1.39**	**0.027**	**Mean = 1.99** **SD = 0.82**	**1.21**	**0.052**	**Mean = 4.31** **Mean = 1.09**

3.4.1 Entrainment

As previously explained in Section 3.3.2, entrainment was assessed as a zero slope in the regression of gait phase onto perturbation number. Similarly, entrainment could be visually inspected by checking whether landmarks in the gait cycle such as the maximum knee flexion maintained a constant phase difference with respect to the rhythmic perturbation pulses or whether these drifted continuously. Figure 3-7 shows two representative trials that evidence the assessment of entrainment by inspection of the linear relationship between the maximum knee flexion and the onset of the continuous rhythmic torque pulses applied by the Anklebot.

Overall, entrainment was observed in 46 out 56 total trials (20 TM, 26 OG). One subject (S6) did not entrain in any of the 4 different trials. The remaining 6 trials identified as not entrained were all TM-slow trials; i.e. entrainment was not observed in 50% of the TM-slow trials. The relationship between plantar-flexion perturbation phase and perturbation number for all entrained gaits can be seen in Figure 3-8.

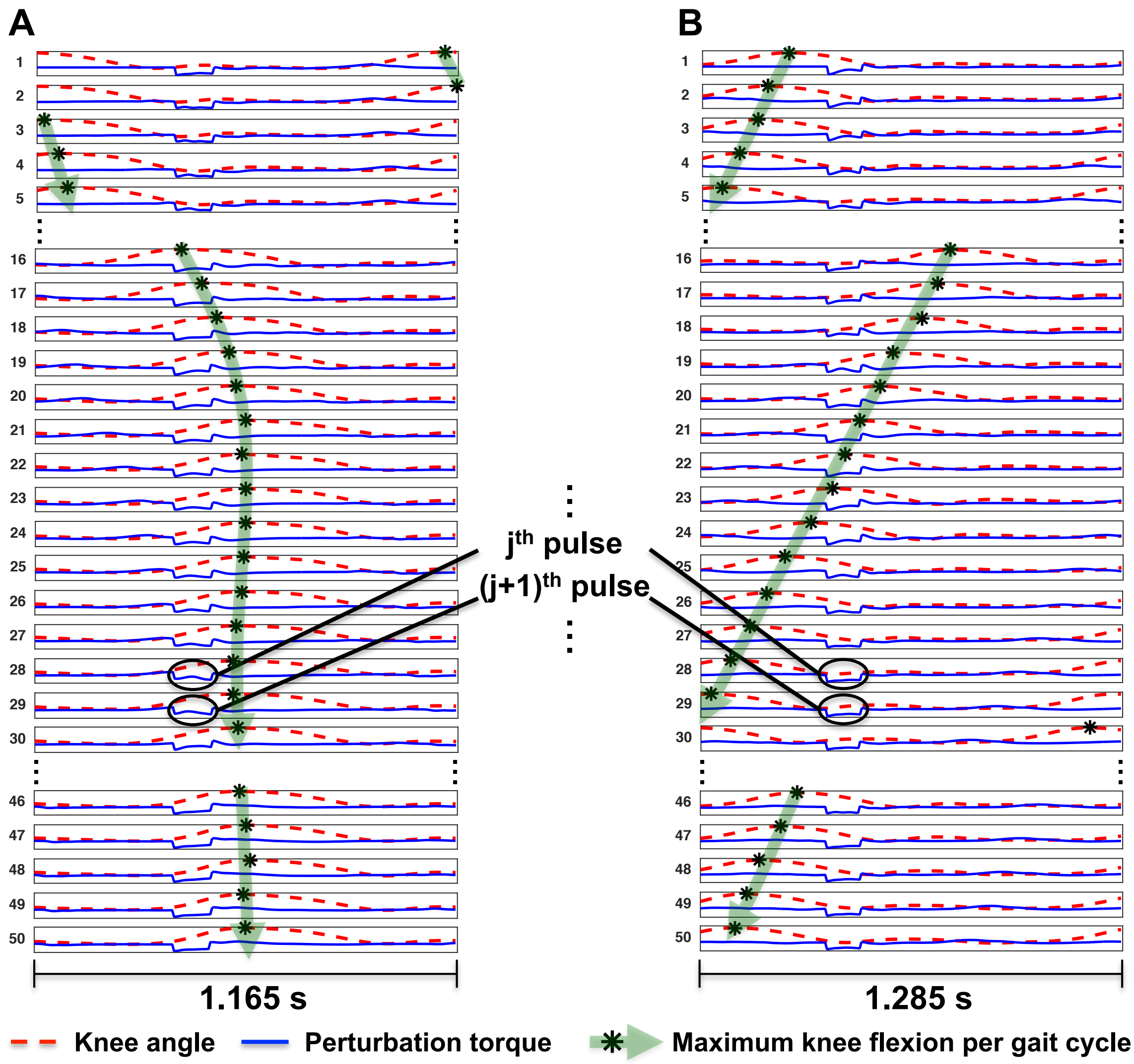

Figure 3-7: Phase relation between the maximum knee flexion in each gait cycle with respect to the plantar-flexion perturbations for "entrained" vs. "not entrained" gaits. **(A)** Typical results for a gait that entrained to "fast" perturbation; the maximum knee flexion drifted initially but eventually converged on a specific phase of the perturbation cycle. **(B)** Typical results for a gait that did not entrain to "slow" perturbation; the maximum knee flexion drifted continuously relative to the perturbation. Each row in **(A)** and **(B)** represents one plantar-flexion perturbation cycle with its duration (τ_p) indicated at the bottom; the knee angle for each perturbation cycle is plotted in each row with the maximum knee flexion landmark identified. The perturbation number corresponding to each row is shown to the left of **(A)** and **(B)**.

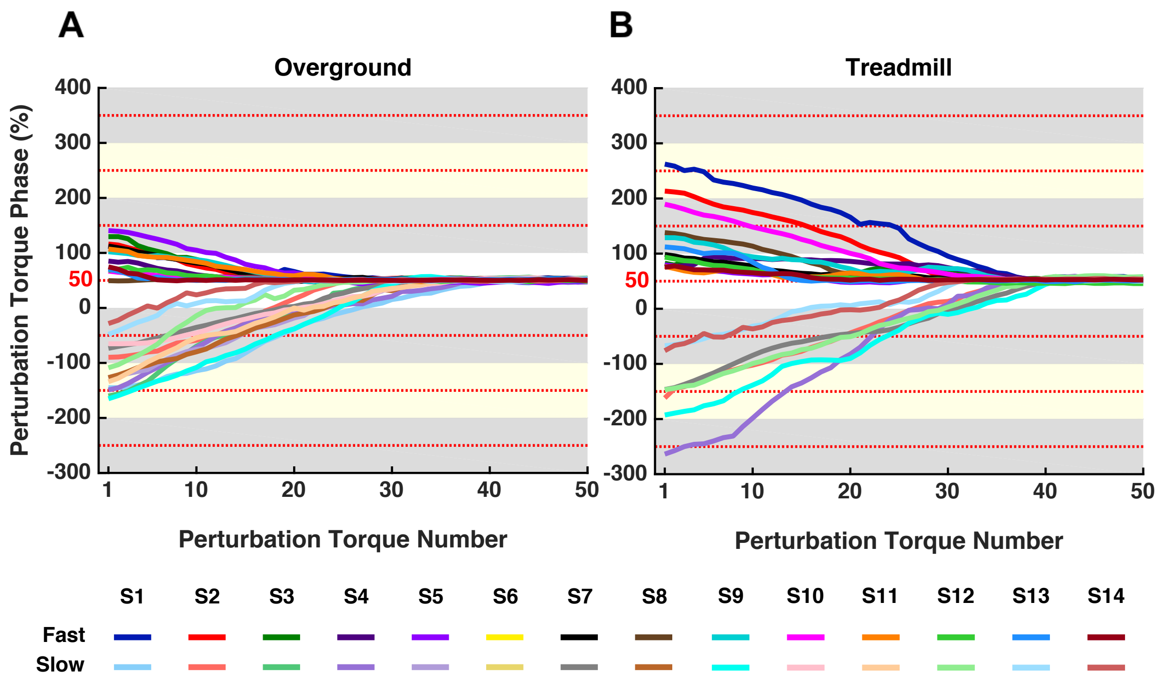

Figure 3-8: Plantar-flexion perturbation phase as a function of perturbation number for all entrained gaits. **(A)** Entrained gaits during overground trials. **(B)** Entrained gaits during treadmill trials. Each color corresponds to a different subject, with a dark and a light shade corresponding to the trials with "fast" and "slow" perturbation respectively. Subject 6 (S6) is not shown since she did not entrain in any of the 4 trials. Other missing lines correspond to trials in which subjects did not entrain.

3.4.2 Phase-Locking in Entrained Gaits

Regardless of the gait phases at which perturbations were randomly initiated (Figure 3-9), subjects who entrained synchronized their gaits with the torque pulses at ∼50% of the gait cycle in the 46 entrained trials. Histograms and a polar plot of gait phase in the last 10 perturbations of entrained gaits are shown in Figure 3-10. The mean φ_{conv} across all entrained gaits was 51.64% (± 2.36%), which was near the boundary between the terminal stance and pre-swing phases. This coincides with the interval of maximum ankle plantar-flexion torque, known as 'push-off' [25].

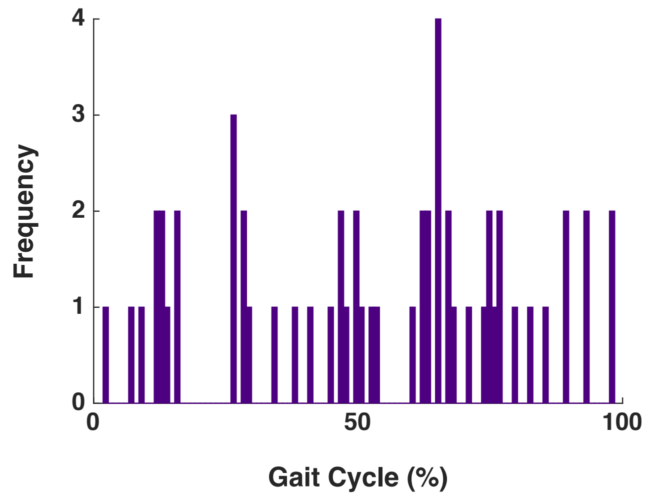

Figure 3-9: Histogram of the randomly selected gait phases corresponding to the first plantar-flexion perturbation applied in all 56 trials.

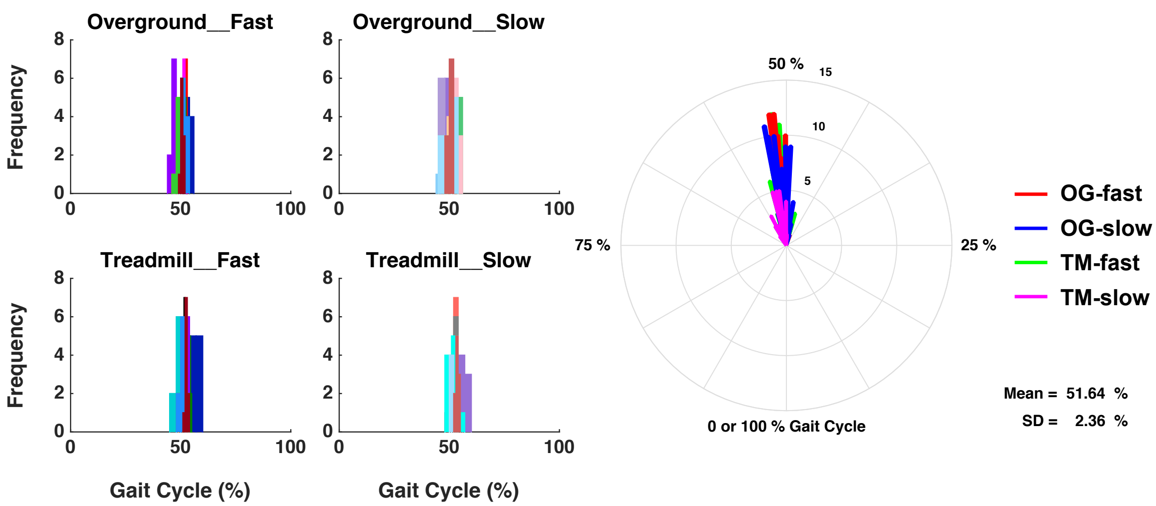

Figure 3-10: Histograms and polar plot of gait phases in the last 10 plantar-flexion torque pulses of entrained gaits. Distribution of the gait phase (φ_{conv}) for each of the 4 conditions for all 14 subjects. Colors in the histogram bars correspond to different subjects as in Figure 3-8

Figure 3-11 shows the mean onset of phase convergence between subjects for the four conditions. The two-factor ANOVA evaluating the onset of phase convergence revealed significant main effects for both walking environment and perturbation period ($p < 0.001$, $F_{1,42} = 19.61$ and $p < 0.001$, $F_{1,42} = 19.01$ respectively). The onset of phase convergence was earlier in OG (Mean = 24.12, SD = 10.26) than in TM trials (Mean = 32.90, SD = 7.13). Similarly, a more rapid gait phase convergence was detected in trials with "fast" τ_p (Mean = 24.04, SD = 10.71) in comparison to those with "slow" τ_p (Mean = 33.00, SD = 6.05). No significant interaction was found between the two factors (p = 0.098).

