MUSCLE SYNERGIES FOR DIRECTIONAL CONTROL OF CENTER OF MASS IN VARIOUS POSTURAL STRATEGIES

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MUSCLE SYNERGIES FOR DIRECTIONAL CONTROL OF CENTER OF MASS IN VARIOUS POSTURAL STRATEGIES

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LIST OF SYMBOLS AND ABBREVIATIONS

ADMG	adductor magnus
APR	Automatic postural response
BFLH	biceps femoris long head
BoS	Base of support
Ci	ith muscle synergy recruitment coefficient
CNS	Central nervous system
CoM	Center of mass
CoP	Center of pressure
CPG	Central pattern generator
EMG	Electromyograph
ERSP	erector spinae
EXOB	external oblique
Fx	Endpoint force in medial/lateral direction
Fy	Endpoint force in anterior/posterior direction
Fz	Endpoint force in vertical direction
GMED	gluteus medius
GRF	Ground reaction force
ICA	Independent components analysis
LGAS	lateral gastrocnemius
MGAS	medial gastrocnemius
NMF/NNMF	Non-negative matrix factorization

PCA	Principle components analysis
PERO	peroneus
PR	Posture response
r	Correlation coefficient
r^2	Coefficient of determination
REAB	rectus abdominus
RFEM	rectus femoris
SEMT	semitendinosus
SOL	soleus
TA	tibialis anterior
TFL	tensor fascia lata
UCM	Uncontrolled manifold
VAF	% variability accounted for
VLAT	vastus lateralis
VMED	vastus medialis
Wi	i^{th} muscle synergy
Wsli	i^{th} muscle synergy from slow walking perturbation responses
Wssi	i^{th} muscle synergy from self-selected walking perturbation responses
Wwi	i^{th} muscle synergy from unperturbed walking

SUMMARY

Our long-term goal is to better understand how the nervous system controls muscles to generate movement. Our overall hypothesis is that the nervous system coordinates muscles by flexibly recruiting muscle synergies, defined here as groups of muscles simultaneously activated in fixed ratios, in order to map high-level task goals into motor actions. Here we studied muscle coordination in the context of balance control – a task that requires multisensory integration and coordination of multiple muscles, yet has a clear goal of controlling the center of mass (CoM), which can be achieved by using different strategies. If muscle synergies are a common mechanism used by the nervous system for balance control, we would expect to see the same muscle synergies used in a variety of strategies. Therefore we investigated the robustness of the muscle synergies in a variety of human postural strategies, such as standing, stepping and walking, to determine whether muscle synergies are a consistent underlying mechanism used by the nervous system. We hypothesized that muscle synergies are recruited to control a task-level variable (e.g. CoM direction) that is not specific to a particular postural strategy.

We demonstrated that similar muscle synergies are used in reactive responses to standing balance perturbations, in reactive stepping responses, in walking, and in reactive postural responses during walking, suggesting a common neural mechanism not only for balance control in various contexts, but for movement in general. The differences in the timing and spatial organization of muscle activity in standing, stepping, and walking postural responses were largely explained by altering the recruitment of a common set of muscle synergies, with the addition of only a single muscle synergy specific to each

behavior. We demonstrated the functionality of muscle synergies by showing that each muscle synergy was correlated with a particular force produced at the ground and component of CoM acceleration both in stepping and in non-stepping postural responses. These results suggest that muscle synergies reflect the neural organization of the motor system, representing motor modules recruited to achieve a common biomechanical function across different postural behaviors. Additionally, muscle synergies used during walking were recruited during atypical phases of the gait cycle in response to an unexpected perturbation, in order to maintain balance and continue walking, suggesting a common neural mechanism for different balance requirements during walking. The compositions of muscle synergies used during walking were similar to those used during walking perturbations as well as standing balance perturbations, suggesting that muscle synergies represent common neural mechanisms for CoM movement control under different dynamic conditions. These results are of interest to a variety of fields such as rehabilitation science, prosthetics, and robotics.

CHAPTER 1

INTRODUCTION

Our long-term goal is to better understand how the nervous system controls muscles to generate movement. There are many more muscles in the body than kinematic degrees of freedom, so how does the central nervous system decide which muscles to activate to perform any given movement? This is Bernstein's degrees of freedom problem (Bernstein 1967). Bernstein proposed that the nervous system reduces the number of elements requiring control by simultaneously activating multiple muscles as a unit. There has been a wealth of work performed since then investigating whether the nervous system activates each muscle independently or instead coordinates movement by simultaneously activating multiple muscles. Here we investigated muscle coordination underlying several motor tasks – standing, stepping, and walking – to gain insight into how the nervous system controls muscles to generate movement.

1.1 Muscle synergies: a simplification strategy for motor control

Muscle synergies have been proposed to be a modular organization for muscle coordination that map high-level task goals, or motor intentions, into motor actions (Chiel et al. 2009; Drew et al. 2008; Giszter et al. 2007; Ting and McKay 2007; Yakovenko et al. 2010). Muscle synergies and other types of modular organization have been used to explain muscle coordination during a variety of motor behaviors in many different species (Cappellini et al. 2006; d'Avella et al. 2006; d'Avella et al. 2003; Drew et al. 2008; Flash and Hochner 2005; Hart and Giszter 2004a; Hart and Giszter 2004b; Kargo

and Giszter 2000; Krishnamoorthy et al. 2004; Latash et al. 2005; Ting and Macpherson 2005; Torres-Oviedo et al. 2006; Yakovenko et al. 2010). The generality of muscle synergies across different motor tasks has been shown in frog kicking, jumping, and swimming (Cheung et al. 2005; d'Avella and Bizzi 2005); as well as in human walking and running (Cappellini et al. 2006), and forward and backward pedaling (Raasch and Zajac 1999b; Ting et al. 1999). Although some muscle synergies are used across multiple tasks, in some instances new synergies may emerge when a new motor task is presented (Cheung et al. 2005; Ivanenko et al. 2005; Robert et al. 2008; Torres-Oviedo and Ting 2010) and the recruitment of existing synergies may be altered (Cappellini et al. 2006; Clark et al. 2010).

Here we define muscle synergies as groups of muscles activated simultaneously with fixed relative gains (Figure 1.1). Each muscle synergy is composed of contributions from multiple muscles; the height of the each bar specifies each muscle's contribution to that synergy. Notice an individual muscle may contribute to multiple synergies. The muscle synergies do not change composition; they are simply activated by a scalar recruitment coefficient, C, which may vary over the time-course of the perturbation response. The recruitment coefficient represents the purported neural command that specifies how that synergy is modulated over time, and how much each synergy will contribute to a muscle's total activity pattern. Therefore we consider muscle synergies to be spatially fixed with temporally varying recruitment patterns. An individual muscle activation pattern can be represented by a linear summation of the activations due to each muscle synergy.

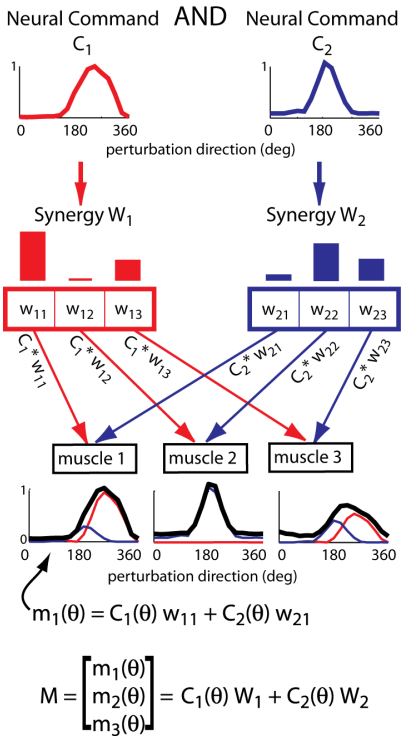


Figure 1.1 Muscle synergy concept. Each muscle activation results from the combination of the activations due to each muscle synergy that contains that muscle.

1.1.1 Different ideas about modularity

In the literature, there are differing ideas about how exactly modularity is implemented in the central nervous system (CNS). Previous work has shown spinal motor primitives are activated to generate a variety of reflex and pattern-generator behaviors in frogs. (Kargo et al. 2010). The primitives are premotor drive impulses that comprise fixed muscle synergies, and these synergies appear to be stereotyped in frogs. These muscle synergies cannot change, but their recruitment may be temporally adjusted and used to compose voluntary movements. Common primitives were identified using ICA on EMG recordings in brainstem and spinal frogs (Hart and Giszter 2004),

suggesting these modules may be implemented purely in the spinal cord. Also, modules used for the wiping reflex in frogs were unchanged after deafferentation (Kargo and Giszter 2000), suggesting their composition is not dependent on somatosensory feedback.

Previous studies of modularity during locomotion have suggested temporally fixed patterns of muscle recruitment occurring at specific times in the gait cycle that are coupled to spatially varying muscle weightings (Cappellini et al. 2006; Ivanenko et al. 2005; Ivanenko et al. 2004). In this organization, the CNS chooses from a set of predefined temporal recruitment patterns to produce a rhythmic behavior in a feedforward manner. The temporally fixed neural commands have access to all of the musculature, and the specific muscles activated vary across trials and contexts. Underlying factors were identified from EMG patterns using PCA with varimax rotation, and five temporal components could reproduce muscle activity during walking (Ivanenko et al. 2004). It is unlikely that a temporally fixed modular organization such as this would be able to explain EMG activity of involuntary or reactive tasks that may rely more heavily on feedback control.

A third view of modularity suggests that synergies are co-varying changes in individual elements of a system that stabilize a value or a time profile of an important performance variable produced by the system (Latash 2008). Thus synergies are only synergies with respect to a particular performance variable. Groups of muscles called m-modes are proposed elemental variables that co-vary to stabilize a performance variable (Krishnamoorthy et al. 2003a; Krishnamoorthy et al. 2004). The m-modes are identified using principal components analysis (PCA) and synergies (the co-variation of these m-modes to stabilize a task variable) are identified using the uncontrolled manifold (UCM

analysis). The composition of m-modes is changed or reshaped under new conditions, such as task, time window, etc. (Danna-Dos-Santos 2007; Robert et al. 2008). This scheme allows for the emergence and modification of an infinite number of synergies with practice, experience, context, etc.

Our hypothesis about the structure of muscle synergies is both similar to and different from the various organizations discussed here. We hypothesize muscle synergies are generally fixed, and only the recruitment of muscle synergies varies across time and condition, consistent with the ideas of Giszter and colleagues. The CNS circuits that branch with varying synaptic weights to motoneurons of muscles in the muscle synergy may indeed be implemented in the spinal cord, but it is possible that they may also exist in other levels of the nervous system, such as brainstem or cortex depending on which motor behavior is being executed. Furthermore, muscle synergy composition may be modified and shaped over the long-term (years) as a result of individual experience, training, and adaptation. An organization consisting of fixed temporal components such as that proposed by Ivanenko and colleagues is unlikely to be used for non-rhythmic or reactive motor behaviors due to the feedback nature of reactive tasks. We do not believe that muscle groups change according to the specific condition or trial, as Latash and colleagues have suggested. However, we do believe that muscle synergies are recruited in order to control a task-level function, consistent with Latash's definition of "synergy".

1.1.2 Muscle synergies related to task-level functions

The recruitment of these muscle synergies, or motor modules, may be related to specific biomechanical functions necessary to accomplish a behavioral goal (Berniker et

al. 2009; Chiel et al. 2009; Giszter et al. 2007; Raasch and Zajac 1999; b; Ting and McKay 2007). The biomechanical outputs related to muscle synergies depend upon the motor task being performed. In human finger spelling, muscle synergies are correlated with common hand postures (Weiss and Flanders 2004), whereas in frog kicking, jumping, and swimming, shared muscle synergies may be activated to implement whole limb movements common to these locomotor behaviors (Cheung et al. 2005; d'Avella and Bizzi 2005). Another study showed that in human walking, muscle synergies were activated to achieve various functions such as weight support, forward propulsion of the body, and deceleration of the leg (Neptune et al. 2009a).

1.2 Balance control

Here we studied muscle coordination in the context of human balance control. Although it may seem "simple", balance control is actually a complex task which requires the integration of multiple sensory modalities (visual, vestibular, and proprioceptive), and which requires coordination of multiple muscles across several joints. Additionally, accurately maintaining balance is required as the foundation of a variety of other voluntary motor tasks, such as standing, walking, running, and jumping.

The overall goal in balance control is to maintain the center of mass (CoM) over the base of support (BoS). CoM position, velocity, and acceleration are variables that we can experimentally measure relatively easily, making balance control an ideal task for investigating relationships between muscle activation and functional goals. Furthermore, there is a wide range of strategies people use in order to maintain balance, such as

standing, stepping, reaching out to grasp a handrail, etc., providing a means for us to understand common principles that underlie muscle coordination in a variety of contexts.

Current methods for studying balance control include measuring human responses to unexpected perturbations of the support surface. These responses include kinematics, kinetics, and electromyographic (EMG) activity. Individual muscle postural responses to support surface translations are characterized by a small burst that is attributed to reflex pathways, followed by a larger burst (around 100 ms after perturbation onset). This later activation, the automatic postural response (APR), is an involuntary response that changes with the direction of perturbation, as represented by muscle tuning curves. Here we studied muscle coordination during the APR in various postural tasks.

Humans use various strategies to maintain balance response to perturbations. To maintain balance without moving the feet, muscles in the legs are activated, resulting in forces generated at the ground to restore the CoM to its initial position above the base of support (BoS) (Horak and Macpherson 1996; Horak and Nashner 1986). These responses in which balance is maintained without moving the feet have previously been called "fixed support" responses, and are referred to here as "non-stepping". Other strategies for maintaining balance are called "change-in-support" strategies, which include reaching out to catch hold of a support and taking a step to recover balance (Grin et al. 2007; Maki and McIlroy 1997). In these responses, the BoS is expanded, and the CoM is pushed out further away from the starting position. The muscle coordination underlying change-in-support strategies is much less understood.

1.3 Muscle synergies and balance control as a framework for understanding neural control of movement

1.3.1 Muscle synergies are used in standing balance control

A few muscle synergies can account for spatial, temporal, and inter-trial variations in muscle activation patterns in human standing responses to perturbations (Torres-Oviedo and Ting 2007). However, muscle synergies underlying more dynamic balance tasks (such as stepping and walking) in humans have largely been unstudied. Previous work has shown that subjects use the same muscle synergies when they are perturbed while standing at a variety of initial stance configurations, such as wide or narrow stance (Torres-Oviedo 2007). Thus the synergies are robust even when the biomechanics of the task are different, which demonstrates that muscle synergies may indeed be a general neural control mechanism for standing balance control. This idea of generality of muscle synergies across motor tasks has not been thoroughly explored. In this work, I have applied the muscle synergy analysis to postural tasks that are less understood than standing, but that may be more relevant to daily activities, such as stepping and walking. This is a novel approach to understand the neural control in these tasks.

Many studies have suggested controlled variables in balance control. For instance, some propose that center of pressure (CoP) shifts, segmental kinematics, or dynamic torques across multiple joints are being controlled in postural tasks (Alexandrov et al. 2001; Danna-Dos-Santos et al. 2007; Grasso et al. 1998; Grasso et al. 2000;

Shemmell et al. 2007). However, these studies do not demonstrate relationships between EMG changes and the controlled variable. Others have correlated the controlled variable to EMG changes by associating them with a selected strategy for maintaining balance. For instance, the non-stepping ankle strategy is concerned with maintaining upright stance, whereas the non-stepping hip strategy may be used to control CoM position. In either case, characteristic muscle patterns can be identified (Horak and Macpherson 1996). Another prior study correlates muscle activity in postural responses with forces generated at the ground (Jacobs and Macpherson 1996), and it has even been shown in cats that muscle synergies are recruited to control forces at the ground (Ting and Macpherson 2005; Torres-Oviedo et al. 2006).

A limitation of these previous studies linking EMG and controlled variables is that they have only considered a single condition. If the muscle synergies truly are a general mechanism for posture control, and they have a specific task-level goal they are recruited to control, we expect to see this variable correlated with muscle synergy recruitment across multiple conditions. In cats, the muscle synergies correlated with forces were used in multiple stance distances and across rotations and translations, validating that ground reaction force (GRF) is the controlled variable (Torres-Oviedo et al. 2006). In chapter 2, we identify correlations between muscle synergy recruitment, forces under the foot, and CoM acceleration in non-stepping and stepping postural responses.

1.3.2 The stepping strategy

Although people with balance impairments more often use a stepping strategy to regain balance than a non-stepping one (Schulz et al. 2005), stepping balance responses are less studied than standing balance responses. In clinical studies, the kinematics of stepping are characterized, but the underlying neural mechanisms have not been addressed, and limited work has addressed muscle activation patterns underlying the stepping response. Stepping and non-stepping responses are initiated at the same latencies following perturbation, yet the magnitude of muscle activation is increased in stepping responses (Horak and Macpherson 1996; McIlroy and Maki 1993a). Also, the kinetics of a stepping response are very different from a standing task, largely due to the swinging leg. However, the goal in both of these tasks is still to maintain the CoM over the BoS, suggesting that common neural mechanisms underlie these two strategies despite the differences in muscle activation and force generation.

1.3.3 Balance control during walking

Although walking is a relevant motor task that most people perform every day, the strategies used for balance control during walking are not understood. During locomotion, balance is always controlled, but may require separate control circuits from the ongoing walking pattern. Walking is a dynamic condition in which the CoM is not usually located over the base of support of either stance foot (MacKinnon and Winter 1993). When a perturbation is encountered while walking, the CoM is moving when the perturbation response needs to be activated, as opposed to standing balance, when the CoM is initially stationary, or moving only very slightly due to postural sway. Perhaps

the walking circuit can account for upright posture, yet a posture circuit must be activated for unexpected movements. There is a need to understand the muscle coordination involved in a task that combines posture and locomotion components that can be distinguished from one another. Studies have administered perturbations while a person walks across the force plate (Tang et al. 1998), however, only forward perturbations are administered, similar to slipping on a wet surface or banana peel. In reality, people may encounter a variety of perturbations while walking. Postural responses to multidirectional perturbations during walking have not yet been characterized, nor have the muscle coordination patterns underlying these responses.

Prior work has demonstrated muscle synergies underlie cycle-by-cycle variability in cyclic behaviors such as pedaling and walking (Clark et al. 2010; Ting et al. 1999). The sequence of muscle activation patterns during locomotion has been characterized in humans (Prilutsky et al. 1998; Rose and Gamble 1994), and muscle coordination during locomotion has been identified in cats (Krouchev et al. 2006), and humans (Ivanenko et al. 2004). Yet the strategies used for balance control during walking are not understood. Although muscle synergies can explain cyclic behaviors and postural responses, they have not been examined during postural perturbations encountered while walking. In chapter 3, we indentify muscle synergies used during walking and demonstrate these are modulated in response to a perturbation to account for the postural response. In chapter 4, we demonstrate similar muscle synergies are used for walking and balance control.

1.4 Thesis overview

Here I investigated the robustness of muscle synergies as a simplification strategy for postural control in a variety of postural tasks. Additionally, I identified biomechanical functions associated with the recruitment of muscle synergies in various postural tasks. The three postural tasks studied here have different initial conditions for the CoM movement as well as different desired motions of the CoM. Nevertheless, we *hypothesize* that the same muscle synergies are robustly used during multiple tasks that require neural control of the CoM. In a non-stepping postural response to a backward perturbation, the CoM is initially thrust forward due to the perturbation, and the desired CoM motion is backward to recover balance without stepping (Figure 1.2). In a stepping postural response to a forward perturbation, the CoM is initially thrust backward due to the perturbation, and the desired CoM motion is also backward as the subject steps back to catch their balance. Can the same muscle synergies be recruited to produce this backward CoM acceleration in both of these cases? Likewise can the same muscle synergies be recruited to produce a forward CoM movement during non-stepping responses to forward perturbations, stepping responses to backward perturbations, as well as walking and perturbation responses during walking? Here we investigated whether the same muscle synergies are recruited to produce a common biomechanical function of directing the CoM in a variety of postural behaviors, such as standing, stepping, and walking. Alternatively, muscle synergy recruitment may instead be related to the perturbation direction, as similar perturbations will produce similar initial sensory input in each of these conditions.

In Chapter 2, I identified a set of common muscle synergies used in both non-stepping and stepping postural responses. Furthermore, each muscle synergy was associated with a force produced at the ground and an acceleration of the CoM, suggesting that muscle synergies in postural tasks are recruited to produce forces at the ground in order to direct CoM motion. In Chapter 3, I identified muscle synergies used during walking that can be modulated to account for perturbation responses in 4 directions. Finally, in Chapter 4, I expanded our investigation of perturbations during walking to include multiple perturbation directions and explicitly compared the muscle synergies used to respond to perturbations during standing postural responses.

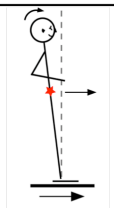
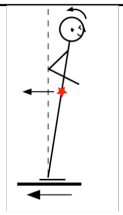
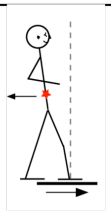
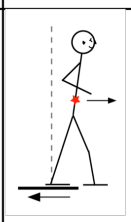
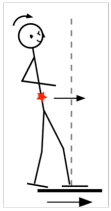
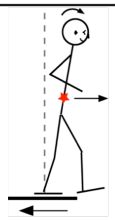
	Forward Perturbation			Backward Perturbation		
		Initial CoM direction	**Desired CoM direction**		**Initial CoM direction**	**Desired CoM direction**
Non-stepping		BACK	FWD		FWD	BACK
Reactive stepping		BACK	BACK		FWD	FWD
Response during walking		BACK	FWD		FWD	FWD

Figure 1.2 Overall study design. We studied three postural tasks which have similarities and differences in both initial CoM movement resulting from a perturbation and desired CoM motion required to maintain balance depending on the response strategy selected

and task goals. This figure illustrates the initial and desired CoM movement directions in all three postural tasks for two perturbation directions (forward and backward).

1.5 Significance

Motor control deficits resulting from an impaired nervous system have been identified in various pathologies such as cerebral palsy and Parkinson's disease. The coordination of muscles that is the intermediate step between a neural command and a visible motor output is still largely not understood. Here we examined the muscle coordination underlying several postural tasks in order to better understand motor control in general. Furthermore, we identified functional outputs related to the recruitment of muscle synergies; it is important to know the purpose, or function, of the muscle synergies to be useful clinically because diagnoses are made based upon functional deficits.

In an attempt to eventually apply our knowledge to adults with deficits, here we chose to look at the nervous system outputs under optimal conditions. We did this by examining muscle coordination in young, healthy adults from the GA Tech and Emory communities. This is a necessary precursor that permits a better understanding of the underlying causes of impairments. Once we have identified the neurophysiological mechanisms that underlie muscle coordination and postural control in young, healthy subjects, we will have a meaningful metric that may help us better understand and identify impairments. This will allow for the development of targeted therapies to address these impairments, such as training programs to develop a desired muscle synergy structure. Finding that the same muscle synergies are used for posture control in

a variety of tasks, such as standing, stepping, and walking, will be useful for clinical tests of synergy structure, diagnosing impairments, and proposing better treatment strategies.

CHAPTER 2

MUSCLE SYNERGIES IN NON-STEPPING AND STEPPING POSTURAL BEHAVIORS

This chapter was submitted to the *Journal of Neurophysiology* and is currently in review.

Chvatal SA, Torres-Oviedo G, Safavynia SA, and Ting LH. Common muscle synergies for control of center of mass and force in non-stepping and stepping postural behaviors. *J Neurophysiol* (in review).

We investigated muscle activity, ground-reaction forces, and center-of-mass (CoM) acceleration in two different postural behaviors used for standing balance control in humans to determine whether common neural mechanisms are used in different postural tasks. We compared *non-stepping responses*, where the base of support (BoS) is stationary and balance is recovered by returning CoM back to its initial position, to *stepping responses*, where the BoS is enlarged and balance is recovered by pushing the CoM away from the initial position. In response to perturbations of the same direction, these two postural behaviors resulted in different muscle activity and ground-reaction forces. We hypothesize that a common pool of muscle synergies producing consistent task-level biomechanical functions is used to generate these different postural behaviors. Two sets of support-surface translations in 12 horizontal-plane directions were presented,

first to evoke stepping responses and then to evoke non-stepping responses. EMGs in 16 lower-back and leg muscles of the stance leg were measured. Initially (~100 ms latency), EMG, CoM acceleration, and forces were similar in non-stepping and stepping responses, but diverged in later time periods (~200 ms), when stepping occurred. We identified functional muscle synergies using non-negative matrix factorization that quantified correlations between muscle synergy recruitment levels and biomechanical outputs. Functional muscle synergies that produce forces to restore CoM position in non-stepping responses were also used to displace the CoM during stepping responses. These results suggest that muscle synergies represent common neural mechanisms for CoM movement control under different dynamic conditions: stepping and non-stepping postural responses.

2.1 Introduction

Muscle synergies have been proposed to be a modular organization for muscle coordination that map high-level task goals, or motor intentions, into motor actions (Chiel et al. 2009; Drew et al. 2008; Giszter et al. 2007; Ting and McKay 2007; Yakovenko et al. 2010). Here we explicitly tested this hypothesis by investigating the relationship between muscle synergy recruitment and functional motor outputs in two postural tasks–stepping and non-stepping responses to perturbations–that achieve the same motor intention of maintaining upright balance using different motor actions. Muscle synergies and other types of modular organization have been used to explain muscle coordination during a variety of motor behaviors in many different species (Cappellini et al. 2006; d'Avella et al. 2006; d'Avella et al. 2003; Drew et al. 2008; Flash and Hochner 2005; Hart

and Giszter 2004a; Hart and Giszter 2004b; Kargo and Giszter 2000; Krishnamoorthy et al. 2004; Latash et al. 2005; Ting and Macpherson 2005; Torres-Oviedo et al. 2006; Yakovenko et al. 2010). The generality of muscle synergies across different motor tasks has been shown in frog kicking, jumping, and swimming (Cheung et al. 2005; d'Avella and Bizzi 2005); or in human walking and running (Cappellini et al. 2006); or in forward and backward pedaling (Raasch and Zajac 1999; Ting et al. 1999). Although some muscle synergies are used across multiple tasks, in some instances new synergies may emerge when a new motor task is presented (Cheung et al. 2005; Ivanenko et al. 2005; Robert et al. 2008; Torres-Oviedo and Ting 2010) and the recruitment of the synergies may be altered (Cappellini et al. 2006; Clark et al. 2010).

The recruitment of these muscle synergies, or motor modules, may be related to specific biomechanical functions necessary to accomplish a behavioral goal (Berniker et al. 2009; Chiel et al. 2009; Giszter et al. 2007; Raasch and Zajac 1999; Ting and McKay 2007). Muscle synergies in humans have been correlated with foot kinematics in locomotion (Ivanenko et al. 2003; Ivanenko et al. 2006) and foot acceleration in pedaling (Ting et al. 1999). The biomechanical outputs related to muscle synergies depend upon the motor task being performed. In human finger spelling, muscle synergies are correlated with common hand postures (Weiss and Flanders 2004), whereas in frog kicking, jumping, and swimming, shared muscle synergies may be activated to implement whole limb movements common to these locomotor behaviors (Cheung et al. 2005; d'Avella and Bizzi 2005). In balance control, we found that muscle synergies in the cat are recruited to produce specific force vectors at the ground that are robust across changes in postural configuration (Ting and Macpherson 2005; Torres-Oviedo et al.

2006). Although these correlations indicate possible muscle synergy functions, the stimuli triggering the studied movements and the behavioral outputs were also directly related. Therefore, one purpose of this study was to determine whether muscle synergies map high-level task goals into actions independently from sensory inputs triggering the postural response.

In feline standing balance control, it has been hypothesized that several muscle synergies are recruited in order to control center of mass (CoM) kinematics by modulating end-point forces (McKay and Ting 2008; Torres-Oviedo et al. 2006), but similar studies have not been conducted in human balance control. Our previous work in human balance control has shown that the same muscle synergies can account for balance responses across a variety of standing conditions (Torres-Oviedo and Ting 2010), suggesting these motor modules may produce biomechanical functions generally needed for balance control. It is likely that these biomechanical functions are related to the control of CoM motion. Human balance control is complex as a broad range of postural behaviors is available in response to perturbations, such as the so-called hip- and ankle-strategies (Horak and Macpherson 1996; Runge et al. 1998), stepping (McIlroy and Maki 1993b), or using the upper extremities for stabilization (Maki and McIlroy 1997). In any variation of the standing balance task, maintaining balance requires keeping the CoM above the base of support (BoS) (Massion 1992; Scholz et al. 2007; Ting et al. 2009). During feet-in-place postural response behaviors, however, the muscles recruited for postural stabilization depend upon the direction of CoM motion, rather than the local changes in joint angle displacements (Carpenter et al. 1999; Gollhofer et al. 1989; Ting and Macpherson 2004). Similarly, CoM kinematics can predict the activation time

course of distal and proximal muscles (Welch and Ting 2008), suggesting a neural command reflecting CoM kinematics could activate multiple muscles across the body.

Here we used support-surface perturbations to elicit both stepping and non-stepping postural responses, allowing us to test the hypothesis that muscle synergies are recruited to achieve the biomechanical output of controlling CoM, independent of the sensory input triggering the response. In non-stepping postural responses to perturbations, the feet stay in place and the CoM is returned back to its initial position above the feet. Conversely in stepping responses, the COM is expanded by taking a step, which results in the CoM being displaced even further from the initial position. Therefore in these two behaviors, the motor output, or desired direction of CoM movement, is opposite in response to the same direction of perturbation which evokes similar sensory inputs in the two cases. Comparing these two postural behaviors allows dissociation between patterns of somatosensory input (due to perturbation direction), the associated patterns of muscular output, and the resultant CoM motion.

In order to use muscle synergy analysis to examine stepping responses, it was first necessary to characterize muscle activity in multidirectional stepping responses more thoroughly. Very few studies have examined the patterns of EMG during stepping responses and compared these patterns to those observed in non-stepping responses (Horak and Macpherson 1996; McIlroy and Maki 1993a). The magnitude of initial EMG is increased in stepping responses compared to non-stepping responses (McIlroy and Maki 1993a), but the time course of muscle activity during stepping and non-stepping responses has not been compared. Furthermore, stepping responses in directions other than anterior/posterior and medial/lateral directions have not been examined.

Multidirectional tuning curves are necessary in order to fully evaluate patterns of underlying muscle synergies. Therefore, in this study we compared the initial time course of muscle activity in stepping and non-stepping responses, and characterized muscle activity tuning during stepping responses to multidirectional perturbations other than anterior/posterior and medial/lateral previously investigated (Perry et al. 2000; Zettel et al. 2002).

We hypothesize that by differentially recruiting a common pool of muscle synergies with specific biomechanical functions, the CNS can direct the movement of the CoM in both non-stepping and stepping postural responses. We first determined whether the same muscle synergies were recruited in both stepping and non-stepping postural response to perturbation or whether different sets of muscle synergies were recruited during these two postural strategies. Furthermore, we examined whether the recruitment of muscle synergies in both types of response were related to a consistent biomechanical function such as to displace the CoM or to produce particular forces in a particular direction, or whether the recruitment was related to perturbation direction. We predicted the same muscle synergies would be used in the stance leg during both stepping and non-stepping postural behaviors to produce similar forces at the ground and CoM acceleration in the two behaviors, but that the recruitment of these functional muscle synergies would differ across stepping and non-stepping responses depending on the desired direction of CoM motion. Alternatively, if muscle synergies were instead patterned in direct response to somatosensory feedback, we would expect to see the same muscle synergies activated for the same perturbation directions in both non-stepping and stepping responses – even when the resulting CoM acceleration was in opposite directions.

2.2 Methods

In order to determine whether the same muscle synergies are recruited during non-stepping and stepping postural behaviors, and whether they are related to a behavioral goal, we recorded human postural responses to support surface translations. Twelve ramp-and-hold perturbation directions were applied in the horizontal plane, and the presentation order was randomized. Subjects were instructed to maintain their balance, and to step with their left foot if a step was necessary to recover their balance. Subjects participated in two sets of perturbations: the first was a larger, faster set that caused a stepping response, the second was a smaller, slower set, during which they maintained balance without moving their feet. Muscle synergies were extracted from the non-stepping condition and the stepping condition individually and compared; muscle synergies extracted from non-stepping were subsequently used to reconstruct the stepping trials. If the stepping data were not sufficiently explained by the non-stepping muscle synergies, additional stepping-specific muscle synergies were then extracted. Finally, we identified functional muscle synergies by incorporating kinematic and kinetic data into our dataset for analysis in order to determine whether the recruitment of muscle synergies was correlated to the production of a consistent biomechanical function.

2.2.1 Data Collection

Eight healthy subjects (5 male, 3 female) between the ages of 21 and 27 were exposed to two sets of support-surface translations according to an experimental protocol that was approved by the Institutional Review Boards of Georgia Tech and Emory. Subjects stood on a platform that translated in 12 equally spaced directions in the

horizontal plane (see Figure 2.1). They were instructed to maintain balance without stepping if possible, but if a step was necessary, to step with their left foot. This was done to ensure steps would be reactive and not voluntary, intentional steps. Two blocks of ramp-and-hold perturbations in each of these 12 directions were presented. In the stepping block, the platform's displacement was 23 cm, velocity was 45 cm/s and acceleration was 0.75g. In the non-stepping block, the platform's displacement was 12.4 cm, velocity was 35 cm/s, and acceleration was 0.5g. The perturbation directions were randomized during each block of perturbations to minimize anticipatory adjustments and increase response variability. Due to the influence of prior trials on a subject's response (Horak and Nashner 1986), we first collected the stepping block of trials and then the non-stepping block of trials. Five trials of each condition (stepping and non-stepping) in each of the 12 directions of perturbation were collected. In the stepping condition, all subjects took a step in response to perturbations in all directions. Occasionally subjects stepped with their right foot and these trials were excluded from the analysis. In the non-stepping condition, all subjects maintained balance without taking a step.

Since many muscles are required for the muscle synergy analysis, surface EMG activity was recorded at 1080 Hz from sixteen lower back and leg muscles on the subject's right side, which was the stance leg in stepping responses. The muscles recorded include: vastus lateralis (VLAT), rectus femoris (RFEM), rectus abdominis (REAB), biceps femoris, long head (BFLH), semitendinosus (SEMT), adductor magnus (ADMG), erector spinae (ERSP), abdominal external oblique (EXOB), vastus medialis (VMED), tibialis anterior (TA), medial gastrocnemius (MGAS), lateral gastrocnemius (LGAS), soleus (SOL), peroneus (PERO), tensor fasciae latae (TFL), and gluteus medius

(GMED). EMG data were high pass filtered at 35 Hz, de-meaned, rectified, and low-pass filtered at 40 Hz, using custom MATLAB routines. Additionally, kinetic data were collected at 1080 Hz from force plates under the feet (AMTI, Watertown, MA) and kinematic data were collected at 120 Hz using a motion capture system (Vicon, Centennial, CO) and a custom 25-marker set that included head-arms-trunk (HAT), and bilateral thigh, shank, and foot segments (Winter 1990). CoM acceleration was calculated from ground reaction forces (F=ma), and CoM position was calculated using kinematic data and the Vicon Plug-in-Gait model. CoM velocity computed from differentiated marker data matched well with the CoM velocity computed from integrated force data. The CoM displacement and velocity were not used in the functional muscle synergy analysis.

2.2.2 Data Processing

To account for temporal variations in muscle activity, four time bins were analyzed: one before the perturbation and three during the automatic postural response. The platform moved at 500 ms after the beginning of the trial. A background period beginning 50 ms after we began collecting data and ending 170 ms before the perturbation onset was analyzed in order to determine the resting activity of each muscle. The automatic postural response (APR) has been well-characterized and occurs ~100 ms following the perturbation (Horak and Macpherson 1996); due to temporal variations in muscle activity during this APR, we further divided it into 3 time bins. Each one lasted 75 ms and began 100 ms (PR1), 175 ms (PR2) and 250 ms (PR3) after the perturbation (see Figure 2.1 gray shaded areas). Mean muscle activity for each muscle during each

time bin was calculated for each trial. These numbers were assembled to form a data matrix, which consisted of 4 time bins x 12 directions x 5 trials x 2 conditions = 480 points for each of the 16 each muscles. For display purposes, each muscle's EMG values were initially normalized to the maximum value across all time periods, perturbation directions, and conditions so that each value was between 0 and 1. Prior to extracting muscle synergies, each muscle vector was normalized to have unit variance to ensure equal weighting in the muscle synergy extraction.

Kinetic and kinematic variables were also analyzed to determine whether muscle synergy activations were consistently correlated with a particular behavioral goal. Ground reaction forces (GRF) were rotated such that the vertical forces were aligned with the limb axis (defined by the vector between the hip and ankle markers), as in Torres-Oviedo et al. (2006). The time bins used to consider ground reaction forces were 60 ms after the PR time bins used for EMG data, due to electromechanical delays (Jacobs and Macpherson 1996). Therefore, the time windows for the 3 PR periods were 160-235, 235-310, and 310-385 ms following perturbation onset for forces. Background forces were subtracted from the forces in each time period, so the force data represents a change from background. In order to use non-negative matrix factorization (described later), the positive and negative components of the forces were separated, resulting in 6 additional data rows to be included in the matrix (Fx+, Fx-, Fy+, Fy-, Fz+, and Fz-). For display purposes, each row was normalized to the maximum value across all time periods, perturbation directions, and conditions, so that each value was between 0 and 1. Similarly, CoM acceleration data were analyzed the same way as GRF. CoM acceleration was averaged over 3 time periods: 160-235, 235-310, and 310-385 ms

following perturbation onset, and background CoM acceleration was subtracted out. The positive and negative components were separated, each row normalized to the maximum value, and then averaged over the same time periods as were used for GRFs. Each functional variable was added into the data matrix of EMG data for extraction of functional muscle synergies, which is described below. The large passive forces that occur in the vertical force component due to perturbation dynamics and changes in weight bearing were a confounding factor. In some perturbation directions (leftward), the vertical forces were mostly passive in the stepping condition, due to the movement of the platform rather than active muscle activation. Because we were primarily interested in the directional control of forces in the horizontal plane due to muscle synergy recruitment, we included only the 4 components of horizontal-plane force (Fx+, Fx-, Fy+, Fy-) in the muscle synergy analysis. As with the EMG data, each row was normalized to have unit variance before extracting functional muscle synergies to ensure a uniform representation of variance across the data pool.

2.2.3 Extraction of Muscle Synergies

We extracted muscle synergies from the data matrix of EMG recordings using nonnegative matrix factorization (NNMF) described by Lee and Seung (Lee and Seung 1999; Tresch et al. 1999), which has previously been used for muscle synergy analysis (Ting and Macpherson 2005; Torres-Oviedo and Ting 2007). This is a linear decomposition technique that assumes that a muscle activation pattern, M, in a given time period which was evoked by a perturbation in a particular direction is comprised of a linear combination of a few muscle synergies, W_i, that are each recruited by a synergy

recruitment coefficient, c_i. Therefore, a particular muscle activation pattern at a particular time in response to a particular perturbation would be represented by:

$$M = c_1W_1 + c_2W_2 + c_3W_3 + \ldots$$

W_i specifies the muscles involved in synergy i and their relative contributions. Each component of W_i represents the contribution of one particular muscle to that synergy, and an individual muscle may contribute to multiple synergies. The muscle synergies do not change composition across conditions, and each one is multiplied by a scalar recruitment coefficient, c_i, which changes over time and across conditions. The recruitment coefficient, c_i, is hypothesized to represent the neural command that specifies how that synergy is modulated over time, and how much each synergy will contribute to a muscle's total activity pattern (Ting 2007). After extracting functional muscle synergies, the unit variance scaling was removed from data so that each muscle, kinetic, and kinematic variable ranged from 0-1 to permit data inspection and interpretation.

To select the number of muscle synergies that could best reproduce our data we extracted 1-16 synergies from 60% of the non-stepping trials for each subject, and used these to reconstruct the EMG data from the remaining non-stepping trials (for cross validation) and from the stepping trials. These were termed "shared" muscle synergies. We selected the fewest number of "shared" muscle synergies (*Nsyn*) that could adequately reconstruct the muscle responses in the non-stepping condition. The goodness of fit of the data reconstruction using the muscle synergies was quantified by the data variability accounted for (VAF), defined as 100 x uncentered Pearson's correlation coefficient (Torres-Oviedo et al. 2006; Zar 1999). We selected *Nsyn* that accounted for at least 90% of the overall non-stepping data variability (i.e., VAF >90%). Note that overall

VAF was found by calculating VAF for the entire non-stepping dataset. Moreover, we also had a local criterion in which *Nsyn* accounted for at least 75% of the data variability in each muscle and each condition. Muscle VAF and condition VAF were calculated by considering only a portion of the non-stepping dataset. Muscle VAF for each muscle quantified the extent to which the muscle synergies accounted for variability in the activity of individual muscles across all time bins, perturbation directions, and trials. Condition VAF for each perturbation direction quantified the extent to which the muscle synergies accounted for the variability in muscle activation patterns formed by the response of all 16 muscles to a single perturbation direction during one time bin across all 5 trials. This local fit criterion was more stringent and ensured that relevant features of the data set were reproduced. The number of muscle synergies was increased until they could account for > 75% muscle VAF in each muscle and for > 75% condition VAF in each perturbation direction, and further increased if local fits were improved. However, if an additional muscle synergy contributed evenly to the VAF across muscles and perturbation directions, it was not included because it likely represented noise in the data rather than variations due to trial or perturbation direction. *Nsyn* was also validated using factor analysis (FA): 1-16 factors were extracted and the log likelihood of each was plotted vs. number of factors. *Nsyn* was chosen by finding the point on the log-likelihood curve where curvature is greatest (Tresch et al. 2006).