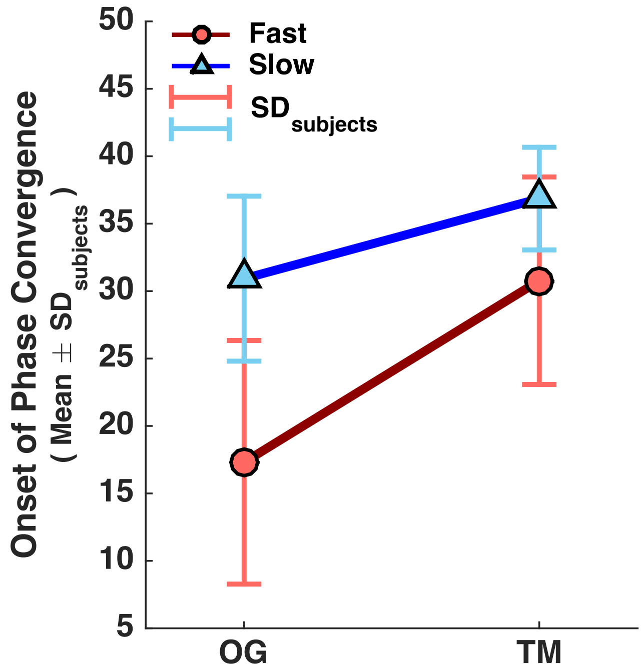

Figure 3-11: Mean plantar-flexion perturbation number corresponding to the onset of phase convergence. Convergence in "slow" perturbation periods took longer than for "fast" perturbation periods. Treadmill trials (TM) showed slower phase convergence than overground trials (OG). Error bars indicate the standard deviation of the onset of phase convergence across subjects by perturbation period and walking environment.

3.4.3 Immediate Effects of Plantar-flexion Perturbations on Stride Duration Variability

Figure 3-12 shows errorbars corresponding to the walking periods (Mean ± SD) of all fourteen subjects over the 15 consecutive strides *before* and *during* perturbation in treadmill and overground trials. As previously mentioned it was noted that subjects generally chose a faster cadence during overground walking trials. Figure 3-13 shows a direct comparison of the variability in subjects' stride duration in TM vs. OG trials. Similarly, a direct comparison of the variability in subjects' stride duration *before* vs. *during* perturbation can be seen in Figure 3-14. Visual inspection of these two figures shows trends in stride duration variability to be greater in OG trials *during* perturbation, while these changes are not as noticeable in TM trials.

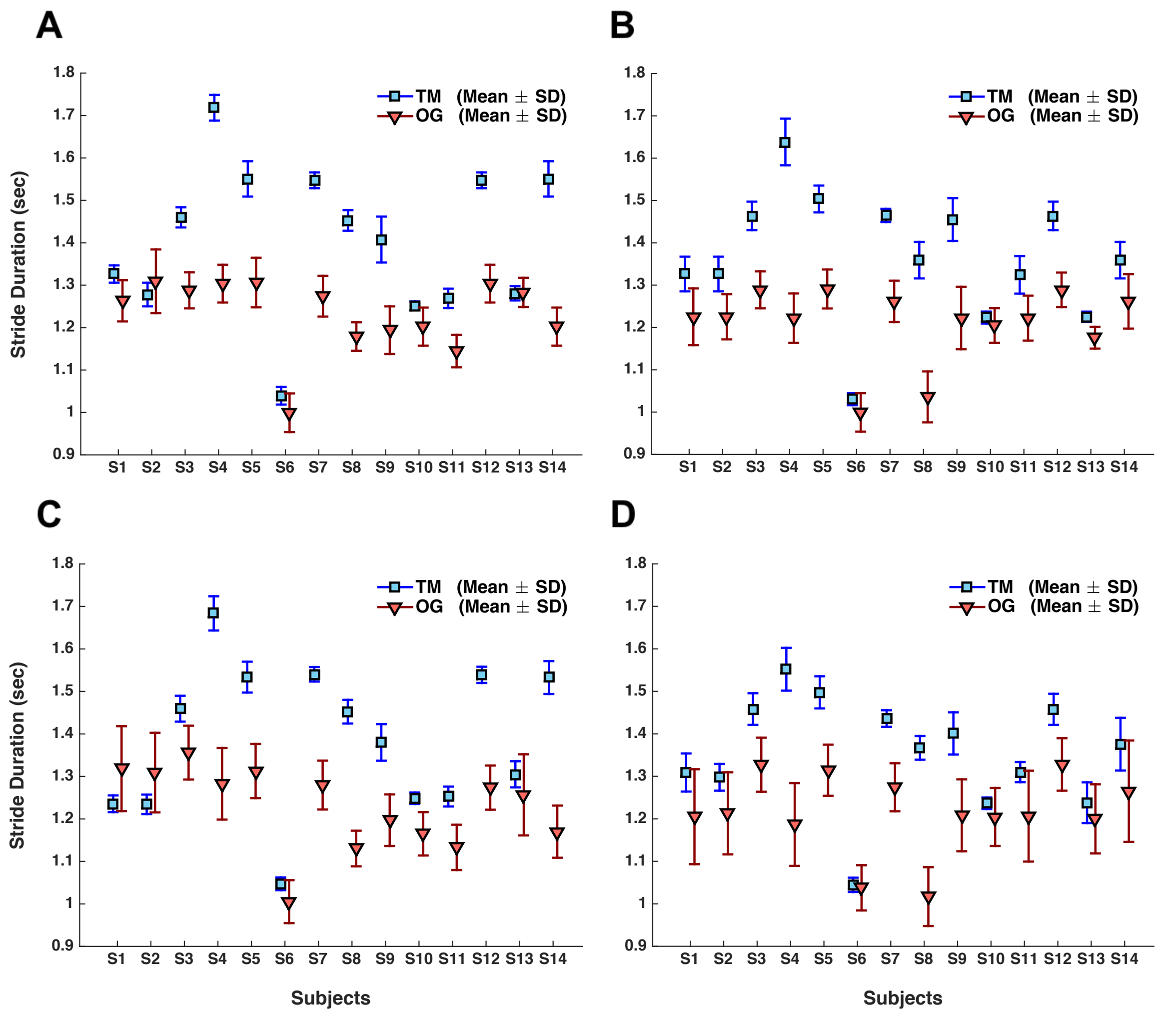

Figure 3-12: Walking periods (Mean ± SD) of all subjects over 15 consecutive strides both *before* and *during* perturbation for treadmill and overground walking trials. **(A)** Distribution of stride durations for the 15 consecutive strides *before* "fast" perturbation. **(B)** Distribution of stride durations for the 15 consecutive strides *before* "slow" perturbation. **(C)** Distribution of stride durations for the first 15 consecutive strides *during* "fast" perturbation. **(D)** Distribution of stride durations for the first 15 consecutive strides *during* "slow" perturbation.

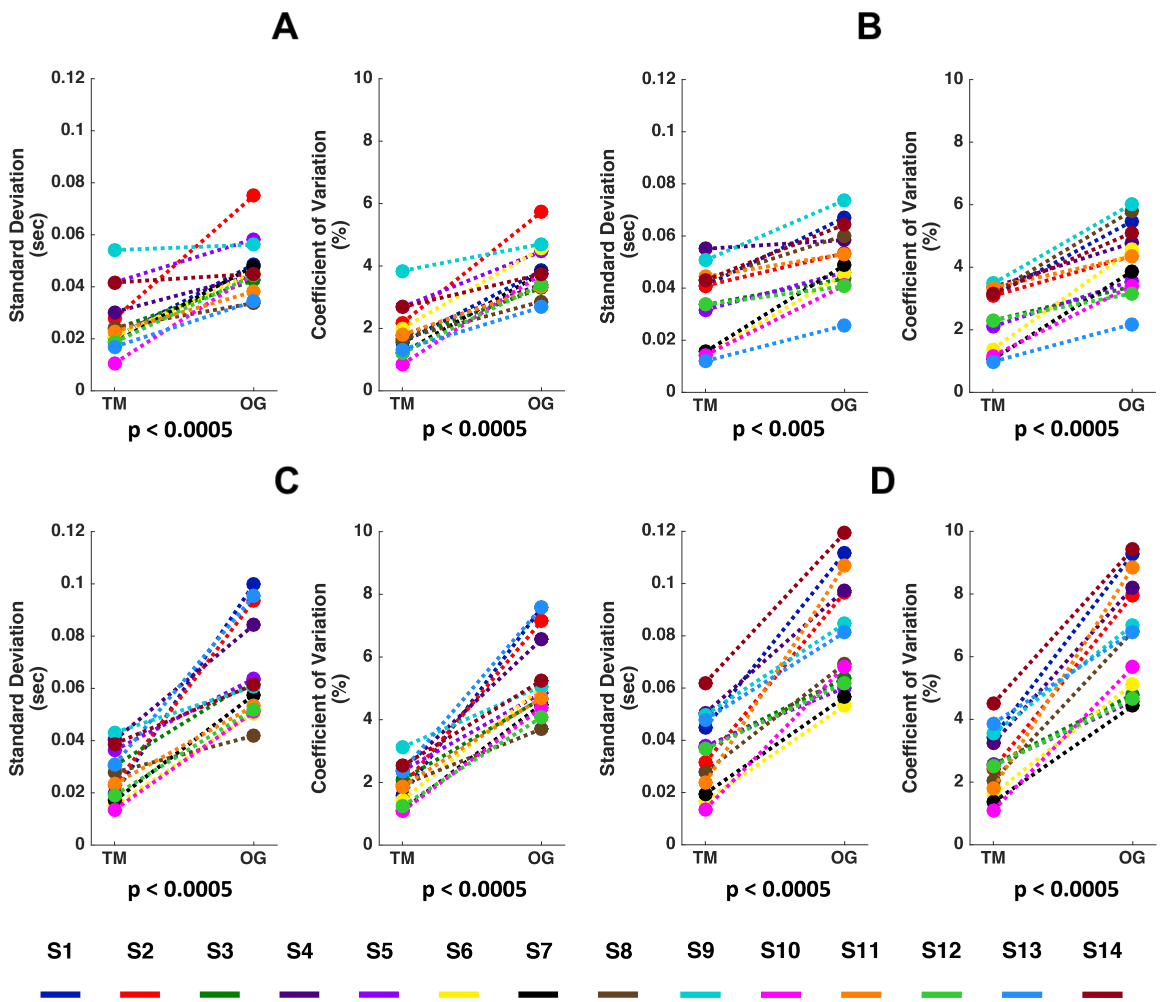

Figure 3-13: Variability (SD and CV) in stride-to-stride duration for all subjects in treadmill and overground walking trials. **(A)** Trends in SD and CV of stride-to-stride duration for the 15 consecutive strides *before* "fast" perturbation. **(B)** Trends in SD and CV of stride-to-stride duration for the 15 consecutive strides *before* "slow" perturbation. **(C)** Trends in SD and CV of stride-to-stride duration for the first 15 consecutive strides *during* "fast" perturbation. **(D)** Trends in SD and CV of stride-to-stride duration for the first 15 consecutive strides *during* "slow" perturbation.

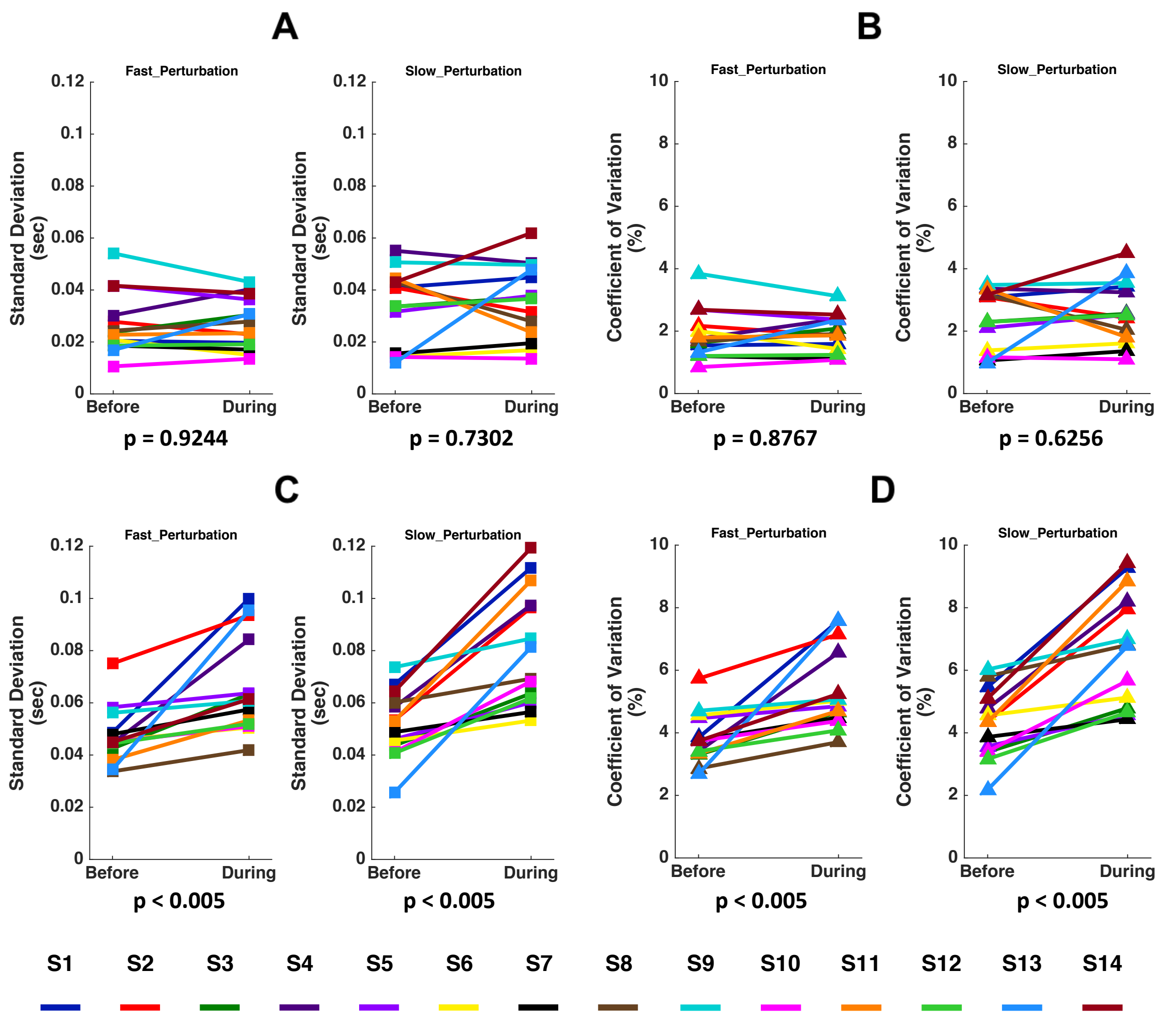

Figure 3-14: Variability (SD and CV) in stride-to-stride duration for all subjects, comparing the 15 consecutive strides *before* and *during* perturbation. (A) Trends in SD of stride-to-stride duration in treadmill trials with "fast" and "slow" perturbation. **(B)** Trends in CV of stride-to-stride duration in treadmill trials with "fast" and "slow" perturbation. **(C)** Trends in SD of stride-to-stride duration in overground trials with "fast" and "slow" perturbation. **(D)** Trends in CV of stride-to-stride duration in overground trials with "fast" and "slow" perturbation.

Two separate three-factor ANOVAs were conducted to evaluate the influence of three independent variables (walking environment, exposure to perturbations, and perturbation period) on subjects' stride duration variability. The two separate ANOVAs differed in the stride duration variability measure: SD or CV across an interval of 15 consecutive strides. In both cases, the walking environment included two values (OG, TM), exposure to perturbations consisted of two values (*before*, *during*[1]), and perturbation period also comprised two values ("slow", "fast"). All main effects were statistically significant at the 5% significance level for both ANOVAs. Table 3.2 and Table 3.3 outline the ANOVA results for both stride-to-stride duration variability measures (SD and CV). No significant 3-factor interaction was found as a result of the full-factorial ANOVA in either SD or CV in stride duration ($p = 0.4514$ and $p = 0.3936$ respectively). Two-way interactions were found between walking environment (OG, TM) and the exposure to perturbations (*before*, *during*) in terms of both SD and CV of stride duration (see Table 3.2 and Table 3.3 for p-values and F-ratios corresponding to these interactions). Post-Hoc analysis revealed that the stride-to-stride duration variability, both in terms of SD and CV, changed significantly in OG trials when comparing the strides *before* and *during* perturbation; however, these changes were not significant in TM trials. In other words, subjects reacted to the applied perturbations by increasing their stride duration variability within the first 15 consecutive strides during overground walking trials. Such increase (or change at all) in stride duration variability was not significant in treadmill walking trials, at least not within the first 15 strides after perturbations were initiated. A graphic representation of the general trends in stride duration variability revealed by both ANOVAs can be seen in Figure 3-15.

[1] This interval comprised the first 15 successive strides immediately after initiating perturbation, but generally before the onset of entrainment. The onset of phase-locking overlapped with part of this interval only in 3 trials.

Table 3.2: Analysis of variance results characterizing the standard deviation of stride-to-stride duration across all conditions in all trials.

Observations (N) = 112			
Source	**DF**	**F-Ratio**	**Prob. > F**
Walking Environment (WE)	1	119.2453	< 0.0001
Exposure to Perturbations (EP)	1	20.3676	< 0.0001
Perturbation Period (PP)	1	9.5420	0.0026
WE × EP	1	16.8608	< 0.0001
EP × PP	1	1.0463	0.3087
WE × PP	1	0.0751	0.7846
WE × EP × PP	1	0.5714	0.4514

Table 3.3: Analysis of variance results characterizing the coefficient of variation of stride-to-stride duration across all conditions in all trials.

Observations (N) = 112			
Source	**DF**	**F-Ratio**	**Prob. > F**
Walking Environment (WE)	1	183.6967	< 0.0001
Exposure to Perturbations (EP)	1	24.8087	< 0.0001
Perturbation Period (PP)	1	12.9956	0.0005
WE × EP	1	19.7884	< 0.0001
EP × PP	1	1.4233	0.2356
WE × PP	1	0.4392	0.5090
WE × EP × PP	1	0.7339	0.3936

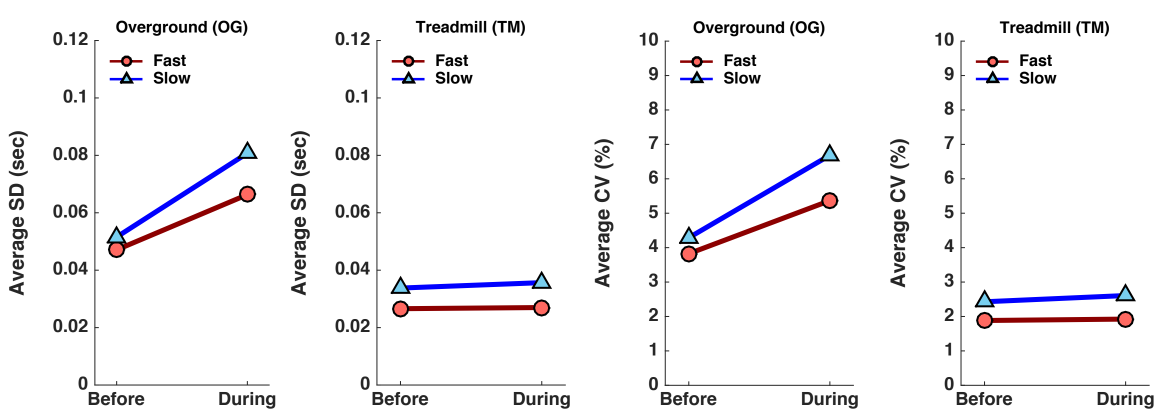

Figure 3-15: Average variability (SD and CV) in stride duration across all subjects in all trials conducted. Both the SD and CV of stride-to-stride duration were significantly different *before* and *during* perturbation in overground trials. No significant changes in stride-to-stride duration were found in treadmill trials when comparing strides *before* and *during* perturbation.

3.4.4 Post-Perturbation Walking

Subjects' stride duration over the 15 strides *before* perturbation, the last 15 strides *during* perturbation, and the first 15 strides *after* perturbation were analyzed using T-tests with 95% confidence level. Stride duration *before* and *during* was not significantly different in 7 of the 56 trials conducted. Of those 7 trials, 5 were identified as not entrained (Figure 3-16 (A)). The other 2 trials with no significant difference in stride duration between *before* and *during* perturbation were identified as entrained and both corresponded to the same subject (1 TM and 1 OG).

Persistence of the entrained gait was previously defined in Section 3.3.5 as no significant difference in stride duration *during* and *after* perturbation. Such persistence was detected in 31 out of 46 entrained trials (Figure 3-16 (B)). A breakdown of these 31 trials by combination of walking environment and perturbation period can be seen in Table 3.4. Of the 15 entrained trials with no significant persistence of the entrained gait, 11 were TM and 4 were OG trials. In 8 of those 15 trials, the subjects' cadence within the first 15 strides *after* perturbation had begun to return back to its pre-perturbation value (Figure 3-16 (C)); i.e. it was significantly different from both its value *before* and *during* perturbation. In the remaining 7 entrained trials with no persistence of the entrained gait, the subjects' cadence *after* perturbation had returned to the pre-perturbation value within 15 strides (Figure 3-16 (D)); i.e. it was significantly different from its value *after* perturbation, yet not significantly different from its value *before* perturbation.

Table 3.4: Number of trials with persistence of the entrained gait period across all four conditions.

	TM-slow	TM-fast	OG-slow	OG-fast	Total
Total Number of Trials	14	14	14	14	56
Entrained Trials	7	13	13	13	46
Trials with Persistence of the Entrained Gait Period	2	7	10	12	31
	TM = 9		**OG = 22**		

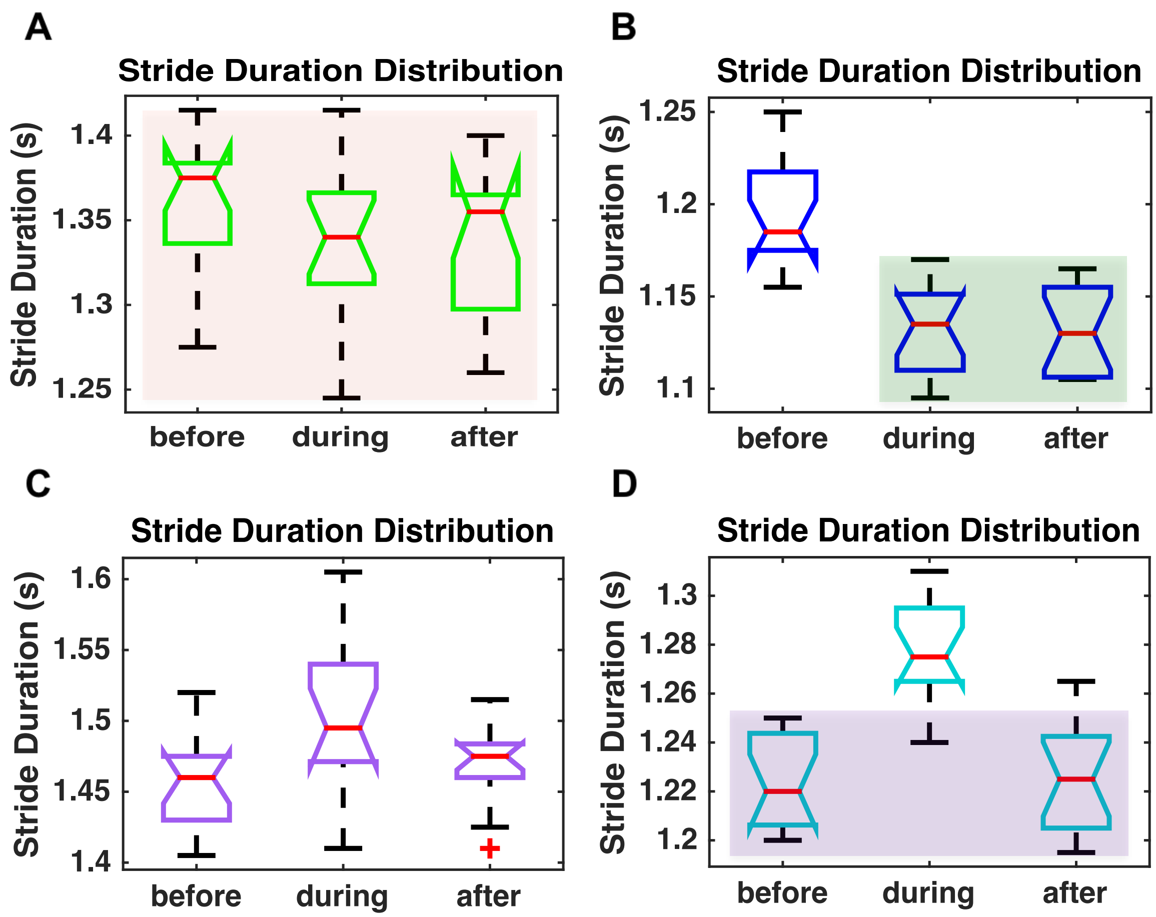

Figure 3-16: Persistence of the entrained gait period for representative trials. **(A)** No significant difference in stride duration *before*, *during*, and *after* perturbation, corresponding to a gait that did not entrain. **(B)** No significant difference between stride duration *during* and *after* perturbation, corresponding to an entrained gait with persistence of stride period. **(C)** Significant difference between stride duration *before* and *during* perturbation, as well as *during* and *after* perturbation, corresponding to an entrained gait with no persistence of stride period. **(D)** Significant difference between stride duration *before* and *during* perturbation, as well as *during* and *after* perturbation, but no significant difference *before* and *after* perturbation, corresponding to an entrained gait with no persistence of stride period since it had returned to the pre-perturbation period.