To validate *Nsyn* we compared the overall VAF using the identified muscle synergies to the overall VAF using muscle synergies extracted from shuffled data. We estimated 95% bootstrap confidence intervals (CI) for the overall VAF when using 1 to 16 muscle synergies extracted from the original data and 1 to 16 muscle synergies

extracted from a shuffled data set. We used bootstrapping with replacement (Cheung et al. 2009; Efron 1993) to resample each data matrix. The overall VAF due to reconstruction by either the 1 to 16 muscle synergies extracted from the original data or the 1 to 16 muscle synergies selected from shuffled data was calculated for 500 resampled datasets to generate confidence intervals. VAF values were sorted, and 95% confidence interval bounds were estimated by selecting the 2.5 and 97.5 percentiles of the VAF distribution. In the shuffled version of the original data matrix, each muscle's data were shuffled independently, therefore, this shuffled data matrix contained the same values, range, and variance for each muscle, but the relationships between muscle activations were removed. The VAF CI found using the muscle synergies extracted from the original dataset was compared to the VAF CI found using muscle synergies from shuffled data.

"Stepping-specific" muscle synergies were extracted from stepping data that was not accounted for by the "shared" muscle synergies described above. To this end, we used an iterative algorithm that held fixed the shared muscle synergies extracted from non-stepping data while optimizing a new set of muscle synergies, termed "stepping-specific", extracted from the remainder of the variability in the stepping data not accounted for by the shared muscle synergies (Cheung et al. 2009; Torres-Oviedo and Ting 2010). In this iterative process the recruitment coefficients of shared and stepping-specific muscle synergies were also optimized. We extracted 1-5 stepping-specific muscle synergies and selected the fewest number of muscle synergies (shared and specific) that could adequately reconstruct the stepping responses, as measured by VAF > 90% of the overall data, and > 75% of the muscle and condition VAF (described above).

Moreover, to validate the shared and stepping-specific muscle synergies we compared them to muscle synergies extracted from data in both conditions (i.e., non-stepping and stepping) and from data in each condition alone. The quantification of similarity between muscle synergy sets is described in the *Data Analysis* section.

To determine if the muscle synergy activations were related to a particular biomechanical function or behavioral goal, we extracted 1-16 functional muscle synergies from a data matrix of non-stepping trials that contained muscle activity as well as forces under the feet and CoM acceleration (forces and CoM acceleration were lagged 60ms behind EMG, as discussed above). Because we used NNMF to extract muscle synergies, all of the input data needed to be positive; therefore positive and negative components of force and CoM acceleration were separated as previously described. Functional muscle synergies were extracted from non-stepping data first, and then used to reconstruct the stepping data. If necessary, stepping-specific functional muscle synergies were also extracted. As a validation, functional muscle synergies were also extracted from EMG and force data without CoM acceleration data, and from EMG and CoM acceleration data without force data included.

2.2.4 Data Analysis

Once N_{syn} and an appropriate number of stepping-specific functional muscle synergies (if needed) were selected, the functional muscle synergies were used to reconstruct the EMG, force, and CoM acceleration patterns for the stepping and non-stepping trials. Measured data and reconstructed data were compared for a particular muscle, force, CoM acceleration component, or perturbation direction for each of the five

trials to examine the ability of the synergies to account for inter-trial variations. Similarity between measured and reconstructed data was quantified using r^2 and VAF (Torres-Oviedo et al. 2006; Zar 1999). We also examined whether the functional muscle synergies could account for temporal and spatial variations in muscle activation, force, and CoM acceleration patterns.

Similarity between two different sets of muscle synergies was determined by calculating correlation coefficients (r) between each muscle synergy vector in the first set and each in the second set. A pair of muscle synergies was considered "similar" if they had $r > 0.623$, which corresponds to the critical value of r^2 for 16 muscles at $p=0.01$ ($r^2=0.388$). An additional analysis was performed to ensure the muscle synergy "matches" we selected were more similar than would be expected by chance. We calculated the expected mean r (μ) and standard deviation (σ) based on comparing the first set of muscle synergies with 22,000 random permutations of the elements of the second set of muscle synergies. Then we transformed the r-values between our actual synergy comparison to the standard normal variable, Z, using $Z = X - \mu / \sigma$, where X is the r-value between one synergy in the first set and one in the second set. An r greater than 0.623 corresponds to a Z-score > 2.409, indicating the pair of muscle synergies is statistically more similar than would be expected by chance ($p < 0.008$). All of the muscle synergy pairs that we call "similar" met this criterion.

2.3 Results

For all subjects, a few muscle synergies reproduced both stepping and non-stepping responses to multidirectional balance perturbations, accounting for temporal,

spatial, and inter-trial variability in muscle activation patterns as well as task-level variables such as GRF and CoM acceleration. Different patterns of muscle activity were observed in these two very different tasks, resulting in variations in muscle tuning. Common muscle synergies in the stance leg were used in both non-stepping and stepping responses. In stepping responses, one additional stepping-specific muscle synergy was required in all subjects, perhaps providing stabilization to the stance limb to swing the stepping limb forward. Furthermore, functional muscle synergies (which included forces and CoM accelerations) were able to account for force direction and CoM acceleration direction in both non-stepping and stepping responses.

2.3.1 Non-stepping vs. stepping responses

In all subjects, following perturbations, CoM movement and forces under the stance foot were initially similar in both behaviors (PR1), but diverged in PR2 or PR3 in stepping versus non-stepping behaviors. For example, forces during a 300° perturbation were initially similar in stepping and non-stepping (Figure 2.1, PR1). In both conditions the right leg was initially unloaded in PR1 as a result of the perturbation. In non-stepping behaviors the right limb was slowly loaded again after PR3 as the subject regained balance (Figure 2.1). However in stepping responses, the right limb was rapidly loaded during PR2 so that the subject could take a step with the left leg, and then the right leg was slowly unloaded as body weight was redistributed onto both legs after PR3. (Figure 2.1, compare PR1 to PR3). Similarly, for all subjects the CoM was initially accelerated and displaced away from the feet in both stepping and non-stepping responses to balance perturbations (e.g. Figure 2.2). However, in stepping responses, the CoM continued

moving in the same direction away from the feet in the later time periods (PR2 and PR3), whereas in non-stepping responses, the CoM was accelerated in the opposite direction returning the CoM back above the feet during PR2 and PR3 (Figure 2.1).

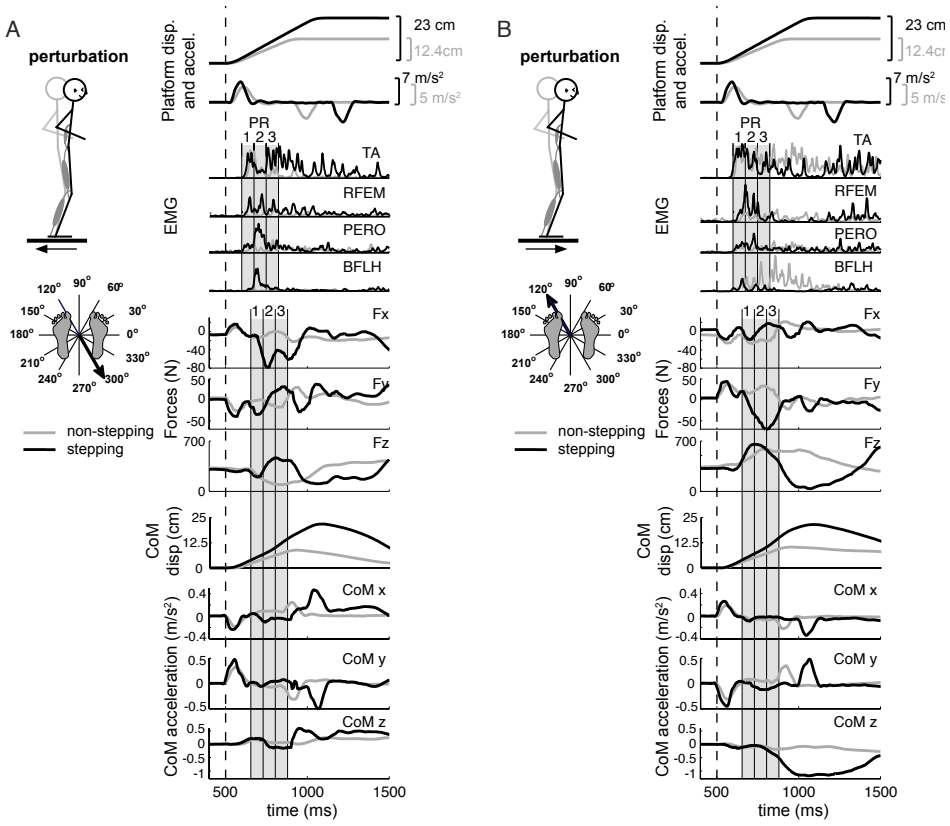


Figure 2.1 Example of postural responses to a backward and rightward perturbation of the support surface (A), and to a frontward and leftward perturbation of the support surface (B). Balance perturbations were induced by ramp-and-hold perturbations in 12 evenly spaced directions in the horizontal plane. Platform displacement and acceleration profiles used to induce non-stepping (gray) or stepping (black) responses are shown. EMG responses occur ~100 ms after the onset of platform motion (vertical dashed line). Shown here are tibialis anterior (TA), rectus femoris (RFEM), peroneus (PERO), and biceps femoris long head (BFLH) EMG responses. Mean EMG activity was calculated for 3 time bins during the automatic postural response (PR), indicated by the shaded region, beginning 100ms (PR1), 175ms (PR2), and 250ms (PR3) following perturbation, as well as one background time period. Ground reaction forces under the right foot as well as center of mass (CoM) position and acceleration are also shown.

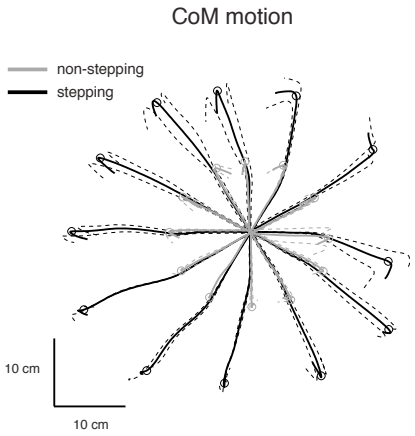


Figure 2.2 Center of mass (CoM) displacement during non-stepping (gray) and stepping (black) responses to perturbations, from 500ms before the perturbation until 150ms after the platform stopped moving. Shown are the mean and standard deviation for the 5 trials in each direction for one subject. The circle at the hook of each trace marks the point at which the platform stopped moving. In both conditions, the CoM was initially displaced 10-12 cm in the direction opposite the platform movement. In non-stepping responses, the CoM then moves back towards the starting position, whereas in stepping responses, the CoM continues moving away from the starting position as the subject took a step.

Likewise, following perturbations, EMG activity was initially similar in the two behaviors (PR1), but diverged at later time points depending upon which behavior was used (Figure 2.1). The latencies to muscle onset and initial muscle activation patterns (PR1) were similar in both non-stepping and stepping responses. The latency to step initiation ranged from 130-280ms after perturbation onset. Across all perturbation directions, muscles had the same tuning in both behaviors during PR1 (Figure 2.3). The tuning directions in non-stepping responses stayed the same throughout the postural response. However, in stepping responses, the muscle tunings were dramatically different by PR3. For example, during PR3, PERO was most active during stepping responses for rightward lateral perturbations, whereas it was most active for leftward

lateral perturbations during non-stepping responses (Fig 3, PR3). Likewise, SOL was most active in stepping responses for leftward, forward perturbations, but in non-stepping responses it was most active for leftward, backward perturbations in PR3.

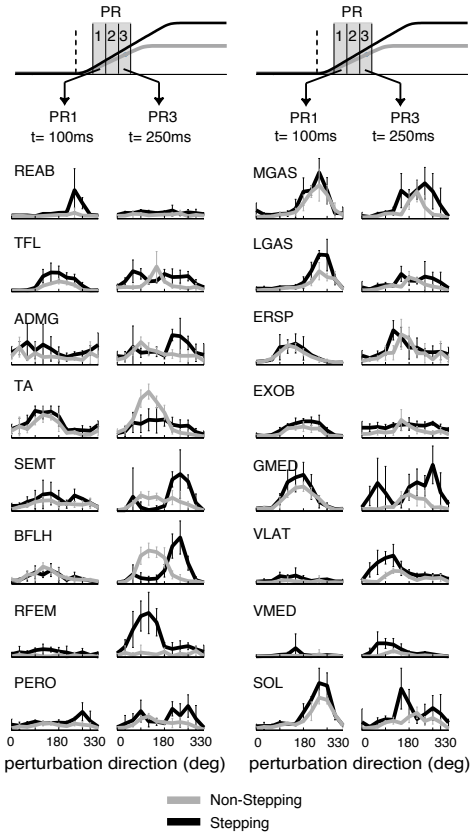


Figure 2.3 Muscle tuning curves for all 16 muscles during non-stepping (gray) and stepping (black) responses during time windows PR1 and PR3 for a representative subject. Muscle tuning curves vary in magnitude over all perturbation directions, and their shapes vary from muscle to muscle, over time, and between non-stepping and stepping responses. Shown are the mean tuning curves ± standard deviations for 5 trials in each perturbation direction, presented randomly.

2.3.2 Muscle synergies were shared between non-stepping and stepping responses

In non-stepping postural responses, four to six muscle synergies per subject were sufficient to account for >90% total variability and >75% variability in each muscle and

condition (all 4 time bins, 12 perturbation directions, and 5 trials of each) in the EMG data. These values are several confidence intervals higher than would be expected by chance. Confidence intervals for VAF of extracted muscle synergies did not overlap with VAF confidence intervals of muscle synergies extracted from shuffled data except for the case where only one muscle synergy was extracted (Figure 2.4A, Subject 1). Five muscle synergies were selected for subject 1, and the VAF CI confirmed this selection since this was the lowest number of muscle synergies required for the upper bound of the CI to exceed 90% VAF (Cheung et al. 2009) The lower bound of the VAF CI for 5 muscle synergies was 2.45 CIs above the VAF CI for 5 muscle synergies extracted from shuffled data (Figure 2.4A). Across subjects, the lower bound of the VAF CI for the selected number of muscle synergies (4-6 muscle synergies per subject) was 2.51 ± 0.79 CIs above the same number of muscle synergies extracted from shuffled source data.

Several analyses demonstrated that muscle synergies used in the stance leg were shared between stepping and non-stepping responses. Figure 2.4B shows the results for one of the multiple comparisons performed between muscle synergy sets in a sample subject. Muscle synergies extracted from non-stepping data were shuffled 22,000 times and compared to muscle synergies extracted from stepping to generate a distribution of r-values expected by chance (Figure 2.4B). Note that the r-values that result when comparing muscle synergies extracted from the non-stepping data to those extracted from the stepping data fall beyond the threshold of r-values expected by chance ($r > 0.623$ corresponding to a Z-score > 2.409) (Figure 2.4B). Four of the five muscle synergies extracted from non-stepping in subject 1 were similar to four of the five muscle synergies extracted from stepping in the same subject ($r > 0.74$) (Figure 2.4B). The distribution of

Z-scores for the r-values between all muscle synergies extracted from stepping and non-stepping was bimodal, with the muscle synergies considered to be similar clustered toward the upper end of the distribution. Across subjects, in stepping responses, five to seven muscle synergies were required; 4-6 of the stepping muscle synergies were similar to those from non-stepping, and there was one additional muscle synergy used only during stepping responses. Furthermore, when muscle synergies were extracted from a data matrix containing both non-stepping and stepping trials, similar muscle synergies were identified (Figure 2.4C). Four muscle synergies were found to be similar across all four different extractions using different data pools (Figure 2.4C). To illustrate the range of fits, Figure 2.4C displays examples of a muscle synergy that was very similar across extractions (W_5) and another muscle synergy which had relatively low r values, but was still considered similar (W_1).

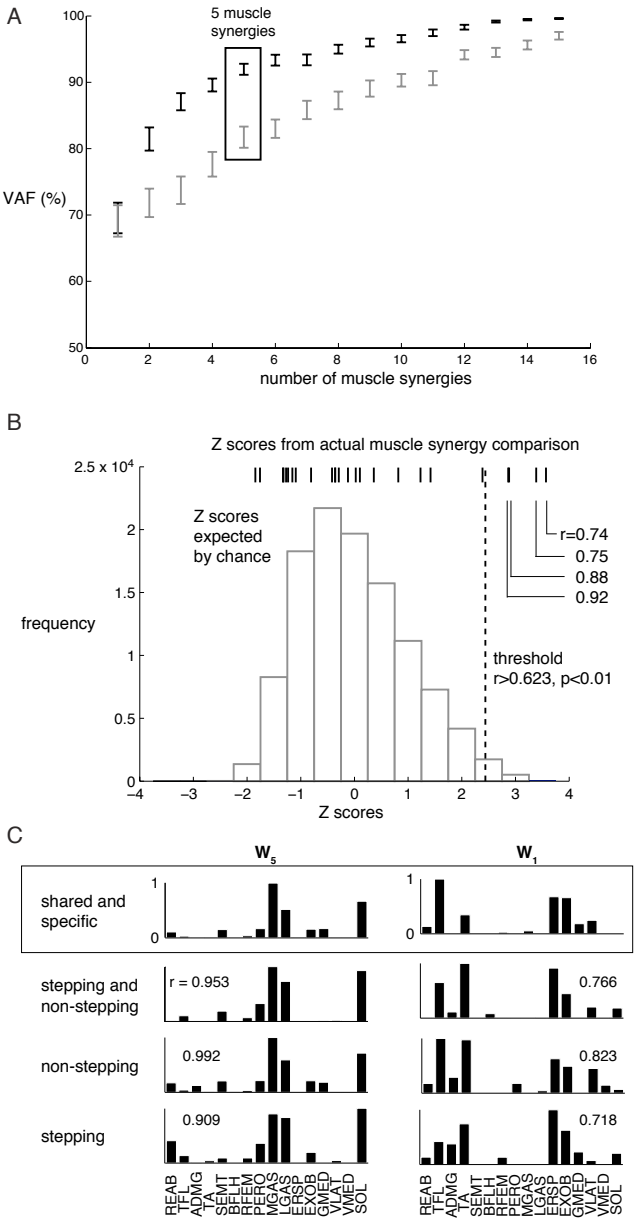


Figure 2.4 Confidence intervals of reconstruction VAF and muscle synergy comparison. A) 95% confidence intervals (CI) of the reconstruction VAF estimated using bootstrapping (black lines) and 95% CIs of the reconstruction VAF when muscle synergies were extracted from a shuffled matrix of the same data (gray lines). For subject 1 (shown here), five muscle synergies were selected, and the lower bound of the VAF CI for 5 muscle synergies was 2.45 CIs above the VAF CI for 5 muscle synergies extracted from shuffled data. B) Demonstration of the criteria used to quantify muscle synergy similarity. Muscle synergies extracted from shuffled non-stepping data were compared to muscle synergies extracted from stepping to generate a distribution of Z-scores for how similar two muscle synergies are predicted to be based on chance (gray histogram). The Z-scores for the comparisons between the actual muscle synergies from non-stepping and

the muscle synergies from stepping are shown as black vertical lines. A pair of muscle synergies was considered "similar" if r > 0.623, corresponding to a Z-score > 2.409 (dotted vertical line). For subject 1, four of the five muscle synergies extracted from non-stepping were similar to four of the five muscle synergies extracted from stepping. C) Comparison of muscle synergies extracted from various combinations of data. Shown are two muscle synergies, W5 and W1, from a representative subject. Shared and specific: muscle synergies extracted from 60% of non-stepping trials and used to reconstruct the remaining non-stepping data as well as stepping responses. This was the final processing method selected and these are the muscle synergies shown in Figure 2.5. All other extracted muscle synergies are compared to these. Stepping and non-stepping: muscle synergies identified from all of the non-stepping and stepping data combined into one large data matrix. Shown are r values from comparing these vectors to these identified using the shared/specific algorithm. Non-stepping: muscle synergies extracted from all of the non-stepping data only. Stepping: muscle synergies extracted from all of the stepping data only. Extracted muscle synergies were similar regardless of the datasets used for analysis, suggesting that they are conserved across conditions.

Therefore, for the rest of our analyses, muscle synergies were extracted from 60% of non-stepping trials ("shared synergies") and used to reconstruct the remaining non-stepping trials (cross-validation) as well as the stepping data. The shared muscle synergies could account for 93±1% of the overall variability (VAF between EMG and reconstruction for the entire dataset) and 79±7% variability across muscles and conditions in the non-stepping behavior (average VAF for individual muscles and conditions, across all subjects). These shared muscle synergies also could account for 85±3% of the overall variability and 72±7% variability across muscles and conditions in the stepping behavior. With the addition of one extra "stepping-specific" muscle synergy, the overall variability accounted for was increased to 91± 2% in stepping, and 81±4% variability across muscles and conditions. For all subjects, these muscle synergies were similar to those extracted from each behavior individually and together (r = 0.83 ± 0.10; Figure 2.4C). The compositions of the shared muscle synergies were similar to those found previously during non-stepping postural responses (Torres-Oviedo

and Ting 2007) and were comprised of muscles spanning multiple joints (Figure 2.5). In each subject, there was an additional muscle synergy used in stepping that was not found in non-stepping responses which was typically composed of the vasti and RFEM, as well as GMED, a muscle important in walking. It was strongly activated for forward perturbations (in which the subject takes a step backwards), perhaps providing forces to stabilize the stance limb or push the swing leg backward.

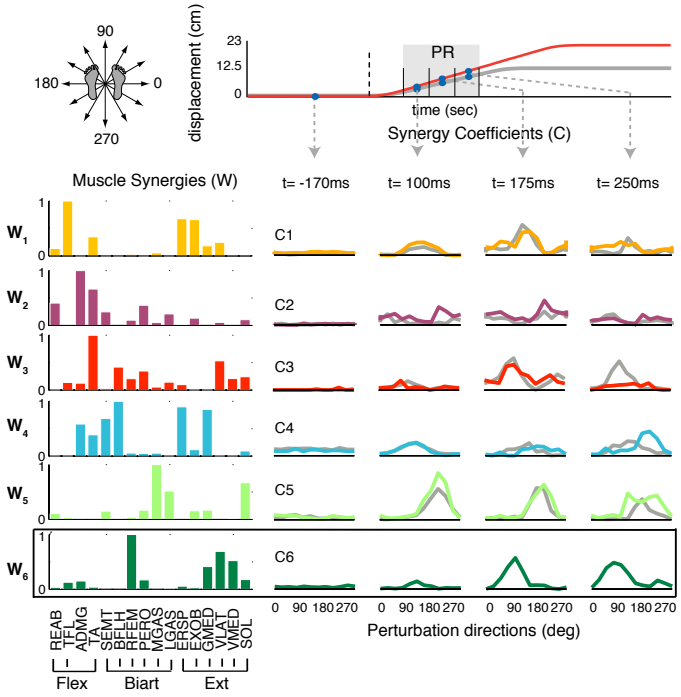


Figure 2.5 Muscle synergy vectors and recruitment coefficients for a representative subject. Muscle synergy vectors W_1-W_5 were extracted from EMG data during non-stepping responses and used to reconstruct stepping responses. W_6 is an additional stepping-specific muscle synergy required to achieve a good reconstruction of stepping responses. Shown are the average muscle synergy recruitment coefficients for 5 trials in each perturbation direction for both non-stepping responses (gray) and stepping responses (color). Directional tuning of muscle synergies can be observed over the 3 response time bins, as well as differences in muscle synergy recruitment between non-stepping and stepping responses.

2.3.3 Muscle synergy recruitment tuning curves explain individual muscle differences in non-stepping and stepping responses

In all subjects, the muscle synergy tuning curves initially had similar tuning directions (PR1 and PR2), but later (PR3) changed tuning direction if a stepping behavior was selected. Similar to individual muscle tuning, muscle synergy tuning with respect to perturbation direction was maintained across all three time bins during non-stepping responses (Figure 2.5, gray curves), but changed by PR3 in stepping responses (Figure 2.5, colored curves). In this subject as well as the others, each muscle synergy had the same tuning in PR1 and PR2 in both non-stepping and stepping responses. In non-stepping responses, this same tuning was maintained in PR3, whereas for stepping responses, the tuning of some of the muscle synergies changed. For example, W_3 (Figure 2.5, red), comprised mainly of TA and quadriceps muscles, was recruited in forward perturbations in PR1 and PR2 in both stepping and non-stepping responses, as well as PR3 in non-stepping, as the subject had fallen backward and was trying to pull their body forward to restore balance. In PR3 in stepping responses, however, W_3 was recruited much less, as the subject had switched behaviors and had begun to take a step backward. Instead, the subject used the stepping-specific muscle synergy, W_6 (Figure 2.5, dark green), in forward perturbations during PR2 and PR3, when the switch had been made to a stepping behavior. During stepping responses, W_4 (Figure 2.5, blue) changed from being recruited in forward, leftward perturbations in PR1 to being recruited for backward, leftward perturbations by PR3. These trends were seen in multiple subjects.

The shifts in muscle synergy tuning direction could explain the patterns of muscle activity (and individual muscle tuning curves) observed in both non-stepping and stepping behaviors (comparison between real and reconstructed tuning curves in both non-stepping and stepping: r^2=0.77±0.24, VAF=94±6%; Figure 2.6). For example, BFLH changed tuning in PR3 in stepping responses, and it was activated by W_4 (Figure 2.6, blue). TA turned off during PR3 in stepping responses, and it was activated by W_3 (Figure 2.6, red). VLAT had similar tuning during PR3 in non-stepping and stepping, but was activated by different synergies. In non-stepping, W_3 (Figure 2.6, red) was responsible for activating VLAT, whereas in stepping, the stepping-specific muscle synergy W_6 (Figure 2.6, green) activated VLAT. Thus the muscle synergies were able to reproduce changes in muscle activation patterns with both perturbation direction and time.

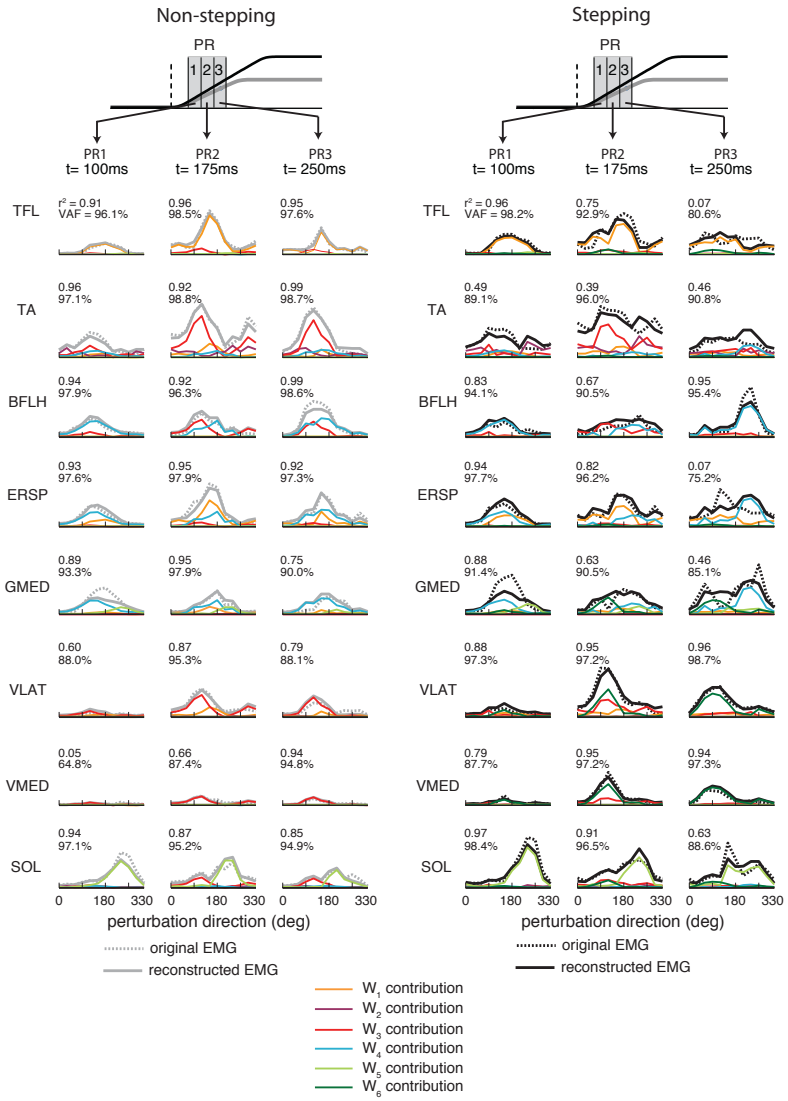


Figure 2.6 Reconstructions of the muscle tuning curves using the muscle synergies shown in Figure 2.5. Original data are shown by a dashed line and reconstructed data are shown by a solid line (non-stepping in gray and stepping in black). The contribution of each muscle synergy to the reconstruction is shown by the corresponding colored line, all of which are added to generate the total reconstruction. Average r^2 between each muscle tuning curve and the muscle synergy reconstruction is 0.77±0.24, and average variability accounted for (VAF) between each muscle tuning curve and the muscle synergy reconstruction is 94±6%.

2.3.4 Functional muscle synergies reveal correlations between muscle synergies and task-level goals

The composition and tuning of the muscle synergies within each subject were not changed by including force and CoM acceleration in the analysis, illustrating that force and CoM acceleration tuning curves were well correlated with muscle synergy tuning curves (Figure 2.7). For all subjects, the muscle synergy composition was preserved when muscle synergies were extracted from EMG and forces only, EMG and CoM acceleration only, as well as EMG, forces, and CoM acceleration together ($r=0.83\pm0.12$). Similarly, the muscle synergy tuning curves were conserved when the functional variables were included in the analysis. Because of the similarities in functional muscle synergies observed when extracting functional muscle synergies from non-stepping or stepping responses individually, we used the same approach here as we had used to identify muscle synergies: functional muscle synergies were extracted from the non-stepping data and used to reconstruct the stepping data.

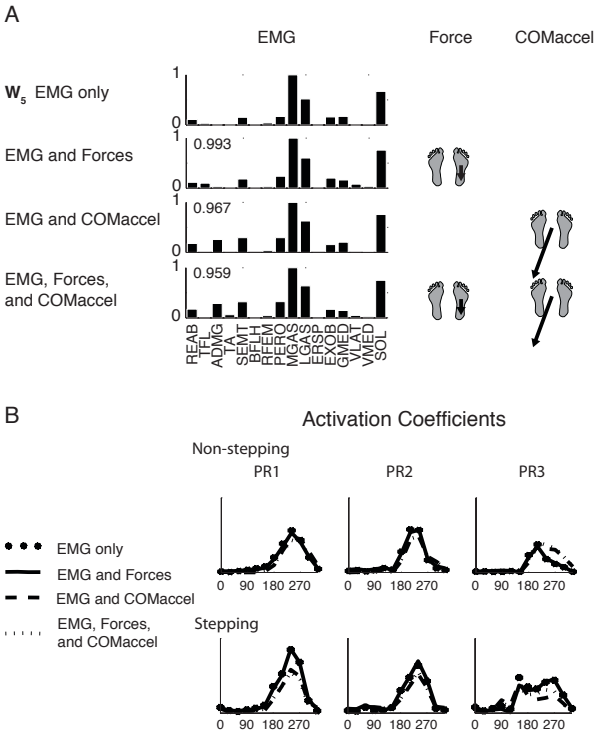


Figure 2.7 Comparison of functional muscle synergies extracted from various combinations of data for a representative subject. Functional variables such as applied forces at the ground and center of mass (CoM) acceleration taken from time windows 60ms after the EMG time windows were included in the analysis and functional muscle synergies were identified. Including the functional variables did not change the composition or recruitment of the identified EMG muscle synergies (r values comparing the muscle synergy vectors are shown). A) Comparison of the muscle synergy vector W_5 extracted from 1: EMG data only, 2: EMG and force data, 3: EMG and CoM acceleration data, and 4: EMG, force, and CoM data. Shown are the EMG portions of each of the functional muscle synergies, which were not changed by including the functional variables, as well as the force and CoM acceleration vectors identified from each extraction. B) Muscle synergy recruitment tuning curves from each of the aforementioned combinations of data. Including the functional variables did not affect the muscle synergy tuning, validating that those forces and CoM accelerations are consistently produced 60ms after that muscle synergy is recruited.

Each functional muscle synergy was composed of specific vectors of EMG, force at the ground and CoM acceleration (Figure 2.8). Because the forces and CoM acceleration values we included were delayed 60ms after the EMG values, we presumed they were the result of recruiting that muscle synergy. For example, in 90º perturbations,

the body initially fell backward, and then in non-stepping responses, appropriate muscles were activated to produce a force forward (W_3, Figure 2.8, red) and accelerate the CoM forward (W_2, Figure 2.8, purple) to return the CoM above the feet. However, in stepping responses, in PR3, W_3 (Figure 2.8, red) was turned off and W_6 (Figure 2.8, dark green) was instead recruited, consistent with producing a force forward and accelerating the CoM backward as the subject stepped backward. One extra functional muscle synergy was required when CoM acceleration is included, comprised only of rightward CoM acceleration, tuned for rightward perturbations, presumably correlated to activity in the other leg, since no muscle synergies in the stance leg were activated for that perturbation direction.

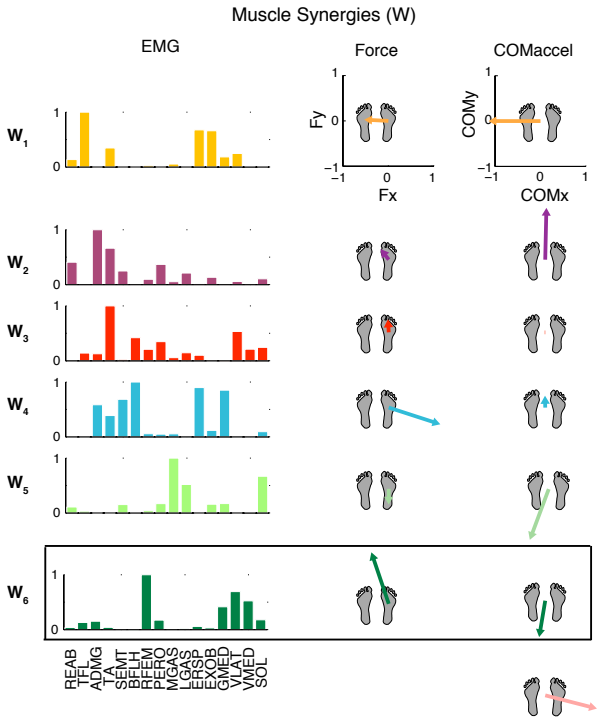


Figure 2.8 Functional muscle synergies for a representative subject. Functional variables such as applied forces at the ground and center of mass (CoM) acceleration taken from time windows 60ms after the EMG time windows were included in the analysis and functional muscle synergies were identified. Shown are the muscle synergies along with the force and CoM acceleration vector associated with each muscle synergy. The pink

CoM acceleration trace is a component identified by the functional muscle synergy analysis that is not attributable to muscle activity in the stance leg.

The functional muscle synergies containing EMGs and biomechanical variables explained variations in EMG, force direction, and CoM acceleration data in both behaviors. EMG and CoM accelerations were well reconstructed for both non-stepping and stepping responses in terms of both direction and magnitude using the functional muscle synergies (r^2=0.77±0.24, VAF=91±11%; Figure 2.9). The forces during stepping responses that were predicted by the functional muscle synergies from non-stepping were in the appropriate directions, but some of the magnitudes were underpredicted (r^2=0.70±0.12, VAF=68±2%), perhaps due to the much larger forces involved when the other leg was lifted off the ground. The r^2 for force reconstructions is comparable to that of EMG and COM reconstructions, but the VAF for force reconstructions is much lower, indicating the force tuning curve shapes were well reconstructed by the muscle synergies, but the magnitudes were not predicted as well. Functional muscle synergies extracted from stepping alone contained larger forces in the same direction as in non-stepping, which may have been due to the different loading conditions in stepping.

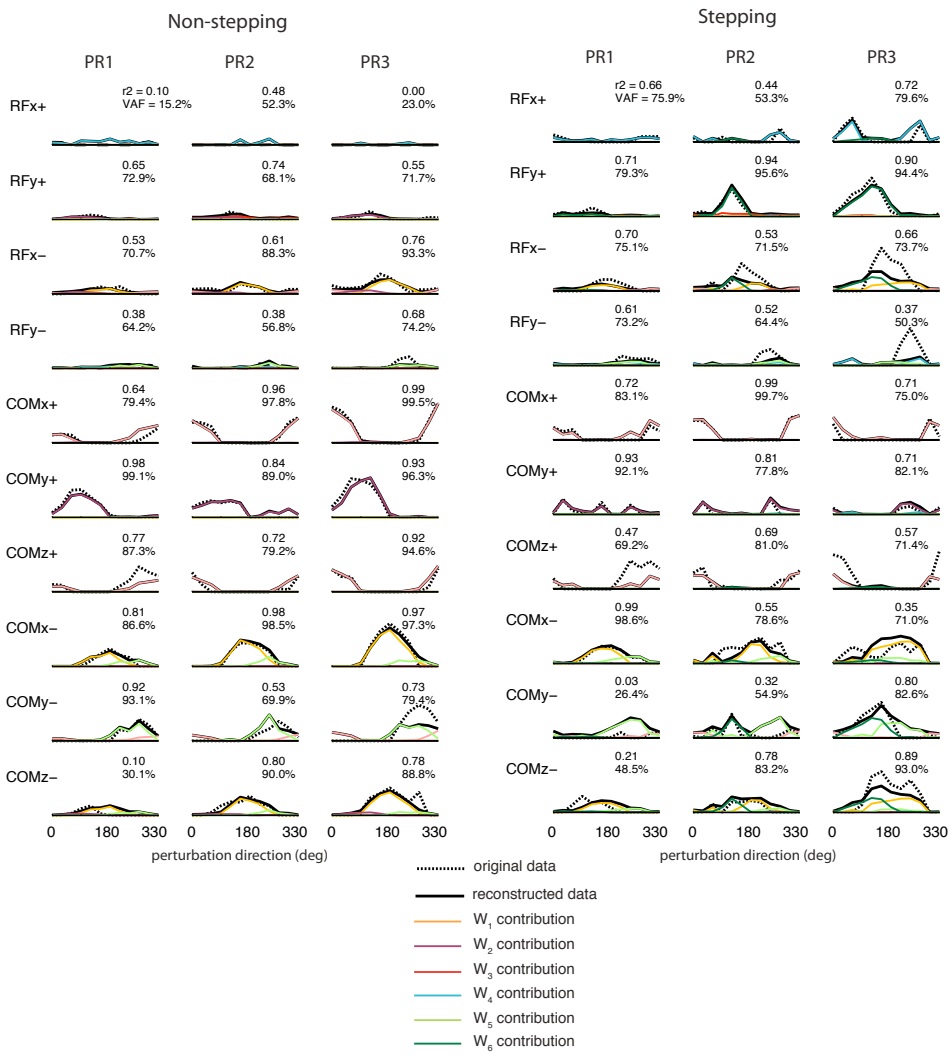


Figure 2.9 Reconstructions of the force and CoM tuning curves using the functional muscle synergies shown in Figure 2.8. Original data are shown by a dashed line and reconstructed data are shown by a solid line (non-stepping in gray and stepping in black). The contribution of each muscle synergy to the reconstruction is shown by the corresponding colored line, all of which are added to generate the total reconstruction. Goodness-of-fit is indicated by r^2 and VAF between each force or CoM acceleration tuning curve and the muscle synergy reconstruction.

2.3.5 Similar muscle synergies were found across subjects

In general, the muscle synergies were robust across subjects**.** Different subjects had different numbers of muscle synergies, but there were commonalities in composition

and tuning of muscle synergies across subjects. W_5 was similar across all 8 subjects ($r=0.74\pm0.07$) and W_4 was similar across 7 of 8 subjects ($r=0.82\pm0.06$). The muscle synergies also performed similar functions, as evidenced by the muscle synergy recruitment tuning curves (Figure 2.10). The subject without W_4 used a different muscle synergy to respond to perturbations in the same direction as W_4, as illustrated by the similarity in the tuning curves of the subject's muscle synergy and that of W_4 in the other subjects. W_3 was another shared synergy similar across 6 subjects ($r=0.75\pm0.05$) and W_1 was similar across 4 subjects ($r=0.75\pm0.10$); the remaining subject had different muscle synergies with similar directional tuning. A few other muscle synergies were unique to individual subjects. Additionally, the stepping-specific muscle synergy, W_6, found in 5 of the 8 subjects was similar across subjects ($r=0.67\pm0.05$) and was recruited for the same perturbation directions.

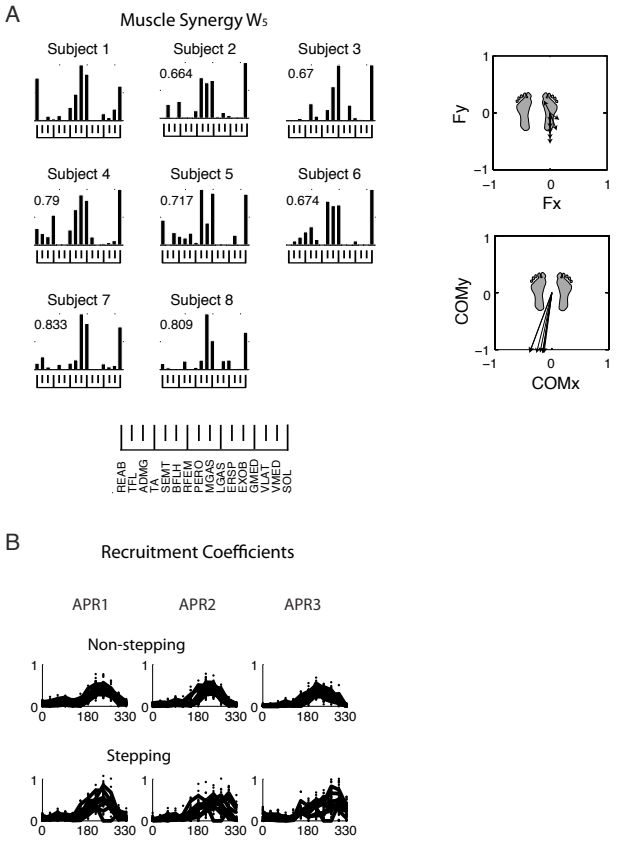


Figure 2.10 Comparison of muscle synergy W_5 and its corresponding force vector and CoM acceleration vector (A), as well as the corresponding recruitment tuning curve (B) across all subjects. One muscle synergy (W_5) was very similar across all subjects, another was similar across 7 of the 8 subjects (W_4), one was similar across 6 subjects (W_3), one muscle synergy was similar across 4 subjects (W_1) and the remaining muscle synergies were subject-specific. In some cases, subjects would use a different muscle synergy to produce a similar force or CoM acceleration, indicating the different strategies people have learned in order to maintain balance.

2.4 Discussion

Our results suggest that muscle synergies reflect the neural organization of the motor system, representing motor modules recruited to achieve a common biomechanical function across different postural behaviors. We observed that the same muscle synergies were recruited during postural behaviors with different movement dynamics (stepping

and non-stepping), but most importantly, their recruitment was determined by the desired direction of CoM motion and not by the perturbation direction. These results demonstrate that the identified muscle synergies do not simply reflect somatosensory patterns triggering the responses, but rather motor modules flexibly recruited to produce biomechanical functions required to stabilize the CoM. Therefore, our results suggest there are separate sensory and motor transformations used by the nervous system to interpret sensory inflow and to construct motor outputs. Consistent neural structures may thus be flexibly accessed and differentially recruited during different motor behaviors by breaking motor activities into their component tasks.

We observed diverse postural responses that became increasingly more complex over time, suggesting the involvement of higher neural centers. While the initial long-latency muscular activity (~100 ms) associated with the automatic postural response was similar in stepping and non-stepping responses, patterns of muscle activity diverged after about 200 ms when a stepping strategy was selected. This observation was consistent across multidirectional postural responses, despite the fact that step latencies varied by direction and step type (i.e., lateral versus crossover steps). We observed lateral and crossover steps in our study due to the constraint that subjects were required to step with the left leg, however, subjects may naturally choose to use crossover steps even when they are not prompted to do so (King and Horak 2008; Perry et al. 2000). Prior studies have also demonstrated similar muscle onset latencies in the same muscles for non-stepping and stepping responses (Burleigh et al. 1994; McIlroy and Maki 1993a), but the changes in the patterns of muscular activity over time were not investigated. Similarly, it has been suggested that stepping responses are triggered only after the failure of a non-

stepping postural response (Horak and Nashner 1986), but our data suggest that stepping muscle activity is initiated before significant destabilization of the body occurs (McIlroy and Maki 1993a). Moreover, the initial muscular response latency during stumbling has been shown to be the same (~50ms), even when later muscle activity (~120ms) corresponding to distinct corrective strategies differ (van der Linden et al. 2007). Long-latency postural response activity at about 100 ms has been demonstrated to be unaffected by cortical pathways (Woollacott and Shumway-Cook 2002) and the concurrent performance of voluntary motor tasks (Trivedi et al. 2010). Only later muscle activity (~150-350 ms) is modified by attentional factors (Woollacott and Shumway-Cook 2002) or secondary motor goals (Trivedi et al. 2010). Thus, the sequence of postural response events following a perturbation may reflect the sequential and increasingly complex influences of nested hierarchy of neural mechanisms (Ting et al. 2009).

Our results suggest muscle synergies represent a common underlying motor structure for postural responses that is independent of specific sensory patterns. We observed the same set of muscle synergies were recruited when the desired CoM acceleration to recover balance was the same in the stepping and non-stepping responses, but the perturbation directions triggering the responses were different. The differences in the timing and spatial organization of individual muscle activity in the stepping and non-stepping responses were largely explained by altering the recruitment of a common set of muscle synergies, with the addition of only a single muscle synergy specific to the stepping behavior. Shared and specific muscle synergies have also been demonstrated across different motor behaviors such as frog swimming, kicking, and jumping (Cheung

et al. 2009; Cheung et al. 2005; d'Avella and Bizzi 2005; Hart and Giszter 2004a; Kargo and Giszter 2000), human balance control (Torres-Oviedo and Ting 2010), and primate hand movements such as grasping (Acharya et al. 2008; Hamed et al. 2007; Overduin et al. 2008). In contrast, a few studies using principal components analysis (PCA) rather than NMF have shown that muscle synergies or m-modes are all reshaped under new conditions (task, time window, etc.) (Danna-Dos-Santos et al. 2007; Robert et al. 2008). The differences in the identified motor modules may reflect a limitation of the chosen decomposition method (Ting and Chvatal 2010; Tresch et al. 2006), or perhaps differences in the type of motor task. Deafferentation studies further support the idea that muscle synergy composition is largely conserved in the absence of somatosensory feedback (Cheung et al. 2005; Giszter et al. 2007; Kargo and Giszter 2000). Moreover, our results suggest muscle synergy recruitment for balance control is determined by task variables such as CoM motion rather than local sensory inputs. This idea is supported by previous studies showing that opposite somatosensory patterns during rotations and translations of the support-surface can elicit the same functional muscle synergies to restore balance (Torres-Oviedo et al. 2006). Although somatosensory feedback is essential for the timing of postural responses (Inglis et al. 1994; Stapley et al. 2002), the muscle activity in the initial postural response reflects task variables such as CoM motion (Gollhofer et al. 1989; Nashner and Mccollum 1985) rather than simple joint angle changes (Nashner 1977; Ting and Macpherson 2004). Task-level information can be derived from aggregate afferent information in the dorsal root ganglia (Weber et al. 2007), as well as in the dorso-spinal cerebellar tract (DSCT) (Bosco et al. 1996). Patterning of the initial postural response is also thought to involve brainstem pathways

(Deliagina et al. 2008; Macpherson et al. 1997). We demonstrated that similar initial patterns of sensory information could differentially recruit the same set of muscle synergies over time. These results are consistent with the fact that the same muscle synergies are also conserved across a wide range of different postural configurations in both humans (Torres-Oviedo and Ting 2010) and cats (Torres-Oviedo et al. 2006). Taken together, muscle synergies appear to be a feature of motor output organization, and are not simply emergent from patterns of sensory inputs alone.

Our results support the idea that muscle synergies are used to organize the musculoskeletal system to produce a predictable biomechanical function (Chiel et al. 2009; Ting and McKay 2007), even in different postural behaviors. We previously demonstrated a consistent relationship between muscle synergy recruitment and endpoint force production in cats across multiple postural configurations (Ting and Macpherson 2005; Torres-Oviedo et al. 2006). The stepping and non-stepping responses to the same support-surface perturbation direction elicited different muscle activity and accelerated the body in different directions. However, our functional muscle synergy analysis revealed common relationships between patterns of muscle activity and the desired biomechanical function across both behaviors. The different individual outputs observed in non-stepping and stepping responses – such as kinematics, forces, and EMGs – arise from recruiting the same muscle synergies in order to accelerate the CoM in an appropriate direction to maintain balance. We observed that during human balance control the functional muscle synergies in humans were aligned with anterior-posterior and medial-lateral directions, whereas in cats, more diagonal forces were observed, possibly due to differences in the upright stance adopted by humans as opposed to the

quadrupedal stance of cats (Dunbar et al. 1986). Muscle synergy recruitment in other motor behaviors has also been related to functional outputs (Ajiboye and Weir 2009; Clark et al. 2010; Krishnamoorthy et al. 2004; Weiss and Flanders 2004), suggesting that muscle synergies are organized according to function in a variety of contexts.

Because of the different mechanical dynamics of non-stepping and stepping responses, we only characterized the gross relationships between muscle activity and horizontal plane acceleration/force direction; however dynamic musculoskeletal simulations would be necessary to make a more quantitative assessment of the biomechanical functions of muscle synergies. Based on prior postural response studies (Jacobs and Macpherson 1996), we assumed that changes in force resulting from muscle activity could be measured at a fixed electromechanical delay of 60 ms following muscle activity. Typically this is a reasonable assumption in the early phases of the postural response because the subject begins by standing quietly, and forces change relatively little prior to the muscle onset latency. In certain perturbation directions evoking stepping responses, the perturbation caused passive loading and unloading that occurred prior to muscle activation changes. Therefore we chose to exclude vertical forces from our analysis and concentrate on the relationship between muscle synergy recruitment and horizontal force generation. Further, we concentrated on the force directions rather than magnitudes of the forces in stepping responses because changes in magnitude might be largely due to nonmuscular, passive dynamics of the body when falling before the step is taken. In some cases the dynamic forces may still have masked the direction of force produced by the muscle synergy. For example, in backward perturbations, the muscle synergies did not correctly predict the CoM acceleration direction during stepping

(Figure 2.9, CoMy–), presumably because the subject fell forward despite recruitment of a muscle synergy that would tend to accelerate the CoM backward. Although a dynamic model of stepping responses would be necessary to accurately differentiate active versus passive changes in force (Berniker et al. 2009; Kargo et al. 2010; Kautz and Hull 1993; McGowan et al. 2010; Neptune and Herzog 2000; Neptune et al. 2009b), a detailed and validated human model of muscle to force interactions during standing balance control is not currently available. Therefore, while not ideal, this analysis provides evidence of directional control of the CoM that results from the recruitment of muscle synergies, and is predictive if not mechanistic.

The decomposition of forces into positive and negative components was based on physiological and methodological reasons and allowed us to reveal possible physiological functions for muscle synergies. First, this separation of forces was made based on previous studies in postural control demonstrating that positive and negative changes in force generation are attributed to different groups of muscles (Jacobs and Macpherson 1996). This is further validated by the relationships previously found between muscle synergy activation and limb force outputs during the initial period of the postural responses in the cat (Ting and Macpherson 2005; Torres-Oviedo et al. 2006). Second, we explicitly separated the components into positive and negative vectors to allow the NNMF synergy extraction algorithm to separately identify correlations between positive and negative changes in forces and EMGs. This is particularly acceptable in postural responses since background levels of muscle activity and forces are low and opposite perturbation directions recruit antagonistic sets of muscles. Thus, we did not use alternative analyses that allow both negative and positive synergy recruitment – such as

PCA – because we believe they are not adequate to reveal physiological relationships between force and muscle activity in this behavior. For example, PCA would allow a muscle to have a negative activation to produce a force in a negative direction (Ting and Chvatal 2010). On the other hand, our analyses attributed positive and negative changes in forces to the recruitment of different muscle synergies – which describes better the antagonistic actions of muscle groups in balance control (Jacobs and Macpherson 1996).

Despite limitations of the analysis techniques, our data indicate that the addition of stance-limb forces or CoM acceleration did not alter the composition of the extracted muscle synergies, suggesting that there was a causal, linear relationship between muscle activity patterns and biomechanical outputs. Our analysis was also competent to reveal a component of CoM acceleration that was not attributable to muscle activity in the stance leg. For example, all subjects had one functional muscle synergy comprised only of CoM acceleration in the rightward and upward directions and no muscle activity tuned for rightward perturbations in non-stepping responses and the early portion of stepping responses (see Figure 2.8). This is consistent with our previous study showing a muscle synergy tuned to rightward perturbations is only revealed during one-legged balance control but not during two-legged balance control (Torres-Oviedo and Ting 2010). Presumably, during two-legged balance control, muscle activity in the left leg (not recorded here) is responsible for producing rightward CoM acceleration in response to rightward perturbations. Furthermore, our functional muscle synergy analysis was competent to decompose the stance-limb forces into components that were attributable to muscle activity in the stance limb versus other sources.

Muscle synergies may reflect spinal and brainstem structures mediating motor control across a variety of behaviors and contexts. Neurophysiological evidence suggests that initial postural responses in the limbs are not simply local reflexes, but rather an activation of a motor pattern to achieve a biomechanical goal (Carpenter et al. 1999; Dufosse et al. 1985). Neurons in the pontomedullary reticular formation (PMRF) are recruited during both reactive and anticipatory postural adjustments (Schepens et al. 2008); these firings are not correlated to individual muscle activity, but discharge in a manner consistent with the goal of restoring equilibrium (Stapley and Drew 2009). It is possible that there exist neural networks that specify the recruitment commands to a muscle synergy (C) which branch with different synaptic weights to the motoneurons of the muscles in the synergy (W) (Hart and Giszter 2010). Motoneuron synchronization has been observed in learning balance tasks (Boonstra et al. 2009), which is consistent with the fact that the recruitment, but not the structure of muscle synergies can be modulated to explain the variation in muscle activity across postural configurations (Torres-Oviedo et al. 2006; Torres-Oviedo and Ting 2010), walking speeds (Clark et al. 2010), as well as in hemi-paretic stroke subjects (Clark et al. 2010). While such modules have been hypothesized to be encoded in the spinal cord for some tasks (Hart and Giszter 2010; Saltiel et al. 2001), postural responses likely require brainstem involvement (Deliagina et al. 2008; Macpherson et al. 1997), possibly in addition to spinal centers (Drew 2008). It remains to be seen whether the same muscle synergies are used in both reactive and voluntary postural tasks, however, similar muscle tuning curves are generated during human whole body reaching tasks as in postural responses to

perturbation (Leonard et al. 2009), suggesting that motor modules may be accessible by voluntary and reactive postural tasks in humans.

CHAPTER 3

SELECTION AND MODULATION OF MUSCLE SYNERGIES DURING PERTURBATIONS TO WALKING

This chapter is in preparation for submission to the *Journal of Neurophysiology*.

Chvatal SA and Ting LH. Selection and modulation of muscle synergies during perturbations to walking. *J Neurophysiol* (in prep).

Our prior work has demonstrated that fixed sets of motor modules called muscle synergies underlie cycle-by-cycle variability in walking and trial-by-trial variability in multidirectional postural responses. Here, we examined whether muscle synergies extracted from walking can account for perturbation responses during walking. We also examined the effect of walking speed on muscle synergy composition and perturbation responses. In unperturbed walking trials, subjects walked along a straight 7.5m path, either at self-selected speed (~1.2 m/s) or slow speed (~0.7 m/s). Subjects stepped on a perturbation platform set flush with the floor at the midpoint of the path. In walking perturbation trials, the platform translated in one of 4 directions (anterior, posterior, medial, and lateral) in the horizontal plane when the subjects stepped on it with their right foot. EMGs of 16 lower-back and right leg muscles were measured. The number and composition of muscle synergies was similar across the two walking speeds. During

walking, perturbations in all four directions caused transient modulation in the activity of walking muscle synergies in the stance limb in most trials. Our results demonstrate that motor patterns used during walking can be recruited in a feedback manner to explain the additional variability caused by an unexpected perturbation during walking in most conditions.

3.1 Introduction

Prior work has demonstrated muscle synergies underlie cycle-by-cycle variability in cyclic behaviors such as pedaling and walking (Clark et al. 2010; Drew et al. 2008; Krouchev et al. 2006; Ting et al. 1999). This suggests the central pattern generator (CPG) for walking recruits muscle synergies in order to account for typical variations in walking, such as slight differences in foot placement, step timing, etc., from one cycle to the next. Here we challenge this hypothesis further by increasing the variability during walking using induced perturbations, to determine the effect of increased variability on muscle synergy recruitment. Afferent information from the periphery influences the central pattern (Dietz 2003), but it is not known if the sensory feedback from a perturbation will disrupt muscle coordination patterns for walking. Can an imposed perturbation during walking elicit differential recruitment of the same muscle synergies used during regular walking, or is a different neural strategy required for the greater variability imposed by a perturbation? Here we examine the muscle synergies underlying walking and the extent to which they are modified when a perturbation is encountered during walking.

Previous work suggests muscle synergy recruitment during locomotion is related to a particular phase of the gait cycle (Ivanenko et al. 2004), but we hypothesize that instead muscle synergy recruitment is related to a global biomechanical function, and that muscle synergies may be recruited at atypical times in the gait cycle depending on the task demands. Prior work suggests muscle synergies may be a mechanism the NS uses to coordinate muscles to produce specific biomechanical functions in order to achieve a behavioral goal (Chiel et al. 2009; Giszter et al. 2007; Ting and McKay 2007). In balance control, muscle synergies in the cat are recruited to produce specific force vectors at the ground that are robust across changes in postural configuration (Ting and Macpherson 2005; Torres-Oviedo et al. 2006). It has been hypothesized that in human standing balance control muscle synergies are recruited in order to control center of mass (CoM) kinematics by modulating end-point forces (McKay and Ting 2008; Torres-Oviedo et al. 2006).

Perhaps muscle synergies used during walking are also recruited to control the CoM. Even though walking is a dynamic condition in which the CoM is not usually located over the base of support of either stance foot (MacKinnon and Winter 1993), the CoM still needs to be controlled during walking to maintain forward momentum and lateral stability. Studying perturbations during walking allows us to investigate the neural control required when an unexpected center of mass (CoM) shift comes during a previously predictable CoM motion.

Here we investigated the neural mechanisms underlying responses to multidirectional perturbations encountered during walking by examining muscle synergies. Although phase and function are coupled in regular walking, here we use

perturbations to decouple them so that we can test whether muscle synergies are phase-dependent or related to function. If muscle synergies are related to a global biomechanical function such as controlling the CoM, we expect to see the same muscle synergies used for walking and for perturbation responses during walking. If instead muscle synergies are phase-dependent, we would expect to see additional muscle synergies used for perturbation responses during walking. We studied perturbations to the stance leg during walking at two different speeds – self-selected and slow – to determine if walking speed affects perturbation responses or muscle synergy structure and recruitment. We studied multidirectional perturbations because the neural mechanisms underlying these responses are unknown. We hypothesized that the same muscle synergies used to control the CoM during walking would be recruited to recover from perturbations during walking. We demonstrate muscle synergies used during walking were recruited in a feedback manner in order to account for the perturbation response during walking for most muscles and perturbation directions.

3.2 Methods

In order to determine whether the same muscle synergies are recruited during postural responses to perturbations in different dynamical contexts, we recorded postural responses to ramp and hold translations of the support surface during regular walking as well as translations during walking. Four perturbation directions were applied in the horizontal plane, and the presentation order was randomized. Muscle synergies were extracted from the unperturbed walking condition and used to reconstruct the perturbed walking trials.

3.2.1 Data Collection

Nine healthy subjects (4 male, 5 female) between the ages of 18 and 26 were exposed to support surface translations according to an experimental protocol that was approved by the Institutional Review Boards of GA Tech and Emory. In the walking only conditions, subjects walked overground slowly (0.6-0.7m/s) or at a self-selected pace (1.2-1.5 m/s) for approximately 7.5 m, or 7 gait cycles. Subjects listened to a metronome beat 4 times before they began walking each trial and were instructed to try to maintain that pace as closely as possible without hearing a metronome while they were walking. Data collection began on the third step, to eliminate any variability associated with gait initiation. Eight trials of unperturbed walking at each speed were collected at the beginning of the experiment condition, in which the subject knew there would be no perturbation. In the perturbed walking conditions, subjects were told there may or may not be a perturbation while they were walking. As subjects crossed a force plate halfway through the path, the platform translated in one of 4 equally spaced directions in the horizontal plane – anterior, posterior, medial, and lateral (displacement 12.4cm, velocity 40 cm/sec, acceleration 0.7g). The perturbation was applied when the force under the right foot had reached 40% of body weight, occurring when the right leg was in early stance. Perturbation directions were randomized, and three trials of each direction for each speed were collected. For each speed, twelve trials of unperturbed walking were collected randomly in between perturbation trials in order to capture any anticipatory responses ("catch" trials). The walking trials collected for each speed were blocked: a

block of self-selected walking trials was collected and a block of slow walking trials was collected separately. The order of the conditions was randomized for each subject.

Since many muscles are required for the component analysis, surface EMG activity was recorded from sixteen lower-back and leg muscles on the subject's right side, which was the stance leg in perturbed walking. The muscles recorded include: vastus lateralis (VLAT), rectus femoris (RFEM), rectus abdominis (REAB), biceps femoris long head (BFLH), semitendinosus (SEMT), adductor magnus (ADMG), erector spinae (ERSP), abdominal external oblique (EXOB), vastus medialis (VMED), tibialis anterior (TA), medial gastrocnemius (MGAS), lateral gastrocnemius (LGAS), soleus (SOL), peroneus (PERO), tensor fasciae latae (TFL), and gluteus medius (GMED). EMG data were sampled at 1080 Hz, and then high pass filtered at 35 Hz, de-meaned, rectified, and low-pass filtered at 40 Hz, using custom MATLAB routines. Additionally, kinetic data was collected from force plates under the feet (AMTI, Watertown, MA) and kinematic data was collected using a motion capture system (Vicon, Centennial, CO) and a custom 25-marker set that included head-arms-trunk (HAT), thigh, shank, and foot segments.

3.2.2. Data Processing

In the walking conditions, in order to reduce computation time, EMG data were downsampled by averaging the data in 10-ms bins. At least three complete gait cycles for each trial were included in the analysis. Although 8 seconds of data were collected, only the first 4-5 seconds of each trial were included in the analysis, because often the subjects reached the end of the pathway before 8 seconds had passed. The precise endpoint used for each subject and walking speed was determined by including the same number of

steps after the perturbation that were collected before the perturbation, and was roughly twice the average perturbation onset time. Trials were concatenated to form the Data matrix; no time normalization was performed. In the walking only conditions, a Data matrix was formed consisting of 6-8 walking trials with no perturbation. For visualization, each row of each data matrix (each muscle) was normalized to the maximum activation of the unperturbed self-selected speed walking trials. Therefore, the self-selected speed unperturbed walking trials' muscle activations ranged from 0-1, and the slow walking trials as well as the perturbed walking trials were all normalized by the same scaling factors. Before extracting muscle synergies, each muscle is normalized to have unit variance (described later), so this 0-1 normalization was purely for visualization and comparison purposes.

3.2.3 Extraction of Muscle Synergies

We extracted muscle synergies from the data matrix of EMG recordings using nonnegative matrix factorization (NNMF) described by Lee and Seung, 1999 (Lee and Seung 1999; Tresch et al. 1999), which has previously been used for muscle synergy analysis (Ting and Macpherson 2005; Torres-Oviedo and Ting 2007). This is a linear decomposition technique that assumes that a muscle activation pattern, M, in a given time period which was evoked by a perturbation in a particular direction is comprised of a linear combination of a few muscle synergies, W_i, that are each recruited by a synergy recruitment coefficient, c_i. Therefore, a particular muscle activation pattern at a particular time in response to a particular perturbation would be represented by:

$$M = c_1W_1 + c_2W_2 + c_3W_3 + \ldots$$

W_i specifies the muscles involved in synergy i and their relative contributions. Each component of W_i represents the contribution of one particular muscle to that synergy, and an individual muscle may contribute to multiple synergies. The muscle synergies do not change composition across conditions, and each one is multiplied by a scalar recruitment coefficient, c_i, which changes over time and across conditions. The recruitment coefficient, c_i, is hypothesized to represent the neural command that specifies how that synergy is modulated over time, and how much each synergy will contribute to a muscle's total activity pattern (Ting 2007).

To determine whether postural muscle synergies are recruited during perturbations to walking, first muscle synergies from unperturbed walking patterns were identified. Each row of the Data matrix (each muscle) was normalized to have unit variance before extracting muscle synergies, and then this normalization is un-done after extracting, to return the data and muscle synergies back to the previous scaling. To determine if bin size affects the muscle synergy structure, and to validate the identified muscle synergies underlying walking are robust, we extracted muscle synergies from data binned in 20ms bins, 50 ms bins, 100 ms bins, and 200ms bins. To determine if anticipation of a perturbation affected the walking pattern and which muscle synergies were recruited during this anticipation, muscle synergies were extracted separately from unperturbed walking trials in which the subjects knew there would be no perturbation, and from unperturbed walking "catch" trials. Furthermore, to determine if walking speed affects muscle synergy recruitment, muscle synergies were extracted separately from self-selected walking catch trials and slow walking catch trials. Similarity between muscle synergies extracted from each speed individually was quantified by calculating

the correlation coefficient (r) between the muscle synergy vectors. A pair of muscle synergies having r>0.623 were considered similar, which corresponds to the critical value of r^2 for 16 muscles (r^2=0.388; p=0.01; see Chapter 2 for muscle synergy comparison details). When we were satisfied that similar muscle synergies are recruited during walking at different speeds, one set of muscle synergies was extracted from a Data matrix consisting of both self-selected walking catch trials and slow walking catch trials, and these muscle synergies were termed "walking" muscle synergies.

The number of muscle synergies required to explain any of these data sets was determined by selecting the least number of synergies that could adequately reconstruct the muscle responses during the unperturbed walking condition (*Nsyn*). The goodness of fit of the data reconstruction using the muscle synergies was quantified by variability accounted for (VAF), defined as 100 x uncentered Pearson's correlation coefficient (Torres-Oviedo et al. 2006; Zar 1999). *Nsyn* accounted for greater than 85% VAF overall. We added the further local criterion that muscle synergies also account for greater than 75% VAF in each muscle. This local fit criterion is more stringent and ensures that relevant features of the data set are reproduced. The number of muscle synergies is increased if local fits were improved. However, if an additional muscle synergy contributed evenly to the VAF across muscles and perturbation directions, it was not included because it likely represented noise in the data rather than variations due to trial or perturbation direction. *Nsyn* was also validated using factor analysis (FA): 1-12 factors were extracted and the log likelihood of each was plotted vs. number of factors. *Nsyn* was chosen by finding the point on the log-likelihood curve where curvature is greatest (Tresch et al. 2006).

3.2.4 Data Analysis

To investigate whether the ongoing walking muscle synergies were differentially recruited during perturbations to walking, the walking muscle synergies were used to reconstruct the perturbed walking trials. VAF and r^2 correlations between measured EMG and reconstructed EMG were computed for a time window 100ms to 400ms after perturbation onset to determine how well the walking muscle synergies can explain the perturbation response.

To visualize which muscle synergies were recruited during postural responses in walking, we quantified the additional walking muscle synergy recruitment required during perturbation responses when compared with unperturbed walking. To this end, we found the area under the recruitment coefficient curve (Cmag) for each muscle synergy during the time window 100ms to 400ms following perturbation onset for each perturbation trial. Likewise, we found the area under the recruitment coefficient curves (Cmag) for the same time window in unperturbed walking catch trials, although instead of based on perturbation onset, this window was based on the vertical force under the right foot corresponding to the force under the foot when a perturbation was triggered in perturbation trials. We averaged Cmag for each muscle synergy across perturbation trials with perturbations in the same direction, and expressed these as percentages of the unperturbed walking Cmag, for each walking speed.

To quantify kinematic modifications in the perturbed gait cycle, we calculated left leg step length and step width, as well as right leg stance time. Left leg step length and width were found by subtracting the heel marker position of the right foot from the heel

marker position of the left foot at the beginning of left stance immediately following the perturbation. The anterior/posterior distance between the left heel and right heel was step length and the medial/lateral distance between the left heel and right heel was step width. These were averaged across trials of the same perturbation direction for each speed and compared to the left step length and width on unperturbed walking catch trials for the step in which the subject crossed the force plate. Additionally, right foot stance times were averaged across perturbed walking trials of the same direction for each speed and compared to unperturbed walking stance times. Stance phase for each foot was determined using heel marker positions.

To determine if the same functional walking muscle synergies are consistently used across subjects, we grouped muscle synergies and calculated the correlation coefficients (r) between all synergy vectors across all subjects. Similar muscle synergies were defined as those having $r>0.623$, which corresponds to the critical value of r^2 for 16 muscles ($r^2=0.388$; $p=0.01$; see Chapter 2 for muscle synergy comparison details). To allow for individual differences when comparing across subjects, we also noted those muscle synergy pairs having $r>0.497$, which corresponds to the critical value of r^2 for 16 muscles using $p=0.05$. This less stringent criterion was also imposed to determine if there were any additional similar muscle synergies across subjects while allowing for individual differences across subjects.

3.3 Results

For all subjects, a few muscle synergies could reproduce walking patterns regardless of walking speed and subjects' anticipatory state. Furthermore, the same

muscle synergies were differentially recruited in response to an unexpected perturbation encountered while walking, and could explain the majority of responses to anterior, posterior, medial, and lateral perturbations during walking.

3.3.1 EMG activity during walking

EMG activity during walking was similar in all unperturbed walking trials, regardless of the subjects' anticipatory state. As has been described before, TA and PERO were active during swing and in early stance, quadriceps (VLAT, VMED, and RFEM) were active at the end of swing and in early stance, hamstrings (SEMT, BFLH) were active during early stance and again in late stance during slow walking, and gastrocnemius muscles were active during midstance and during swing in slow walking. These patterns were also observed during perturbation trials for the step cycles before and after the cycle which included the perturbation.

The magnitude of ongoing muscle activity and perturbation responses depended on walking speed. The magnitude of the ongoing walking EMG was greater in self-selected speed walking than was observed in slow walking (Figure 3.1A). However, the magnitude of the perturbation response relative to the ongoing walking muscle activity was greater in slow walking, as evidenced just after perturbation onset for perturbed walking trials. The muscles that responded to a perturbation during walking were different depending on the perturbation direction. For instance, anterior perturbations elicit posture responses in TA, PERO, and quadriceps, whereas lateral perturbations elicit posture responses in TFL, GMED, and PERO (Figure 3.1B). Although GMED activity

appears low, the posture response is quite high relative to the ongoing muscle activity, indicating it does play a role in medial/lateral stability as has been shown previously.

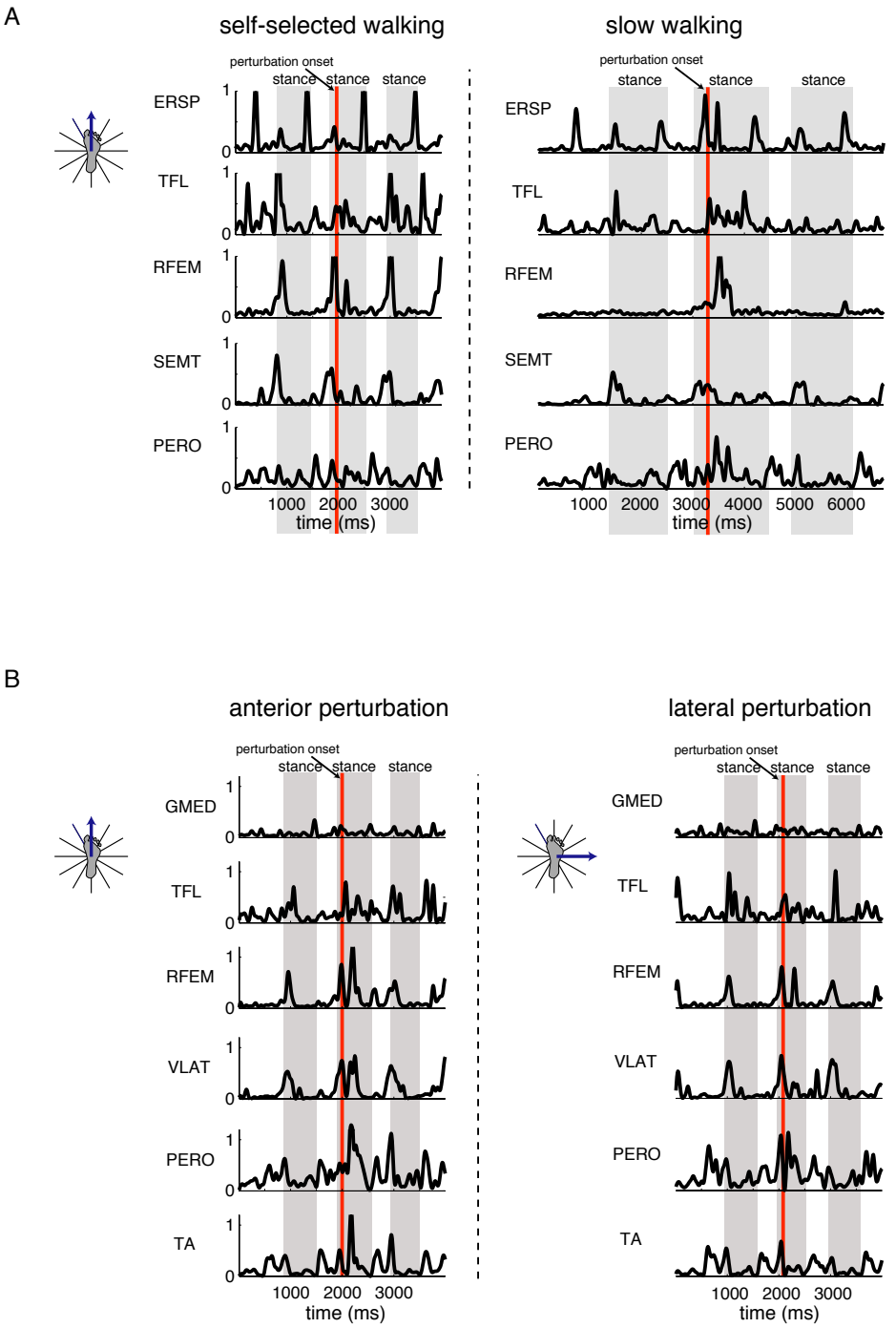


Figure 3.1 Comparison of EMG across walking speeds and perturbation directions. A) EMG during perturbed self-selected speed and slow walking. Red vertical line indicates perturbation onset of an anterior perturbation. Gray shaded boxes indicate stance phase. The magnitude of the ongoing walking EMG was greater in self-selected speed walking than slow walking, but the magnitude of the perturbation response relative to the ongoing walking muscle activity was greater in slow walking. B) EMG during perturbed self-selected speed walking. Shown are one trial that contained an anterior perturbation and one with a lateral perturbation. Different muscles were activated during the perturbation response (time window 100-400ms following perturbation onset) depending on the perturbation direction.

3.3.2 Muscle synergies extracted from various conditions

The composition of muscle synergies underlying walking is not affected by the size of the time window used to smooth the data, validating the robustness of the walking muscle synergies (Figure 3.2). Muscle synergies extracted from walking data binned into 200ms bins, 100ms bins, 50ms bins, 25 ms bins, 10 ms bins, and no bins were similar ($r = 0.93 \pm 0.08$). For bin sizes of 10ms, 25ms, and 50ms, all muscle synergies were similar to those extracted from data which had not been binned at all. For bin sizes of 100ms or 200ms, one muscle synergy was no longer similar to the one extracted from the other bin sizes ($r=0.40$), but all other muscle synergies were similar to those extracted from data which had not been binned at all. Therefore, we selected a 10ms bin in order to reduce computation time and improve visualization while retaining small (and possibly important) variations in muscle activity. The muscle synergies extracted from data binned into 10ms bins were nearly identical to those extracted from data which had not been binned at all ($r=0.98 \pm 0.02$).

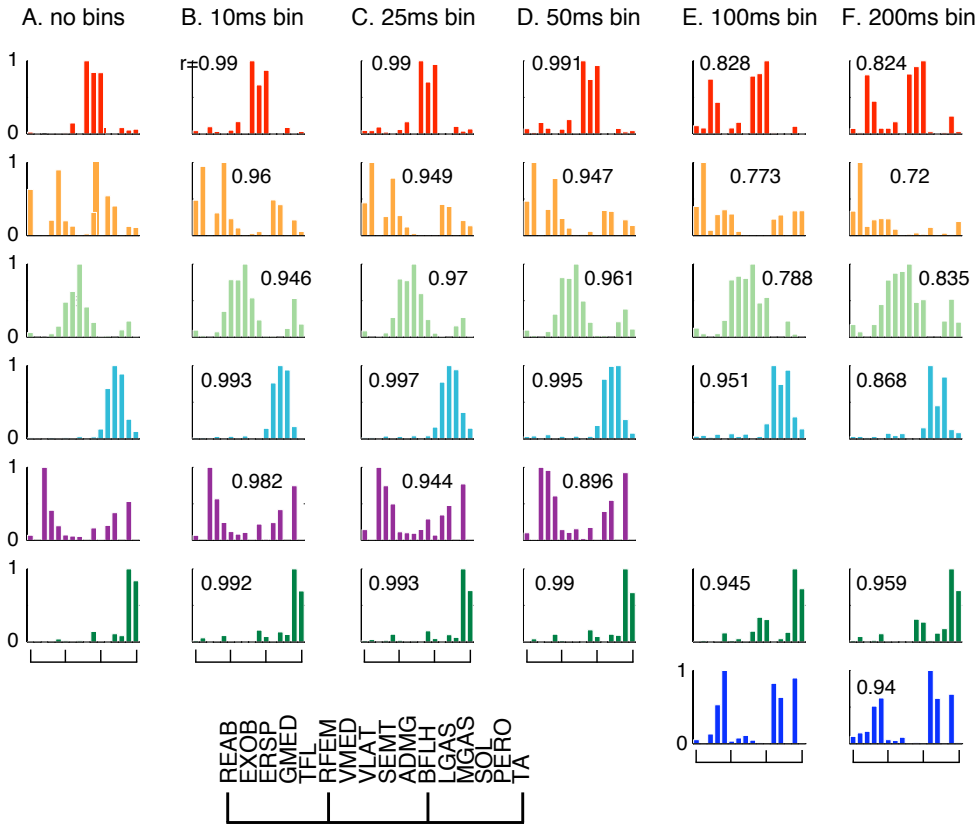


Figure 3.2 Comparison of muscle synergies extracted from walking data binned into different time bins. Shown are the muscle synergies extracted from slow walking catch trials which have either been A) not binned, B) binned into 10ms bins, C) binned into 25ms bins, D) binned into 50ms bins, E) binned into 100ms bins, or F) binned into 200ms bins. Bin size did not affect muscle synergy composition until the bin is 100ms or larger, when only one muscle synergy composition was changed. Correlations between each muscle synergy vector and the corresponding muscle synergy from data that had not been binned at all are shown by r-values.

Muscle synergies were generally robust across walking speeds. 6-8 muscle synergies from self-selected and slow walking data combined were sufficient to explain the variability in the data. Muscle synergies extracted from self-selected speed walking alone were generally similar to those extracted from slow walking alone, and both were similar to muscle synergies extracted from self-selected speed walking and slow walking

together ($r=0.90\pm0.07$, Figure 3.3). Six subjects had one muscle synergy that was used in one walking speed but not used in the other walking speed, usually composed of hamstring or trunk muscles. In four of these subjects, this muscle synergy was identified in the muscle synergies extracted from the combined data consisting of both walking speeds, so the combined set of muscle synergies contain all muscle synergies used in both walking speeds. However, in two subjects, the muscle synergy used only in one walking speed was not identified in the set of muscle synergies extracted from combined data (Figure 3.3).

Muscle synergy composition was generally unaffected by anticipation of a perturbation. For six subjects, the same number of muscle synergies were identified from walking trials in which subjects knew there would be no perturbation as were identified from walking catch trials in which no perturbation was given but one was expected. The composition of the muscle synergies extracted from these two conditions was similar ($r=0.93\pm0.07$, Figure 3.4). For two other subjects, one additional muscle synergy was used in walking catch trials but not in regular walking trials. This additional muscle synergy involved hamstring and/or trunk muscles, depending on the subject. For the remaining subject, one additional muscle synergy with strong contribution from TFL was identified in regular walking trials that was not used in walking catch trials.