3.5 Discussion

3.5.1 Behavioral Evidence of a Nonlinear Neuro-Mechanical Oscillator Underlying Human Locomotion

Human bipedal locomotion displays some fundamental features indicative of an underlying nonlinear limit-cycle oscillator. In fact, nonlinear oscillators with a limit-cycle have served as competent models of rhythmic pattern generators (including CPGs) [65–68] and stable bipedal walkers (e.g. "passive walkers") [32,70,71]. A distinctive characteristic of nonlinear limit-cycle oscillators is entrainment to an external rhythmic perturbation. The experiments presented in this chapter demonstrated gait entrainment to periodic perturbations (i.e. plantar-flexion torque pulses at the ankle joint) in both treadmill and overground walking, together accounting for 46 entrained trials out 56 total trials.

To minimize voluntary gait synchronization to the imposed perturbations, subjects were asked to perform a distractor task. If gait entrainment was a result of voluntary synchronization, then the onset of phase convergence should have occurred within the first few perturbation cycles. Instead, a rather moderate-to-slow convergence was observed in overground and treadmill trials, occupying 24 and 32 perturbation cycles on average respectively.

To the best of my knowledge, this is the first study demonstrating dynamic entrainment to external periodic plantar-flexion perturbations at the ankle joint during overground walking.

> *I submit that these results show clear, behavioral evidence that a nonlinear neuro-mechanical oscillator with a limit-cycle plays a significant role in human locomotion.*

3.5.2 Gait Entrainment in Overground vs. Treadmill Walking

Previous studies reported no significant differences in the kinematic gait patterns of chronic stroke survivors with and without the Anklebot on the paretic leg during treadmill and overground walking [101]. In the experiments presented in this chapter, TM and OG trials were conducted in the same fashion, but without constraint on fixed speed in the OG trials. However, the gait entrainment results obtained differed significantly in TM and OG trials: gait phase converged faster in OG than in TM trials, taking an average of 24 and 32 perturbation cycles respectively (Figure 3-11).

Furthermore, more trials entrained in OG compared to TM trials. This difference appears to be due to the fixed-speed constraint in TM trials. In order for subjects to entrain to periodic perturbations 50 ms different from their preferred stride period, they had to change their speed, and/or their stride length. Given that the speed was kept constant in TM trials, subjects could only adjust their stride period to eventually match the perturbation period. However, the direct comparison of stride-to-stride duration variability, even *before* perturbation, was significantly different in overground vs. treadmill walking trials. It was noted that subjects' stride duration variability under no perturbation was significantly greater in OG trials (refer to Figure 3-13 (A and B) and Figure 3-15). Greater variability in stride duration could potentially facilitate a faster rate of entrainment to rhythmic perturbations occurring at periods different from subjects' preferred walking periods since they would have more flexibility to gradually change their walking period to match the period of the perturbations. Therefore, it could be concluded the constant speed of the treadmill belt, including the limited length of the treadmill deck, appears to have influenced the gait phase convergence in TM trials.

As previously noted, subjects generally chose a faster cadence during overground walking (refer to Table 3.1). Such significant differences in subjects' walking periods may have influenced the gait entrainment results obtained in OG vs. TM trials. Further experiments are therefore required to address this substantial difference in gait entrainment during treadmill and overground walking, specifically with subjects walking at the same cadence in all different trials.

3.5.3 Faster Phase-Locking at Ankle 'Push-off' in Overground Walking Trials

While entrainment requires phase convergence of the subject's stride duration to the perturbation period, it does not limit such phase convergence to any particular, constant phase. It was previously reported by Ahn and Hogan [98] that gait synchronized with the perturbation at approximately 50% of the gait cycle when subjects walked on a treadmill. The experiments presented in this chapter not only replicated their findings on treadmill walking, but also extended their observation to walking overground. Analysis of gait phase convergence revealed that the average gait phase in the 46 entrained trials was 51.64% ($\pm$ 2.36%) Figure 3-10. It must be emphasized that the final gait phase value was independent of the gait phase at which perturbations were initiated. Perturbations were randomly initiated at various phases of the gait cycle across all trials, which can be seen in Figure 3-8 and Figure 3-9. Hence, the end of double stance ($\sim$50% of the gait cycle) may be regarded as the "global" attractor for phase-locking in gait entrainment to periodic ankle plantar-flexion perturbations [99].

In normal walking, the maximum ankle plantar-flexion torque is exerted at 'push-off' (47-62%), which begins near the end of terminal stance phase (31-50%) and ends during the pre-swing phase (50-62%) [25]. Phase-locking occurring consistently at ankle 'push-off' in the experiments presented in this chapter suggests that gait adapted so that the periodic perturbations mechanically assisted plantar-flexion at the ankle joint, thus facilitating forward propulsion. This observation is of significance for lower-extremity robotic rehabilitation and exoskeleton design since the mechanical perturbations could supply the additional torque needed by patients who cannot produce sufficient propulsion to swing their paretic leg forward. Similarly, it could be reasoned that varying the magnitude and frequency of the torque perturbations to provide assistance as needed may stimulate voluntary participation.

In several entrained trials, it was observed that a torque pulse occurring at 'push-off' was not always accompanied by immediate gait synchronization (phase-locking). Examples of this observation can be seen in Figure 3-8 as several functions of plantar-flexion perturbation phase vs. perturbation number crossed the red horizontal lines corresponding to 50% of the gait cycle, yet there was no entrainment until further along in the trials. If subjects synchronized their gaits with the perturbation where it assisted propulsion—or did not oppose ankle actuation—then why did they not do so at the very first opportunity? Perturbation periods (τ_p) were strictly 50 ms slower/faster than preferred stride duration (τ_0). However, τ_0 was determined as the averaged duration of 15 consecutive strides, measured by a stopwatch and visually estimating the moment of heel strike. Hence, not only could the preferred period be non-stationary, but it also had a variability. As a result, τ_p could be further apart from or closer to subjects' walking cadence when perturbations were initiated. Synchronization to perturbation periods further apart from subjects' stride period required greater changes in cadence. Given the nonlinear nature of the limit-cycle oscillator postulated to underlie human locomotion, entrainment could only occur when the τ_p was sufficiently close to the subjects' stride period. Hence, the perturbation period could have been significantly different from a subject's stride period at the very first opportunity a torque pulse occurred at 'push-off', thus making phase-locking unattainable. In these cases, gradual changes in walking cadence eventually reduced the difference between τ_p and subjects' stride period, leading to entrainment further along.

3.5.4 Gait Entrainment to "Fast" vs. "Slow" Perturbation Periods

The plantar-flexion torque pulses applied to the ankle during double-stance can only act as mechanically assistive pulses, adding positive work. Entrainment to fast perturbation periods ($\tau_p = \tau_p - 50$ ms) required subjects to speed up cadence. Hence, gait entrainment to fast perturbation periods might be due to the positive work added by the mechanically assistive perturbations. A simple model presented by Ahn and Hogan reproduced this behavior [99].

In contrast, entrainment to "slow" perturbation periods ($\tau_p = \tau_p + 50$ ms) cannot solely be attributed to a mechanical response to assistive perturbations. Ahn and Hogan's model was capable of reproducing entrainment and phase-locking only when the perturbation periods were faster than preferred stride period [99]. However, the experiments presented in this chapter also demonstrated gait entrainment to "slow" perturbations, which therefore cannot be attributed only to mechanics. Entrainment to "slow" perturbation periods required subjects to slow down their cadence even though the mechanically assistive plantar-flexion torque pulses caused them to speed up, at least locally.

Analysis of immediate effects of perturbations of gait timing variability within the first 15 strides *during* perturbation revealed a significant main effect for the perturbation period factor ("slow" vs. "fast"). Stride duration variability *during* perturbation was, in fact, significantly greater when subjects were exposed to "slow" perturbations (Figure 3-15). The "slow" plantar-flexion perturbations delivered in these experiments are contradictory in nature. This type of perturbations could supply positive work during double-stance, which would facilitate a faster cadence, while at the same time demanding slower walking periods for subjects to match the period of the "slow" perturbations. Such conflicting nature of the "slow" plantar-flexion perturbations may have indeed led subjects to increase their stride duration variability in an attempt to find a compromise between the two opposing factors in order to eventually entrain their gaits to the perturbations. On the other hand, the behavioral evidence in terms of stride-to-stride duration variability in trials involving "fast" perturbation periods was quite different. While there was a significant increase in gait timing variability between the 15 strides *before* perturbations and the first 15 strides *during* "fast" perturbation, such increase was not as prominent as in trials involving "slow" perturbations (Figure 3-14).

The evidence presented in this chapter indicates that subjects' immediate reaction to the perturbations was typically to increase their stride duration variability. Such increase, however, led to a greater number of entrained gaits in trials involving "fast" perturbation periods since it was plausibly easier for subjects to take advantage of the mechanically assistive pulses to speed up and match the imposed ("fast") period. Additionally, the fact that phase-locking occurred significantly later in "slow" perturbation periods is consistent with this reasoning. In fact, gait entrainment in treadmill walking was only detected in 50% of the total trials.

In all, the results presented in this chapter suggest the hypothesis that gait entrainment may not simply be the result of peripheral mechanics in human walking. Instead, gait entrainment seems to require a more complex interaction between the neuro-muscular periphery and the gravito-inertial mechanics in human locomotion.

3.5.5 Persistence of the Entrained Gait during Post-Perturbation Walking

Persistence of the entrained gait after the perturbation was observed in 67% of the entrained trials (31 out of 46 entrained trials). A correlation was found between the rate of gait phase convergence and the post-perturbation walking. The faster the rate of phase-locking, the greater the number of trials exhibiting persistence of the entrained gait. Altogether, trials with persistence showed the onset of entrainment on or before the 33rd perturbation torque pulse. Thus, subjects who continued walking at the perturbation period had walked 17 or more consecutive strides at that particular cadence during perturbation. Overall, the adapted cadence persisted in more entrained trials with overground walking than in treadmill walking. I speculate that this difference is due to the faster gait phase convergence detected in overground walking; i.e. subjects maintained the perturbation period in more overground trials because they walked at that cadence for a greater number strides after the onset of entrainment.

Persistence of the entrained gait for at least 15 consecutive post-perturbation strides is not sufficient to determine how much longer subjects would maintain the adapted walking cadence. Previous studies of robot-aided upper-extremity rehabilitation have demonstrated that while progress in motor recovery made in one therapy session did not necessarily carry through to the next session, significant improvements were detected over the course of many therapy sessions [101]. Similar long-term results might be obtained for lower-extremity rehabilitation through gait entrainment to mechanical perturbation, even if the entrained gait did not persist long after perturbation in each therapy session. Further studies are necessary to test the possible locomotor control improvements in impaired human subjects over many gait entrainment therapy sessions.

Chapter 4

Rhythmic Dorsi-flexion Perturbations to the Ankle Joint

In the previous chapter, experimental results were presented to characterize the entrainment of human locomotion to rhythmic plantar-flexion perturbations applied to the ankle joint during treadmill and overground walking. This chapter presents experimental data to characterize gait entrainment to ankle dorsi-flexion perturbations instead. Additionally, this chapter discusses the implication of this new series of experimental results in identifying the mechanical vs. neural contributions of the entrained oscillator to human walking.

4.1 Introduction

Humans exhibit locomotor behavior that is much more sophisticated than that of many inspiring dynamic walkers [71,107–109] developed after McGeer's pivotal work in legged locomotion [32,70]. For instance, in soccer, the foot is used to manipulate a ball with remarkable dexterity, while simultaneously maneuvering through a continually changing environment. Even routine walking is characterized by a remarkably repeatable trajectory of the foot [112]. Indeed, it has been shown that subjects adjust their minimum toe clearance using subtle adjustments of lower-limb kinematics in order to avoid small obstacles [113].

These observations suggest that higher-level processes adjust peripheral muscle activation and joint recruitment to control the kinematics of the foot.

The experimental study presented in the previous chapter presented evidence of the non-negligible role of nonlinear limit-cycle oscillators in human locomotor control and their sensitivity to different walking environments—treadmill vs. overground. A complementary approach to assess the strength of such limit-cycle oscillator is to test the robustness of entrainment. If entrainment is primarily mediated by peripheral neuro-mechanics, it should be sensitive to the form of the mechanical perturbation. The experiment presented in the previous chapter used plantar-flexion square pulses; this subsequent experiment applied dorsi-flexion square pulses of the same amplitude (10 N·m) and duration (100 ms) as before. In the following sections, the experimental protocols and results are described in detail.

Importantly, in the previous experiment, gait entrainment to plantar-flexion square pulses was always accompanied by phase-locking; the pulse always occurred at the same specific phase of stance—ankle 'push-off'. In this subsequent experiment, if **(1)** gait entrainment to dorsi-flexion square pulses sill occurs, and **(2)** phase-locking is detected at the same gait phase, this behavior cannot be attributed to a purely mechanical effect independent of neural control.