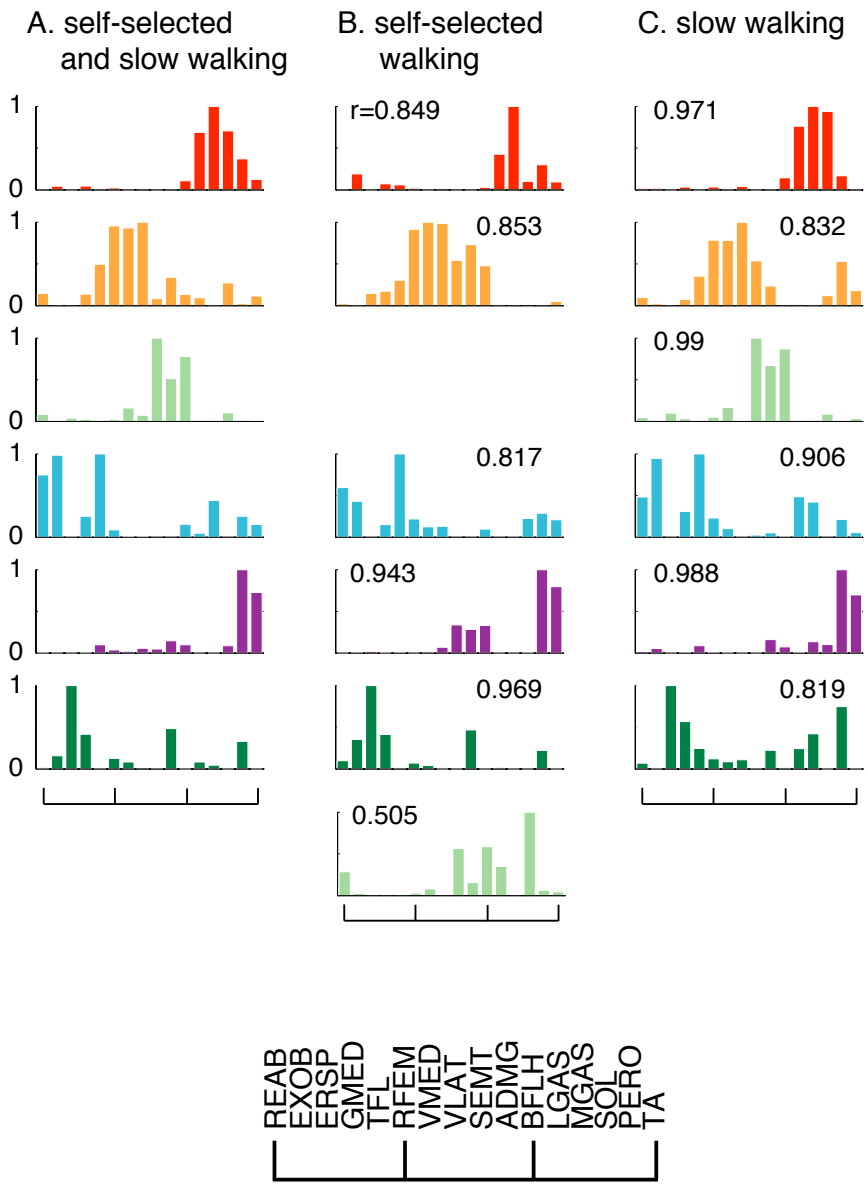


Figure 3.3 Comparison of muscle synergies extracted from different walking speeds. A) Muscle synergies extracted from slow walking trials and self-selected speed walking trials combined; B) muscle synergies extracted from slow walking catch trials; and C) muscle synergies extracted from self-selected speed walking catch trials. Generally walking speed did not affect indentified muscle synergies. Correlations between each muscle synergy vector and the corresponding muscle synergy from self-selected and slow walking data combined are shown by r-values.

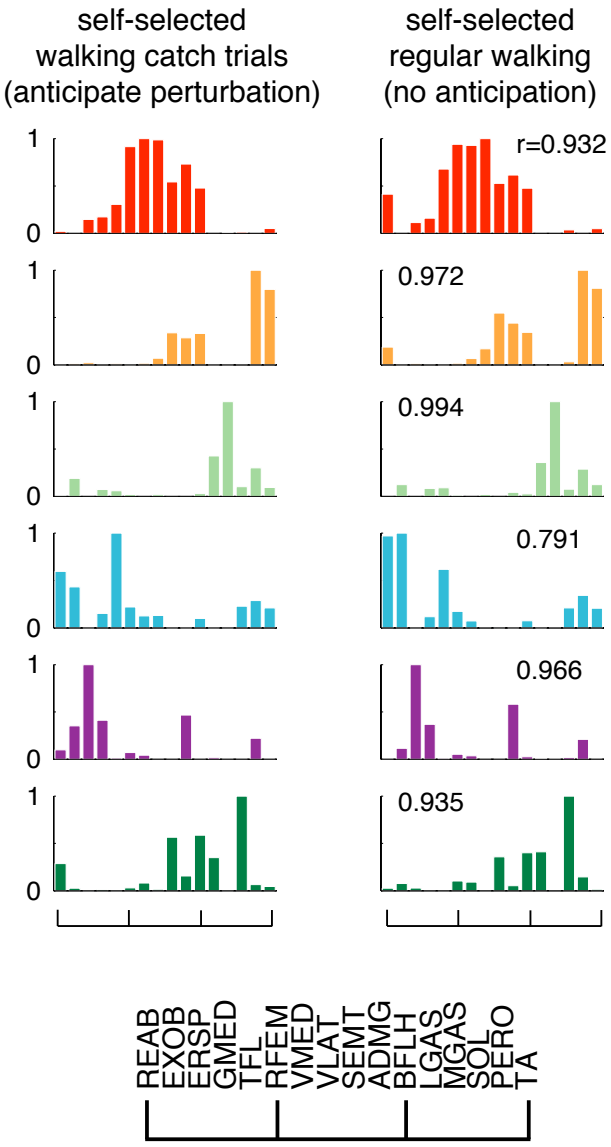


Figure 3.4 Muscle synergies extracted from unperturbed self-selected speed walking with and without anticipation. A) Muscle synergies extracted from (A) walking catch trials (with anticipation) and (B) walking control trials (no anticipation) have similar composition and recruitment. Correlations between muscle synergy vectors are shown by r-values.

3.3.3 Muscle synergies from unperturbed walking can explain posture responses

6-8 muscle synergies extracted from unperturbed self-selected and slow walking data combined for each subject were sufficient to explain 89±3% of the overall variability in the data, and 89±6% of the variability in each muscle across both walking speeds. Each muscle synergy was generally composed of muscles spanning one particular joint or muscles that have a similar function (Figure 3.5, W). For example, W1 had strong contributions from LGAS, MGAS, and SOL, all plantar flexors, and W2 had strong contributions from VLAT, VMED, and RFEM, all knee extensors. These trends in muscle synergy composition were observed in all subjects. Muscle synergies were generally recruited during particular phases of the gait cycle, such as W1 recruited during late stance, and W2 recruited during early stance. However, a few muscle synergies were recruited throughout the gait cycle, composed usually of trunk muscles, such as W4 (Figure 3.5).

Examining the recruitment coefficients of muscle synergies across time, trial, and perturbation direction reveals that the variability in the data is explained by recruiting the same muscle synergies for feed-forward walking, anticipation, and the feedback postural response. When subjects encountered a perturbation during walking, the muscle synergies from unperturbed walking were recruited to account for the perturbation response. In response to a forward perturbation during slow walking, W2, W5, and W6 were recruited strongly 100-400ms after the perturbation (Figure 3.5). Additionally, W2 was recruited even before the perturbation was presented, likely due to anticipation of the perturbation.

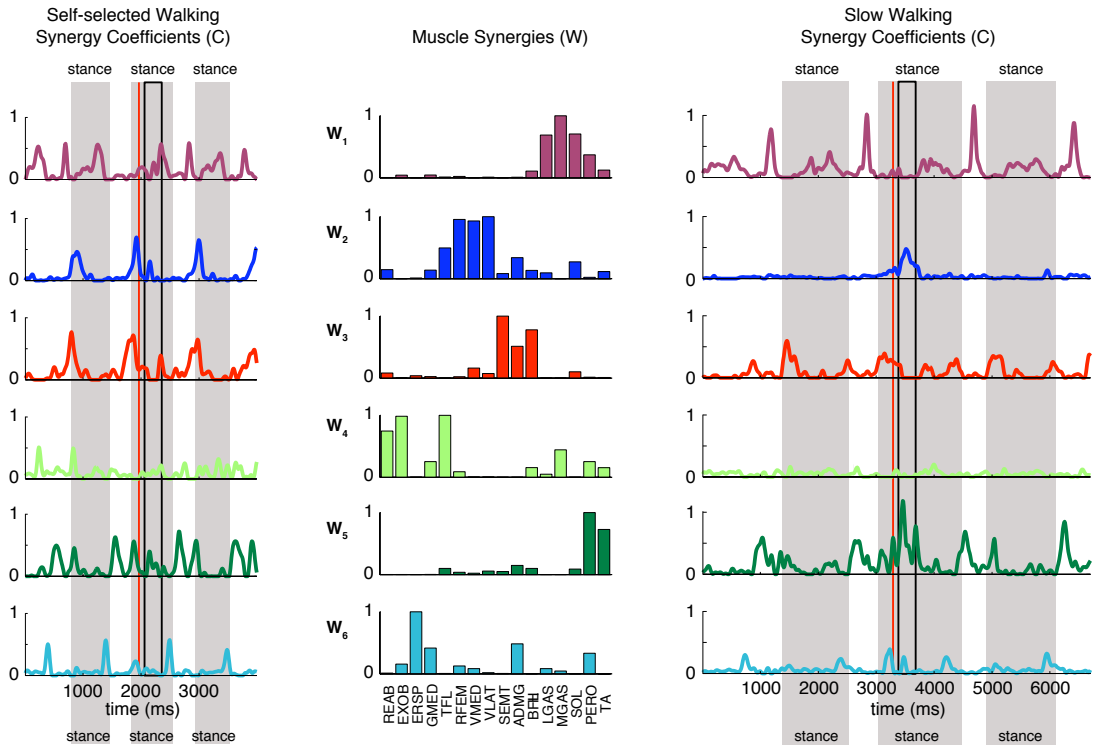


Figure 3.5 Walking muscle synergies and recruitment coefficients for an anterior perturbation trial. Muscle synergies were extracted from self-selected and slow walking catch trials and used to reconstruct perturbed walking trials. Shown are the recruitment coefficients for an anterior perturbation trial at each walking speed.

Walking muscle synergies can explain most of the variability in perturbed walking data at both self-selected and slow speeds (Figure 3.6). For perturbations in the four cardinal directions (anterior, posterior, medial, and lateral), the ongoing walking muscle synergies were differentially recruited to account for the perturbation response. Most of the EMG activity resulting from the perturbation is observed 100-400ms following the perturbation. The muscle activity during this window predicted by recruiting ongoing walking muscle synergies is similar to the recorded EMG during this time window for the majority of all muscle responses, no matter the walking speed or perturbation direction (VAF=91±8.7%, individual muscle reconstructions, Figure 3.6).

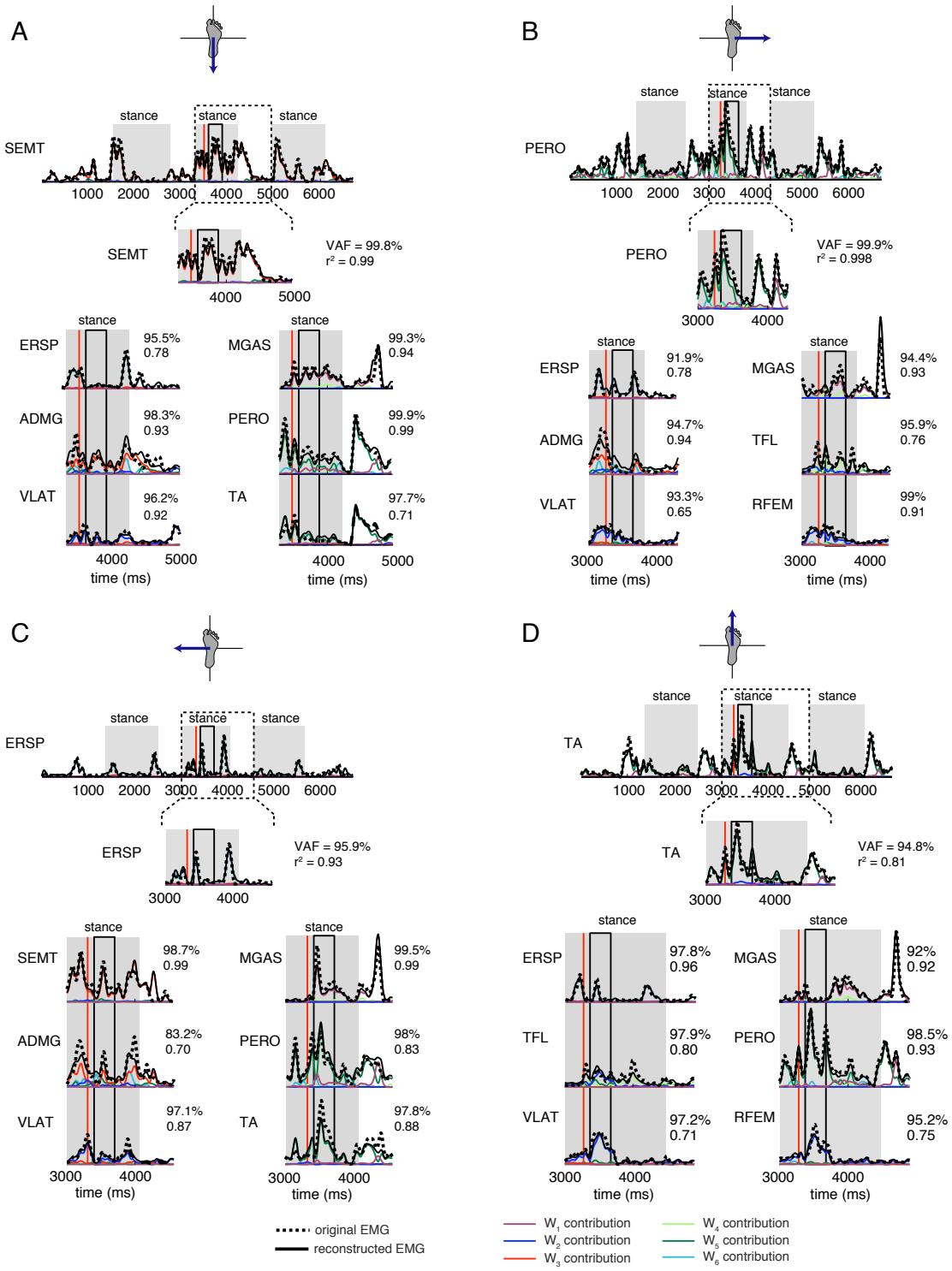


Figure 3.6 Reconstructions of EMG in several perturbed walking trials using the muscle synergies shown in Figure 5. Original data are shown by a dashed black line and reconstructed data are shown by a solid black line. The contribution of each muscle synergy to the reconstruction is shown by the corresponding colored line, all of which are added to generate the total reconstruction. Average VAF between each muscle activation

pattern and the muscle synergy reconstruction is 91±8.7%. A) posterior perturbation during slow walking, B) lateral perturbation during slow walking, C) medial perturbation during self-selected walking, and D) anterior perturbation during self-selected walking. Shown are VAF and r^2 between each EMG and the reconstruction using the walking muscle synergies.

Occasionally a muscle responded to a perturbation and this additional muscle activity was not well reconstructed using the muscle synergies from walking. Of the 8 subjects, 2 walking speeds, 16 muscles, 4 perturbation directions, and 3 trials in each direction (3456 total reconstructions), this was the case for 134 reconstructions (3.8% of all reconstructions). For example, in one lateral perturbation trial, the posture response in TA was overpredicted using the muscle synergies from unperturbed walking, although the responses in the other muscles are well reconstructed (Figure 3.7A). In another subject, the posture responses to an anterior perturbation during walking in VMED and TA were overpredicted using their walking muscle synergies, whereas the posture response in TFL in the same trial was underpredicted using their walking muscle synergies (Figure 3.7B).

3.3.4 Quantification of additional muscle synergy recruitment accounting for perturbation response

Specific muscle synergies were recruited to account for the perturbation response in specific perturbation directions (Figure 3.8). In self-selected speed walking, generally 2-3 muscle synergies were recruited additionally during the perturbation response for each perturbation direction. For example, in self-selected speed walking lateral perturbations, W5 was strongly recruited during the time window 100-400ms after

perturbation onset, whereas W6 was recruited only slightly more than in unperturbed walking (Figure 3.8A). In anterior perturbations, W2 and W5 were strongly recruited during the time window 100-400ms after perturbation onset, relative to unperturbed walking (Figure 3.8B). In medial perturbation directions, W3 is recruited much more than in unperturbed walking, along with W2 and W5. The large additional recruitment of muscle synergies observed in anterior and medial perturbations may indicate greater instability in those directions. In slow walking, generally 1-2 muscle synergies were additionally recruited during perturbation responses. In slow walking, muscle synergy recruitment immediately following the perturbation was not much greater than in unperturbed walking, except W2 was very strongly recruited in anterior perturbations (Figure 3.8B).

3.3.5 Some compensations were made by the swing leg

Different perturbation directions resulted in differential placement of the swing leg following the perturbation (Figure 3.9). A longer step taken by the left leg was observed following posterior perturbations, and shorter steps followed anterior perturbations (Figure 3.9A). Lateral perturbations resulted in a wider step taken by the left leg just after the perturbation, whereas medial perturbations generally resulted in a cross-over step to maintain balance (Figure 3.9B). The right leg stance duration was increased in anterior perturbations, likely due to the additional time required to restore the CoM motion to a forward direction after the perturbation caused it to temporarily accelerate backward (Figure 3.9C). Right leg stance duration was decreased in posterior perturbations as subjects quickly stepped the left foot down to continue walking forward.

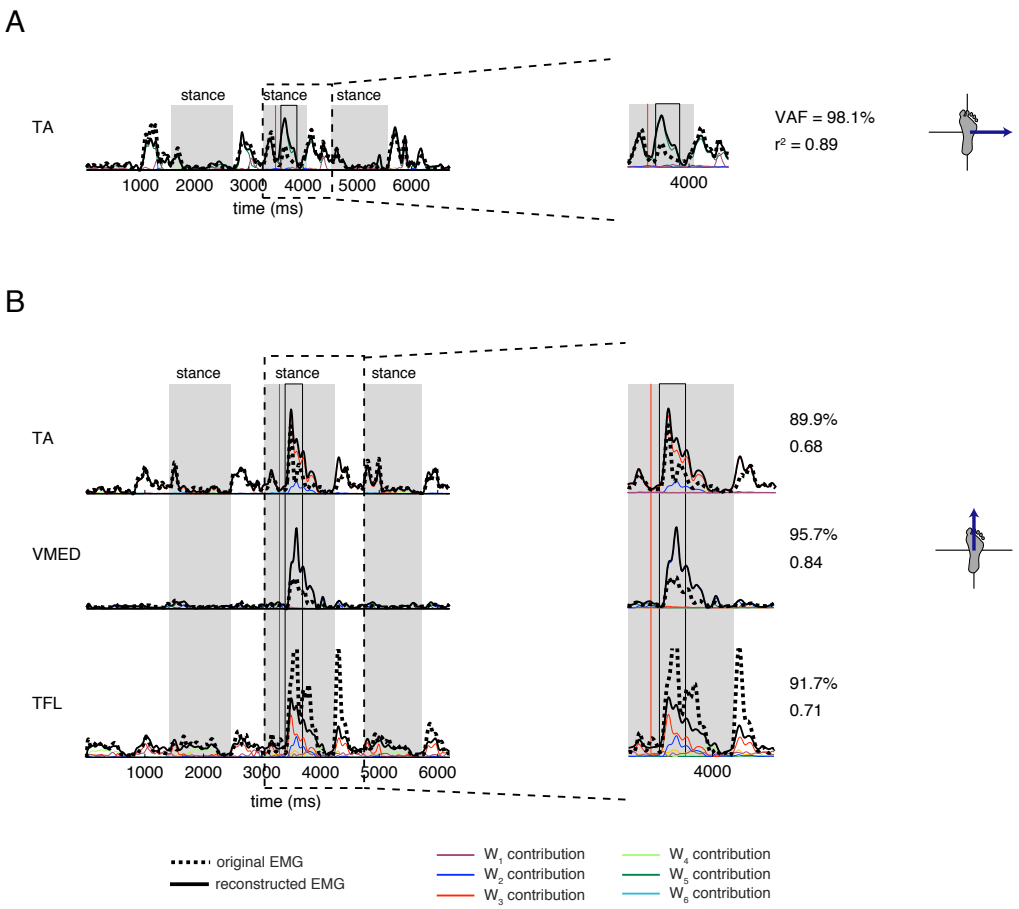


Figure 3.7 Reconstructions of EMG using the walking muscle synergies for a few trials and muscles that were not well reconstructed. A) A lateral perturbation during walking in which the postural response in TA was overpredicted by the walking muscle synergies shown in Figure 5. Original data are shown by a dashed black line and reconstructed data are shown by a solid black line. The contribution of each muscle synergy to the reconstruction is shown by the corresponding colored line, all of which are added to generate the total reconstruction. B) Another subject; anterior perturbation during walking in which the postural response in TFL was underpredicated by their walking muscle synergies (not shown), and the postural responses in VMED and TA were overpredicted by the walking muscle synergies. Shown are VAF and r^2 between each EMG and the reconstruction using the walking muscle synergies.

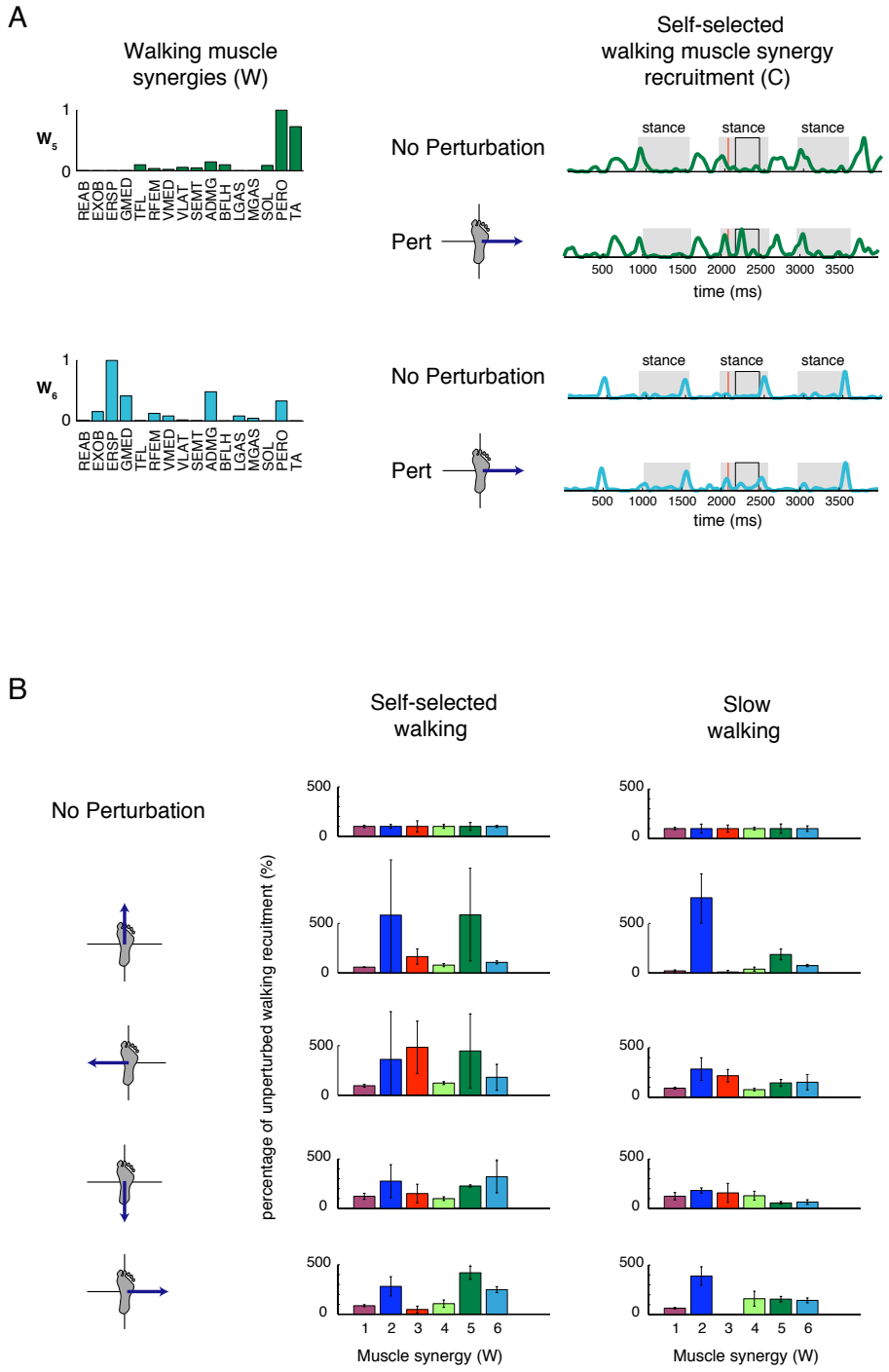


Figure 3.8 Quantification of the additional muscle synergy recruitment that accounts for perturbation responses during walking. A) Two muscle synergies (W_5 and W_6) and their recruitment coefficients for one trial of unperturbed walking and one trial of walking with a lateral perturbation. In perturbation trials, the magnitude of the recruitment coefficient for each muscle synergy was averaged during the time window 100-400ms after

perturbation and expressed as a percentage of the magnitude of the coefficient during the same window in unperturbed walking. B) Average and standard deviation of the magnitudes of muscle synergy recruitment in perturbation responses during walking expressed as a percentage of unperturbed walking recruitment magnitudes across trials of the same perturbation direction. In self-selected speed walking, generally 2-3 muscle synergies were recruited extra during the perturbation response for each perturbation direction. In slow walking, generally 1-2 muscle synergies were additionally recruited during perturbation responses. Different muscle synergies were recruited during perturbation responses in different directions.

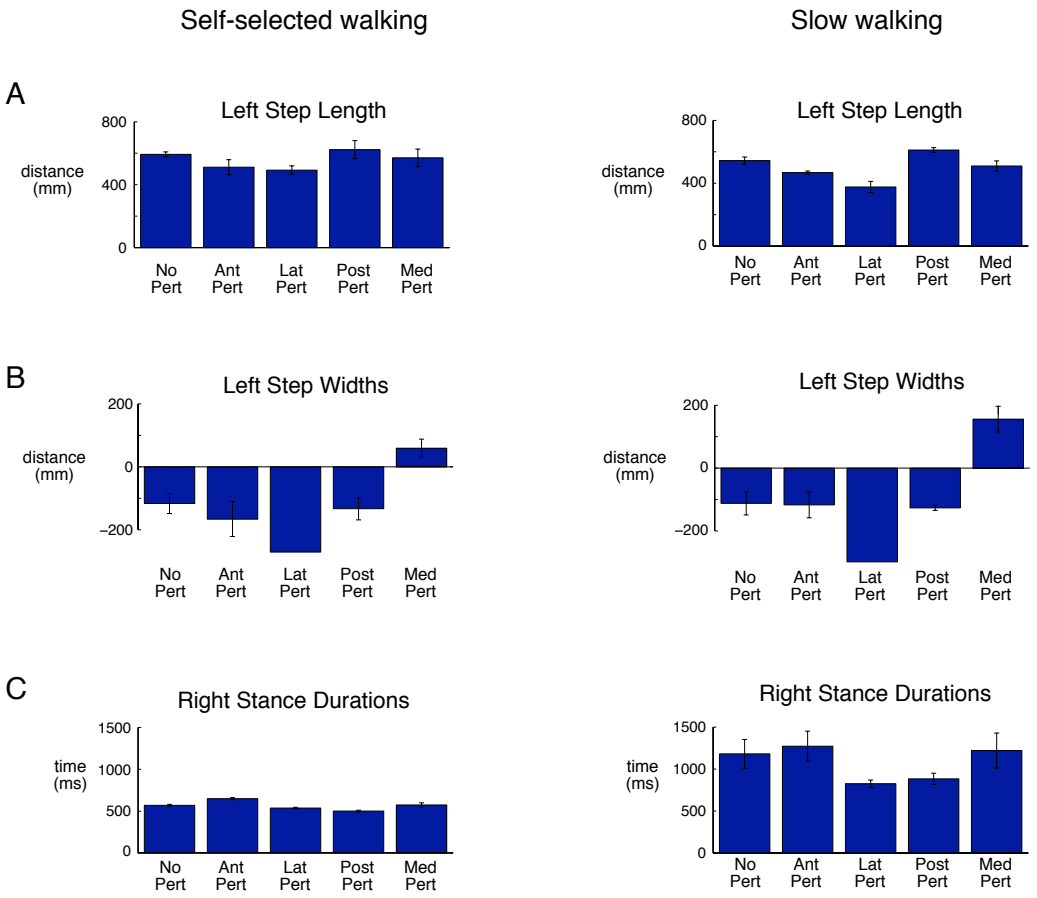


Figure 3.9 Swing leg (left leg) step length (A) and width (B) for self-selected speed walking without perturbations and for each direction of perturbation, illustrating the differential placement of the swing leg used to recover from perturbations. Step lengths and widths are relative to the right foot. Shown are the mean and standard deviation for the left leg step length and width across trials for the one step immediately following the perturbation. C) Right leg stance times for the stance phase which includes the perturbation. Shown are the mean and standard deviation across trials of the same perturbation direction. Anterior perturbations cause a longer stance phase, whereas posterior perturbations shortened stance.

3.3.6 Similar muscle synergies were found across subjects

Different subjects used different numbers of muscle synergies during walking, but there were some commonalities in composition of muscle synergies across subjects (Figure 3.10). W1 and W2 were similar across all subjects (r=0.73±0.14, and r=0.78±0.12, respectively). The muscle synergies were recruited during similar phases of the gait cycle across subjects: W1 recruited during mid- to late stance, and W2 recruited during early stance. W3 was another shared muscle synergy similar across 8 subjects (r=0.86±0.15) and used during late swing and early stance. Subject 2 used a different muscle synergy during late swing/early stance. W5 was similar across 7 subjects (r=0.77±0.14), W6 was similar across 6 subjects (r=0.73±0.13), and W4 was similar across 5 subjects (r=0.82±0.12). A few other muscle synergies were unique to individual subjects, perhaps reflecting prior experience or training.

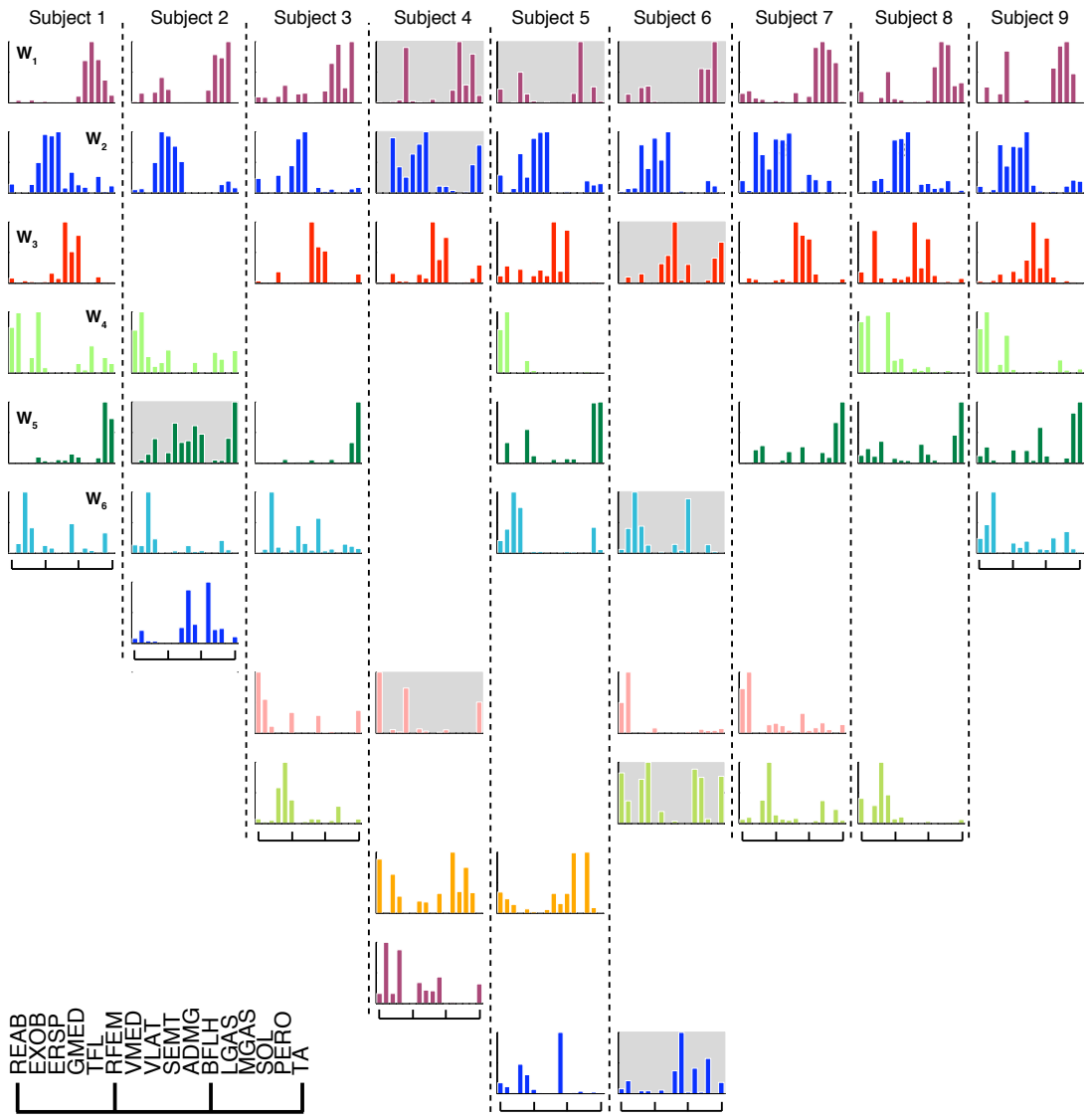


Figure 3.10 Comparison of walking muscle synergies across subjects. Two muscle synergies were similar across all subjects (W1 and W2), and another was similar across 8 subjects (W3). One muscle synergy was similar across 7 subjects (W5), one was similar across 6 subjects (W6), and one was similar across 5 subjects (W4). Similar muscle synergies have r>0.623 (p=0.01) when compared with the corresponding muscle synergy found in Subject 1. Synergies indicated with a gray background have r>0.497 (p=0.05), but less than 0.623 when compared with Subject 1.

3.4 Discussion

Our results demonstrate that muscles synergies used during walking can be recruited in a feedback manner to explain the additional variability caused by an unexpected perturbation during walking in most conditions. We examined whether muscle synergies could help us identify or distinguish feed-forward balance control associated with walking from feedback balance control required in light of an unexpected disturbance. In general, the same muscle synergies were used for both types of balance control, suggesting a common neural mechanism for different balance requirements during walking. Occasionally the walking muscle synergies could not explain the postural muscle activity following a perturbation, so other mechanisms may have been contributing in those instances.

The walking muscle synergies identified here are similar to those that have been described previously (Clark et al. 2010; Neptune et al. 2009a), although we identified a greater number of muscle synergies because we recorded a larger number of muscles. We recorded from 16 muscles as opposed to their 8, including many trunk and medial/lateral muscles which were not included in their study, so we identified 2 muscle synergies in addition to the 4 they identified. The two extra muscle synergies identified here, W_4 and W_6 (Figure 3.5), are composed predominantly of trunk muscles. W_4 is recruited in early stance and throughout the gait cycle and W_6 is recruited in late stance, acting to propel the trunk forward and then stabilize the trunk at the end of stance, respectively. The walking muscle synergy recruitment timings are also similar to those that have been previously identified (Ivanenko et al. 2004). The additional component

identified here (W_4) has strong contributions from muscles REAB and EXOB, which were not recorded in the referenced previous study. It was recruited during early stance in some trials and minimally recruited throughout the entire gait cycle in other trials, possibly providing trunk stabilization during walking. Several muscle synergies were conserved across subjects (Figure 3.10), which may indicate an evolutionary advantage to using these muscle synergies, or may reflect the biomechanics of walking. Other muscle synergies were subject-specific, and may reflect individual differences in prior experiences, training, etc.

Walking muscle synergies were recruited extra on the step in which a perturbation was expected, even before the perturbation was initiated, illustrating the differential recruitment of muscle synergies in anticipation of a perturbation (see Figure 5, W2 recruitment increased before perturbation onset in slow walking). The increased cycle-by-cycle variability induced by feed-forward anticipation was explained by recruiting the same muscle synergies used during unperturbed walking. Anticipation reflects cognitive influences, and this voluntary modification suggests the anticipatory recruitment of the same muscle synergies was possibly achieved via a different pathway from that which recruits muscle synergies in regular walking.

The walking muscle synergies were differentially recruited in a feedback manner in reactive responses to perturbations during walking, suggesting that the recruitment of muscle synergies is not strictly phase dependent, but perhaps instead is related to a biomechanical function, such as controlling the CoM. Walking muscle synergies were recruited in response to perturbations at phases in the gait cycle where they are not typically recruited. Within a single gait cycle we observed modifications in muscle

activity due to the perturbation that are not simply deletions or enhancements of bursts that are already there in walking. Rather than resetting or modifying the CPG pattern, the CPG was able to recruit muscles during a phase that is not typical (McCrea and Rybak 2008). Similarly, previous work in cycling has shown muscle activity during a non-typical phase, demonstrating no phase-resetting (Ting et al. 2000; Ting et al. 1998). This suggests two possibilities: 1) The CPG itself was modified to account for the perturbation, or 2) a postural loop was activated that recruited the same muscle synergies used for walking. It is possible that there exists a CPG controller and a postural controller which both have access to the same set of muscle synergies.

Here we showed the same muscle synergies are used for feed-forward walking (with feedback contributions) and feedback posture responses, as well as anticipation, suggesting that they must be broadly accessible. Walking patterns are thought to be generated spinally, but posture responses generally are considered initiated from higher centers such as brainstem (Honeycutt et al. 2009), due to the necessary integration of various sensory modalities. Current evidence suggests spinal circuits alone cannot generate the coordinated muscle activity required following postural perturbations (Pratt 1994). Our results suggest the muscle synergies themselves are implemented in the spinal cord, but accessible via numerous descending pathways, and their recruitment may be modifiable via cortical control (Drew et al. 2008). A previous study of perturbations to walking showed that responses to afferent input during walking are organized at the spinal level and modulated by supraspinal centers (Field-Fote and Dietz 2007).

As other studies have shown, here we observed that afferent input from the stance limb influenced control of the swing limb (Dietz and Duysens 2000; Dietz et al. 1989;

Reisman et al. 2005; Tang et al. 1998; Ting et al. 2000). Although we did not record EMG from the swing limb (left leg), the differential placement of the foot following perturbations in different directions suggests compensatory mechanisms are used in the NS in response to the afferent input from the perturbed stance limb. Another study supports this idea by finding that balance control during walking is achieved by preprogrammed muscle synergies that may be triggered by multiple sensory cues (Misiaszek 2003).

Here we have shown that postural responses during walking can be explained by walking muscle synergies in most instances, but there were a few muscles/perturbation directions in which the walking muscle synergies either under or over-predicted the perturbation response (Figure 3.7). It is possible that postural muscle synergies were recruited in addition to walking ones to account for the perturbation responses in these instances. Further study is required to expand our examination of perturbation responses during walking to see whether similar neural mechanisms are used for balance control in walking when compared with standing balance.

CHAPTER 4

COMMON MUSCLE SYNERGIES FOR WALKING AND BALANCE CONTROL

This chapter is in preparation for submission to the *Journal of Neurophysiology*.

Chvatal SA and Ting LH. Common muscle synergies for walking and balance control. *J Neurophysiol* (in prep).

Our previous work has demonstrated that fixed sets of motor modules called muscle synergies underlie cycle-by-cycle variability in walking and trial-by-trial variability in multidirectional postural responses. Here, we compared muscle synergies extracted from trials in which subjects encountered a postural perturbation during overground walking to those extracted from trials of either the walking or postural task alone. In walking control trials, subjects walked along a straight 7.5m path. At the midpoint of the path, subjects stepped on a perturbation platform that was flush with the floor. In walking perturbation trials, the platform translated in one of 12 directions in the horizontal plane when the subjects stepped on it with their right foot. In perturbation control trials, subjects maintained balance in response to the same perturbations while standing quietly on the platform. EMGs of 16 muscles in the lower-back and right leg were measured. Although the number of muscle synergies extracted using nonnegative

matrix factorization was greater in walking (6-8 muscle synergies) than in postural perturbations (5-6 muscle synergies), their composition was similar. Muscle synergies extracted from standing balance perturbations and perturbations during walking had similar composition and were recruited for similar perturbation directions. Specific muscle synergies that were only used in one condition were robust across subjects. We have shown similar muscle synergies are used for walking and balance control, suggesting a common neural mechanism for not only balance control in various contexts, but for movement in general. The same muscle synergies appear to be accessible from multiple commands, such as feed-forward recruitment of muscle synergies during walking and feedback recruitment during a postural response.

4.1 Introduction

When two tasks are performed simultaneously, such as in a postural response during walking, it is unclear whether the necessary muscle activations for each task are simply superimposed. Very few studies have considered muscle coordination underlying a situation in which two tasks are performed at the same time. One study suggests that when a subject performs a voluntary task during walking, an additional activation component is simply superimposed on the walking activations to account for the additional voluntary task (Ivanenko et al. 2005). A different study found that when a reaction task (e.g. an arm pull) is performed while walking, the arm movement is not affected by the walking pattern (Haridas et al. 2005). These two studies suggest the two tasks are independent, and have independent control mechanisms that are both activated. However, other studies involving more than one task have shown that typically the

dynamics of the two tasks are not simply juxtaposed (Yiou and Schneider 2007). Instead, it seems that one task will take precedence over another. For example, when subjects perform a voluntary task during a postural perturbation, the posture response takes priority and is expressed (Muller et al. 2007), which suggests the two control mechanisms are not activated simultaneously.

Walking and balance control are two distinct tasks that are hypothesized to be differentially organized, yet have a common goal of controlling the center of mass (CoM). Generally, walking is thought to be achieved via the activation of a spinal CPG with modifications from higher neural centers. However, evidence suggests spinal circuits alone cannot generate the coordinated muscle activity required following postural perturbations (Macpherson and Fung 1999; Pratt et al. 1994), so balance control likely requires involvement from brainstem structures (Deliagina et al. 2008; Macpherson et al. 1997). Are the same neural strategies used for walking used for reactive posture responses? In chapter 2, we showed that muscle synergies are recruited in order to direct the movement of the center of mass (CoM) in standing balance tasks. In a response to a perturbation during walking, the ongoing CoM movements as well as the desired CoM movement are different than in a standing balance perturbation. Even so, EMG responses to perturbations during walking have been observed at a latency of 90-120ms following perturbation onset (Misiaszek 2003; Tang et al. 1998), consistent with the timing of standing postural responses. Therefore, it is possible that similar muscle synergies are recruited to direct the CoM for both walking and reactive posture responses

Although muscle synergies used during walking and standing balance control have been studied in isolation, limited work has been done examining the neural

mechanisms mediating balance control during walking. Walking naturally requires balance control, but it is unknown whether the same neural mechanisms responsible for walking are also controlling balance during walking. When an unexpected disturbance is encountered during walking, are the muscle synergies that underlie a postural response superimposed with the ongoing walking pattern? Here we investigate muscle synergies used to respond to multidirectional perturbations during walking. Previously we have demonstrated that muscle synergies can explain cycle-by-cycle variability in cyclic behaviors such as pedaling and walking (Clark et al. 2010; Ting et al. 1999), as well as trial-by-trial variability in multidirectional postural responses (Torres-Oviedo and Ting 2007). The generality of muscle synergies across cyclic motor tasks has been shown in human walking and running (Cappellini et al. 2006; Raasch and Zajac 1999; Ting et al. 1999) and in forward and backward pedaling (Raasch and Zajac 1999; Ting et al. 1999). In chapter 3, we showed that in most cases, muscle synergies used during walking are recruited differently to account for perturbation responses during walking. We studied four perturbation directions and examined the effect of perturbations on the ongoing walking patterns by using walking muscle synergies to reconstruct perturbation responses.

It is possible that the muscle synergies used during walking are actually the same ones recruited for balance tasks. The generality of muscle synergies across balance tasks has been shown in human stepping and non-stepping responses to standing balance perturbations (Chapter 2). In Chapter 3 we examined walking muscle synergies and whether they could explain perturbation responses during walking. Here we explicitly compared the muscle synergies used for standing balance control with those used for

walking and for perturbation responses during walking. We focused on the perturbation response during walking (rather than the entire walking trial as examined in study 3), and compared muscle synergies used for balance control during standing and walking to determine whether muscle synergies are robustly used across both walking and balance tasks. We studied walking and postural responses to perturbations to the stance leg in 12 directions during standing and during walking at two different speeds – self-selected and slow. We hypothesized that the same muscle synergies are recruited to control the CoM during walking as are used to control the CoM in standing postural responses. We demonstrate muscle synergies used during walking were also used during perturbations to walking and in standing balance perturbations.

4.2 Methods

In order to determine whether common muscle synergies are recruited during postural responses to perturbations in different dynamical contexts, we recorded postural responses to ramp and hold translations of the support surface during standing balance as well as during walking at both self-selected and slow walking speeds. Perturbations in twelve directions in the horizontal plane were delivered in random order in each condition. Muscle synergies were extracted from both the standing balance and walking conditions, as well as from additional trials of unperturbed walking. Muscle synergies and recruitment coefficients from each condition were compared to give insight into neural mechanisms underlying each condition.

4.2.1 Data Collection

Eight healthy subjects (4 male, 4 female) between the ages of 19 and 26 responded to support surface translations according to an experimental protocol that was approved by the Institutional Review Boards of Georgia Institute of Technology and Emory University. All subjects participated in each of the three experimental conditions (standing balance, self-selected speed walking, and slow walking). The order in which the conditions were presented was randomized for each subject.

In the standing balance condition, subjects stood on an instrumented platform that translated in 12 equally spaced directions in the horizontal plane (see Figure 4.1). Subjects were instructed to maintain balance without stepping if possible. A block of ramp-and-hold perturbations in each of 12 directions evenly spaced in the horizontal plane was presented. The platform's displacement was 12.4 cm, velocity was 35 cm/s, and acceleration was 0.5 g. The perturbation directions were randomized within the block of perturbations to minimize subject anticipatory adjustments and increase variability. Five trials of each of the 12 directions of perturbation were collected. All subjects were able to maintain balance without taking a step.

In the walking conditions, subjects walked overground slowly (0.6-0.7m/s) or at a self-selected pace (1.2-1.5 m/s) for approximately 7.5 m, or 7 gait cycles. Subjects listened to a metronome beat 4 times before they began walking during each trial and were instructed to maintain that pace as closely as possible while walking after the metronome was silenced. In slow trials the metronome was set at 60 bpm, and in self-selected trials the metronome pace was determined by having the subject walk at their own pace when they first arrived. Subjects began walking with their right foot, and data

collection began on the third step, to eliminate any variability associated with gait initiation. A single block of walking trials was collected for each walking speed. Eight trials of unperturbed walking were collected at the beginning of each block, in which the subject knew there would be no perturbation. In the remaining trials, subjects were told that there may or may not be a perturbation. Twelve trials of unperturbed walking were collected randomly in between the perturbation trials in order to capture any anticipatory responses. In perturbed trials, perturbations (displacement 12.4 cm, velocity 40 cm/sec, acceleration 0.7g) were applied as subjects crossed the instrumented platform halfway along the path, during early stance phase of the right leg. The platform was instrumented with force plates (AMTI, Watertown, MA), and the perturbation was applied when the ground reaction force at the right foot had reached 40% of body weight. The timing of the perturbation during gait was important – it is possible to have inhibition of sensory feedback at different times depending on the task conditions. Preliminary work showed a perturbation had a lesser effect on the ongoing walking pattern if encountered during late stance. Perturbation direction was randomized, and three trials of each direction for each walking speed were collected.

Surface EMG activity was recorded from sixteen muscles of the lower-back and leg on the subject's right side, the side of the stance leg in perturbed walking. Muscles recorded included: vastus lateralis (VLAT), rectus femoris (RFEM), rectus abdominis (REAB), biceps femoris long head (BFLH), semitendinosus (SEMT), adductor magnus (ADMG), erector spinae (ERSP), abdominal external oblique (EXOB), vastus medialis (VMED), tibialis anterior (TA), medial gastrocnemius (MGAS), lateral gastrocnemius (LGAS), soleus (SOL), peroneus (PERO), tensor fasciae latae (TFL), and gluteus medius

(GMED). EMG data were sampled at 1080 Hz, high pass filtered at 35 Hz, de-meaned, rectified, and low-pass filtered at 40 Hz, using custom MATLAB routines. Additionally, kinetic data was collected from force plates under the feet, and kinematic data was collected using a motion capture system (Vicon, Centennial, CO) and a custom 25-marker set that included head-arms-trunk (HAT), thigh, shank, and foot segments.

4.2.2 Data Processing

In the unperturbed walking conditions, at least three complete gait cycles for each trial were included in the analysis. In order to reduce computation time, EMG data were downsampled by averaging the data in 10-ms bins. Each trial consisted of 4-5 seconds of walking data that was analyzed. The precise endpoint used for each subject and walking speed was determined by including the same number of steps after the perturbation as were collected before the perturbation. Time-courses of EMG from unperturbed walking trials of each subject were concatenated to form the data matrix used for subsequent muscle synergy analysis; no time normalization was performed. The activation of each muscle in each subject was normalized to the maximum activation observed during the unperturbed walking trials at the self-selected walking speed. The elements of each row of the data matrix (each muscle) constructed from unperturbed walking trials at the self-selected speed therefore ranged from 0-1. Identical normalization factors from the unperturbed self-selected walking conditions were used for all other conditions of each subject (see below). Before extracting muscle synergies, each muscle was normalized to have unit variance.

In the standing balance condition, in order to account for temporal variations in muscle activity, three time bins during the automatic postural response were analyzed. The automatic postural response (APR) has been well-characterized and occurs ~100ms following the perturbation (Horak and Macpherson 1996). Due to variations in muscle activity during this APR, we further divided it into three 75 ms time bins beginning 100 ms (PR1), 175 ms (PR2) and 250 ms (PR3) after perturbation onset (Figure 4.1A gray shaded areas). Mean muscle activity for each muscle during each time bin was calculated for each trial. These numbers were assembled to form the data matrix used for subsequent muscle synergy analysis, which consisted of 3 time bins x 12 directions x 5 trials = 180 points for each of the 16 each muscles. For display purposes, each muscle's EMG values were normalized to the same scaling factors as were using in self-selected speed unperturbed walking.

In the perturbed walking conditions, a small time window following the perturbation containing postural response activity was analyzed similarly to the standing balance condition. Mean muscle activity was calculated during three time bins beginning 100 ms, 175 ms, and 250 ms after the perturbation, and assembled to form the Data matrix (Figure 4.1B gray shaded areas). For perturbed walking, the Data matrix consists of 3 time bins x 12 directions x 3 trials = 108 points for each of the 16 each muscles. Each muscle's EMG values were normalized to the same scaling factors as were used in self-selected speed unperturbed walking, to permit data inspection and comparison.

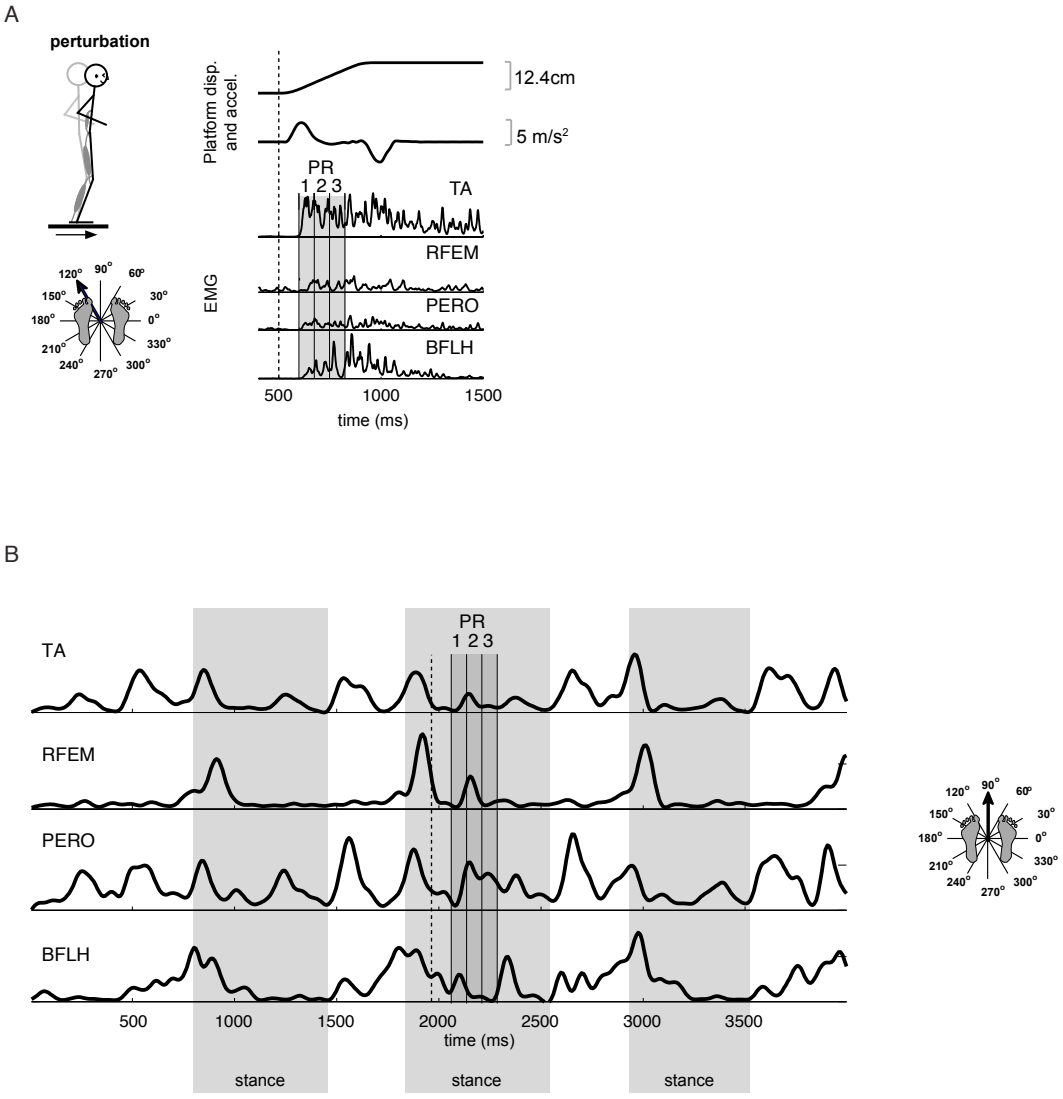


Figure 4.1 Examples of EMG during a standing balance posture response and a walking posture response. A) Example of postural responses to a forward and leftward perturbation of the support surface. Standing balance perturbations were induced by ramp-and-hold perturbations in 12 evenly spaced directions in the horizontal plane. Platform displacement and acceleration profiles used to induce responses are shown. EMG responses occur 100-ms after the onset of platform motion (vertical dashed line). Shown here are tibialis anterior (TA), rectus femoris (RFEM), peroneus (PERO), and biceps femoris (BFLH) EMG responses. Mean EMG activity was calculated for 3 time bins during the automatic postural response (PR), indicated by the shaded region, beginning 100ms (PR1), 175ms (PR2), and 250ms (PR3) following perturbation. B) Example of EMG during self-selected walking and the response to a forward perturbation administered during walking. Ramp-and-hold perturbations in 12 evenly spaced directions were administered during early stance while subjects walked at either self-selected or slow speeds. Shown here are TA, RFEM, PERO, and BFLH EMG during

walking and the postural response. Mean EMG activity was calculated for 3 time bins during the walking postural response (PR), indicated by the shaded region, beginning 100ms (PR1), 175ms (PR2), and 250ms (PR3) following perturbation.

4.2.3 Extraction of Muscle Synergies

Prior to extracting muscle synergies, each muscle vector in the Data matrix was normalized to have unit variance to ensure equal weighting in the muscle synergy extraction. We extracted muscle synergies from each data matrix of EMG recordings using nonnegative matrix factorization (NNMF) (Lee and Seung 1999; Tresch et al. 1999), which has previously been used for muscle synergy analysis (Ting and Macpherson 2005; Torres-Oviedo and Ting 2007). NNMF is a linear decomposition technique that assumes that a muscle activation pattern, M, in a given time period is comprised of a linear combination of a few muscle synergies, W_i, that are each recruited by a synergy recruitment coefficient, c_i. Therefore, a particular muscle activation pattern, M, at a particular time in response to a particular perturbation would be represented by:

$$M = c_1W_1 + c_2W_2 + c_3W_3 + \ldots$$

where W_i specifies the relative contributions of the muscles involved in synergy i. Each component of W_i represents the contribution of one particular muscle to that synergy, and an individual muscle may contribute to multiple synergies. The muscle synergies do not change composition across conditions, and each one is multiplied by a scalar recruitment coefficient, c_i, which changes over time and across conditions. The recruitment coefficient, c_i, is hypothesized to represent the neural command that specifies how that synergy is modulated over time, and how much each synergy will contribute to a muscle's total activity pattern (Ting 2007). After extracting muscle synergies, the unit

variance scaling was removed from data so that each muscle's data was returned to the scale where 1 is the maximum activation during self-selected speed unperturbed walking, in order to permit comparison of responses and muscle synergies across conditions.

First muscle synergies were extracted from unperturbed walking patterns in order to later compare with muscle synergies used during postural responses. Since we previously showed that the similar muscle synergies are identified when each walking speed is analyzed individually (see Chapter 3), one set of muscle synergies was extracted from a data matrix consisting of both self-selected speed unperturbed walking catch trials and slow unperturbed walking catch trials, and these muscle synergies were termed "walking" muscle synergies. The goodness of fit of the data reconstruction using the muscle synergies was quantified by variability accounted for (VAF), defined as 100 x uncentered Pearson's correlation coefficient (Torres-Oviedo et al. 2006; Zar 1999). The number of muscle synergies selected *(Nsyn)* was determined by choosing the least number of synergies that could account for greater than 90% of the overall VAF. We added the further local criterion that muscle synergies also accounted for greater than 75% VAF in each muscle. This local fit criterion was more stringent and ensured that relevant features of the data set are reproduced. *Nsyn* was also validated using factor analysis (FA): 1-12 factors were extracted and the log likelihood of each was plotted vs. number of factors. *Nsyn* was chosen by finding the point on the log-likelihood curve where curvature is greatest (Tresch et al. 2006).

Next, muscle synergies were extracted from the postural responses in each of the remaining three perturbed conditions: standing balance, slow walking, and self-selected walking. For each dataset, we selected the least number of muscle synergies (*Nsyn*) that

satisfied both the global criterion of reconstructing at least 90% of the overall variance (VAF ≥ 90%) as well as the local criterion of reconstructing at least 75% of the variability in each muscle and each perturbation direction. VAF for each muscle quantified the extent to which the muscle synergies accounted for variability in the activity of individual muscles across all time bins, perturbation directions, and trials. VAF for each perturbation direction quantified the extent to which the muscle synergies accounted for the variability in muscle activation patterns formed by the response of all 16 muscles to a single perturbation direction during one time bin across all trials.

4.2.4 Data Analysis and Muscle Synergy Comparison

Once *Nsyn* was selected for each condition, the muscle synergies were used to reconstruct the EMG patterns, and measured and reconstructed data were compared for a particular muscle, time bin, and perturbation direction for each trial to examine the ability of the muscle synergies to account for inter-trial variations. Similarities between measured and reconstructed data were quantified using r^2 and VAF (Torres-Oviedo et al. 2006; Zar 1999). To determine similarity in muscle synergies used for walking and balance control, the muscle synergies were compared across conditions. When comparing two sets of muscle synergies, we calculated correlation coefficients (r) between each muscle synergy vector in the first set and each in the second set. A pair of muscle synergies were considered "similar" if they had $r > 0.623$, which corresponds to the critical value of r^2 for 16 muscles (r^2=0.388; p=0.01; see Chapter 2 for muscle synergy comparison details). To determine if similar neural mechanisms are used for walking and balance control, we compared walking muscle synergies with muscle

synergies extracted from standing balance perturbations and walking perturbations. Across perturbation conditions, we compared the tuning curves of similar synergies to determine if they were recruited for similar perturbation directions in different contexts. We examined the composition and tuning of any condition-specific muscle synergies to determine their potential functions.

4.3 Results

For all subjects, a few muscle synergies reproduced both walking patterns and responses to multidirectional balance perturbations, accounting for temporal, spatial, and inter-trial variability in muscle activation patterns in walking, balance, and combined walking and balance tasks. The majority of muscle synergies extracted from standing balance perturbations and perturbations during walking had similar composition and were recruited for similar perturbation directions. Any identified muscle synergies that were only used in one condition were robust across subjects.

4.3.1 Individual muscle activation differs across perturbation conditions

Muscle tuning curves demonstrate that muscle activation was different during the postural response in standing balance perturbations than during postural responses while walking slowly or at a self-selected speed (Figure 4.2). For example, ERSP was activated for the same perturbation directions in all conditions (forward and leftward), but was activated much more strongly in walking perturbation responses than in standing perturbation responses. TFL was recruited during forward/leftward standing postural responses, but was recruited following rightward perturbations during walking. Other

muscles were recruited for the same perturbation directions, and roughly the same magnitudes, in both standing and walking conditions. For example, MGAS was recruited strongly for backward perturbations in both standing and walking conditions.

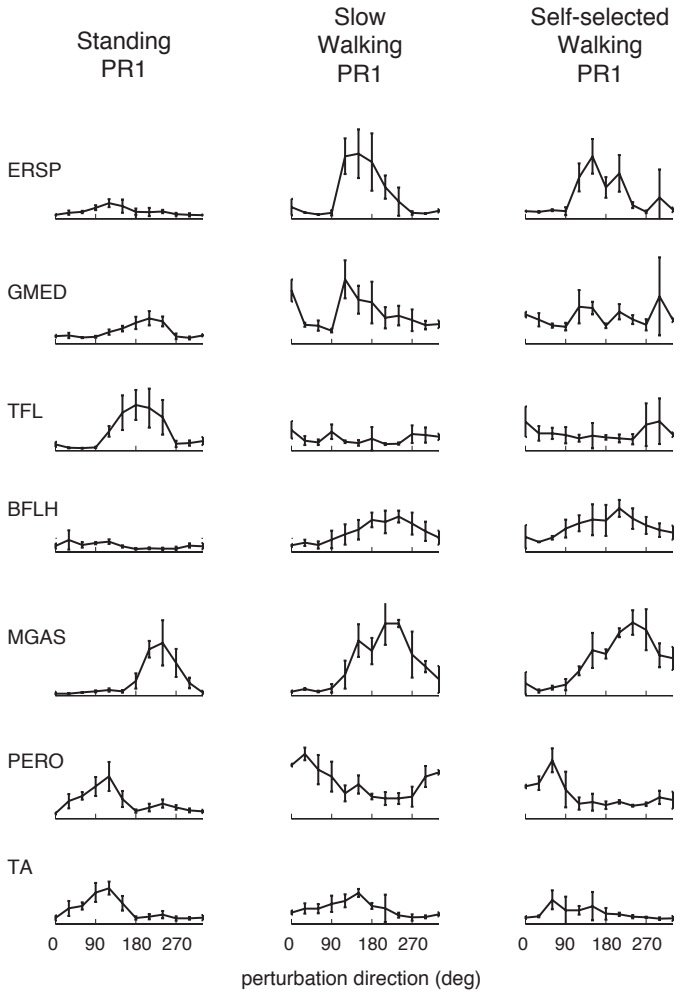


Figure 4.2 Muscle tuning curves from standing balance perturbations and perturbations during slow and self-selected walking. Shown are the tuning curves for seven muscles (ERSP, GMED, TFL, BFLH, MGAS, PERO, and TA) during time window PR1 for a representative subject. Shown are the mean tuning curves ± standard deviations for 5 trials in each perturbation direction, presented randomly. Muscle tuning curves vary in magnitude across perturbation directions, and their shapes vary from muscle to muscle. Some muscles have consistent tuning across perturbation conditions (standing, slow walking, self-selected walking), while other muscles have different tuning across conditions.

4.3.2 Similar muscle synergies were used in standing balance and unperturbed walking

Although unperturbed walking generally required a greater number of muscle synergies than standing postural responses, the compositions of the muscle synergies used for walking and standing postural control were similar (Figure 4.3). In unperturbed walking, six to eight muscle synergies from walking data from both walking speeds were sufficient to explain the variability in the EMG data (VAF overall=89±3%, muscle VAF=88±6%). In postural responses to standing balance perturbations, five to six muscle synergies per subject were sufficient to account for >90% total variability and >75% variability in each muscle and condition (all 3 time bins, 12 perturbation directions, across 5 trials of each) in the EMG data. For three of seven subjects, all of the muscle synergies used in standing postural responses were also used in walking. For the remaining four subjects, all but one to two postural muscle synergies were also used in walking. The postural muscle synergies used in standing balance but not in walking usually either had large contributions from TFL and were active for medial/lateral perturbations, or had large contributions from TA and PERO and were active for anterior perturbations. Muscle synergies used in unperturbed walking that were not used in standing balance postural responses were only weakly recruited during slow walking (Ww6, Figure 4.4). These muscle synergies were comprised of hip/trunk muscles and were recruited throughout various phases of the gait cycle in both slow and self-selected walking (unlike the other walking muscle synergies that are recruited at particular phases), suggesting they may play a role in trunk stabilization during walking.

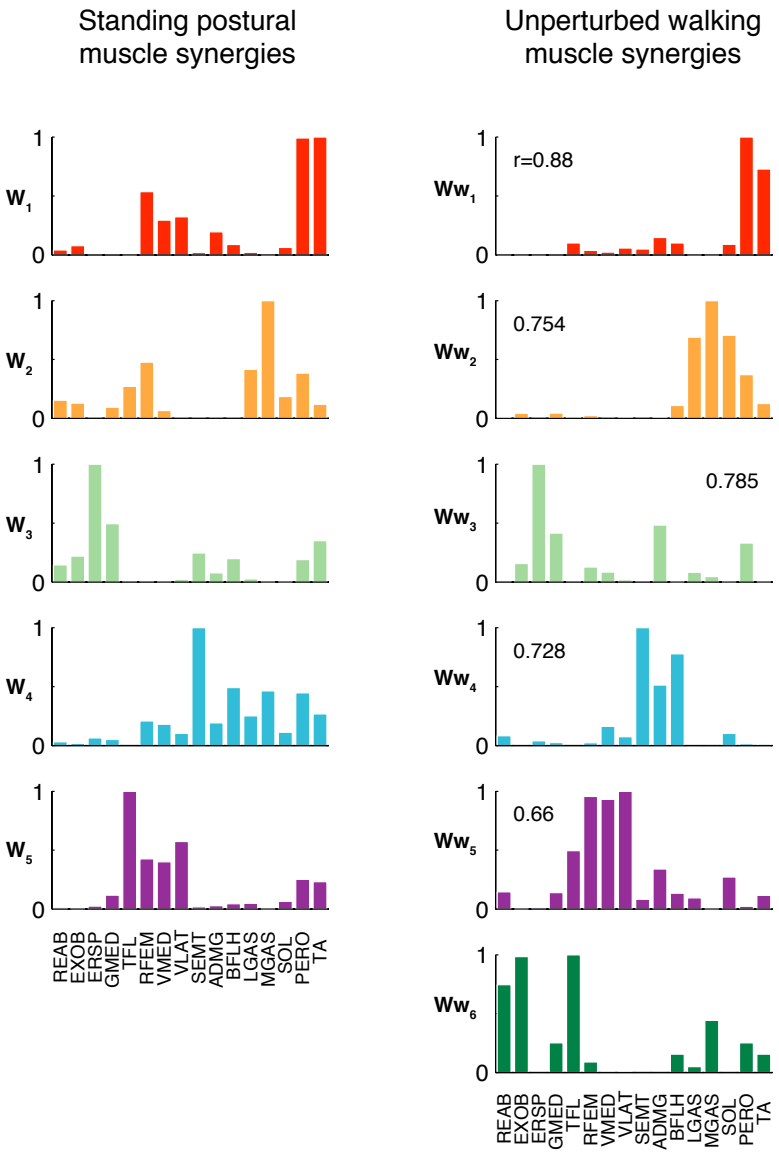


Figure 4.3 Comparison of standing postural muscle synergies and unperturbed walking muscle synergies. A pair of muscle synergies having r > 0.623 was considered similar. Muscle synergies extracted from standing balance perturbation responses were similar to those extracted from the entire timecourse of many trials of unperturbed walking. In this subject, one additional muscle synergy was identified from walking that is not used in standing postural responses. Correlations between muscle synergy vectors are shown by r-values.

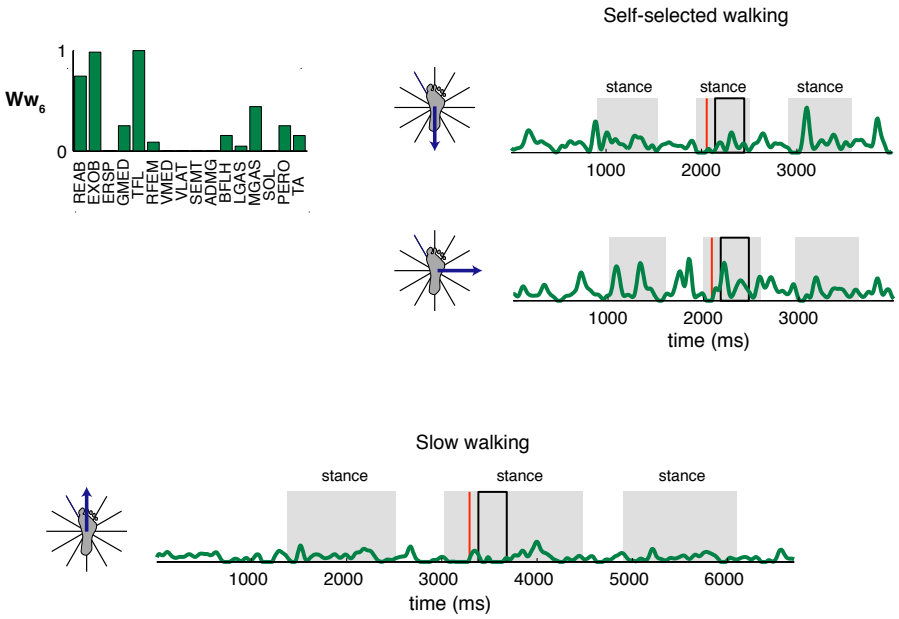


Figure 4.4 Muscle synergy recruitment coefficients for muscle synergies that were specific to regular walking. Ww6 was recruited during walking but not during postural responses in any condition. Shown are the recruitment coefficients for the trials containing: a backward perturbation during self-selected walking, a lateral perturbation during self-selected walking, and a forward perturbation during slow walking. Ww6 is weakly recruited in slow walking and recruited throughout the gait cycle in self-selected walking, suggesting it plays a trunk stabilization role during walking.

4.3.3 Similar muscle synergies were used during standing balance and perturbed walking

Muscle synergies extracted from perturbed walking postural responses were also similar to the muscle synergies from standing postural responses (Figure 4.5). For five of seven subjects, all but one of the muscle synergies extracted from slow walking perturbation responses were identified in standing perturbation responses. For the other two subjects, two muscle synergies were identified in slow walking posture responses that were not used in standing posture responses. Furthermore, all but one of the muscle

synergies extracted from self-selected walking perturbation responses were used in the other perturbation response conditions. There were generally two muscle synergies extracted from self-selected speed walking perturbation responses that were not used in standing perturbation responses, one of which was similar to the muscle synergy specific to slow walking perturbation responses (Figure 4.5). The other self-selected speed walking postural response muscle synergy that was not used in standing balance was similar to a walking muscle synergy for most subjects.

4.3.4 Muscle synergy tuning reveals the function of muscle synergies across conditions

Many similar muscle synergies were identified across all perturbation conditions (standing, slow walking, and self-selected walking) and most were recruited for the same perturbation directions in all conditions (Figure 4.6). W1, W2, and W3 were used in standing perturbation responses as well as postural responses during both slow and self-selected walking. W2 was recruited for backward perturbations in all conditions, and W3 was recruited during postural responses to medial/lateral perturbations in all conditions. Some muscle synergies were recruited for different perturbation directions in the different conditions. For example, W1, comprised of strong contributions from TA and PERO, was recruited for forward and backward perturbations in standing postural responses, but was instead recruited for lateral and forward perturbations in slow walking postural responses and self-selected postural responses. Although differentially recruited, the same muscle synergies could account for perturbation responses in standing and walking conditions.

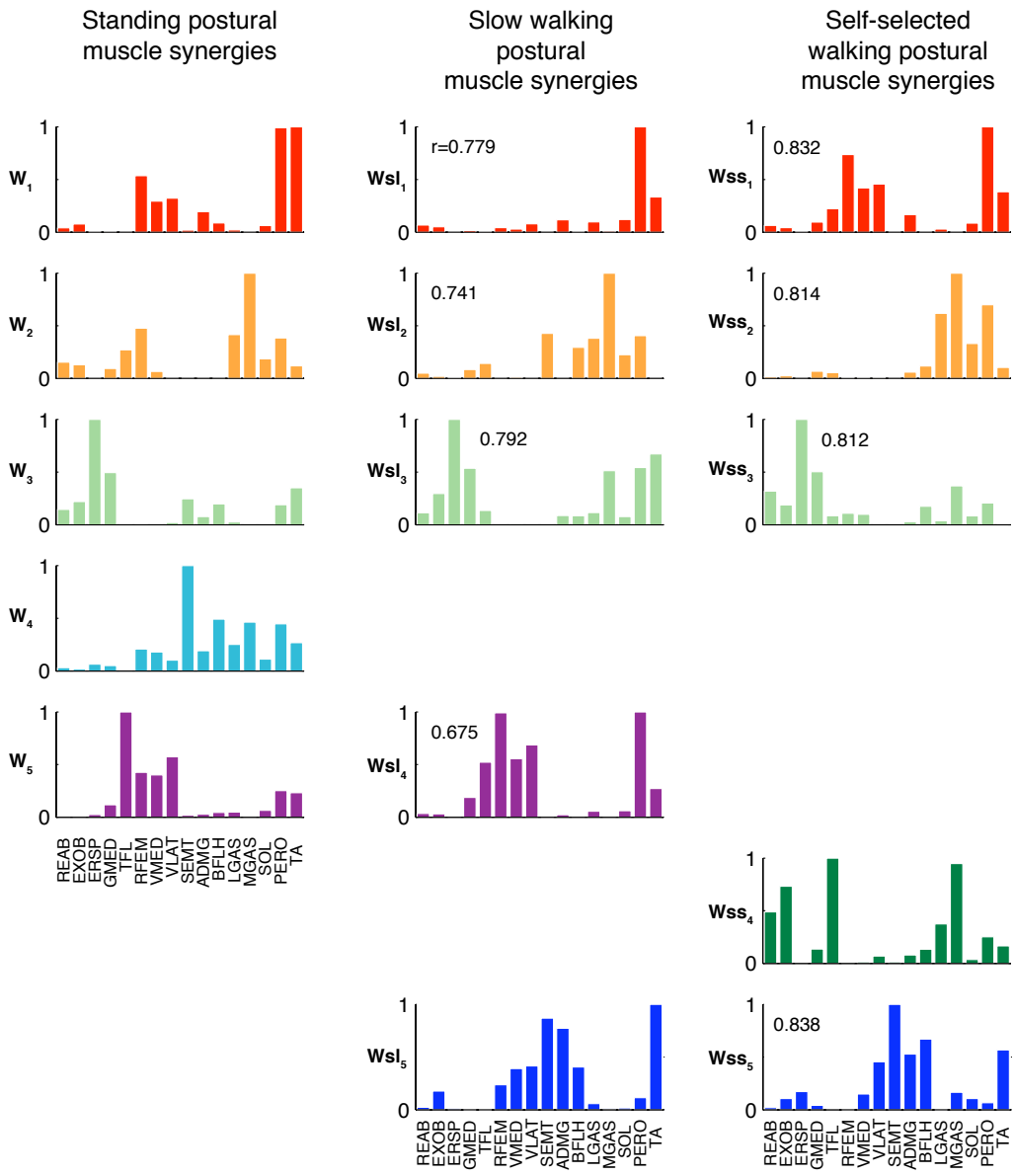


Figure 4.5 Comparison of muscle synergies extracted from perturbation responses in the 3 conditions studied here (standing balance, slow walking, and self-selected walking). Muscle synergies were extracted from the 3 PR time periods (100-325 ms following perturbation) in each condition. All but one of the muscle synergies used in slow walking postural responses was similar to those used in standing balance postural responses. All but one of the muscle synergies used in self-selected walking perturbation responses was similar to those used in standing and/or slow walking postural responses. Correlations between each muscle synergy vector and the corresponding muscle synergy from standing balance are shown by r-values.

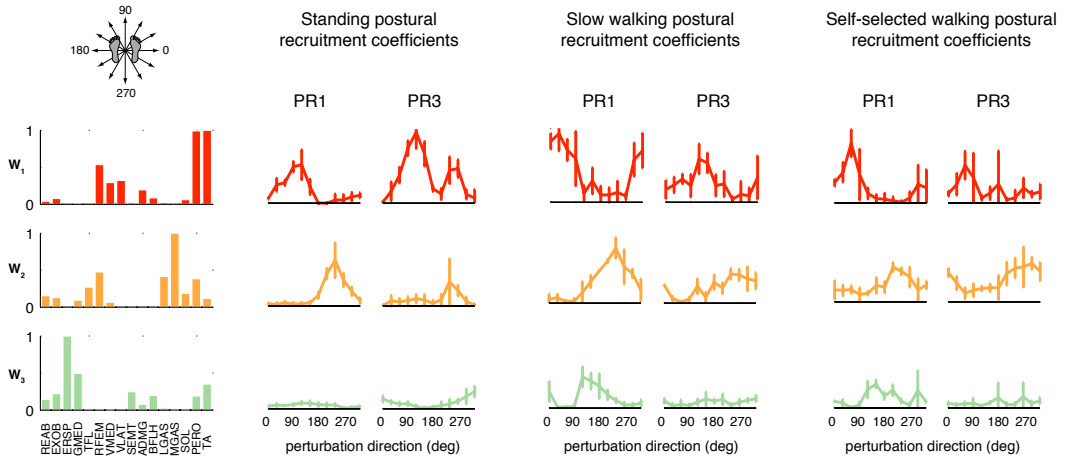


Figure 4.6 Muscle synergy recruitment tuning curves for similar muscle synergies across standing and walking perturbation responses. W1, W2, and W3 were used in standing perturbation responses as well as postural responses during slow and self-selected walking. W2 was recruited for backward perturbations in all conditions, whereas W3 was recruited for medial/lateral perturbations. W1 was recruited for anterior/posterior perturbations in standing postural responses, and for anterior and lateral perturbations in walking postural responses.

The muscle synergies specific to walking perturbation responses were strongly recruited for medial/lateral perturbations. One muscle synergy used in slow and self-selected walking perturbation responses (Wsl5 and Wss5 see Figure 4.5) had strong contributions from hamstring muscles and TA, and was recruited following medial perturbations during walking (Figure 4.7A). An additional muscle synergy identified during self-selected postural responses (Wss4), was similar to a muscle synergy used in unperturbed walking (Ww6, Figure 4.3, r=0.86), and was not strongly recruited in any perturbation direction, so it possibly instead was playing a trunk stabilization role. In another subject, the additional muscle synergy used in walking postural responses that

was not used in standing postural responses had strong contributions from PERO and TFL and was recruited in response to lateral perturbations during slow and self-selected walking (Figure 4.7B). Several subjects used a muscle synergy with similar composition and tuning to this one, which resembles a muscle synergy previously identified that emerges in postural responses when a subject is standing on one leg (Torres-Oviedo and Ting 2010).

The muscle synergies specific to standing perturbation responses were usually recruited for forward and backward perturbations. W4 was recruited for both forward and backward perturbations in PR2 and strongly recruited for backward perturbations in PR3 in standing postural responses, but was not used in walking postural responses (Figure 4.8A). Interestingly, W4 was used during regular walking (see Figure 4.3). Four subjects had a muscle synergy tuned for backward perturbations in standing that was not used in walking perturbation responses. Another subject had a muscle synergy with strong contributions from REAB, EXOB, and TA, which was strongly recruited following forward perturbations in standing but was not used in walking postural responses (Figure 4.8B). A separate set of four subjects had a muscle synergy tuned for forward perturbations in standing that was not used in walking perturbation responses.