4.2 Methods

The same fourteen healthy subjects who participated in the previous series of experiments (presented in Chapter 3) agreed to participate in this second series of experiments, which was conducted on the same day as the previous trials. All participants gave informed consent in accordance with procedures approved by the Institutional Review Board (IRB) of the Massachusetts Institute of Technology (MIT). The purpose of the study was to compare the subjects' walking performance on a standard treadmill versus overground while exposed to a series of rhythmic dorsi-flexion perturbation applied to the ankle joint via a wearable robot.

4.2.1 Equipment and Protocols

Each subject performed 2 trials on the same Sole Fitness F80 treadmill (with a 0.84 m $\times$ 1.90 m deck) as before, and another 2 trials walking overground in the same large corridor at MIT previously used for the ankle plantar-flexion perturbation trials. For both walking conditions, "slow" and "fast" perturbation periods were delivered. In all trials, subjects performed the same cognitive distractor task previously requested: listing countries, cities, animals, etc. in alphabetical order (one category at a time).

The Anklebot was once again used in this new series of experiments to deliver the periodic square torque pulses of magnitude –10 N·m and duration 100 ms, in the same fashion as previously outlined in Chapter 3. The robot's torsional spring-and-damper behavior was also maintained in these trials, with 5 N·m/rad stiffness and 1 N·m·sec/rad damping, referenced to a constant equilibrium position measured from the subject's upright posture. Subjects' knee angle was recorded throughout the trials using the potentiometer embedded in the Anklebot's knee brace. As before, subjects wore a harness to distribute the weight of the Anklebot over the upper body.

4.2.2 Treadmill vs. Overground Trials

In treadmill trials, subjects were asked to adjust the speed of the treadmill to a comfortable walking speed, which was maintained constant throughout the duration of any one trial. As before, a treadmill trial (TM) began with subjects walking at their preferred speed and their preferred stride duration (τ_0) was measured as the average duration of 15 consecutive strides. The perturbation period (τ_p) was then selected to be 50 ms "slower" (TM-slow) or "faster" (TM-fast) than the subjects' preferred stride duration (τ_0). To maintain similarities with the previous series of ankle plantar-flexion perturbation experiments, each one of these trials was also divided into 3 sections: *before*, *during*, and *after*. The *before* section consisted of 15 strides with no perturbation. The *during* section comprised 50 consecutive perturbations. In the *after* section the robot stopped exerting the torque pulses but maintained its spring-damper behavior. Subjects stopped walking and the trial terminated immediately afterwards.

In overground trials (OG), subjects were asked to walk at their preferred walking speed. These trials differed from treadmill trials in that there was no fixed-walking-speed constraint. As before, subjects' preferred walking period (τ_0) was measured using the first 15 consecutive strides after subjects had achieved their comfortable walking speeds. Overground trials were conducted in the same fashion as treadmill trials, including one trial with "slow" (OG-slow) and one with "fast" (OG-fast) perturbation periods.

4.3 Data Analysis

The gait cycle was estimated once again based on knee angle measurements recorded by a potentiometer embedded in the Anklebot's knee brace. The knee angle profile was normalized from 0 to 100% to define a gait phase for each stride, with 100% defined as the maximum knee extension adjacent to heel strike (refer to Figure 3-3). All data collected from onboard sensors were recorded at a sampling rate of 200 Hz. Subjects' stride durations *before*, *during*, and *after* perturbation were compared to evaluate the effect of the mechanical perturbations on subjects' walking cadence. Statistical significance was set at a 5% significant level.

4.3.1 Assessment of Entrainment

As previously explained, while the dorsi-flexion perturbations were delivered at a constant period throughout each trial, the onset of the torque pulses could vary with respect to landmarks in the gait cycle (e.g. the maximum knee flexion) given its 50 ms difference from the preferred stride period. Consequently, the phase of the gait cycle at which perturbations occurred would not necessarily be constant. Entrainment to the applied perturbations requires subjects' gaits period must be the same as the period of the imposed torque pulses; i.e. each pulse must to occur at the same phase of the gait cycle.

As in the previous experiments outlined in Chapter 3, the gait phase corresponding to each perturbation was determined as the percentage of the gait cycle that coincided with the onset of the torque pulse. Entrainment was identified as zero slope included in the 95% confidence interval corresponding to the linear regression of gait phase onto perturbation number applied to the last 10 perturbations in each trial. If the null hypothesis was accepted (H_0: m = 0), then the gait was considered *entrained*. Trials for which H_0 was rejected were defined as *not entrained* to "slow" perturbations (m > 0) or *not entrained* to "fast" perturbations (m < 0) (refer to Figure 3-5 for representative cases of *entrained* and *not entrained* trials).

4.3.2 Converged Gait Phase

The converged gait phase value (φ_{conv}) was determined as the mean gait phase corresponding to the greatest number of consecutive perturbations[1] lying within an interval $\varphi_{\text{conv}} \pm 2\sigma$, where σ corresponds to the standard deviation of the gait phases at which the last 10 perturbations occurred. Thus, the onset of converged gait phase or phase-locking was determined as the first perturbation to lie within the defined interval. The dependent measures, gait phase and onset of phase convergence, were submitted to a 2 (TM vs. OG) $\times$ 2 (Slow vs. Fast) ANOVA using SAS JMP® statistical software package [110] to evaluate gait phase convergence for each entrained gait.

4.3.3 Persistence of the Entrained Gait

Gaits that entrained to the imposed perturbation could be subjected to persisting changes in stride duration periods even after the torque perturbations

[1]When determining φ_{conv}, it was deemed acceptable for up to 3 consecutive perturbations to lie outside the interval, provided the subsequent perturbation re-entered the interval (refer to Figure 3-6 for a representative trial demonstrating this scenario).

had been discontinued. Persistence of the entrained gait was evaluated by comparing the subjects' walking frequency *during* and *after* perturbations. Such persistence was present when the periods of the last 15 strides *during* perturbation and the 15 strides immediately *after* perturbation did not differ significantly when evaluated using T-tests with 95% confidence level.

4.4 Results

A total of 56 ankle dorsi-flexion perturbation trials were conducted with the fourteen healthy subjects who were recruited to participate in the experiments. Each subject completed 4 consecutive trials (2 TM and 2 OG) in randomized order. None of the subjects requested to opt out of the experiment nor reported pain or significant discomfort during their participation in any of the trials. The subjects who agreed to participate in this second series of experiments were the same subjects who participated in the previously discussed experiments with ankle plantar-flexion perturbations (refer to Chapter 3). Table 4.1 shows each subject's preferred treadmill speed and walking periods *before* perturbation during both treadmill and overground walking (refer to Table 3.1 in Chapter 3 for additional details on subjects' gender and height). As in the previous ankle plantar-flexion perturbation trials, subjects were allowed to select their preferred walking speed (in both TM and OG) and these could differ from trial to trial even within the same subject. As previously reported, the mean stride duration (*before* perturbation) for all 14 subjects was significantly lower in overground trials; i.e. subjects always chose a faster cadence during overground walking. Similarly, the standard deviation and coefficient of variation of stride duration (*before* perturbation) was always significantly greater in overground trials (see Table 4.1).

Table 4.1: Subjects' ID, preferred treadmill speeds, and walking periods *before* ankle dorsi-flexion perturbations. Abbreviations—SD: standard deviation; CV: coefficient of variation (SD/Mean)

Subject ID	**Preferred Treadmill Speed (m/s)**	**Preferred TM Stride Period *Before* Perturbation (s)**			**Preferred OG Stride Period *Before* Perturbation (s)**		
		Mean	**SD**	**CV%**	**Mean**	**SD**	**CV%**
S1	0.80	1.33	0.041	3.08	1.23	0.067	5.45
S2	0.89	1.32	0.039	2.95	1.20	0.053	4.42
S3	0.67	1.46	0.024	1.64	1.29	0.043	3.35
S4	0.72	1.72	0.030	1.75	1.22	0.058	4.75
S5	0.72	1.50	0.032	2.13	1.29	0.046	3.57
S6	1.56	1.03	0.014	1.36	0.99	0.046	4.65
S7	0.76	1.55	0.019	1.23	1.27	0.048	3.78
S8	0.76	1.45	0.024	1.66	1.04	0.060	5.77
S9	0.85	1.46	0.051	3.49	1.22	0.074	6.07
S10	0.98	1.22	0.014	1.15	1.20	0.041	3.42
S11	0.89	1.27	0.023	1.81	1.22	0.053	4.34
S12	0.85	1.55	0.019	1.23	1.31	0.045	3.44
S13	0.89	1.28	0.017	1.33	1.18	0.026	2.20
S14	0.89	1.36	0.043	3.16	1.26	0.064	5.08
All Subjects	**Mean = 0.87** **SD = 0.22**	**1.39**	**0.027**	**Mean = 1.99** **SD = 0.82**	**1.21**	**0.052**	**Mean = 4.31** **Mean = 1.09**

4.4.1 Entrainment

In this second series of experiments, entrainment was also assessed as a zero slope in the regression of gait phase onto perturbation number. Figure 4-1 shows two selected trials in which the phase difference between the maximum knee flexion and the rhythmic perturbation pulses can be visually inspected to assess entrainment. The gait in Figure 4-1(A) entrained to the perturbations since the landmarks in the gait cycle maintained a constant phase difference with the continuous rhythmic torque pulses applied by the Anklebot. Conversely, the gait in Figure 4-1(B) did not entrain to the perturbations since the maximum knee flexion drifted continuously with respect to the periodic torque perturbations.

Overall, entrainment was observed in 50 out 56 total trials (23 TM, 27 OG). In the first series of ankle plantar-flexion perturbation experiments, subject (S6) did not entrain in any of the 4 different trials. In the this second series of ankle dorsi-flexion perturbation experiments, however, subject S6 entrained in the 2 overground trials but did not entrain in the 2 treadmill trials. The remaining 4 trials identified as not entrained were 3 TM trials and 1 OG trial. The relationship between dorsi-flexion perturbation phase and perturbation number for all entrained gaits can be seen in Figure 4-2.

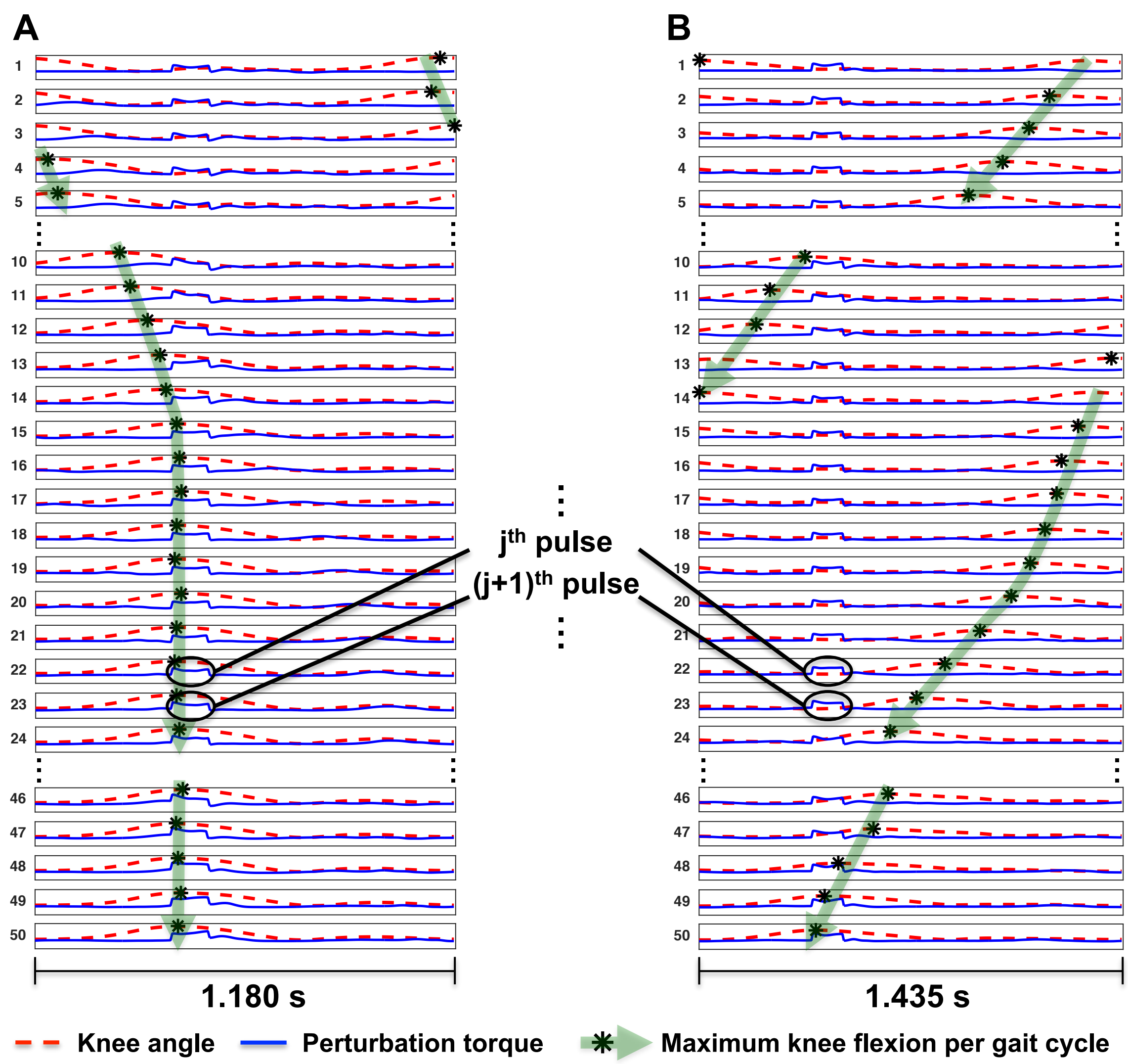

Figure 4-1: Phase relation between the maximum knee flexion in each gait cycle with respect to the dorsi-flexion perturbations for "entrained" vs. "not entrained" gaits. **(A)** Typical results for a gait that entrained to "fast" perturbation; the maximum knee flexion drifted initially but eventually converged on a specific phase of the perturbation cycle. **(B)** Typical results for a gait that did not entrain to "slow" perturbation; the maximum knee flexion drifted continuously relative to the perturbation. Each row in **(A)** and **(B)** represents one dorsi-flexion perturbation cycle with its duration (τ_p) indicated at the bottom; the knee angle for each perturbation cycle is plotted in each row with the maximum knee flexion landmark identified. The perturbation number corresponding to each row is shown to the left of **(A)** and **(B)**.