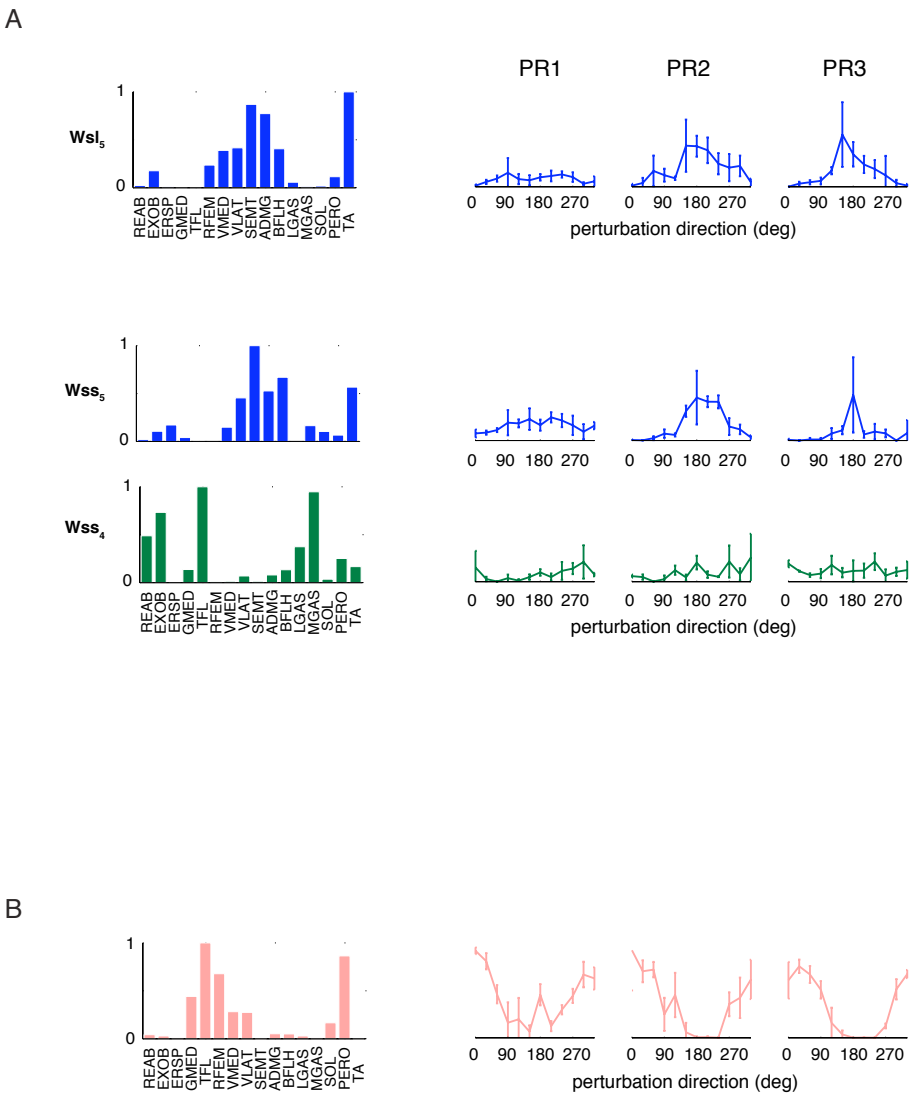


Figure 4.7 Muscle synergy recruitment tuning curves for muscle synergies that were specific to walking postural responses. A) Wsl5 and Wss5, tuned for medial perturbation directions, were used during walking postural responses but not standing postural responses. Wss4 was used during self-selected walking postural responses and regular walking, but not during slow walking or standing postural responses. B) A muscle synergy used during walking postural responses but not standing postural responses for another subject, tuned for lateral perturbations during walking. Muscle synergies used in walking postural responses that were not used in standing postural responses were recruited for medial or lateral perturbation directions.

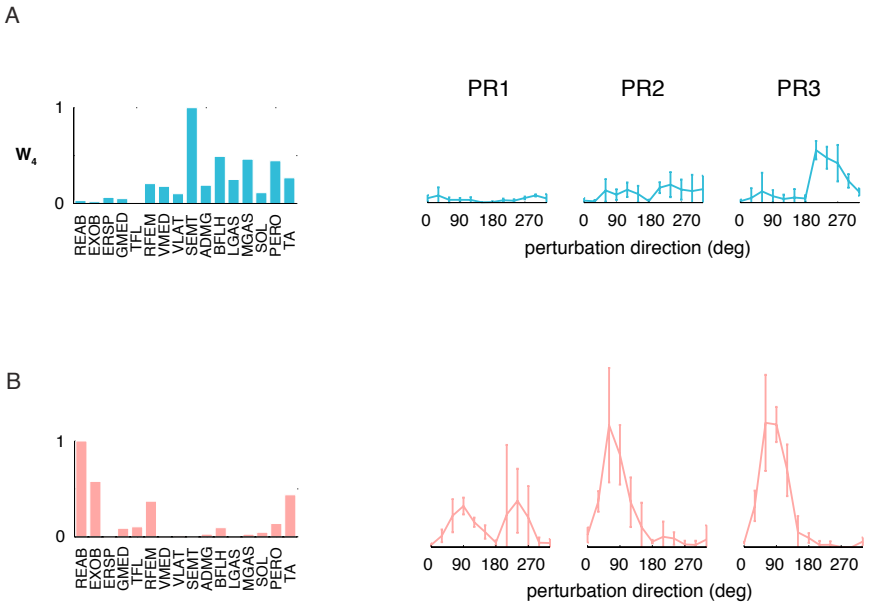


Figure 4.8 Muscle synergy recruitment tuning curves for muscle synergies that were specific to standing postural responses. A) W4, tuned for backwards perturbations, was used during standing postural responses but not walking postural responses. B) A muscle synergy used during standing postural responses but not walking postural responses for another subject, tuned for forward perturbations while standing. Muscle synergies used in standing postural responses that were not used in walking postural responses were recruited for forward or backward perturbation directions.

4.4 Discussion

We have shown that similar muscle synergies are used for walking and balance control, suggesting a common neural mechanism for not only balance control in various contexts, but for movement in general. Our results demonstrate that muscle synergies are recruited from a common pool to generate walking patterns as well as respond to perturbations during standing and walking. The same muscle synergies appear to be accessible from multiple commands, such as feed-forward recruitment of muscle synergies during walking and feedback recruitment during a postural response. The CNS

appears to be using an integrated motor program built from shared (and some more specialized) motor modules in a variety of motor tasks.

Differences between muscle synergies used in the various conditions studied here reflect differences in the functional demands of the tasks in the different contexts of each condition. For instance, the extra muscle synergies identified from walking perturbation responses that were not used in standing perturbation responses were tuned for medial/lateral perturbation directions (Figure 4.7). Their composition and tuning was similar to the task-specific muscle synergy identified previously that emerged when a subject responded to standing balance perturbations while standing on one leg (Torres-Oviedo and Ting 2010). The perturbation here was administered during early stance while the subject was standing on one leg only, so these additional muscle synergies needed to be recruited. In standing postural responses it is likely that the left leg contributed largely to maintaining balance in the medial/lateral directions. Perhaps these muscle synergies would also be used in different walking situations that require greater medial/lateral corrections, such as turning or walking in a circle.

Likewise, most of the muscle synergies found in standing perturbation responses that were not used in walking perturbation responses (usually only one muscle synergy per subject) were tuned for anterior/posterior perturbations (Figure 4.8). Presumably during walking the forward momentum of the body moves the body forward so an extra muscle synergy is not needed to pull the body forward. Similarly, in walking the overall goal is to continue progressing forward, so an additional muscle synergy that would pull the body backward is not needed either. Any extra muscle synergies used in unperturbed walking that were not used in perturbation responses tended to have very low recruitment

during slow walking and were active throughout different portions of the gait cycle in self-selected walking (Figure 4.4). These muscle synergies (usually one per subject) were comprised of hip/trunk muscles, suggesting they may be playing a role in trunk stabilization during walking. Despite these differences in muscle synergies recruited in each condition, generally the muscle synergies identified here were robustly used across distinct motor tasks of balance and locomotion.

Several biomechanical functions are common across walking and postural control, and may explain why similar muscle coordination patterns are used in both tasks. In balance control, the CoM must be maintained above the base of support (BoS) to prevent falling. Even though walking is a dynamic condition in which the CoM is not usually located over the base of support of either stance foot (MacKinnon and Winter 1993), the CoM still needs to be controlled to maintain a certain speed during walking. Additionally, both walking and balance control require additional functions such as body support and trunk stabilization. In addition to these shared functions, other functions are performed during walking, such as limb propulsion and deceleration each gait cycle, trunk propulsion, and foot placement. Nevertheless, the muscle synergies used during balance control tasks were also used during walking, and thus were able to account for all of these various functions.

Our results suggest these muscle synergies are encoded in the CNS and accessible via multiple pathways. Walking patterns are thought to originate from activation of a spinal CPG, but can be modified by higher centers (McCrea and Rybak 2008). Here the walking patterns likely had some involvement from the cortex due to the instructions given to the subjects. There was an aspect of intentionality to their walking because they

were instructed to try to match a specific walking speed, which they heard in advance via a metronome. Perhaps the muscle synergies themselves are implemented in the spinal cord, but accessible via numerous descending pathways, and their recruitment may be modifiable via cortical control (Drew et al. 2008). A previous study of perturbations to walking showed that responses to afferent input during walking are organized at the spinal level and modulated by supraspinal centers (Field-Fote and Dietz 2007). Although walking patterns are generally considered to be feedforward, the posture response is considered to be reactive, and likely requires modulation from brainstem or other higher centers due to the multiple sensory modalities which are integrated to generate a coordinated responses (Deliagina et al. 2008; Macpherson et al. 1997). Nevertheless, the same muscle synergies were recruited for these reactive postural responses, during both walking and standing still. Therefore, it appears that multiple pathways in the CNS can and do recruit the same modules to achieve different tasks.

CHAPTER 5

CONCLUSIONS

5.1 Significance

Complications resulting from falls are a leading cause of death among the elderly (Anderson et al. 2004). Thus, it is important to better understand and improve balance and postural control. Here we have identified the muscle coordination underlying postural control in healthy, young subjects, as a first step toward our eventual goal of applying our knowledge to adults with deficits. This is a necessary precursor that permits a better understanding of the underlying causes of impairments that are associated with walking and maintaining balance. Once we can determine a mechanism underlying balance control problems in neuromuscular disease or deficit, it would be possible to develop appropriate, targeted therapies to address it, including training programs to develop the desired muscle synergy structure and activation patterns, thereby improving patients' ambulation and independence.

Here we have shown that the same muscle synergies are used for balance control in a variety of tasks, such as standing, stepping, and walking, which could be useful for clinical tests of synergy structure, diagnosing impairments, and proposing better treatment strategies. Clinicians could measure a patient's responses to perturbations in only one condition, such as standing, and have information concerning their underlying muscle synergies without having to measure responses in multiple conditions. Alternatively, patients may have proper coordination in one behavior, but disrupted coordination in another behavior, which could be identified using muscle synergies.

Knowing the typical muscle coordination patterns should aid in identification of disrupted muscle coordination, as has been demonstrated in the muscle synergies of stroke patients (Clark et al. 2010). The robust muscle coordination we identified here may be of interest to a variety of fields such as rehabilitation science, prosthetics, and robotics.

5.2 Robust muscle synergies for CoM control across multiple motor tasks

We conclude that muscle synergies represent a mechanism for simplifying muscle coordination in a variety of motor tasks and contexts. Muscle synergies were robustly used across static and dynamic postural tasks, as well as for muscle coordination during walking. Here we showed similar muscle synergies used during reactive non-stepping postural responses, reactive stepping responses, walking, and postural responses during walking (Figure 5.1), behaviors that had previously been studied separately. Furthermore, the muscle synergies were related to task-level goals, rather than local variables. For example, the same muscle synergies were recruited to produce a backward CoM acceleration in both a non-stepping response to a forward perturbation and in a backward step elicited in response to a backward perturbation. Therefore the NS may only need to compute the desired CoM motion or force at the ground and recruit the appropriate muscle synergies to achieve that desired motion.

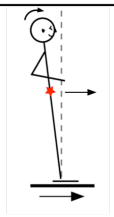
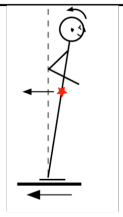
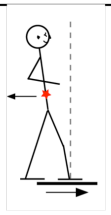
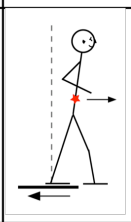
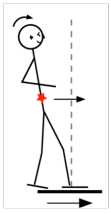
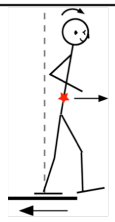
	Forward Perturbation			Backward Perturbation		
		Initial CoM direction	**Desired CoM direction**		**Initial CoM direction**	**Desired CoM direction**
Non-stepping		BACK	FWD		FWD	BACK
Reactive stepping		BACK	BACK		FWD	FWD
Response during walking		BACK	FWD		FWD	FWD

Figure 5.1 Overall study design. We studied three postural tasks which have similarities and differences in both initial CoM movement resulting from a perturbation and desired CoM motion required to maintain balance depending on the response strategy selected and task goals. The same muscle synergies were recruited according to desired direction of CoM motion across postural behaviors and walking.

Here we demonstrated that similar muscle synergies are used for walking and balance control, suggesting a common mechanism for not only balance control in various contexts, but for movement in general. The differences in the timing and spatial organization of individual muscle activity standing, stepping, and walking postural responses were largely explained by altering the recruitment of a common set of muscle synergies, with the addition of only a single muscle synergy specific to each behavior. The timing and amount of muscle synergy recruitment varied across these behaviors to

account for the differences in individual muscle activity we observed. This is consistent with previous results demonstrating shared and specific muscle synergies across different motor behaviors such as frog swimming, kicking, and jumping (Cheung et al. 2009; Cheung et al. 2005; d'Avella and Bizzi 2005; Hart and Giszter 2004a; Kargo and Giszter 2000). Furthermore, the muscle synergies identified here can explain both proactive and reactive balance strategies, accounting for both feed-forward and feedback balance control during walking as well as feedback balance control in response to unexpected disturbances.

Our results support the idea that muscle synergies are used to organize the musculoskeletal system to produce a predictable biomechanical function (Chiel et al. 2009; Ting and McKay 2007), even in different postural behaviors. We previously demonstrated a consistent relationship between muscle synergy recruitment and endpoint force production in cats across multiple postural configurations (Ting and Macpherson 2005; Torres-Oviedo et al. 2006). Here we showed not only that the same muscle synergies were recruited during behaviors with different movement dynamics, but more importantly, their recruitment was determined by the desired direction of CoM motion (Figure 5.1). In non-stepping postural responses, a forward perturbation thrusts the body backward, and muscles are activated to return the CoM forward to the initial position. In stepping postural responses, a forward perturbation thrusts the body backward, and the appropriate muscles are activated in order to take a step backward, moving the CoM further away from the starting position. In backward perturbations, the body is thrust forward, and in non-stepping responses the CoM is returned backward to the initial position, whereas in stepping responses the CoM is moved further away as a forward step

is taken. In both the non-stepping response to a forward perturbation, and the stepping response to a backward perturbation, the desired CoM direction is forward. In these two contexts, the perturbation direction is different, resulting in different sensory input, the body is oriented differently, and the overall motion is different, but the goal of moving the CoM forward is the same. Similarly, in walking conditions, the CoM is already moving at perturbation onset, whereas in standing postural responses it is initially stationary, and the goal following any perturbation direction is to regain balance and continue moving the CoM forward. Despite the differences in sensory, biomechanical, and neural conditions in these three behaviors (standing, stepping, and walking), similar muscle synergies were recruited to achieve the desired CoM movement.

These muscle synergies were recruited to produce a consistent force at the ground and CoM acceleration in different postural behaviors as well as walking, rather than being recruited consistently according to perturbation direction across behaviors. This is consistent with previous results showing the muscle activity in the initial postural response reflects task variables such as CoM motion (Gollhofer et al. 1989; Nashner and Mccollum 1985) rather than simple joint angle changes (Nashner 1977; Ting and Macpherson 2004). These results demonstrate that the identified muscle synergies do not simply reflect somatosensory patterns triggering the responses, but rather motor modules flexibly recruited to produce biomechanical functions required to stabilize the CoM. Muscle synergy recruitment in other motor behaviors has also been related to functional outputs (Ajiboye and Weir 2009; Clark et al. 2010; Krishnamoorthy et al. 2004; Weiss and Flanders 2004), suggesting that muscle synergies are organized according to function in a variety of contexts.

The idea that muscle synergies are recruited in order to accomplish behavioral goals is consistent with previous work in postural sway showing muscle components, called m-modes, that correspond to the direction of center of pressure changes used to stabilize the body (Aruin et al. 1998, Krishnamoorthy et al. 2004). However, these m-modes we identified using PCA, and their composition changed as the number of postural conditions increased (Krishnamoorthy et al. 2004). Although we believe muscle synergy composition may change over long time scales as a result of individual experience, training, and adaptation, here we have shown that muscle synergy composition is consistent across a variety of postural behaviors. Nevertheless, this work supports hypotheses suggesting muscle synergies are organized in order to achieve task-level goals.

Muscle synergy recruitment during walking also appears to be related to function rather than a specific phase of the gait cycle. Even though walking is a dynamic condition in which the CoM is not usually located over the base of support of either stance foot (MacKinnon and Winter 1993), the CoM still needs to be directed during walking, perhaps explaining why the muscle synergies used during balance control tasks were also used during walking. Previous studies suggest temporally fixed patterns of muscle recruitment occurring at specific times in the gait cycle that are coupled to spatially varying muscle weightings (Cappellini et al. 2006; Ivanenko et al. 2005; Ivanenko et al. 2004). In this organization, the CNS chooses from a set of predefined temporal recruitment patterns to produce a rhythmic behavior in a feedforward manner. The fixed neural commands have access to all of the musculature, and the specific muscles activated can vary across trials and contexts. It is unlikely that a temporally

fixed modular organization such as this would be able to explain EMG activity of involuntary or reactive tasks that rely more heavily on feedback control. Here we studied perturbations during walking in order to determine whether the modularity in walking is organized according to fixed temporal recruitments or instead to fixed muscle groups. We saw muscle synergies recruited during different phases of a single gait cycle in response to a perturbation (such as one synergy recruited during swing as it is during regular walking and recruited again during stance following the perturbation where it is not usually recruited), demonstrating that fixed temporal components would not be sufficient to explain the additional posture response during walking. Instead, fixed muscle synergies with varying temporal recruitment were able to explain both feed-forward walking and feedback posture responses during walking, suggesting their recruitment is more likely related to a task-level function such as controlling the CoM.

5.3 Central neural control of balance and locomotion

Our results in combination with the literature suggest these muscle synergies may be encoded in the CNS and accessible via multiple pathways. It is possible that there are neural networks that specify the recruitment commands to a muscle synergy (C) which branch with different synaptic weights to the motor neurons of the muscles in the synergy (W) (Hart and Giszter 2010). While such modules have been hypothesized to be encoded in the spinal cord for some tasks (Hart and Giszter 2010; Saltiel et al. 2001), postural responses likely require brainstem involvement (Deliagina et al. 2008; Honeycutt et al. 2009; Macpherson et al. 1997), possibly in addition to spinal centers (Schepens et al. 2008). Walking patterns are thought to originate from activation of a spinal CPG, but

also can be modified by higher centers (McCrea and Rybak 2008). Perhaps the muscle synergies themselves are implemented in the spinal cord, but accessible via numerous descending pathways, and their recruitment may be modifiable via cortical control (Drew et al. 2008). This organization is consistent with previous work suggesting fixed motor modules encoded in the spinal cord that might also contribute to voluntary movements (Kargo et al. 2010)

Muscle synergies may reflect neural structures mediating motor control across a variety of behaviors and contexts. Neurophysiological evidence suggests that postural responses in the limbs are not simply local reflexes, but rather an activation of a motor pattern to achieve a biomechanical goal (Carpenter et al. 1999; Dufosse et al. 1985). Current evidence suggests spinal circuits alone cannot generate the coordinated muscle activity required following postural perturbations (Macpherson and Fung 1999; Pratt et al. 1994). Neurons in the pontomedullary reticular formation (PMRF) are recruited during both reactive and anticipatory postural adjustments (Schepens et al. 2008), and these firings are not correlated to individual muscle activity, but discharge in a manner consistent with the goal of restoring equilibrium (Stapley and Drew 2009). Additionally, task-level information can be derived from aggregate afferent information in the dorsal root ganglia (Weber et al. 2007), as well as in the dorso-spinal cerebellar tract (DSCT) (Bosco et al. 1996). Therefore, it can be concluded that consistent neural structures may be flexibly accessed and differentially recruited during different motor behaviors by breaking motor activities into their component tasks.

It appears that multiple pathways in the NS may recruit the same modules to achieve different tasks. The same muscle synergies were recruited for walking and

reactive postural responses in different contexts. It is possible that separate controllers exist for each task – a CPG controller and a postural controller – which both have access to the same set of muscle synergies. It remains to be seen whether the same muscle synergies are used in both reactive and voluntary postural tasks, however, similar muscle tuning curves are generated during human whole body reaching tasks as in postural responses to perturbation (Leonard et al. 2009), suggesting that motor modules may be accessible by voluntary and reactive postural tasks in humans.

5.4 Limitations and Future studies

5.4.1 Different perturbation strengths/types/terrains

In Chapter 3 we showed that balance control during walking can be explained by modulating walking muscle synergies in most instances, but there are a few muscles/perturbation directions in which the walking muscle synergies either under or over-predict the perturbation response. This suggests other studies that examine various perturbation strengths, directions, walking speeds, etc. to find the breaking point after which walking muscle synergies are no longer sufficient. Perhaps postural muscle synergies are recruited in addition to walking ones to account for the perturbation responses in these instances.

It would be interesting to examine muscle synergies used while subjects walk on unfamiliar terrains, such as foam or rocks. Perhaps they might initially use a different strategy or different muscle synergies as they are initially cautious, but as they become familiar with the terrain, they may continue to use the same "preferred" muscle synergies

that were used during regular overground walking. If subjects do use some different muscle synergies or strategies initially and then return to their preferred walking muscle synergies when walking on different terrains, that would open the door to a variety of short-term adaptation studies as well, that would examine how long it takes for subjects to return to their preferred patterns.

5.4.2 Role of the other leg

In this work, we examined muscle synergies and forces at the ground in the stance leg only. Although we did relate this muscle activity to CoM acceleration, which is a whole-body measure that accounts for contributions from both limbs, it would be interesting to characterize the muscle synergies and forces produced in the other leg to gain a better understanding of the bilateral coordination involved in these postural and locomotor behaviors. In chapter 2, we identified a component of CoM acceleration not associated with muscle activity in the stance leg, which we presumed was due to muscle activity in the other leg, but in the future it would be useful to quantify the left leg muscle activity and correlations to task-level variables. Our lab is now equipped to record 32 muscles as opposed to 16; future studies will examine muscle synergies in each limb individually for comparison, as well as bilateral muscle synergies and their relationships to task-level goals.

5.4.3 Other task-level goals

Here we quantified relationships between muscle synergy recruitment and task-level goals of forces at the ground and CoM acceleration. In feline standing balance

control, it has been hypothesized that several muscle synergies are recruited in order to control center of mass (CoM) kinematics by modulating end-point forces (McKay and Ting 2008; Torres-Oviedo et al. 2006), therefore here we investigated correlations between muscle synergy recruitment and forces at the ground to see if similar relationships exist in human balance control. The CoM is a likely control variable, because although several strategies may be used to maintain balance in various contexts, in any variation of the standing balance task, maintaining balance requires keeping the CoM above the base of support (BoS) (Massion 1992; Scholz et al. 2007; Ting et al. 2009). Also, previous work has shown that during non-stepping postural responses, the muscles recruited for postural stabilization depend upon the direction of CoM motion, rather than the local changes in joint angle displacements (Carpenter et al. 1999; Gollhofer et al. 1989; Ting and Macpherson 2004). Therefore we do not believe that muscle synergies are recruited in order to modulate joint angles, or other local variables.

However, other global variables may also be controlled in balance behaviors and locomotion, such as head stabilization or trunk orientation. Alternatively the goal may be to expand the limits of stability. We did not explicitly test whether muscle synergy recruitment is correlated with any of these other task-level variables. In future analyses, we could examine whether recruiting muscle synergies stab ilizes other global variables such as these across various behaviors. Also, we chose to use a 60-ms delay between muscle activity and force/CoM acceleration due to previously reported electromechanical delays (Jacobs and Macpherson 1996). Future work might include testing different, possibly longer delays, such as 100ms, to determine if the chosen delay changes the results.

5.4.4 Voluntary stepping

In Chapter 2 we demonstrated the same muscle synergies were recruited in voluntary postural tasks to direct the motion of the CoM to maintain balance. In Chapter 4 we demonstrated the same muscle synergies are also used during walking, which is a more voluntary task yet still considered automatic. It will be interesting to investigate the muscle synergies used during a voluntary stepping task.

Studying voluntary stepping alongside reactive stepping allows the comparison of two tasks that have the same kinematics and CoM movement, but the command to activate the synergies comes from different levels of the nervous system. The command in a voluntary step comes from motor cortex, but in a reactive step it comes from a lower level, perhaps brainstem, in response to a combination of sensory inputs that provide information about the body orientation and CoM position. Additionally, the displacement of the CoM is achieved slightly different in these two conditions. In reactive stepping, the CoM is displaced initially due to the platform motion, and then further displaced via generation of forces at the ground to cause a step. In voluntary stepping, the initial destabilization and entire CoM displacement results from forces generated by the stance leg. Even so, I predict that the same muscle synergies will be used in the stance leg in the voluntary stepping condition as were used in the reactive non-stepping and stepping tasks. We hypothesize that muscle synergies are activated to perform a specific biomechanical function (such as generate forces at the ground) in order to control the movement of the CoM. Since both of these tasks require control of CoM, I expect to see the same muscle synergies used in both tasks, and only the

recruitment of the muscle synergies will need to change in order to produce observed differences in individual muscle patterns and ground reaction forces. Preliminary results from voluntary stepping are shown in Appendix B.

5.4.5 Other motor tasks

Here we examined muscle synergies in postural strategies and locomotion. Perhaps similar muscle synergies were identified because walking and standing are similar tasks. Much of walking is standing and falling, and although we analyzed the entire gait cycle in chapter 3, in chapter 4 our analysis of perturbed walking was limited to the small time window immediately following the perturbation during stance. It would be interesting to examine the muscle synergies underlying other motor tasks, such as running, turning, backward walking, etc. Since all of these tasks still require control of the CoM, we expect at least some of the same muscle synergies will be used in these tasks as we observed during the walking and postural tasks studied here. As motor tasks become increasingly complex, more areas of the CNS are required for successful execution. It is unknown whether the CNS can still access the same muscle synergies robustly used to direct the CoM in walking and balance tasks during more complex tasks such as these.

5.4.6 Studies of skill and deficit

So far we have examined muscle synergies in healthy, young adults, in order to better understand normal muscle coordination in ideal circumstances. However, the eventual goal is to use what we have learned in healthy subjects to better understand

neuromuscular and functional deficits in impaired populations, in order to develop better treatments and rehabilitation strategies that try to achieve the desired muscle coordination, thereby improving people's motor control and daily functioning. Improved muscle coordination could hopefully lead to improved control of the CoM, which may increase a person's limits of stability, thereby decreasing falls. Previous work has shown stroke patients use fewer muscle synergies in the paretic leg compared to the non-paretic leg and healthy controls (Clark et al. 2010). It appears that these impaired modules represent a merging of normal modules, suggesting that the appropriate neural structures may be intact, yet inaccessible. Muscle synergy structure in other pathological conditions as well as normal aging has not been thoroughly explored. We propose the number of muscle synergies available to accomplish motor tasks will be reduced with pathologies.

Conversely, muscle synergy structure in highly skilled populations has not been thoroughly examined either. We might expect to see Tai Chi masters or highly skilled dancers recruit a greater number of muscle synergies during postural tasks, because they have learned and practiced fine motor movements for many years. We observe young, healthy subjects using anywhere from 5-7 muscle synergies during postural tasks; perhaps this discrepancy in number across individuals is due to their prior experiences and training. It would be interesting to compare the number, structure, and recruitment of muscle synergies across a wide range of populations, ranging from highly skilled all the way to balance impaired.

5.4.7 Changes in muscle synergies over time

We hypothesize that on short time scales (days), muscle synergy composition is invariant, and only the recruitment of the muscle synergies vary. Preliminary work has shown the same muscle synergies are used from one consecutive experiment day to the next. However, it is unclear how muscle synergies change over longer time periods (years). Individual experience, training, and adaptation all may affect muscle synergy composition over time. Acquiring specialized skills may reveal additional muscle synergies, or new muscle coordination patterns may result during the course of normal development (from infancy to adulthood) or aging. As muscles are consistently activated together, perhaps new networks are formed or reinforced that branch to the motoneurons of the coordinated muscle groups. As people age, muscle synergies may merge or become less accessible, resulting in decreased flexibility of movements and decreased or delayed control over the CoM. These could be investigated by comparing the muscle synergies used by specialized populations (as discussed above), or by a longitudinal study following the same population over time, such as following a group of children for a number of years until they are adults.

5.4.8 Translating our methods into a clinical setting

Currently, muscle synergies are identified after subjects perform a variety of postural or locomotor tasks over the course of a 3-hour experiment. In order to obtain enough data for the analysis, subjects perform hundreds of trials. The perturbation platform we use in the lab is large and expensive. It is unrealistic to expect these perturbation platforms will ever be widely available and cost-effective, and elderly or

impaired populations will be unable to withstand such long and tedious experimental protocols. Additionally, the NNMF analysis we use to identify muscle synergies is difficult, and probably not appealing to clinicians. Therefore, a more practical means of assessing a person's muscle synergy structure is needed, one that can be performed quickly and efficiently. This would include a perturbation system that still delivers relevant perturbations mimicking those experienced in daily living, but is portable and inexpensive, as well as a user-friendly method of analyzing EMG and identifying muscle synergies.

In conclusion, the robust muscle coordination we identified here in healthy adults will be useful to a variety of fields such as rehabilitation science, prosthetics, and robotics. It provides a framework with which to compare altered muscle coordination as a result of skill, adaptation, or deficit. These results will provide a baseline for future studies to develop targeted rehabilitation therapies or more realistic prostheses.

APPENDIX A

DECOMPOSING MUSCLE ACTIVITY IN MOTOR TASKS

This chapter was originally published in *Motor Control*

Ting LH and Chvatal SA. Decomposing muscle activity in motor tasks: methods and interpretation. In: *Motor Control*, edited by Danion F, and Latash, Mark L. Oxford, 2010.

In this chapter, we examine methodologies for dimensional analysis and linear decomposition of multivariate data sets and discuss their implicit hypotheses and interpretations for muscle coordination of movement. We present tutorials (available for download at http://neuro.gatech.edu/groups/ting/PMCtutorial.html) to compare how two common methods, principal components analysis (PCA) and non-negative matrix factorization (NMF), decompose electromyographic signals into underlying components. To facilitate the integration of such mathematical techniques with physiological hypothesis testing, we focus on developing an intuitive understanding to the two techniques. A simple two-dimensional tutorial is provided, focusing on how orthogonality constraints in PCA and non-negativity constraints in NMF impact the resulting data decomposition and physiological relevance. Examples are presented using real data sets from human balance control and locomotion, examining the structure of the resulting components, their robustness across tasks, and their implications for various

muscle synergy hypotheses. We address practical issues and caveats in organizing datasets, the selection of the appropriate number of components, and considerations and pitfalls of experimental design and analysis, as well as suggestions and cautions for interpreting results. Based on these comparisons, and on the work in the visual system over the last decade, we present evidence for the increased neurophysiological relevance of the factors derived from NMF compared to PCA.

A.1 Introduction

How do humans and animals move so elegantly through unpredictable and dynamic environments? Why does this question continue to pose such a challenge? During any motor task, many physiological elements throughout the body must be coordinated, such as limbs, muscles, neurons, etc. A major question in motor control is: How do the overall functions and characteristics of movements arise from the functional arrangement and coordination of both neuromuscular elements and environmental interactions? Although modern technology allows us to collect an unprecedented amount of data on the activity of neurons, muscles, and limbs during a wide variety of behaviors, we still lack an understanding of how individual elements of the body interact to produce the many movements we perform, let alone characteristics such as grace or clumsiness.

Interpreting both structure and variability in the motor system and relating it to the resulting biomechanical and behavioral outputs remains a grand challenge in understanding how we move. Nikolai Bernstein noted the fact that motor behaviors never repeat themselves exactly, even when the same task is performed in succession (Bernstein 1967). On the other hand, he also noted that characteristic output patterns

occur even when a motor task is performed by different sets of muscles, such as when drawing shapes or letters on a piece of paper versus on a blackboard, or with a different appendage. Similarly, more recent studies also demonstrate that the performance of a motor task, such as reaching to a target, can occur quite consistently even when there is a great deal of variability in the underlying joint motions or torques contributing to that task (Newell and Carlton 1988; Latash et al. 2002; Ko et al. 2003; Reisman and Scholz 2006). These findings highlight the fact that the our bodies have a large number of degrees of freedom in the joints, muscles, and neurons that allow them to be flexible and functionally reconfigured to perform the same task, as well as different tasks (see Kelso, Sternad, this volume). During any so-called coordinated movement, synchrony and similarity are observed across many different kinematic, kinetic, electromyographic, and neural signals (Bernstein 1967; Macpherson 1991). But, when looking across a wide behavioral repertoire, the synchrony and coordination observed in one movement may be abolished in another, such that fluctuations in the spatiotemporal dynamics of the multiple measures may appear coordinated in one instance and independent in another (Bernstein 1967; Macpherson 1991). Such differences are potentially due to both changes in the neural control of muscles, as well as to changing interactions of the body with the environment under various conditions.

Controlling movements requires not only organizing physiological processes for movement, but also requires consideration of the complex interactions of forces acting between the organism and the environment. Bernstein defined the coordination of movement as: “the process of mastering redundant degrees of freedom of the moving organ, in other words, its conversion to a controllable system” (Bernstein 1967). By

"controllable" Bernstein meant that coordinated motor activity causes predictable biomechanical events, such as force generation and motion, that allow us to reliably perform a motor task. Thus, understanding movement requires characterizing the degrees of freedom of the physiological system that are used in the performance of any particular movement, the reconfiguration of such degrees of freedom in the performance of divergent movements (see Latash, this volume), and the relationships of these degrees of freedom to the biomechanical interactions that ultimately generate the movement (see Prilutsky, this volume). Gathering large sets of data during natural movements is becoming increasingly easier, thus allowing us to characterize coordination across many variables at different levels of the motor system; however, interpreting such large data sets and analyzing them to test motor control hypotheses remains a challenge.

Computational methods for analyzing large set of data are now easily accessible and available; however, the utility of such methods for providing insight into motor control is debated. Can such techniques help us to understand increasingly large data sets? Can quantitative analysis provide further insight than that which scientists have gathered from observation? Are automated pattern-recognition techniques able to reveal that which an experienced scientist can see when examining raw data? What are the potential benefits and pitfalls of using such techniques? These questions will be addressed in this chapter.

Here, our goal is to provide instructive tutorials to provide an intuitive guide to the similarities and differences between two primary techniques used for the analysis and decomposition of multiple signals in motor control and neuroscience, as well as in engineering fields: principal components analysis (PCA) and non-negative matrix

factorization (NMF) (Lee and Seung 1999). Although comprehensive texts on the quantitative aspects of these techniques are readily available (Ramsay and Silverman 2005), we present methods for understanding how the properties of each technique affect the decomposition and physiological interpretation of muscle activation patterns in a simple example and in actual data from postural control and walking. We have chosen two commonly used linear decomposition techniques that render the most divergent results; however, similar principles could be used as a basis for comparing other decomposition techniques, such as independent components analysis (ICA) or k-means analysis (Tresch et al. 2006). We will discuss the interpretations and implications of the results and how such techniques might be used to understand principles of motor coordination, as well as give insight into the function of the nervous system in translating goal-level intentions into specific muscle activation patterns for movement.

A.2 Basic Properties and Differences Between PCA and NMF: A Simple Example

Although PCA and NMF are similar in their underlying concept and mathematical representations, there are key differences in their implementation and in the resulting components. Both PCA and NMF are linear decomposition techniques that assume that the set of measured data is composed of linear combinations of a smaller number of underlying elements (Fig. A.1A). That is, given a number of simultaneous observations of multiple data channels, any particular observation could be represented as:

$$M_j = c_{1j} W_1 + c_{2j} W_2 + \ldots + c_{nj} W_n + \text{error} \qquad \text{(Eq. 1)}$$

Here, M_j is a vector that represents measurements of multiple channels of data (Fig. A.1B); for example, the activity of *m* muscles at a given time point, arranged in a column.

On the right side of the equation, the components or basis functions W_i are vectors, also of length *m*, that represent invariant patterns of activity across those different channels. The pattern of muscle activity can be described by *n* scalar values c_{ij}, each of which specifies the contributions of each component to the measured muscle activation pattern M_j. If there are *m* muscles and $n < m$ components, then the representation of M_j in terms of the components W_i and the weight or scaling factors c_{ij} is lower-dimensional than simply stating the value of each element of M_j. Such linear decomposition techniques therefore test the hypothesis that, over a large number of observations of M_j, the components W_i remain fixed, but the scaling factors c_{ij} are allowed to change and are sufficient to account for all of the variations of the data measured across different conditions. When analyzing muscle activation patterns, the modules W_i are often referred to as muscle synergies (Tresch et al. 1999; Cheung et al. 2005; Ting and Macpherson 2005; Torres-Oviedo and Ting 2007) or M-modes (Danion et al. 2003; Krishnamoorthy et al. 2004; Latash et al. 2007). In this context, the hypothesis is that muscle synergies remain fixed, but activation of these synergies can vary, resulting in observed variations in individual muscle activity.

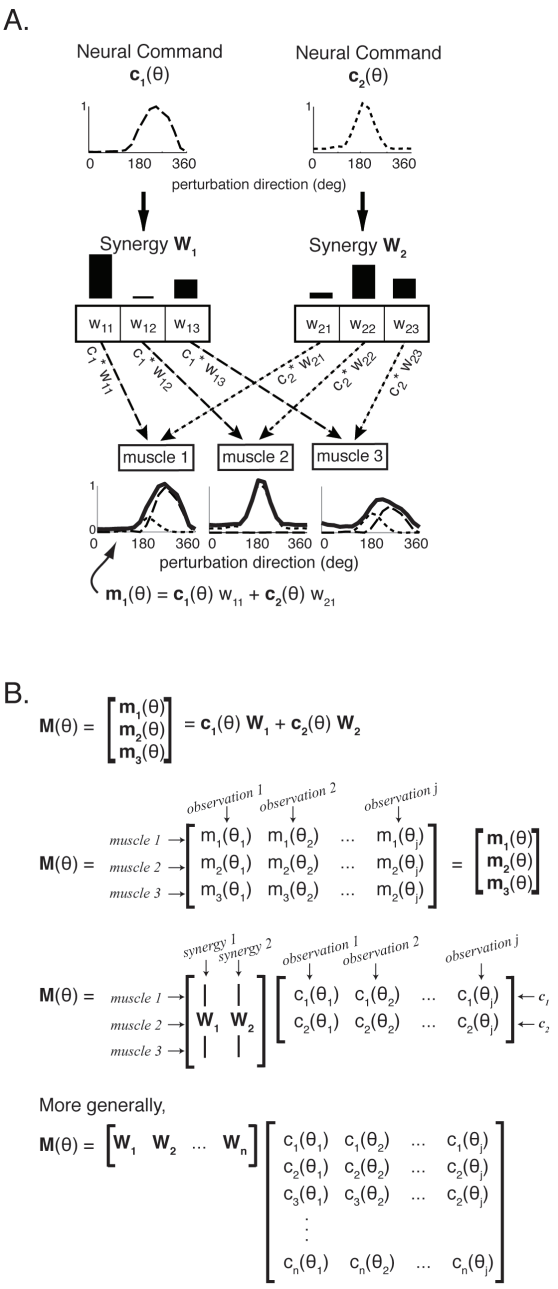


Figure A.1 Electromyograph (EMG) data decomposition schematic and muscle synergy concept. A: Any pattern of multiple muscle activation can be represented as a linear combination of the activations of that muscle by each muscle synergy component. In this example, there are $n = 2$ components and $m = 3$ muscles, thus M(q) can be represented in terms of the lower-dimensional combination of muscle synergies (components, W_i) and activation commands ($c_i(q)$). B: Organization of the data matrix and the structure of the W and c matrices.

Although similar in concept, in practice, PCA and NMF are quite different; each method decomposes the variability with a given data set in very different ways. PCA is an analytical technique, meaning that the components are found through a straightforward set of computations. Therefore, it is easy to use and there are readily available algorithms included in most data processing software packages. This is possible because PCA requires that the components be orthogonal (e.g., perpendicular) to each other, creating a unique solution to any decomposition. Furthermore, it is relatively straightforward to select the appropriate number of components needed to explain a given data set based on a cutoff value for the variance accounted for. In contrast, NMF is found using a search algorithm, which means that it has to start with a set of random components and iteratively improve on them until an adequate proportion of the variability in the dataset is accounted for. Components generated by repeated searches will not be numerically identical but will be similar. Because NMF constrains both the weights $c_{i,}$ as well as all of the elements of the components, W_i to be non-negative, the problem is what is called *convex*. That is, there are no local minima for the search to be "stuck" in, therefore components from multiple searches are numerically similar. In a non-negative space, it is not possible for the components to be orthogonal; however, they must be independent, meaning that no component can be defined as a linear combination of the other components. The iterative technique also requires that the number of components be specified in advance, so that multiple searches must be done to determine the right number.