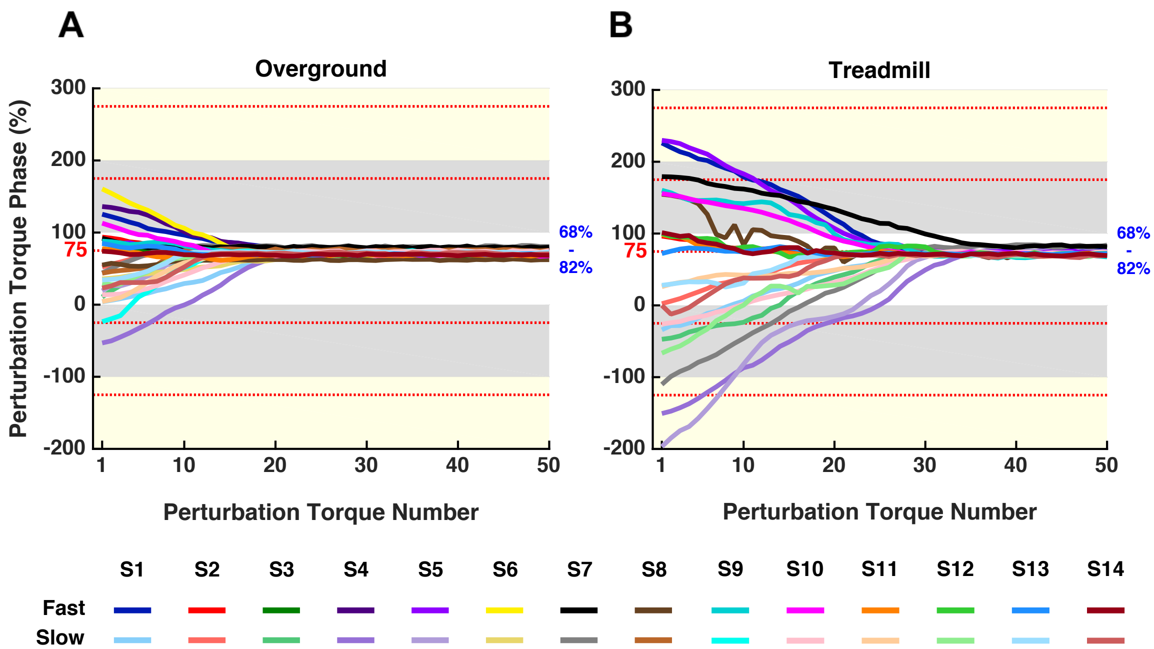

Figure 4-2: Dorsi-flexion perturbation phase as a function of perturbation number for all entrained gaits. **(A)** Entrained gaits during overground trials. **(B)** Entrained gaits during treadmill trials. Each color corresponds to a different subject, with a dark and a light shade corresponding to the trials with "fast" and "slow" perturbation respectively.

4.4.2 Phase-Locking in Entrained Gaits

As can be appreciated in Figure 4-3, the ankle dorsi-flexion perturbations delivered by the Anklebot were initiated randomly at various phases of the gait cycle. Interestingly, subjects who entrained to the imposed perturbations consistently synchronized their gaits with the torque pulses between 68 and 82% of the gait cycle in the 50 entrained trials. Histograms and a polar plot of gait phase in the last 10 perturbations of entrained gaits are shown in Figure 4-4. The mean φ_{conv} across all entrained gaits was 71.92% ($\pm$ 4.28%), which was near the end of 'initial swing'of the leg wearing the Anklebot. This coincides with the interval of ankle dorsi-flexion torque for toe clearance from the ground [25].

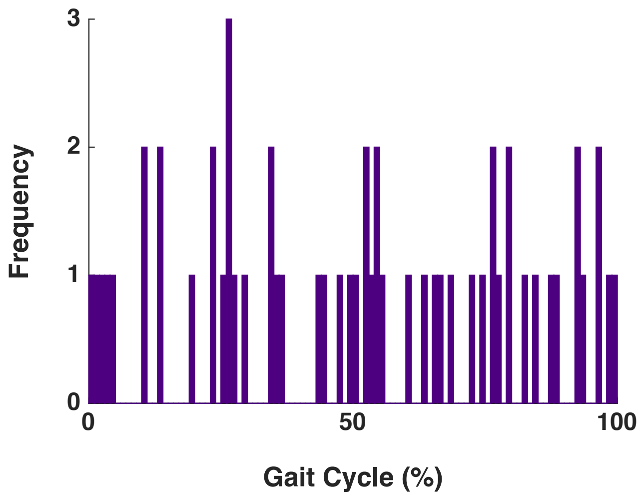

Figure 4-3: Histogram of the randomly selected gait phases corresponding to the first dorsi-flexion perturbation applied in all 56 trials.

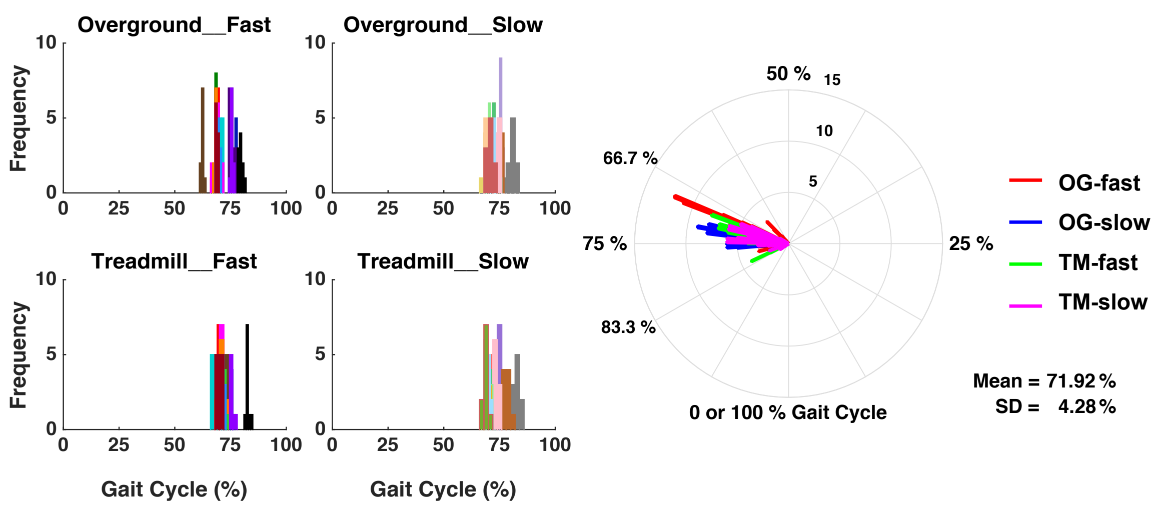

Figure 4-4: Histograms and polar plot of gait phases in the last 10 dorsi-flexion torque pulses of entrained gaits. Distribution of the gait phase (φ_{conv}) for each of the 4 conditions for all 14 subjects. Colors in the histogram bars correspond to different subjects as in Figure 4-2

Figure 4-5 shows the mean onset of phase convergence between subjects for the four conditions. The two-factor ANOVA evaluating the onset of phase convergence revealed a significant main effect for walking environment ($p < 0.001$, $F_{1,46} = 41.87$). On the other hand, no significant main effect was found for perturbation period ($p = 0.3700$). Onset of phase convergence was earlier in

OG (Mean = 15.56, SD = 6.07) than in TM trials (Mean = 26.70, SD = 5.92). No significant interaction was found between the two factors (p = 0.8169).

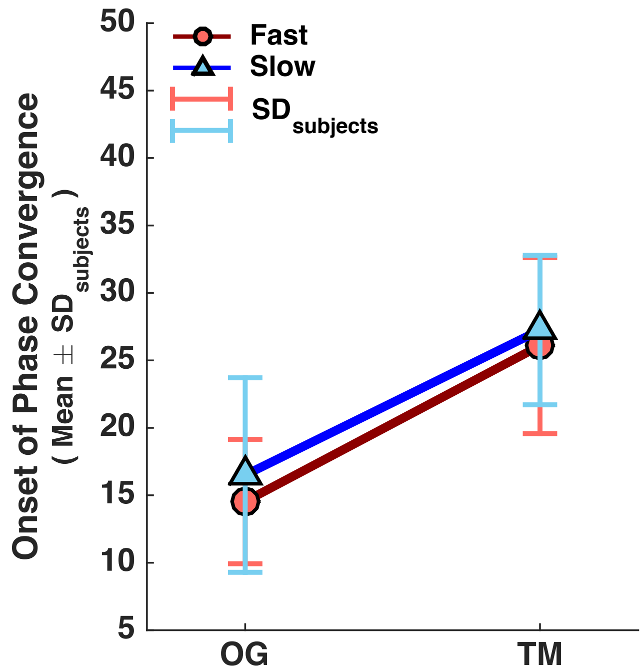

Figure 4-5: Mean dorsi-flexion perturbation number corresponding to the onset of phase convergence. Treadmill trials (TM) showed slower phase convergence than overground trials (OG). However, no significant differences were found between convergence to "slow" and "fast" perturbation periods. Error bars indicate the standard deviation of the onset of phase convergence across subjects by perturbation period and walking modality.

4.4.3 Post-Perturbation Walking

Subjects' stride duration over the 15 strides *before* perturbation, the last 15 strides *during* perturbation, and the first 15 strides *after* perturbation were analyzed using T-tests with 95% confidence level. Stride duration *before* and *during* was not significantly different in 4 of the 56 trials conducted. Of those 4 trials, 1 was identified as not entrained. The other 3 trials with no significant difference in stride duration between *before* and *during* perturbation were identified as entrained and corresponded to two different subjects (2 TM and 1 OG).

Persistence of the entrained gait was previously defined as no significant difference in stride duration *during* and *after* perturbation. Such persistence of the entrained gait was only detected in 8 out of 50 entrained trials (6 TM, 2 OG). No significant difference in stride duration *before* and *during* perturbation was found in 1 of those 8 trials exhibiting persistence of the entrained gait. Of the 42 entrained trials with no significant persistence of the entrained gait, 17 were TM and 25 were OG trials. In 17 of those 42 trials, the subjects' cadence within the first 15 strides *after* perturbation had begun to return back to its pre-perturbation value; i.e. it was significantly different from both its value *before* and *during* perturbation. In the remaining 25 entrained trials with no persistence of the entrained gait, the subjects' cadence *after* perturbation had returned to the pre-perturbation value within 15 strides; i.e. it was significantly different from its value *after* perturbation, yet not significantly different from its value *before* perturbation.

4.5 Discussion

4.5.1 Faster Phase-Locking during 'Initial Swing' in Overground Walking Trials

As mentioned in the previous chapter, gait entrainment requires phase convergence of the subject's stride duration to the perturbation period; however, such phase convergence is not strictly limited to any particular constant phase. In other words, subjects can synchronize their gaits with the perturbations occurring at any one phase of the gait cycle, say at heel strike, during mid stance, initial swing, etc. Remarkably, analysis of the of the gait phase convergence in the experiments presented in this chapter revealed that the average gait phase in the 50 entrained trials was 71.92% ($\pm$ 4.28%) (Figure 4-4), which corresponds to the segment of 'initial swing'in the gait cycle. As in the experiments presented in the previous chapter, the converged gait phase to ankle dorsi-flexion perturbations was independent of the gait phases at which perturbations were initiated. In all trials, perturbations were randomly initiated at various phases of the gait cycle (see Figure 4-2 and Figure 4-3). According to these results, the moment of 'initial swing'in the gait cycle could be regarded as the "global" attractor for phase-locking in gait entrainment to ankle dorsi-flexion perturbations.

The gait cycle can be divided into two main phases: Stance and Swing. According to Perry's assessment of the gait cycle, the Stance phase can be subdivided into: Initial Contact (0-2%), Loading Response (2-12%), Mid Stance (12-31%), Terminal Stance (31-50%), and Pre-Swing (50-62%) [25]. Similarly, the Swing phase can be subdivided as follows: Initial Swing (62-75%), Mid Swing (75-87%), and Terminal Swing (87-100%). The ankle experiences a series of plantar-flexion and dorsi-flexion torques throughout the gait cycle, including two major dorsi-flexion peaks. The first of these peaks takes place during mid/terminal stance and it is known as 'ankle rocker' [25]. At this point of the gait cycle, the ankle acts as the axis of rotation while the limb rolls forward and advances as the result of momentum. The purpose of the 'ankle rocker' is to dorsiflex the ankle to facilitate limb advancement over the stationary foot while ensuring limb and trunk stability. This particular type of ankle dorsi-flexion is often defined as 'passive' since it is mainly the result of shank moving towards the forefoot while the limb advances due to momentum. The second ankle dorsi-flexion peak occurs during initial/mid swing and its purpose is to ensure foot clearance from the ground to allow limb advancement. In the literature, this type of ankle dorsi-flexion is often regarded as 'active' since it is the result of the forefoot moving towards the shank not due to momentum but in response to muscle activation to ensure toe clearance.

The experiments presented in this chapter revealed that subjects who entrained their gaits established a phase relationship with the perturbations occurring at 71.92% ($\pm$ 4.28%) of the gait cycle, which corresponded mainly to the end of 'initial swing'. This part of the gait cycle overlaps with the second ankle dorsi-flexion peak previously described, which ensures foot clearance from the ground. Thus, it appears subjects gait adapted so that the periodic perturbations assisted dorsi-flexion at the ankle joint to facilitate foot-ground clearance and limb advancement.

Foot clearance represents a critical event in the gait cycle; specifically, foot clearance deficit can not only hinder limb advancement but also increase the risk of falls [114]. Consistent phase-locking during 'initial swing'to assist foot-ground clearance and limb advancement is a particular observation which may have potential significance for lower-extremity rehabilitation.

Hemiparesis is a muscle weakness affecting one side of the body, which is a common condition in stroke survivors. It is, in fact, what leads to inefficient limb clearance due to reduced ankle excursions during the swing phase. The traditional method for assisting foot-ground clearance during the swing phase involves the use of an ankle-foot orthosis (AFO) to maintain the ankle in a dorsi-flexed position throughout the gait cycle [115]. However, AFOs can be bulky and often restrict ankle movement, which may hinder other tasks and in turn prevent the transferring of re-learned gait patterns to normal walking conditions [116]. Gait entrainment to mechanical dorsi-flexion perturbations at the ankle joint could, in fact, stand as an alternative, minimally-encumbering approach to assist neurologically-impaired patients with foot-clearance during swing in both treadmill and overground walking.

Neurologically-impaired patients are known to have less effective plantar-flexion during ankle 'push-off', which *may* compromise subsequent dorsi-flexion during swing phase and foot-ground clearance—possibly leading to the foot scuffing often observed in this population [117,118]. Hence, the mechanical perturbations could supply the additional torque needed by patients who cannot produce sufficient ankle dorsi-flexion during 'initial swing'to accomplish proper foot-clearance with their paretic leg. Similarly, it could be reasoned that varying the magnitude and frequency of the torque perturbations to provide assistance as needed may stimulate voluntary participation.

As with the previous experiments, this second series of trials reveal significant differences in gait entrainment to dorsi-flexion perturbations at the ankle joint in treadmill versus overground walking. Specifically, the number of entrained gait during overground walking was higher than in treadmill walking (27 vs. 23 entrained gaits). In addition, the rate of gait phase convergence (i.e. the number of torque pulses required for entrainment) was faster in overground compared to treadmill walking trials (15.56 vs. 26.70 torque pulses). In a study with 22 unimpaired (young and older) adults walking on a treadmill and overground, treadmill walking elicited significantly reduced foot-ground clearance [111]. This particular finding is consistent with previous studies reporting significantly lower vertical reaction forces at 'push-off'in treadmill walking compared to overground locomotion [74, 119]. If less foot-ground clearance is required during normal treadmill locomotion and the dorsi-flexion perturbations assisted foot-ground clearance, then it is reasonable that subjects entrained to the perturbations predominantly during overground trials since foot-clearance appears to be more critical in that walking environment.

Given that there is another prominent ankle dorsi-flexion in the normal gait cycle, which occurs during mid/terminal stance, it is interesting to see that none of the subjects synchronized their gait with the perturbations occurring at this portion of the gait cycle. The 'ankle rocker'also requires ankle torque in the same direction as the one caused by the dorsi-flexion perturbations, so why was phase-locking not detected at that point? The mid/terminal stance phases overlap with a major functional task in the gait cycle ensuring stability and forward progression: single limb support. At this point, the one leg on the ground is the main support element guaranteeing stability (the other leg is in the air during its own Swing phase). In these experiments the gait cycle is defined based on the leg wearing the Anklebot, which means a torque pulse occurring during mid/terminal stance phases would be applied to the ankle that is on the ground (i.e. the supportive limb). Dorsi-flexion ('toe-up') perturbations occurring at this point of the gait cycle *may* destabilize the supportive limb, which may be why entrainment to the perturbations at this portion of the gait cycle was unattainable. This observation is consistent with previously reported evidence of locomotor control strategies being adapted to overcome environmental factors that may compromise stability, such as the treadmill belt moving the single-supportive limb behind the upper-body [79, 90–92], or in this case the imposed torque pulse perturbations.

As in the previous series of plantar-flexion experiments, it was noted that in several entrained trials a torque pulse occurring during 'initial swing'was not always accompanied by immediate gait synchronization. Examples of this observation can be seen in Figure 4-2 as several functions of dorsi-flexion perturbation phase vs. perturbation number crossed the red horizontal lines corresponding to 75% of the gait cycle, yet there was no entrainment until further along in the trials. In general, entrainment was achieved through gradual changes in walking cadence to reduce the difference between τ_{p} and subjects'stride period, and not as an immediate result to a perturbation occurring during 'initial swing'for the first time.

4.5.2 Persistence of the Entrained Gait during Post-Perturbation Walking

Persistence of the entrained gait after the perturbation was observed in 16% of the entrained trials (8 out 50 entrained trials). In the majority of the entrained trials not exhibiting persistence of the entrained gait (42) subjects' cadence had either returned to the pre-perturbation period (59.52%) or started drifting back to their preferred walking period (40.48%) within the first 15 strides after discontinuing the perturbations. In the previous chapter, persistence of the entrained gait after discontinuing the plantar-flexion torque pulses—detected in 67% of the entrained trials—was discussed as an observation with plausible implications in gait therapy. However, in the case of gaits entrained to dorsi-flexion perturbations, the lack of persistence of the entrained walking period calls for further investigation to understand the feasibility of this particular strategy to assist locomotor recovery.

Ankle dorsi-flexion to achieve foot-ground clearance during swing is closely related to limb advancement. Significant changes in ankle dorsi-flexion during 'initial swing'after phase-locking with the periodic dorsi-flexion perturbations are likely to have impacted other gait parameters such as step length and/or cadence. Entrainment to the perturbation may have elicited ranges of motion of the lower limb that were not typical for subjects to maintain during post-perturbation walking. Perhaps maintaining the new gait parameters once the ankle assistance was discontinued demanded greater metabolic cost. Humans tend to minimize metabolic cost during locomotion [120]; hence, it is plausible that subjects returned to their preferred walking periods in an attempt to resume their normal gait parameters and optimize metabolic cost. However metabolic cost and gait parameters such as step length and cadence were not measured in these experiments.

In the spectrum of locomotor therapy, persistence of the entrained gait would be ideal since it would imply retention of the re-learned locomotor patterns, such as normal cadence, step length, proper foot-ground clearance, etc. However, the lack of persistence of the entrained walking period in these experiments with unimpaired subjects does not necessarily imply the ineffectiveness of the proposed new strategy for locomotor therapy. Previous studies of robot-aided upper-extremity rehabilitation have demonstrated that while progress in motor recovery made in one therapy session did not necessarily carry through to the next session, significant improvements were detected over the course of many therapy sessions [121]. Similar long-term results might be obtained for lower-extremity rehabilitation through gait entrainment to mechanical perturbation, even if the entrained gait did not persist long after perturbation in each therapy session. Furthermore, retention of the re-learned gait patters may be significantly improved by *how* the ankle assistance—via periodic dorsi-flexion perturbations—is designed and applied. Regulation of human locomotion is sensitive to sensory feedback related to the limb [39,40] and the skin of the foot [41,42]. Considering the reliable phase-locking 'initial swing', which may have assisted foot-ground clearance, the gait entrainment and walking cadence may be dependent on the profile of the torque. Thus, refinement of the imposed mechanical perturbation may not only improve efficacy of the proposed gait rehabilitation strategy, but also contribute to a more profound understanding of the mechanics involved.

4.5.3 Contributions of the Neuro-mechanical Oscillator to Gait Entrainment

An important question that remained unanswered from previous chapters referred to the extent of the mechanical and neural contributions of the nonlinear limit-cycle oscillator postulated to underlie human locomotion leading to the observed gait entrainment to mechanical ankle perturbations. The experiments presented in Chapter 3 revealed that subjects synchronized their gaits with the imposed plantar-flexion perturbations such that the torque pulses provided mechanical assistance with forward propulsion during ankle 'push-off'. However, the fact that subjects were capable of entraining to both "slow" and "fast" perturbation periods indicated that entrainment was not only due to mechanics, but instead there was a neural factor involved in these results.

The results presented in this chapter, however, cannot be attributed to mechanics alone since phase-locking occurred consistently during 'initial swing' (at 71.92% $\pm$ 4.28% of the gait cycle) when the foot was in the air. While in these experiments the dorsi-flexion perturbations assisted with the natural motion of the ankle after phase-locking was achieved, these torque pulses did not influence the mechanical work done. Additionally, the simple model previously presented by Ahn and Hogan [99], which was capable of reproducing gait entrainment to "fast" plantar-flexion perturbation periods, cannot reproduce entrainment to "slow" plantar-flexion perturbation periods or to dorsi-flexion perturbations.

4.5.4 Hierarchical Organization of Human Locomotion—*Episodic Supervisory Control*

Overall, the gait entrainment results presented in this thesis seem to require a neural adaptation that cannot be easily ascribed to biomechanics, suggesting a hierarchical organization (Figure 4.6) between the supra-spinal nervous system and the spinal neuro-mechanical periphery: *episodic supervisory control*. Information transmission causes substantial delays—as much as hundreds of milliseconds—and muscles respond rather slowly relative to the mechanical dynamics of walking. Sophisticated theoretical approaches to motor control, such as stochastic optimal feedback, do not seem to address this particular problem. Hierarchical organization of human locomotors control in accordance with *"central supervisory control of a semi-autonomous periphery"* stands as a different approach to address this particular problem.

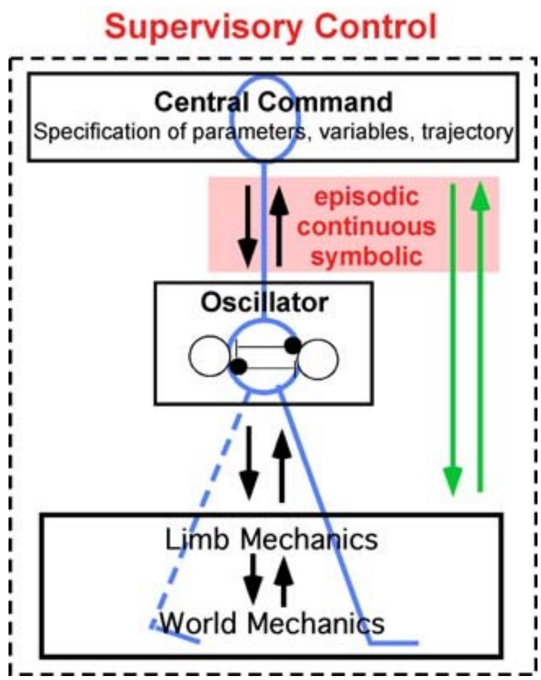

Figure 4-6: Supervisory control of dynamic walking. Low-level circuits and mechanics comprise a nonlinear oscillatory dynamic system. High-level processes may intervene episodically or continuously. Top-down commands may specify oscillator parameters or limb trajectories transmitted through low-level circuits (black arrows) or may address biomechanics directly (green arrows).