In the following set of tutorials, we use a simple two-dimensional example of a simulated dataset to illustrate the differences in how PCA and NMF decompose

variability in the dataset. For all three examples, simulated muscle activity data are fabricated by assuming that there are two underlying components, which can be interpreted as muscle synergies, W_1 and W_2 that each define a different ratio between the activity of two muscles (Fig. A.2A, *gray bars*). These components can also be drawn as vectors on a two-dimensional plot (Fig. A.2A, *gray arrows*). A set of data, M, is created by randomly assigning the activation level of each component (c_1 and c_2) from a uniform distribution between 0 and 1. Each data point, or observation M_j, can be represented as a vector $[m_{1j}\, m_{2j}]$, and plotted as a single point on a set of axes representing the level of activation of muscle 1 versus muscle 2 (Fig. A.2A). The tutorials are available for download as part of the supplementary materials, at http://neuro.gatech.edu/groups/ting/PMCtutorial.html.

A.2.1 Orthogonality Versus Independence

The constraints of orthogonality and independence in PCA, and independence without orthogonality in NMF, account for the large differences between the components extracted by each technique. In this example, the activity of each component was equally weighted, so that the data is scattered evenly between the two vectors, W_1 and W_2, used to create the data (Fig. A.2A). When PCA is applied to the data, two components are extracted (Fig. A.2B). The first aligns with the center of the long axis of the data and accounts for 87% of the variability. Because the scaling factors can be positive or negative, the direction that W_1 points does not matter, only the line it defines. The second component must be at a right angle to the first component to satisfy orthogonality. It accounts for a much smaller portion of the variability, only 13%. Neither PCA

component looks like the original components used to generate the data. Using NMF, the extracted components are similar to the original components, W_1 and W_2, used to generate the data, appearing at the edges of the data points (Fig. A.2C). The variability accounted for by each component is similar, 49% and 51%, respectively. Although the components are not orthogonal, the addition of a second component nonetheless increases the set of possible patterns of muscle activation between muscles 1 and 2.

A.2.2 PCA Is Descriptive; NMF Is Prescriptive

PCA, much like a multiple regression, describes the mean and residual variance from the mean in successive principal components. Before identifying the components, the original dataset is typically demeaned; if this is not done, then the first principal component represents the mean value of each variable across the dataset. Otherwise, as in this example, the first principal component in PCA describes the largest deviation from that mean in each muscle across a given dataset. Each additional component describes the orthogonal direction containing the next largest deviations from that mean. In our two-dimensional example, it means that, if the first component changes, then the second component must also change. The percentage of variability accounted for by each component decreases monotonically, describing the degree to which the dataset varies in the corresponding direction. Because PCA allows for both negative and positive values for the scaling factors, it is possible to describe any point on the plane with two independent components derived from data in that plane, regardless of the direction that they point (Fig. A.2B). Data with multiple dimensions can be restricted to a plane by choosing only the first two principal components.

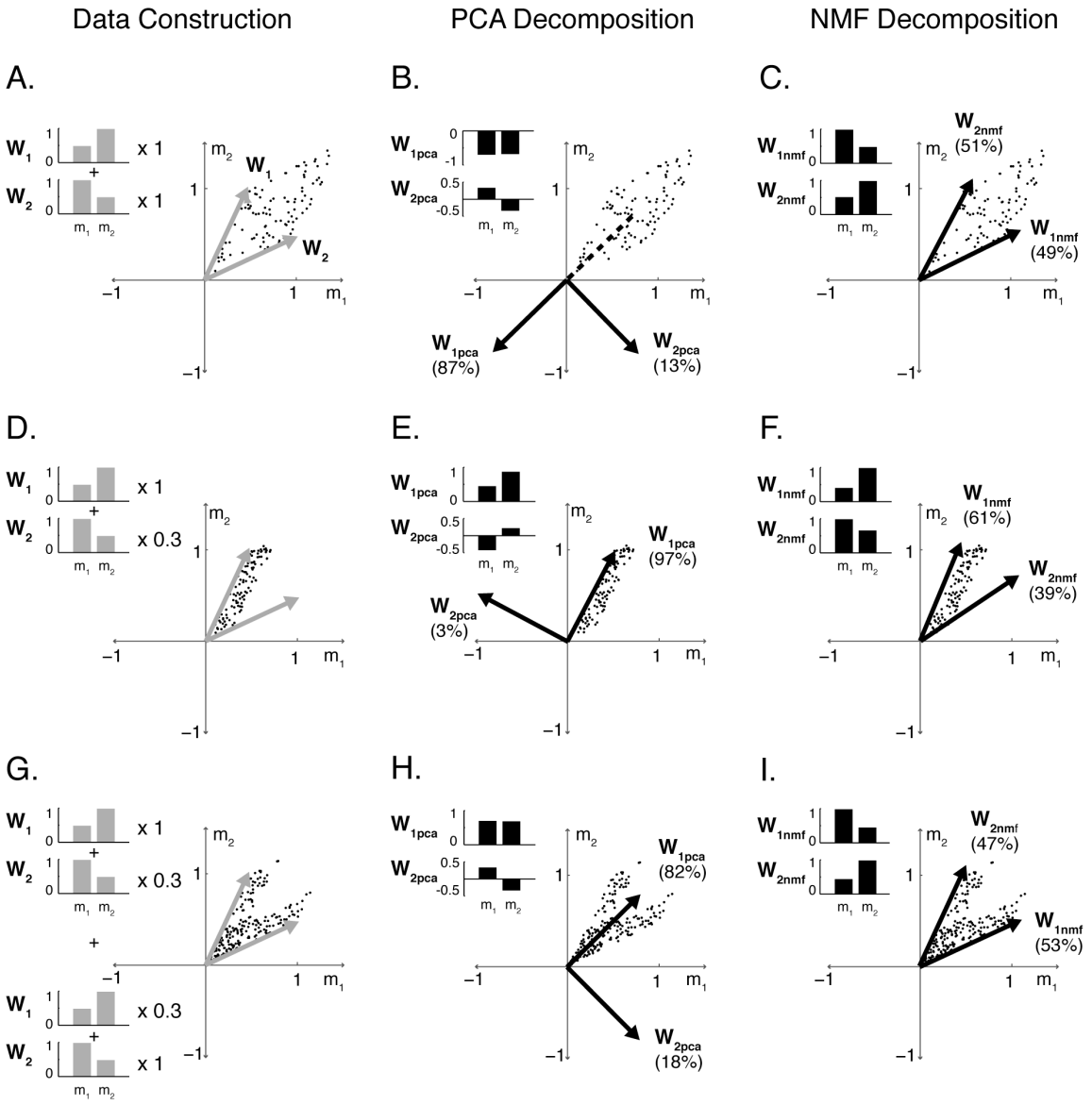


Figure A.2 A 2-D example illustrating differences between components identified using principal components analysis (PCA) and non-negative matrix factorization (NMF). A: Data is constructed using two components specifying fixed ratios of muscle activation between two muscles, W_1 (m_1=0.5*m_2) and W_2 (m_1=2*m_2). The contribution of each component for a given observation, or data point, is found by multiplying each component by a scaling factor (c_1 and c_2) selected from a uniform distribution ranging from 0–1. B: Components identified using PCA to decompose the data from A. The percentage of total data variability that each component accounts for is shown beside each vector. The first component is directed along the long axis of the data cloud, and the second is constrained to be in the orthogonal direction. C: Components identified using NMF to decompose the data from A. Components are found near the edges of the data cloud. Note the similarity to the original components (W_1 and W_2) used to generate the data. D: Data is constructed using the same two components as in A, except now it is

weighted towards using W_1. In order to generate this data, $\mathbf{c_1}$ was taken from a uniform distribution between 0 and 1, whereas $\mathbf{c_2}$ was taken from a uniform distribution between 0 and 0.3. E: Components identified using PCA to decompose the data from D. W_{1pca} looks similar to W_1, reflecting the bias towards W_1 in the generation of the data set, but W_{2pca} is different from W_2. F: Components identified using NMF to decompose the data from D. Despite the bias in the generation of the data set, these components are similar to those used to generate the data, as well as the components identified in C. G: Data is constructed using the same two components as in A and D, except now part of the data is weighted towards using W_1 and part is weighted towards using W_2. To generate this data, c_1 was taken from a uniform distribution between 0 and 0.3, whereas c_2 was taken from a uniform distribution between 0 and 1, and this was included along with the data from D. H: Components identified using PCA to decompose the data from G. W_{1pca} passes between the two "clouds" of data where the mean values of m_1 and m_2 lie, and the components look similar to those identified in B. I: Components identified using NMF to decompose the data from G. Again the components are similar to those used to generate the data.

In NMF, the components prescribe a subspace within which all data points must lie. Because of the non-negativity constraints, only the points lying between the two components can be described (e.g., Fig. A.2A). Thus, components from NMF tend to identify the edges of the dataset and define a convex hull, or polygon, within which all of the feasible data points lie (e.g., Fig. A.2C). The condition of independence requires that each additional component increase the allowable subspace, as no two components can be represented as a linear combination of other components. Because there is no constraint on orthogonality, it is also possible for one component to change and the others to remain the same.

Therefore, the non-negativity constraints within NMF make it more restrictive than PCA, delimiting regions of the low-dimensional space that cannot be reached. Although dimension reduction can be achieved in both techniques by examining only the first few components, NMF imposes further restrictions. Components derived from PCA tend to *describe* the major direction of the data without imposing restrictions within the

space defined by those components. In contrast, NMF *prescribes* a subspace in which possible combinations of muscle activity lie, restricting the expressible data points using those components.

Consider an example using the same components, W_1 and W_2, as in the previous tutorial, except this time the data are preferentially weighted toward using W_1 (Fig. A.2D, data construction). This dataset was created from sampling the same muscle activation components as in the prior example, but with a higher activation of W_1 over W_2. Using PCA, both components changed direction compared to the previous tutorial (compare Fig. A.2E and 2B). The first PCA component (W_{1pca}) rotated closer to the mean of the observed pattern of muscle activity and now looks qualitatively similar to the original W_1 used to construct the data (Fig. A.2A), accounting for 97% of the variance. The second component must rotate a similar amount to maintain orthogonality (compare Fig. A.2B and 2E). Both components identified in this case look different from those identified using PCA in the previous example. Thus, PCA describes the data in a similar sense to a mean and standard deviation. In contrast, both components found using NMF (Fig. A.2F) were similar to the components W_1 and W_2 used to generate the data (Fig. A.2D) and to those identified in the previous tutorial (Fig. A.2C). There was a slight shift in the second component simply because there is less variance in that direction, and therefore a larger confidence interval. Thus, the components obtained from NMF identify vectors that prescribe the same space of possible solutions using those two components as in the prior tutorial, even when one component is more heavily weighted than the other.

A.2.3 Physiological Interpretability of PCA Versus NMF Components

In PCA, a component, $W_{i,}$ can contain positive and negative numbers representing relative muscle activation levels, as well as positive and negative weightings, c_i. This means that positive and negative relationships can be inverted easily by negative weighting values. In the context of muscle activation patterns, this equal relationship between positive and negative activation is inconsistent with the transformation between motorneuron action potentials and muscle activity. Although motoneurons no doubt receive inhibitory as well as excitatory neural activity, the inhibitory effect can only be seen on motor output if there is also a high background level of muscle activity. That is, if inhibition occurs when muscles are quiescent, they have no effect on muscle activity due to the rectifying properties of neural transmission. Moreover, excitatory pathways and effects cannot be made inhibitory, and vice versa, so that there is no reason to think that an excitatory pattern would be identical to an inhibitory one. In contrast, in NMF, the components are constrained to be non-negative, which is physiological for neural and muscle output, since neurons are either firing action potentials (positive signal) or else in a resting state (zero signal).

One interesting result of the non-negativity constraint in NMF is that the underlying components resemble a "parts-based" decomposition, in which a series of parts are summed to create a whole. Since each component, or part, that is added cannot be subtracted out through the contributions of another component, the parts must resemble identifiable features of the output. In contrast, allowing negative numbers in PCA means that a given data point is created by addition and subtraction of contributions from different components to a given muscle's activity. The first component describes

the mean, and the next components can add or subtract activity from that mean. Therefore, the resulting data point may bear no resemblance to the identified principal components.

Here, we demonstrate the different ways in which PCA and NMF deal with data that are not evenly distributed. Consider an example using data constructed from the same components, W_1 and W_2, from the first two tutorials, except now part of the data is skewed toward using W_1 and part skewed toward using W_2 (Fig. A.2G). The components identified using PCA are similar to those found in the first tutorial: The first component passes between the two main "clouds" of data, and the second is orthogonal to the first (compare Fig. A.2H to 2B). In contrast, components extracted using NMF look very similar to the original W_1 and W_2 used to generate the data, as well as to those identified in the first two tutorials (compare Fig. A.2I to 2F and 2C). The components lie along the edges of the data "clouds," and therefore can be used to describe any data points between them.

In this example, the components from PCA are directed in similar directions as in first example, with the first component aligned along the mean values of m_1 and m_2 across the dataset (Fig. A.2H). Most of the data points are reached by scaling the contribution of the first component and adding or subtracting a contribution of the second component. However, these components do not resemble the two-armed "parts" of the dataset. In contrast, the components from NMF are again similar to those used to generate the data, and similar to the components found from the two other data sets (Fig. A.2I). Here, the two components from NMF clearly identify two of the underlying "parts" that are obvious in the dataset (similar results can also be achieved through independent

components analysis [ICA] in combination with PCA (Hyvärinen 2001; Tresch et al. 2006).

Similarly, in the original paper describing differences between PCA and NMF, the components underlying decomposition of an image of a face were compared (Lee and Seung 1999). All of the PCA components look like entire faces, which are then added and subtracted together to generate a given face. To generate a face with a medium nose, large eyes, and small mouth, one might imagine starting with the mean face expressed by the first principal component and adding a component with a large nose, large eyes, and medium mouth, then subtracting another component with a small nose, medium eyes, and small mouth. The NMF components, however, are characterized by face parts such as the nose, eyes, and mouth. A face would be generated by selecting a component nose, scaling it by a medium number, selecting a component eyes and scaling it by a larger number, and selecting a component mouth and scaling it by a smaller number. Interestingly, this kind of parts-based decomposition is similar to the type of neural representations observed in the visual and other sensory encoding systems (Olshausen and Field 2004). Accordingly, there has been a shift from the use of PCA to NMF in visual system research (Simoncelli and Olshausen 2001).

A.3 Identifying Components Using PCA and NMF: A Postural Control Example

Taken together, these three tutorials illustrate key differences in how PCA and NMF describe and partition the variability in a given data set, which are relevant to how they can be used to test motor control hypotheses. Although all of the data were generated from the same set of underlying components, the components identified by

PCA changed when the mean levels of muscle activation changed, and all of the components changed simultaneously. NMF has the ability to identify components that are stable across different conditions, but combined differently. This demonstrates how different conclusions regarding the robustness and generality of components might be drawn depending on which decomposition algorithm is used.

In the literature, both PCA and NMF have been used to examine whether stable motor modules are used for generating movements. Several studies have addressed muscle coordination in standing balance control, because muscles in various regions of the body tend to act synchronously, and patterns of muscle activation can be easily related to a direction of body motion. During postural body sway, PCA has been used to identify components, called *M-modes*, that correspond to the direction of center of pressure changes used to stabilize the body (Aruin et al. 1998; Krishnamoorthy et al. 2003a). Similarly, in responses to different directions of perturbation during standing balance control, components from NMF, referred to as *muscle synergies*, have been identified that correspond to the direction of force applied at the ground to stabilize the body (Ting and Macpherson 2005; Torres-Oviedo et al. 2006). However, as the number of postural conditions is increased, the underlying M-modes from PCA are found to change (Krishnamoorthy et al. 2004), whereas the muscle synergies from NMF remain consistent (Torres-Oviedo et al. 2006; Torres-Oviedo and Ting 2010).

Rarely are both techniques used in the same study, so that it is difficult to know whether the differences in the literature reflect the techniques used, the experimental design, or the particular motor tasks tested. Moreover, since NMF requires several decisions on the part of the investigator, choosing the right number of muscle synergies is

not necessarily straightforward, which may also lead to different conclusions being drawn. Here, we provide examples where both PCA and NMF are performed on actual data from one subject during postural responses to multidirectional perturbations.

A.3.1 Introduction to Postural Responses

In order to maintain balance in light of an unexpected perturbation of the support surface, humans and animals must keep the projection of their center of mass (CoM) within the limits of their base of support. Various strategies may be used when balance is disrupted, requiring the activation of different muscles, such as taking a step, grabbing a handrail, or maintaining the feet in place to restore balance. When standing balance is disturbed with a discrete perturbation, first the direction of falling is sensed, and then the appropriate muscles are activated to restore balance. The initial change in muscle activity in the lower limbs does not occur until approximately 100 ms following the onset of a perturbation, and this initial muscle activity is called the *automatic postural response* (APR). Variations are observed even in responses to the same perturbation direction due to attention, expectation, and the like (Woollacott and Shumway-Cook 2002). When many trials and many perturbation directions are examined, the differences observed in individual muscle activations are difficult to interpret (Henry et al. 1998; Horak and Macpherson 1996). One hypothesis is that the nervous system activates these muscles in groups, and decomposition techniques such as PCA and NMF can be used to identify such groups and the relationships between the muscle activations (Krishnamoorthy et al. 2003a; Krishnamoorthy et al. 2003b; Torres-Oviedo and Ting 2007).

To generate the postural data examined here, subjects stood on a platform, which was suddenly moved in one of 12 different directions in the horizontal plane. Electromyographic (EMG) signals were collected from 16 lower trunk and leg muscles from the right side. For each trial, mean muscle activity during three time windows during the APR was calculated: 100–175 ms following perturbation onset (PR1), 175–250 ms (PR2), and 250–325ms (PR3), as well as one background time window before the perturbation began (Fig. A.3A). Therefore, this data set consisted of 16 muscles and 240 conditions (4 time windows × 12 perturbation directions × 5 trials in each direction). All of the data were arranged in a matrix in which each of the 16 rows contains the 240 observed values for a single muscle. The values in each row were normalized to the maximum value in that row, corresponding to the maximum level of muscle activity observed for that muscle across all conditions. Therefore, for each muscle all values ranged from 0 to 1. Before components are extracted using NMF, each muscle was also normalized to have unit variance, meaning that the sum of the squared values in the row equals 1. This allows the variations in each muscle to be considered with equal importance by the algorithm. One practical consideration is that, for NMF, the data should always be presented in the format N muscles × M conditions. However, PCA requires the data be transposed, in the format N conditions × M muscles.

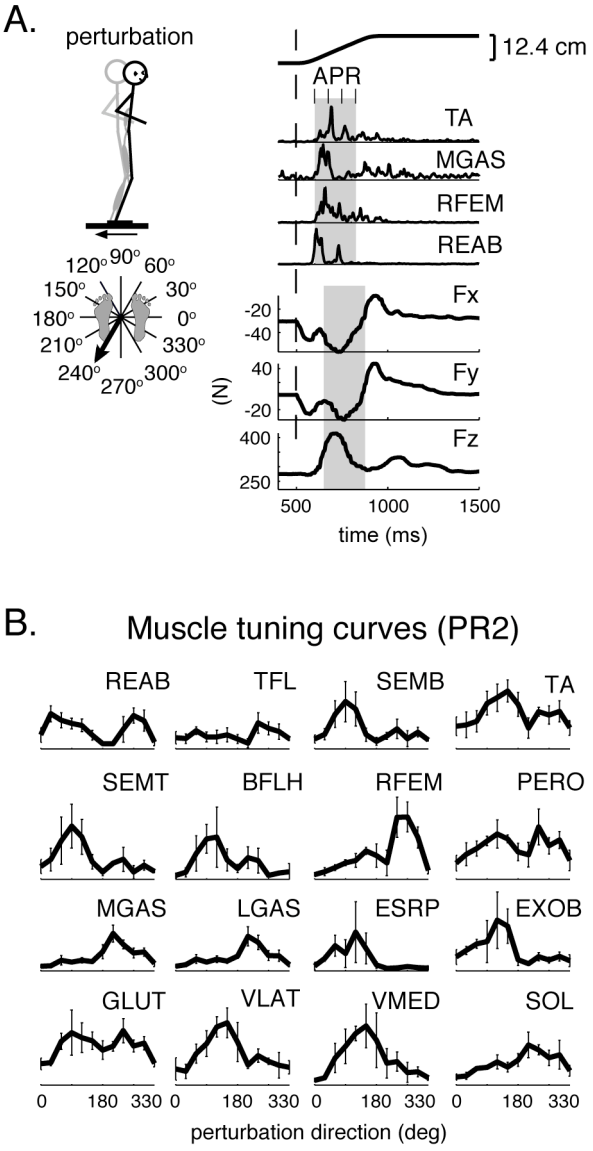


Figure A.3 Example of postural responses to a backward and leftward perturbation of the support surface. A: Platform displacement during the ramp-and-hold perturbation. Electromyograph (EMG) responses occur 100 ms after the onset of platform motion (*vertical dashed line*). Shown here are tibialis anterior (TA), medial gastrocnemius (MGAS), rectus femoris (RFEM), and rectus abdominus (REAB) EMG responses. Mean EMG activity was calculated for three time bins during the APR (*shaded region*), beginning 100 ms (PR1), 175 ms (PR2), and 250 ms (PR3) following perturbation, as well as one background time period. Ground reaction forces under the right foot are also shown. B: Muscle tuning curves generated from 12 evenly spaced perturbation directions, taken from time window PR2. Muscle tuning curves vary in magnitude over all perturbation directions, and their shapes vary from muscle to muscle. In addition to the four muscles shown in A, tensor fasciae latae (TFL), semimembranosus (SEMB),

semitendinosus (SEMT), biceps femoris long head (BFLH), peroneus (PERO), lateral gastrocnemius (LGAS), erector spinae (ERSP), abdominal external oblique (EXOB), gluteus medius (GLUT), vastus lateralis (VLAT), vastus medialis (VMED), and soleus (SOL) were also collected. Shown are the mean tuning curves ± standard deviations for five trials in each perturbation direction, presented randomly.

In response to horizontal plane disturbances, each muscle was preferentially activated for particular perturbation directions (Fig. A.3B). The muscle "tuning curves" demonstrate the directional sensitivity of the muscles. Each muscle is active maximally in a given direction, and less so for other directions. Some muscles have a single preferred direction (e.g., vastus medialis, VMED), whereas others have multiple tuning directions (e.g., rectus abdominus, REAB). The muscle tuning curves demonstrate that each direction of perturbation evokes a different combination of muscle activity. The error bars on the muscle tuning curves also illustrate trial-to-trial variations observed in postural responses. Therefore, across perturbation directions, and even within a perturbation direction, different patterns of muscle activity are evoked. Does this mean that each muscle must have an independent neural command specifying its level of activation (Macpherson 1991)? Using NMF and PCA, we can test the hypothesis that the observed variations can be explained by the activation of a few muscle synergies (Fig. A.1). In the following section, we will compare how NMF and PCA describe postural response data, and include practical issues of selecting the appropriate number of components, and examine the robustness of the components across different postural tasks, specifically, two-legged versus one-legged perturbation responses.

A.3.2 Components of Postural Responses Identified by PCA and NMF

Here, we compare five components selected by NMF and PCA to describe the postural response data for normal, two-legged stance (the procedure for selecting the number of components will be described in a later section).

The components identified by PCA are composed of muscle contributions that are both positive and negative, and are activated by weighting coefficients (or scaling factors) that may also be positive or negative (Fig. A.4A). This example illustrates again that the components are identified in order of the percentage of variance that each explains. The first component describes the mean level of activity of the muscles across all conditions, and therefore has positive contributions from all of the measured muscles, with strong contributions from TA and PERO (Fig. A.4A, W_{1pca}). The first component is also strongly activated for forward (90-degree) and backward (270-degree) perturbation directions, which evoke much more muscle activity than lateral perturbation (Henry et al. 1998). The subsequent components have contributions from fewer muscles, and these contributions are both positive and negative. Additionally, the activation coefficients may be positive or negative for different perturbation directions, and the magnitude of activation decreases with each subsequent component.

The way in which PCA decomposes data can best be illustrated by examining how the components contribute to an individual muscle tuning curve. Due to the positive and negative values taken both by the components and the activation coefficients in PCA, contributions from different components can be added and subtracted to obtain the total predicted muscle activity. An example of this can be seen in the reconstruction of the VMED tuning curve from the individual contributions from each component (Fig. A.4B),

which are found by multiplying the height of the VMED bar in each component with the activation coefficient for a given direction. Thus, each of the contributions resembles a scaled and possibly inverted version of the activation coefficient tuning curves of each component (Fig. A.4A). The resulting tuning curve for VMED is generated by adding all five curves together (Fig. A.4B, *bottom*). Although the peaks of the various contributions can vary, the resulting VMED tuning curve peaks near 90 degrees, and is roughly zero between 180 and 360 degrees. The response of the VMED to the 90-degree perturbation is high, and is due to positive contributions from $W_{1pca,}$ W_{2pca}, W_{4pca}, and W_{5pca} and a negative contribution from W_{3pca} (Fig. A.4B, *bars*). Similarly, in the region between 180 and 360 degrees, negative and positive contributions from all the components cancel each other out, so that the resulting tuning curve is near zero. To reconstruct the tuning curve of MGAS, the same curves are scaled differently and added together. The near-zero activity of MGAS in the 90-degree perturbation direction results from the cancellation of positive and negative contributions, primarily from W_{1pca} and W_{2pca}. In general, when using components identified by PCA, the reconstructions tend to underpredict the recorded muscle activity.

In contrast to PCA, the components and activation coefficients identified by NMF contain only positive values, as constrained by the algorithm. They are identified in no particular order, as evidenced by the percentage of total variance accounted for by each component (Fig. A.4C). Each component has large contributions from a few muscles, and smaller contributions from several other muscles, illustrating the multijoint coordination required for postural control. Each component has a corresponding activation coefficient

that is tuned for a particular range of perturbation directions. These activations are also positive, and the magnitude of activation is similar across all five of the components.

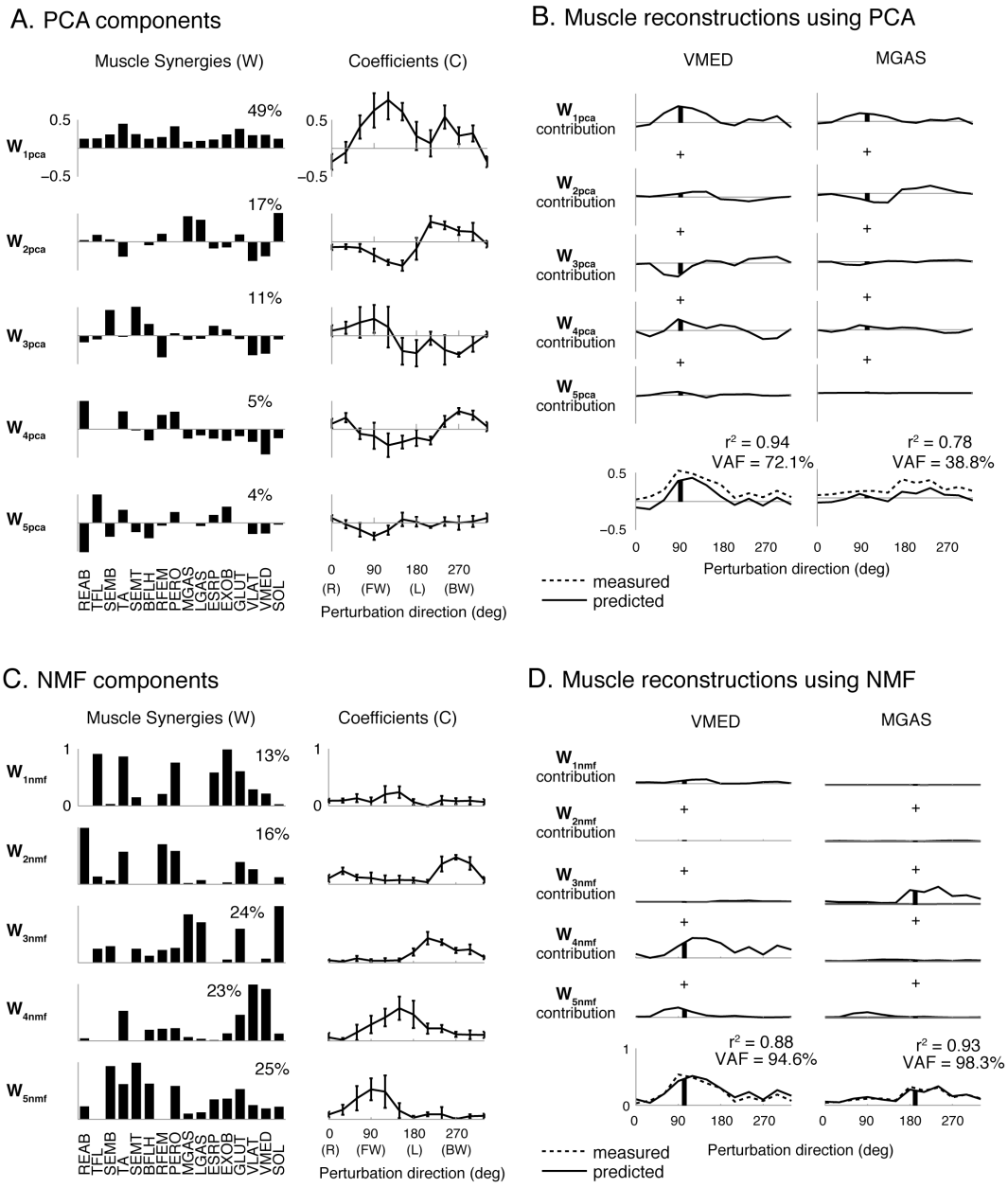


Figure A.4 Components and activation coefficients identified from postural response data using principal components analysis (PCA) and non-negative matrix factorization (NMF). A: Components identified using PCA may have positive and/or negative muscle contributions and activation coefficients. Each bar represents the contribution of that muscle to that component. Percentages indicate the amount of total data variability accounted for by each component. Activation coefficient tuning curves from PR2 are

shown as mean ± standard deviation of five trials. B: Tuning curves created from a single trial in each direction for two muscles reconstructed using the components identified in A. The contribution from each component is added or subtracted to form the reconstructed muscle tuning curve. The original data are shown with a dashed black line and the reconstructed data are shown with a solid black line. The variability accounted for (VAF) by the reconstruction as well as r^2 values are shown for each muscle tuning curve. C: Components identified using NMF have only positive muscle contributions and activation coefficients. Percentages indicate the amount of total data variability accounted for by each component. Activation coefficient tuning curves from PR2 are shown here as mean ± standard deviation of 5 trials. D: Two muscle tuning curves reconstructed using the components identified in C. The contribution from each component is added to form the reconstructed muscle tuning curve. The original data are shown with a dashed black line and the reconstructed data are shown with a solid black line. The variability accounted for (VAF) by the reconstruction as well as r^2 values are shown for each muscle tuning curve.

The reconstruction of the individual muscle tuning curves illustrates the differences between PCA and NMF in the way the components are combined to predict the recorded data. As with PCA, the height of the VMED bar in each NMF component is used to scale the contribution of each component's tuning curve. In this case, since VMED is virtually zero in W_{2nmf} and W_{3nmf}, these components make essentially no contribution to the VMED tuning curve. In contrast to the case with PCA decomposition, the activity of VMED at 90 degrees is due to the additive contributions of three components W_{1nmf}, W_{4nmf}, and W_{5nmf} (Fig. A.4D).

Using NMF, there is no cancellation of features (Fig. A.4D). Each muscle's activity is reconstructed by adding the contributions from each muscle synergy, all of which are positive. Once a feature of the tuning curves is expressed in the contribution of a given component, it cannot be subtracted out. For MGAS, the tuning curve consists primarily of contributions from W_{3nmf}, which causes high activity of MGAS between 180 and 360 degrees, and W_{5nmf}, which is responsible for a low level of activity of MGAS between 0 and 180 degrees.

The separation of the contributions from each component makes it possible to use the patterns of muscle activity within each component to make predictions about the activity of other muscles. In this case, the activity of MGAS between 180 and 360 degrees can be attributed to W_{3nmf}, which coactivates high MGAS activity with high extensor activity in the LGAS, GLUT, and SOL. When MGAS is active between 0 and 90 degrees, its activity is due to W_{5nmf}, which coactivates small MGAS activity with high flexor and hamstring activity in SEMB, TA, and SEMT. This demonstrates that MGAS activity in different perturbation directions results from fundamentally different muscle coordination patterns. It may be a prime mover in 180- to 360-degree perturbations, and a stabilizer in 0- to 90-degree perturbations. The analysis demonstrated that MGAS is strictly covaried with SOL from 180 to 360 degrees, and strictly covaried with TA from 0 to 90 degrees. A traditional correlation analysis would reveal MGAS to be strongly correlated to SOL, and weakly correlated to TA, but it would not be able to decompose the different portions of MGAS activity to one or the other.

Here, the coefficient of determination (r^2) and variability accounted for (VAF), which are measures of goodness-of-fit between the predicted and recorded EMG signals, demonstrate that NMF components can explain the recorded muscle responses more closely than PCA components (NMF average r^2 for all muscles: 0.84, average VAF: 95.5%; PCA average r^2 for all muscles: 0.81, average VAF: 58.9%). Both r^2 and VAF are defined as the coefficient of determination, or percent variability accounted for in the dataset (1 – sum of squares error/total sum of squares). The Pearson correlation coefficient, r, is based on a linear regression with an offset and thus compares only shapes of two curves, allowing for their actual values to differ. VAF is based on a linear

regression that must pass through the origin, and therefore requires that the actual values of the measurements be equal to have a high percent of variability accounted for. In the standard Pearson correlation coefficient (r^2), the sum of squares is taken with respect to the mean, whereas in the uncentered case (VAF), it is taken with respect to zero. In this postural example, PCA reconstructs the shape of the tuning curve well, but not the offset; as expressed by the reasonably high r^2 values, but much lower VAF. In contrast, NMF reconstructs the level of activity well, and allows for more differences in the shape of the curve, which is evidenced in the high VAF values.

A.3.3 Selecting the Appropriate Number of Components Using NMF

In both NMF and PCA, the investigator must determine the number of components required to sufficiently explain the data. With PCA, a cutoff of the total percent variability explained is typically chosen, and the components with the largest contributions are chosen to meet that criterion. A similar criterion can be used in NMF, in which the analysis is run multiple times, each with a different number of components, and VAF can be plotted as a function of component number (Fig. A.5A). In this postural data example, a cutoff of 90% VAF selects four components. Note, however, that the VAF due to one component is very high, so that high VAF values can be misleading in the overall variability because generally they represent a small portion of the data having a large amplitude that contributes the most to the overall data variability.

Whether using PCA or NMF, using the overall variability accounted for to select the number of components may not generate adequate reconstructions of data, particularly when there are certain conditions in which generally less activity occurs, but

which nonetheless are an important feature of the dataset. In the postural control example, the overall level of muscle activity is higher in forward and backward directions. When choosing a smaller number of components, the muscle activity in forward and backward directions tends to be well-explained, whereas activity in lateral directions may not be well-reconstructed. Because muscle activity in lateral directions represents a small fraction of the total variability, it is difficult to discern from the overall VAF scree plot when such variations are accounted for. In both analyses, large differences in the magnitude of the variability across conditions always poses a problem when selecting components.

A number of additional criteria can be imposed to ensure that desired features of the dataset are reconstructed. For our postural control example, we further examined the variability accounted for within subsets of the data. We examined the VAF of each muscle, which ensures that each muscle's tuning curve is well-reconstructed. In certain cases, when a muscle's contribution to the overall variability is low, the features of its tuning curve may not be well reconstructed by the selected number of components, requiring additional components to be added. We then examined the data by perturbation direction, ensuring that the differences in the relative levels of activity by direction do not cause muscle activity in certain directions to be ignored. In these cases, rather than having a smooth increase in VAF as components are added, there tend to be jumps when the salient features are accounted for. Therefore, we specify a minimum %VAF that should be accounted for in all muscles and all perturbation directions, as well as require that the addition of the next component should not drastically improve the VAFs. Ultimately, however, only an experienced researcher examining the reconstructions of the

original raw data traces can determine whether the features accounted for are physiological or are artifacts.

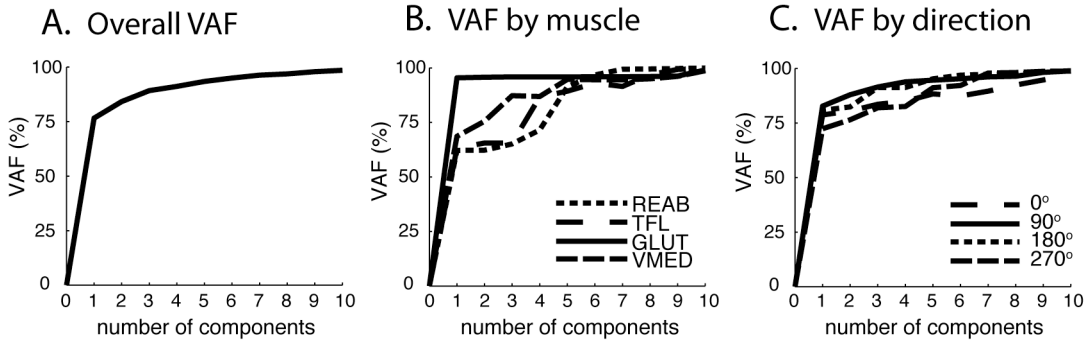


Figure A.5 Scree plots showing variability accounted for (VAF) between the original data and the reconstruction using non-negative matrix factorization (NMF) components for the data shown in Figure A.3. A: VAF for increasing number of components over the entire data set. B: VAF for increasing number of components for four individual muscles: REAB, TFL, GLUT, VMED. One component accounts for variability in GLUT relatively well, three components can explain VMED variability, but five is better at explaining variability in TFL and REAB. **C**: VAF for increasing number of components across individual perturbation directions. Shown here are the four cardinal directions, but the number of components needed was selected by looking at these types of plots for all muscles and all perturbation directions.

The scree plots from the postural response example demonstrate how five components were selected in this case (Fig. A.5). Examining the overall VAF (Fig. A.5A) reveals that one component seems sufficient to explain the variability in the data, using a 75% VAF criterion. However, examining the scree plots for individual muscles reveals that five components are necessary in order for each of the muscles to achieve >75% VAF (Fig. A.5B). These curves demonstrate that the activity of GLUT is well accounted for by the first component, but that activity of the other muscles is not. Three components are necessary for VMED to pass the 75% threshold. However, the addition of the second and third components does not change the VAF of TFL and REAB, as illustrated by the flat part of the lines. The fourth and fifth synergies account for the variability in TLF and

REAB, respectively. Note that the addition of a sixth component does not drastically improve the VAF in any muscle. Therefore, five muscle synergies were chosen. Examining the variability accounted for across the various perturbation directions leads to a similar conclusion (Fig. A.5C). Most directions have >75% VAF using only one or two components, but there is a sizeable improvement from four to five components for backward perturbations (270 degrees).

Finally, the composition of the components should be examined as additional components are added. The sharp jumps in the scree plots of VAF by muscle and by perturbation direction suggest that including an additional component may cause a previous component to split (Fig. A.5B, sharp jump in REAB VAF from four to five components). The number of components selected as sufficient to explain the data should be high enough such that the components have stabilized, and the addition of new components does not significantly change the previous components. In this example, the composition of the components when six components (not shown) were used was compared with the five components identified here and shown not to alter the composition of the five components. Additionally, the reconstructions of the data and the activation coefficients of the sixth component can be used to deduce its contribution to features in the data. If the additional component accounts for a feature, such as a particular burst of muscle activity or tuning direction, that is unaccounted for by the other components, then it may be important; the investigator must decide whether this is a critical and/or physiological feature. If the activation coefficients appear to be evenly distributed across all perturbation directions, it is unlikely to account for a feature associated with muscle activation in a given direction, but is more likely noise.

A.4 Using NMF Versus PCA to Test Motor Control Hypotheses: Standing and Walking

Although it is possible to apply either PCA or NMF to any data matrix, the results may not necessarily provide insight into the underlying physiological mechanisms. It is important to ensure that the results are not artifacts of data collection or experimental design. Both techniques allow the dimension of the dataset to be identified. However, the maximum dimension is limited by the number of muscle signals analyzed, as well as by the number of disparate conditions examined. Therefore, it is critical that the data matrix itself be of high enough dimension such that a reduction in dimension is meaningful. The extraction of components relies on muscles being coordinated in different patterns. Therefore, the number of muscles recorded must be adequately high to capture different patterns of covariation, and the number of experimental conditions or possible variations observed must be of high enough dimension to capture different coordination patterns among the muscles. If muscle activation patterns are truly independent, this will also be reflected in the component analysis.

For example, the early studies of postural responses examined only two directions of perturbation (forward and backward). It was suggested that there were only two muscles synergies necessary, one active for forward perturbations, and another for backward perturbations (Nashner 1977; Horak and Macpherson 1996). However, these finding revealed experimental rather than physiological constraints. If NMF or PCA were applied only to forward and backward perturbations, they would arrive at a similar conclusion because the data only represent two conditions. By examining multiple

perturbation directions, it becomes clear that more than two muscle synergies are needed to describe the full repertoire of postural responses (Macpherson 1988; Macpherson 1991; Henry et al. 1998), but a new muscle synergy is not necessary for each perturbation direction (Torres-Oviedo et al. 2006; Torres-Oviedo and Ting 2007). Similarly, the total number of components that can be extracted is limited by the number of muscles that are recorded. It also depends upon muscles being coactivated during certain conditions and not others. Therefore, if only a few muscles are recorded, it is possible that they would each comprise a single synergy if they are independently activated. Conversely, if they are always coactivated, then they will comprise only a single muscle synergy. Again, sufficient experimental conditions must be tested to demonstrate that the muscles could be coactive or independent, depending upon the condition. Such manipulations in pedaling revealed that certain muscles that are always coactive during forward pedaling may have different patterns of activation in backward pedaling (Ting et al. 1999).