The essence of human level-ground locomotion that is organized to enable *semi-autonomous* ('set and forget') operation entails that the automated control of walking can be interrupted as needed to maneuver or recover from a slip or stumble. According to this hypothesis, the supra-spinal nervous system is considered to be the 'operator'; i.e. it *may—if need be*—mediate the detailed control of the semi-autonomous spinal neuro-mechanical periphery. In other words, the supra-spinal nervous system may behave as a *tele-operator* of the spinal neuro-mechanical periphery. Hence, the burden on higher centers of the brain to methodically control all *'lower-level'* system behavior is reduced, especially given the known delays in neural conduction and limited speed of muscle response.

High-level commands may be in the form of continuous specification of nominal trajectory, but do not have to be; they may specify low-level dynamical system parameters (e.g. stride amplitude, period, etc.), or they may be symbolic (e.g. step sideways to avoid an obstacle). As a result, episodic supervisory control also requires lower levels to be semi-autonomous. In the context of locomotor control, semi-autonomous lower levels must then be capable of robustly stable rhythmic walking with no or minimal high-level intervention. Since robustly sustained autonomous oscillation can only emerge from a nonlinear dynamical system, then *the identified neuro-mechanical oscillator with a limit-cycle attractor must exist in the semi-autonomous lower-levels*. Indeed, this semi-autonomous generation of rhythmic behavior is consistent with previous observations that rhythmic motions activate only primary motor areas, which are significantly fewer brain regions than those activated by discrete motions [122].

Semi-autonomous operation of human level-ground walking may involve a *'self-sustaining neural oscillator'*, such as the rhythmic CPG that has been suggested for animal locomotion. In order to be self-sustaining, such oscillator must be nonlinear[2] and exhibit a limit-cycle. The experiments presented in this thesis have revealed clear, behavioral evidence that a nonlinear neuro-mechanical oscillator with a limit-cycle plays a significant role in human locomotion.

Semi-autonomous operation of human level-ground locomotion may also involve a *'finite-state machine'*—a closed chain of stereotyped actions each triggered by a sensory state resulting from a previous action in the chain. Given the inescapable nonlinearity of intermittent foot-ground contact, such finite state machine must also be nonlinear and may exhibit a limit-cycle.

> *Taken together, the results presented in this thesis suggest that both mechanisms—self-sustaining neural oscillator with a limit-cycle and a closed chain of 'reflex' actions—may be present in level-ground human locomotor control.*

[2] A linear system cannot exhibit self-sustained oscillation (refer to Appendix A)

Chapter 5

Conclusions and Future Work

5.1 Summary of Accomplishments

The graying of the population presents a rapidly growing demand for effective rehabilitation of human motor function. Robot-aided therapy is a promising method to meet this enormous demand and provide effective rehabilitation services. Robots are able to augment and extend the labor-intensive tasks of therapists and provide quantitative measurement of human performance, which is essential for systematic training. However, while robotic technology has proven effective to aid recovery of upper-extremity motor function [11–14], robot-aided lower-extremity therapy is less mature [15–17]. Recent studies report that robotic walking therapy has not matched the efficacy of conventional therapy, and resulted in gaits with different muscle activation patterns than normal gait [15, 16]. Considering the labor-intensive nature of conventional walking therapy, effective robot-aided walking therapy is urgently needed.

Advances in robotic technology and humanoid robotic bipeds suggests that a probable reason for this limitation of current robot-aided locomotor therapy is the *absence of an "effective strategy"* rather than insufficient sophistication of robotic hardware. A plausible explanation for such ineffectiveness is the use of human-interactive robots that may suppress the expression of the *natural oscillatory dynamics of walking*. Indeed, most gait rehabilitation robots emphasize nominal kinematics of lower-limb motion, inadvertently ignoring the natural periodic dynamics of neuro-mechanical oscillators underlying human locomotion [18–20]. Moreover, the majority of experiments and training sessions involving robotic gait rehabilitation are conducted on treadmills that subtly interfere with natural movement control, and consequently, inhibit the transfer of the 're-learned'gait patterns to overground ambulation [94–97].

For reaching movements, motor neuroscience studies have proven the dominant role of kinematics [52–55]. However, the importance of kinematics is substantially less clear for locomotion. Various studies in neuroscience and robotics have provided evidence supporting the role of dynamic oscillations in human walking [32, 59–64, 70–72]. Yet, current approaches to robotic walking therapy still emphasize the nominal kinematics of lower limb motions [18–20]. To overcome the limitations of present robotic locomotor therapy, it is essential to examine the minimal "mechanical components" that contribute to stable locomotion. Essentially, *an effective strategy needs to allow the impaired patients to re-learn how to take advantage of the natural oscillatory dynamics that result from their foot-ground interactions*.

Despite the vast and growing literature, the control of human locomotion is incompletely understood. Hence, a comprehensive characterization of the locomotor control architecture describing the interaction between low-level spinal circuits and high-level processes has not bee established. Rhythmicity is known to be the hallmark of locomotion; however, the source of such rhythm generation in human locomotion has not been concluded. While several studies have suggested the plausible existence of a CPG in the human spinal cord [62–64], others have demonstrated that simple limit-cycle oscillators can exhibit stable human-like walking [10, 32, 59–61, 65–72]. The study presented in this thesis—aimed at understanding the human locomotor control—followed the footsteps of this latter line of research: Dynamic Walking.

A distinctive characteristic of a nonlinear oscillator with a limit cycle-attractor is that it may, under certain circumstances, exhibit *entrainment* and *phase-locking*.

Experiments were conducted to assess the feasibility of gait entrainment to mechanical perturbations at the ankle joint during treadmill and overground walking, in an attempt to investigate the possible contribution of limit-cycle oscillators to human locomotion.

Experimental work with unimpaired human subjects exposed to periodic mechanical perturbations in both plantar- and dorsi-flexion directions concluded *gait entrainment* and *phase-locking* in both treadmill and overground walking. The observation of entrainment to these two different ankle perturbations and walking environments indicated clear behavioral evidence of a nonlinear limit-cycle oscillator underlying human locomotion. Indeed, this oscillator was found to be sensitive to both the type of mechanical perturbation and the walking environment.

In the experiments involving ankle plantar-flexion perturbation, phase-locking allocated the perturbation at ankle 'push-off'such that it assisted propulsion both during treadmill and overground walking. Conversely, in the experiments involving ankle dorsi-flexion perturbation, phase-locking allocated the perturbation at 'initial swing'such that it assisted foot-ground clearance both during treadmill and overground walking. In all, significant differences were found between gait entrainment during treadmill vs. overground: the number of entrained gaits during overground walking was higher and the rate of gait phase convergence was faster than in treadmill walking. Regardless of the gait phases at which perturbations were randomly initiated, subjects' gaits synchronized or phase-locked with the mechanical plantar-flexion or dorsi-flexion perturbation at specific phases of the gait cycle—ankle 'push-off'or 'initial swing', respectively. Overall, a moderate-to-slow gait phase convergence to phase-locking was observed, contrary to what it would be expected should gait entrainment emerge as the result of voluntary synchronization.

> *Taken together, the experimental results presented in this thesis show direct behavioral evidence that, in human locomotion, the spinal neuro-mechanical periphery is governed by a semi-autonomous oscillator with a limit-cycle attractor*.

Specifically, it appears human locomotion is hierarchically organized to enable *episodic supervisory control* of the semi-autonomous spinal neuro-mechanical periphery by the supra-spinal nervous system. These observations should be given due consideration when designing therapeutic robots and exoskeletons to improve human locomotion and/or walking efficiency.

> Although further investigation is required, this study indicates *gait entrainment to mechanical ankle perturbation may be a feasible approach for robot-aided recovery of locomotor function*.

5.2 Implications for Engineering Science

One of the main messages that has been stressed throughout this thesis is that in order for robotic technology to effectively assist locomotor therapy, it must allow the expression of the essential components of human locomotor control—namely its natural oscillatory dynamics. Indeed, robotic technology has shown considerable promise, however it appears to have been misapplied, at least in the field of robotic gait rehabilitation. This study has revealed that, for neuro-motor rehabilitation, robotic technology should shift towards the use of highly back-drivable actuators so that patients' voluntary motion is permitted. For walking rehabilitation in particular, this shift is especially important so that foot-ground interaction is exploited and the natural oscillatory dynamics of locomotion are allowed. Although further investigation is required, this study indicates gait entrainment to mechanical perturbations at the ankle may be a feasible approach for robot-aided walking rehabilitation. Altogether, the results of this research, along with subsequent studies following its footsteps, may challenge the current approaches of robot-aided walking therapy, shifting from strategies that emphasize nominal kinematics of lower-limb motion to strategies that exploit the natural oscillating dynamics of rhythmic locomotion.

The implications of this research will also improve the understanding on human locomotor control, since it has revealed the sensitivity of human walking to different environment, as well as it overall subtlety and adaptability. These observations should be considered when designing therapeutic robots and exoskeletons to improve human locomotion and/or walking efficiency.

5.3 Future Work

Although further investigation is required, this study indicates gait entrainment to mechanical perturbations at the ankle may be a feasible approach for robot-aided walking rehabilitation. First, experiments should be conducted to test the protocol on neurologically-impaired patients to **(1)** quantify the therapeutic effect of gait entrainment to mechanical ankle assistance in both treadmill and overground walking, and **(2)** to refine how periodic assistive torque is applied to maximize its therapeutic effects in the two walking environments.

Furthermore, overground experiments should be performed with unimpaired and impaired subjects to determine the basin of entrainment in these different walking environments. Given the higher number of entrained gaits and the faster gait phase convergence detected during overground walking trials in this thesis, it may follow that the basin of attraction in overground walking is larger than in treadmill walking.

Additional experiments should address entrainment when walking on uneven ground. Increasing the requirement to control foot trajectory may impair or weaken the entrainment phenomenon. Subsequently, these experiments could also involve the transition from uneven to even ground. Based on the results presented in this thesis suggesting episodic supervisory control of walking, changed induces by modification of the mechanical environment may persist after those modifications are removed.

Another unique characteristic of nonlinear limit-cycle oscillators is derived from the steady-state response to a single brief perturbation. When the transient response has died away, a persistent phase shit relative to the perturbation oscillation is typically observed, which is called phase resetting.

The phase-resetting-curve is identically zero for high-level trajectory controller since stable execution of a centrally-specified trajectory means that the system eventually "forgets" the perturbation. On the other hand, the phase-resetting-curve is non-zero for a lower-level rhythm generator. The results presented in this thesis which indicate that the identified nonlinear limit-cycle oscillator underlies the semi-autonomous spinal neuro-mechanical periphery (lower-level). Hence, a brief ankle torque pulse may evoke a non-zero phase shift that will depend on the pre-perturbation gait phase at which the torque pulse was applied.

Specifically in the robotic rehabilitation spectrum, this study may serve as the baseline for future investigation to develop and refine an effective strategy for robot-aided walking therapy that is able to:

(1) stimulate voluntary participation of patients,

(2) facilitate overground training to promote locomotor improvements made in the same environment patients are exposed to in their normal lives, and

(3) allow and exploit the natural oscillating dynamics of human walking through carefully designed human-machine interaction.

Importantly, future work with neurologically-impaired patients must focus on allowing the injured nervous system to express its natural rhythmic dynamics and engage any residual neural circuitry by continuously adjusting features of the robot-aided assistance to the patients' performance. Further investigation along this line of study may help pioneer an innovative *permissive* intervention for locomotor therapy with the key feature of successful upper-extremity robotic therapy: *minimally-encumbering human-robot interaction that provides assistance <u>only</u> as needed.*

Appendix A

Stability Criterion for Self-Sustained Oscillation

The equation of motion for an N-dimensional system in equilibrium, which may be exposed to small perturbations, can be linearly approximated as:

$$[\mathbf{M}][\ddot{x}] + [\mathbf{C}][\dot{x}] + [\mathbf{K}][x] = [0] \tag{A.1}$$

where **[M]**, **[C]**, and **[K]** are real-valued, constant matrices of dimension N $\times$ N. **[M]** describes the inertial mass, **[C]** describes the damping, and **[K]** describes the stiffness of the system. Hence, the corresponding motion of the system in the time domain can be expressed as:

$$[\mathbf{x}] = e^{i\omega t}[\mathbf{a}] \tag{A.2}$$

where $i\omega$ represents the complex roots and **[a]** are the corresponding time-independent vectors—often referred to as the "normal modes" of the system.

The normal modes (eigenvectors), **[a]**, and the associated frequencies (eigenvalues), $\omega^{\mathbf{2}}$, of the system can be found by solving the eigenvalue problem:

$$(-\omega^2[\mathbf{M}] + i\omega[\mathbf{C}] + [\mathbf{K}])[a] = [0] \tag{A.3}$$

$$\mathbf{det}(-\omega^2[\mathbf{M}] + i\omega[\mathbf{C}] + [\mathbf{K}]) = 0 \tag{A.4}$$

According to the Routh-Hurwitz [123] criterion, a linear system cannot exhibit self-sustained oscillation if the matrices [**M**], [**C**], and [**K**] in Eq. (A.1) are all symmetric (i.e. if they are equal to their own matrix transpose, e.g. [**M**]= $[\mathbf{M}]^{\mathrm{T}}$), unless the matrix [**C**] has eigenvalues with non-positive real parts—this is not typically the case for symmetric linear mechanical systems.

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