Once it is established that the number of muscles and conditions is appropriate and can provide enough variability to extract a smaller number of components, the robustness of such components can then be tested across tasks (Krishnamoorthy et al. 2004; Cheung et al. 2005; d'Avella and Bizzi 2005; Torres-Oviedo et al. 2006). The generality of muscle synergies has been shown in a few studies in which synergies were shared between multiple tasks, such as frog kicking, jumping, and swimming, and in human walking/running, and pedaling forward and backward (Raasch and Zajac 1999; Ting et al. 1999; Cheung et al. 2005; d'Avella and Bizzi 2005; Cappellini et al. 2006; Torres-Oviedo et al. 2006). Although some synergies are used in multiple tasks, sometimes new synergies emerge when a new motor task is presented (Ivanenko et al. 2005) or the

activation of the synergies may be adjusted (Cappellini et al. 2006).

Here, we provide two examples of the differences between NMF and PCA when applied to test the robustness of muscle synergies (a) across postural tasks, and (b) during walking.

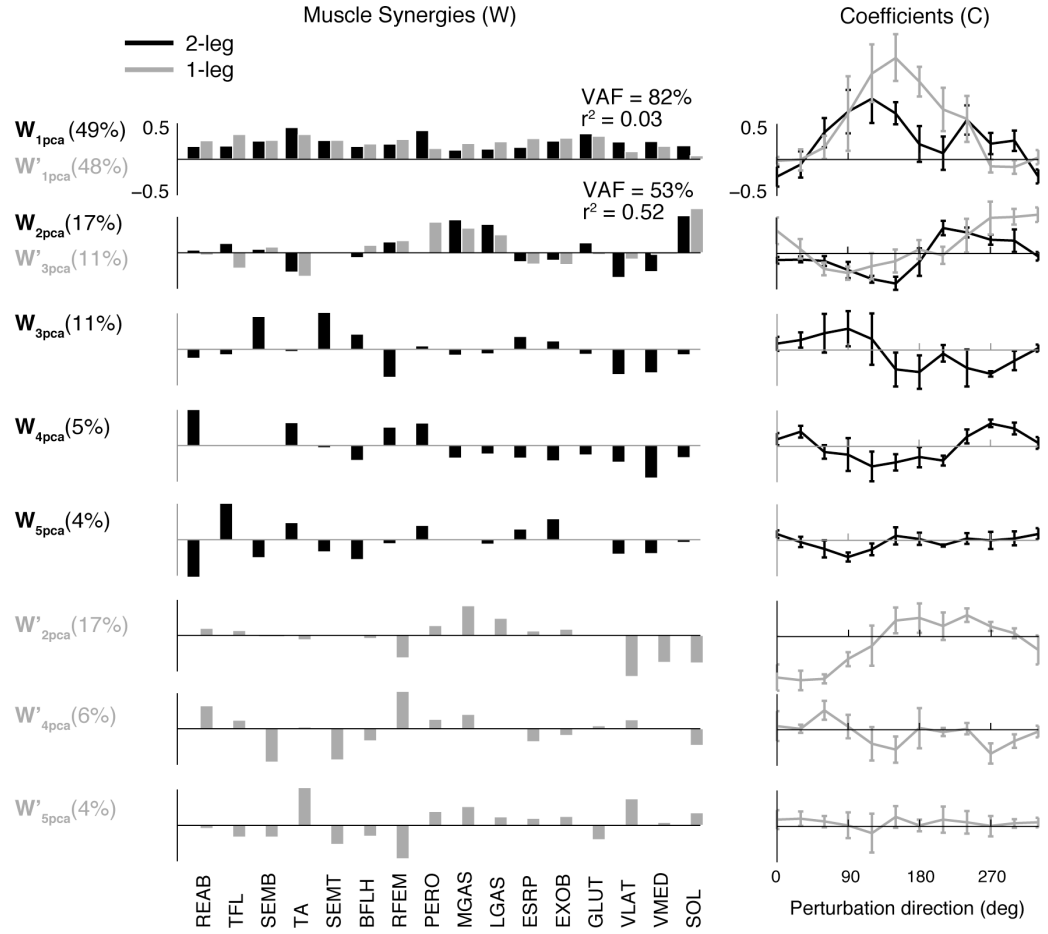
A.4.1 Are Muscle Synergies Stable or Artifact? Shared Versus Specific Components

Here, we used PCA and NMF to test whether muscle synergies are stable across postural tasks by comparing the components extracted from perturbations in two-legged stance extracted above (Fig. A.4) to those from perturbations during one-legged stance. Subjects stood on their right leg and were subject to 12 directions of perturbations of smaller velocity and amplitude than in two-legged stance. One- and two-leg data were recorded in the same session, so that the activity of the 16 lower trunk and leg muscles from the stance side could be directly compared.

When PCA was applied to the one-leg data set to identify muscle synergies, two of the components extracted were similar to those identified from the two-leg postural responses (Fig. A.6A). The first component (W'_{1pca}) is comprised of small contributions from all of the muscles, representing the average responses, so these would be expected to remain the same. Because the similarity between components from one- and two-legged stance are mainly based on the mean level of muscle activity, the VAF provides a better representation of the similarity than r^2 (r^2=0.0291, VAF = 82%). The third component from one-leg responses, W'_{3pca} (Fig. A.6A, *gray bars*), looks similar to the second one identified from two-leg responses, W_{2pca} (Fig. A.6A, *black bars*), suggesting it is more highly activated in two-leg responses. The other components, most of which

account for a smaller percentage of variance, are quite different in the one-leg task compared to the two-leg task (max $r^2 = 0.176$, max VAF=17.5%). Therefore, if PCA were used to identify muscle synergies, the conclusion would be that different muscle synergies are used for one- and two-leg postural responses.

When NMF was applied to the one-leg data set to identify muscle synergies, however, four of the five components were very similar to those used during the two-leg balance responses (r^2=0.27 – 0.76, VAF=51%–85%, Fig. A.6B). The muscle contributions to each of these four components was similar, and the activation coefficient tunings shifted slightly to account for differences in individual muscle tuning curves. The fifth component from two-leg stance (W_{2nmf}) had a large contribution from REAB, a hip flexor, whereas the fifth component in one-leg stance (W'_{5nmf}) has primarily SOL activity, an ankle extensor. This is likely because subjects were more likely to use a hip strategy in two-leg stance compared to one-leg stance. Further, the component used in one-leg stance (W'_{5nmf}) was strongly activated for rightward (0 degree) perturbations. Note that, in the two-leg stance, none of the five components were tuned for rightward perturbation directions (Fig. A.6B). This suggests that when both legs can be used to respond to a rightward perturbation, subjects use muscles in the left leg to restore their balance, but when the left leg is not available, an additional component in the right leg must be activated to compensate for the loss of stability provided by the left leg. These results show that there are similar components that are used across postural tasks, suggesting that the muscle synergies derived from NMF are physiological constraints that the nervous system uses for muscle coordination, and not simply artifacts of the experiment or analysis.


A. PCA
Muscle Synergies (W)
Coefficients (C)
2-leg
1-leg
VAF = 82%
r2 = 0.03
VAF = 53%
r2 = 0.52
W1pca(49%)
W'1pca(48%)
W2pca(17%)
W'3pca(11%)
W3pca(11%)
W4pca(5%)
W5pca(4%)
W'2pca(17%)
W'4pca(6%)
W'5pca(4%)
0.5
−0.5
REAB
TFL
SEMB
TA
SEMT
BFLH
RFEM
PERO
MGAS
LGAS
ESRP
EXOB
GLUT
VLAT
VMED
SOL
0
90
180
270
Perturbation direction (deg)

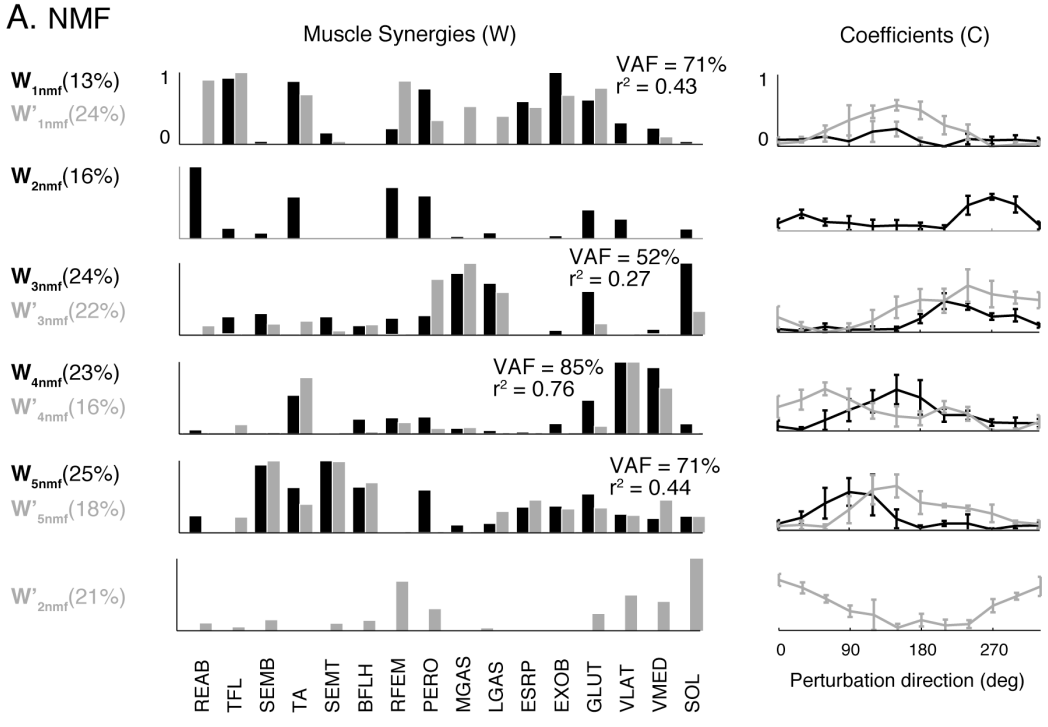

A. NMF
Muscle Synergies (W)
Coefficients (C)
VAF = 71%
r2 = 0.43
VAF = 52%
r2 = 0.27
VAF = 85%
r2 = 0.76
VAF = 71%
r2 = 0.44
W1nmf(13%)
W'1nmf(24%)
W2nmf(16%)
W3nmf(24%)
W'3nmf(22%)
W4nmf(23%)
W'4nmf(16%)
W5nmf(25%)
W'5nmf(18%)
W'2nmf(21%)
1
0
REAB
TFL
SEMB
TA
SEMT
BFLH
RFEM
PERO
MGAS
LGAS
ESRP
EXOB
GLUT
VLAT
VMED
SOL
0
90
180
270
Perturbation direction (deg)

Figure A.6 Comparison between components identified from one-leg postural responses compared to those identified from two-leg postural responses. A: Comparison of components and activation components identified using principal components analysis (PCA). Black bars and lines are two-leg responses (same as in Figure A.4), and gray bars and lines are one-leg responses. Percentages on the left-hand side of each component represent the percent total variability that each component accounts for. Numbers to the right of each component are indicators of how closely the component from one-leg responses matches the one from two-leg responses. Both r^2 and uncentered r^2 (variability accounted for; VAF) are shown. The first component from one-leg (W'_{1pca}) and two-leg responses (W_{1pca}) matches fairly well, and the third component from one-leg responses (W'_{3pca}) matches the second component from two-leg responses (W_{2pca}). Subsequent components do not match; due to the orthogonality constraint of PCA, when one component changed, subsequent components changed also. B: Comparison of components and activation coefficients identified using non-negative matrix factorization (NMF). The same components are used in one-leg and two-leg responses, with the exception of one component that is specific to either condition. The additional component used in one-leg responses is tuned for 0-degree perturbations, which presumably are accounted for by the left leg in two-leg responses. The same components, or muscle synergies, can explain the different individual muscle activations observed between these two tasks, by only changing the activation of the muscle synergies.

Although the example demonstrates the possibility of stable components across tasks, thorough cross-validation tests should be performed to ensure that the components are indeed stable across tasks. Therefore, to draw stronger conclusions about the physiological basis of the components, the results of analyses across different subsets and combinations of the data should be compared (e.g Torres-Oveido and Ting 2010). Apart from extracting components independently from control (e.g., two-leg) and test (e.g., one-leg) tasks, the components from the control condition can be used to reconstruct the test data. If they do not explain a sufficient percentage of the variability, then condition-specific components may be extracted from the remaining variability of the data (Cheung et al. 2005). Additionally, components extracted from the control and test data pooled into one large data set should render similar results. If the same components are identified

in all of these cases, it is more likely that the technique has identified underlying physiological features of the data. In our example using NMF, the same components are identified in one-leg and two-leg stance using all these different combinations (not shown). In contrast, PCA generates different components depending on which data combination is used.

A.4.2 Using Time As a Condition: Muscle Synergies During Walking

When applying PCA and NMF to a continuous motor task, such as locomotion, time can be considered to be a condition. Similar to the different directions of postural perturbations, different coordination patterns across muscles are observed across different time points in the locomotor cycle. However, if muscles are activated in a similar pattern across time, such as in an isometric task, the use of time as a condition may not provide enough variability in the data to allow for meaningful interpretation. In this example, subjects walked freely at a slow (0.7 m/s) pace for at least ten steps each trial. Data were recorded beginning at heel strike of the third to fourth step, so that subjects had already reached a steady-state gait, and each trial includes at least three full stride cycles. Seven trials were included in the data matrix. Sixteen EMG signals were recorded in one leg (Fig. A.7).

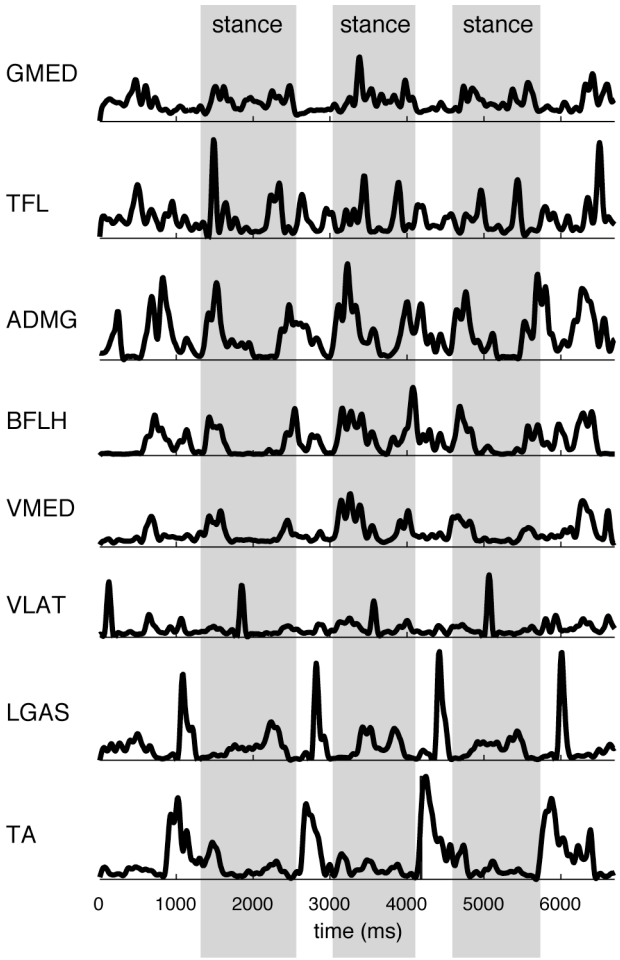


Figure A.7 Example of muscle activity during a forward walking trial. Shown are eight muscles of the 16 recorded. The subject was walking at a speed of approximately 0.7 m/s. The shaded gray boxes indicate stance phase.

To create the data matrix, the mean activity was computed in 10 ms bins over the three steps in each trial. *Binning* has the advantages of smoothing the data, reducing the total number of conditions, thus reducing computation time, while maintaining much of the detail in the variations of the EMG within and across cycles. Note that the muscle activation patterns do not resemble the idealized sinusoidal EMG patterns often found due to smoothing or averaging. Additionally, the pattern of muscle activity and the duration of the stance phase vary from step to step, as does the number of bins. There is no need to stretch or shorten the data across time to obtain a consistent number of data

points per stride. When creating the data matrix, different trials are simply concatenated end to end.

It is important to distinguish between two mutually exclusive hypotheses that can be tested by decomposing walking data into muscle synergies. For both PCA and NMF, the components W_i are assumed to be fixed, whereas the activation coefficients or scaling factors c_i are allowed to vary (Clark et al. 2010). Here we choose W's to refer to fixed muscle activation patterns, whereas we allow c's to vary across time. The data must be structured such that the muscles are the observations (rows for NMF, columns for PCA) and the time windows are the conditions (columns for NMF, rows for PCA). Conversely, it is possible to hypothesize that the timing patterns are stereotypical across cycles, and that the muscle coordination patterns vary (Ivanenko et al. 2004; Cappellini et al. 2006). Fixed timing patterns might be generated by a central pattern-generating neural circuit, with their muscle targets changing with phase. In this case, it is necessary to stretch the cycles in time so that they all have the same number of points. In this case, the data should be transposed, such that the time points are the observations, and the muscles are the conditions, with repeated trials or cycles concatenated. However, in neither analysis can both the components and the timing patterns vary. Either muscular coactivation patterns or timing patterns must be assumed to be the same across all conditions.

Here, we compare six components extracted from one subject's walking data using PCA and NMF (Fig. A.8).

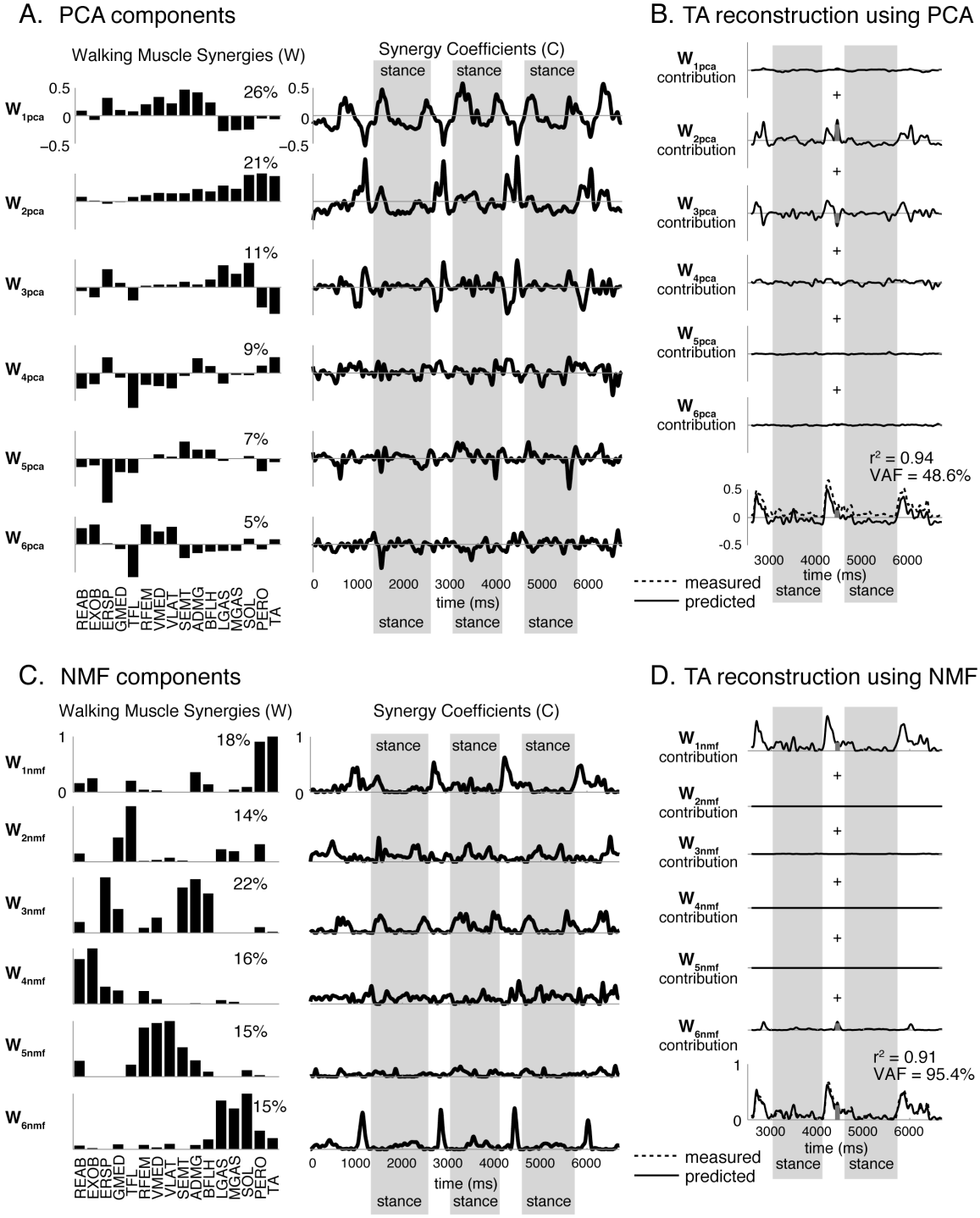


Figure A.8 Components and activation coefficients identified from walking data using principal components analysis (PCA) and non-negative matrix factorization (NMF). A: Components identified using PCA may have positive and/or negative muscle contributions and activation coefficients. Percentages indicate the amount of total data variability accounted for by each component. The shaded gray boxes indicate stance phase. Activation coefficients from one trial of walking (the same trial as in Figure A.7)

are shown. Components from PCA have contributions from many muscles. The first few components have activation patterns that are aligned with particular phases of the gait cycle, whereas the last few have less identifiable patterns. B: TA muscle activity from a single trial reconstructed using the PCA components identified in A. The original data are shown with a dashed black line and the reconstructed data are shown with a solid black line. Variability accounted for (VAF) and r^2 indicate goodness-of-fit. **C**: Components identified using NMF have only positive muscle contributions and activation coefficients. Components from NMF tend to have strong contributions from only a few muscles. Activations coefficients for some components (W_{1nmf}, W_{2nmf}, W_{3nmf}, and W_{6nmf}) are aligned with particular phases of the gait cycle, whereas others may be stabilizing components since they are active throughout the entire trial (W_{4nmf} and W_{5nmf}). **D**: TA muscle activity from a single trial reconstructed using the NMF components identified in C. The original data are shown with a dashed black line and the reconstructed data are shown with a solid black line. VAF and r^2 indicate goodness-of-fit.

Similar to the postural response example, the first component identified using PCA primarily describes the mean level of muscle activity, and the later ones described deviations from that mean. The first two components contained primarily positive contributions from nearly all of the muscles. The first component was activated positively at the beginning and end of stance and activated negatively in swing, whereas the second component was positively activated in swing but negatively activated in stance. The subsequent components all had both negative and positive contributions from different muscles, and their activation coefficients over time decreased in amplitude, but increased in frequency. Although the first three components had peaks that corresponded to identifiable events in the gait cycle and various EMG activity (Fig. A.7), the last three had high-frequency oscillations that were not localized to a particular phase in the locomotor cycle. Reconstructing the TA EMG signal reveals that the activity during swing phase is composed of contributions from two components primarily, although there are small contributions from all components (Fig. A.8B). Both components contribute to the large peak in TA activity. However, the smaller, secondary burst is due to a positive

contribution from W_{2pca} that is largely cancelled by a negative contribution from W_{3pca}. (Fig. A.8B). Note that the r^2 value is quite high, indicating a good match of shape, whereas the VAF level is low, indicating that the predicted EMG amplitudes do not match measured values.

The six components extracted using NMF were quite different from those found using PCA. Each component consists of large contributions from a small number of muscles, and the muscles tend to be grouped according to joint or function. Some of the components were activated at specific points during the gait cycle, such as W_{3nmf} being activated at early stance and again at late stance, W_{1nmf} activated during early swing, and W_{6nmf} during late swing. Other muscle synergies were activated throughout both stance and swing, suggesting that they may be used for stabilization (W_{4nmf} and W_{5nmf}). As in the postural example, the bursts of activity appearing in the activation coefficients resemble the bursts observed in the original EMG data (Fig. A.7). Only two NMF components contribute to TA EMG activity (Fig. A.8D). W_{1nmf} contributes most of the TA activity, including the large burst in early swing phase. The contribution from W_{6nmf} adds a small secondary burst.

Again, the components extracted during walking must also be cross-validated over a number of different test extractions to be sure that they are stable and not artifacts of the way the data are represented. In our NMF analyses, we find components to be stable across time bins sizes of 10 to 100 ms during walking. Components are also stable if fewer trials are analyzed, or if faster walking speeds are analyzed. Moreover, the components extracted from one speed can account for variations in EMG occurring with changes in walking speed (Clark et al. 2010). However, the components change if EMGs

are averaged across strides, and less of the variability from stride to stride is accounted for by components extracted from averaged data.

A.5 Conclusion

Are linear decomposition techniques useful for understanding motor control (Macpherson 1991; Tresch and Jarc 2009)? Ultimately, no decomposition technique is perfect, and much discretion and interpretation must be exercised on the part of the investigator when drawing conclusions from any such analysis. Computational analyses cannot replace the judgment and intuition of the researcher, and ultimately the results must make sense in a physiological context. Therefore, it is critical that the implicit hypotheses, assumptions, and constraints inherent in any technique be understood in order to use it usefully in motor control or other scientific research. In the best-case scenario, a linear decomposition can be a tool that can formally test a hypothesis that the researcher formulates by looking at the raw data and observing the synchrony and variability across multiple EMG signals. It allows different periods of activity within a muscle to be attributed to different underlying components. In the end, the relationship between the derived components and the original data may potentially allow a researcher to draw conclusions about the underlying neural mechanisms if the components do not represent limitations of the recordings, experimental conditions, or other data artifact. Ultimately, to make any sort of physiological conclusion, the extracted components must be interpreted in terms of the known underlying physiological mechanisms and biomechanical outputs. The examples presented here demonstrate intuitively the workings of NMF and PCA, with the aim of informing and aiding in the interpretation of

data. Such exercises can be performed to better understand any kind of decomposition technique, each with its own advantages and disadvantages (Tresch et al. 2006).

Is the added computation useful for understanding motor tasks? In some cases, the answer may be "no," particularly for any kind of initial analysis of a motor task or experimental condition. The technique must appropriately match the hypothesis. Component decompositions can be useful when examining the detailed workings of complex multimuscle coordination. It is useful for comparing complex muscle coordination across different tasks or trials in which muscle activity changes, but the underlying coordination principles may be the same, as we have shown in fast and slow walking (Clark et al. 2010), or one- and two-legged postural control (Torres-Oviedo and Ting 2010). In cases in which repeated measures are not possible, such as in patient populations, highly variable motor patterns are difficult to analyze from traditional techniques that rely on averaging. In this case, a component decomposition can identify whether common underlying elements are being activated across different trials or tasks (Clark et al. 2010). Similarly, the underlying components may provide a better measure of similarity or differences across individuals than the comparison of individual EMG traces (Ting 2007; Ting and McKay 2007). It is possible to identify whether individuals with different EMG patterns have similar underlying components but activate them differently, or if instead they have different numbers or composition of underlying components (Torres-Oviedo and Ting 2007; Clark et al. 2010)

Decomposition can also be useful for understanding the function of the underlying components. These analyses are difficult and do not always work. They require many practical considerations to accommodate limitations of the analysis techniques, and

require the investigator to guess at the correct variables that are being controlled. But if a relationship is not found, it does not mean that there is no functional role for that component. Previous work in postural control has shown in cats that muscle synergies are recruited to control forces at the ground (Ting and Macpherson 2005; Torres-Oviedo et al. 2006). Such an analysis includes biomechanical variables as additional observations (rows) in the data matrix and extracts functional muscle synergies, which are composed of both muscles and functional variables (Torres-Oviedo et al. 2006). However, the application of NMF to biomechanical variables poses a challenge because negative and positive changes in forces necessarily result from different muscle groups requiring them to be partitioned physiologically (Ting and Macpherson 2005; Torres-Oviedo et al. 2006; Valero-Cuevas 2009). Because changes in velocity and position require the integration of forces, the relationship between muscle activity and kinematics is highly redundant, and also difficult to predict without explicit models (Gottlieb et al. 1995; Lockhart and Ting 2007). This redundancy is evident in studies relating the activation of components found using PCA to center-of-pressure shifts in human balance control using the uncontrolled manifold hypothesis (Latash et al. 2002; Krishnamoorthy et al. 2003a; Ting and Macpherson 2005). These studies demonstrate that, although functional roles of individual components may be identified, the variability in their activation may not be reflected in the variability of the output because they are precisely coordinated by higher mechanisms in the nervous system to reduce variations in the desired motor task. Alternately, biomechanical simulation and analysis techniques allow the functional role of the muscle coordination patterns identified by the extracted components to be explicitly tested (Raasch et al. 1997; Berniker et al. 2009; Neptune et al. 2009).

Additionally, the feasibility of robustly using such components to coordinate a repertoire of movement can also be explored (Kargo and Giszter 2008; McKay and Ting 2008; Raasch and Zajac 1999; Valero-Cuevas 2000; Valero-Cuevas et al. 2003). However, it is difficult to build appropriate dynamics models and to record from all of the muscles involved in a movement to use such techniques. Moreover, models of the neural control mechanisms that shape and use the components effectively need to be explored (Berniker et al. 2009). Again, in order for any of these techniques to be useful in relating muscle activity to functional variables, the investigator must have a good understanding of their raw data and the underlying physiological and biomechanical mechanisms in order to interpret the results of the component analysis appropriately.

Do the identified components extracted using computational techniques reflect the organization of neural circuits for movement? One of the attractive features of components from NMF is that they generate a part-based type of representation that appears similar to both neurophysiological observations, as well as to predictions from "sparse-coding" algorithms in sensory systems (Olshausen and Field 2004). The idea is that in a retinotopic, somatotopic, or other sort of spatial sensory map in the nervous system, only a small region is activated for any given stimulus, such as a location in space, or a part of the body. This "sparse" coding means that a minimum of neurons is used to encode a particular feature from among all of the information contained in that map. But, as in PCA, it is also possible to imagine a system in which neurons in the entire map are activated given a particular stimulus, and their net output results in the identification of a particular stimulus. The sparseness property has also been proposed for motor system and is proposed to improve energetic expenditure by reducing the number

of neurons involved in any given behavior, as well as improving computational efficiency, thus reducing the total number of elements that need to be modified during motor adaptation (Olshausen and Field 2004; Fiete et al. 2007; Ting and McKay 2007). Accordingly, localized regions of motor cortex are activated to perform a given movement, and muscle synergies for reaching have been proposed to result from cortico-motoneuronal cells that project to multiple muscles (Graziano and Aflalo 2007; Scott and Kalaska 1997). Similarly, reticulospinal neurons active during postural control (Schepens and Drew 2006; 2004; Schepens et al. 2008; Stapley and Drew 2009) also project to multiple muscles in the limbs and trunk, and interneurons in the spinal cord may facilitate coordination of muscles within and between the limbs during locomotion (Drew et al. 2008; McCrea 2001; Quevedo et al. 2000).

Although, NMF components may provide one computational tool among the many needed to understand the sensorimotor transformations involved in determining how we move, much research is warranted before any of the questions about the utility and interpretability of the resulting components can be resolved. Component decompositions allows large datasets of EMG data and other variables to be decomposed into components that must be interpreted and compared to the organization of neural control systems upstream, and their functional biomechanical outputs downstream. NMF is especially useful for examining neural and muscle activity signals that are inherently non-negative. PCA may prove more useful for analyzing biomechanical variables that take on both positive and negative values without consideration for muscle activity. The continued development of physiologically relevant decomposition techniques combined

with experimental and computational studies may eventually allow us to better understand how learning, adaptation, and rehabilitation occurs in the motor system.

APPENDIX B

VOLUNTARY STEPPING

B.1 Introduction

Previous studies have shown differences in muscle activity and step latency between a reactive step in response to a perturbation and a voluntary step. In voluntary steps (pre-planned steps in which a perturbation is the cue), the muscles were not activated as much as in reactive stepping, and the latency to step is longer due to the presence of an anticipatory postural adjustment (APA) when a step is pre-planned (Horak and Macpherson 1996; Maki and McIlroy 1997; McIlroy and Maki 1993a). The APA which has been observed in voluntary steps consists of initial vertical loading of the stepping foot before lift off, which serves to move the center of mass (CoM) toward the stance foot, ensuring that the body is supported during the movement (Maki and McIlroy 1997). This anticipatory behavior is absent in reactive steps taken in response to a perturbation (McIlroy and Maki 1993a). Even so, I predict that the same muscle synergies will be used in the stance leg in the voluntary stepping condition as were used in the reactive non-stepping and stepping tasks (see Chapter 2). The kinematics and CoM movement will be the same for reactive and voluntary stepping tasks, but the command to activate the synergies will come from different levels of the nervous system. The command in a voluntary step comes from motor cortex, but in a reactive step it comes from a lower level, perhaps brainstem, in response to a combination of sensory inputs that provide information about the body orientation and CoM position.

Additionally, the displacement of the CoM is achieved slightly different in these two conditions. In reactive stepping, the CoM is displaced initially due to the platform motion, then further displaced via generation of forces at the ground to cause a step. In voluntary stepping, the entire CoM displacement results from forces generated by the stance leg. We hypothesize the muscle synergies are activated to perform a specific biomechanical function (such as generate forces at the ground) in order to control the movement of the CoM. Since both of these tasks require control of CoM, I expect to see the same muscle synergies used in both tasks, and only the commands to the synergies will need to change in order to produce the differences in individual muscle patterns that have been observed and required ground reaction forces.

In this study, I plan to identify muscle synergies underlying both reactive and voluntary steps. Thus the biomechanics of the tasks will be identical but the command to the muscles will originate from different levels of the nervous system, giving us an indication of how accessible the muscle synergies are and the role sensory feedback plays in their activation. As a first step, I examined the kinetics, kinematics, and EMG underlying reactive and voluntary stepping in different directions. While a few studies have examined reactive stepping in multiple directions (Maki and McIlroy 1997; Zettel et al. 2002), multidirectional voluntary stepping has not been studied nor compared to reactive stepping.

Here we examined whether the presence of APAs in voluntary steps and absence in reactive steps generalizes to other directions of stepping. The biomechanics of stepping are different depending on the direction of the step; in order to execute the step, muscles are activated differently over different directions. What is the nature and

function of the APA and under what conditions is it necessary? Studies of whole-body reaching have shown that APAs do not necessarily oppose a focal movement, but instead may vary to set up the desired task dynamics (Stapley et al. 1999). Here examined the sequence of events that occured during reactive and voluntary stepping, focusing on the presence or absence of an APA. Furthermore, we investigated the origin and function of the APA by examining its timing relative to muscle activity.

B.2 Methods

First subjects were asked to maintain standing balance as the support surface translated in any of 12 directions in the horizontal plane; they were instructed to step with their left foot if necessary. Next, subjects were asked to voluntarily step with their left foot in the same 12 directions as quickly as possible following the onset of a visual cue. EMG activity was measured from 16 muscles of the right (stance) leg and lower trunk. Mean EMG levels were calculated just before and after step initiation, and EMG tuning curves across directions were examined.

B.2.1 Data Collection

Eight healthy subjects between the ages of 19 and 26 were exposed to two sets of support-surface translations according to an experimental protocol that was approved by the Institutional Review Boards of Georgia Tech and Emory. Subjects stood on a platform that translated in 12 equally spaced directions in the horizontal plane (see Figure 1). They were instructed to maintain balance without stepping if possible, but if a step was necessary, to step with their left foot. This was done to ensure steps would be

reactive and not voluntary, intentional steps. Two blocks of ramp-and-hold perturbations in each of these 12 directions were presented. In the reactive stepping block, the platform's displacement was 23 cm, velocity was 45 cm/s and acceleration was 0.75g. In the non-stepping block, the platform's displacement was 12.4 cm, velocity was 35 cm/s, and acceleration was 0.5g. The perturbation directions were randomized during each block of perturbations to minimize anticipatory adjustments and increase response variability. Due to the influence of prior trials on a subject's response (Horak and Nashner 1986), we first collected the stepping block of trials and then the non-stepping block of trials. Five trials of each condition (stepping and non-stepping) in each of the 12 directions of perturbation were collected. In the stepping condition, all subjects took a step in response to perturbations in all directions. Occasionally subjects stepped with their right foot and these trials were excluded from the analysis. In the non-stepping condition, all subjects maintained balance without taking a step.

For some subjects, the parameters used to induce stepping in the reactive stepping condition actually did not cause the subjects to step, particularly in lateral directions. Increasing the input velocity caused an increase in platform acceleration in cardinal directions, but in diagonal directions caused a curved trajectory. We attempted to get a consistent stepping response in all directions; therefore, the parameter set used during the reactive stepping condition had increased velocity input values for directions 0 and 180, which resulted in a platform acceleration of ~0.95g. A previous study used different displacements for medial perturbations compared with anterior/posterior perturbations due to differences in stability when perturbed in those directions (Macpherson 1988),

confirming this is a reasonable approach to ensure consistent responses across all directions.

Subjects also performed two sets of voluntary steps in multiple directions. A screen in front of the subjects showed empty circles in the same 12 directions as the reactive conditions. In each trial, one of the circles would light up, indicating to the subject which direction they should step. In the voluntary step out and back condition, subjects were instructed to step as quickly as possible towards the direction of the indicator light, using their left foot, and were told the light would turn off once they had shifted their weight to the stepping leg. They were instructed to immediately step back to the starting position when the light turned off. The reason for them to quickly return to the starting position was because in reactive stepping responses, subjects tended to step very quickly, just long enough to catch themselves before falling, and then immediately returned their feet to the center. They shifted ~75% of their weight onto the stepping leg before stepping back to the center. Therefore the weight shift required to turn the light back off in the voluntary step out and back condition matched as closely as possible the weight shift observed in reactive stepping responses. There were no markers on the floor indicating where exactly they should step to; they were simply told to step towards the direction indicated by the light while looking straight ahead. The kinematics of this voluntary stepping task seem to match closely the kinematics of the reactive step, ensuring that any differences we see in muscle activity/synergies are due to the different commands rather than a different movement. Note that if subjects were not instructed to step quickly, the motion of the step looked completely different, so any differences observed could be due to a different movement rather than a different command. This

condition mimicked the reactive stepping in that the subject knows their end goal is to return the CoM to the center.

Subjects also performed a second set of voluntary steps in the voluntary step out and hold condition. In this condition, again subjects stepped quickly towards the direction of the indicator light with their left foot, but this time they were instructed to shift their weight onto the stepping leg (without lifting the right foot) and hold it there. Thus the end goal in this condition was to push the CoM away, similar to a gait initiation step.

Surface EMG activity was recorded from sixteen lower back and leg muscles on the subject's right side, which was the stance leg in all stepping conditions. The muscles recorded included: vastus lateralis (VLAT), rectus femoris (RFEM), rectus abdominis (REAB), biceps femoris, long head (BFLH), semitendinosus (SEMT), adductor magnus (ADMG), erector spinae (ERSP), abdominal external oblique (EXOB), vastus medialis (VMED), tibialis anterior (TA), medial gastrocnemius (MGAS), lateral gastrocnemius (LGAS), soleus (SOL), peroneus (PERO), tensor fasciae latae (TFL), and gluteus medius (GMED). EMG data were high pass filtered at 35 Hz, de-meaned, rectified, and low-pass filtered at 40 Hz, using custom MATLAB routines. Additionally, kinetic data were collected at 1080 Hz from force plates under the feet (AMTI, Watertown, MA) and kinematic data were collected at 120 Hz using a motion capture system (Vicon, Centennial, CO) and a custom 25-marker set that included head-arms-trunk (HAT), and bilateral thigh, shank, and foot segments (Winter 1990). CoM acceleration was calculated from ground reaction forces (F=ma), and CoM position was calculated using kinematic data and the Vicon Plug-in-Gait model.

B.2.2 Data Processing

To distinguish any anticipatory muscle activation from the actual stepping movement, two time bins were analyzed: one prior to step initiation and one following step initiation. Step initiation and APA onset were defined by divergences in GRF. Step initiation was defined as the time when the right foot began rapidly loading while the left foot began unloading, and APA onset was the time when the left foot began loading while the right foot started unloading. To analyze forces, two time bins were defined: the APA period which lasted from APA onset to step initiation, and the Step period which last from step initiation until 200ms after step initiation (Figure B.1, gray shaded regions). To analyze EMG patterns that would have been responsible for generating these force shifts, each time bin was shifted back by 60ms to account for electromechanical delays. Therefore, for EMG analysis, the APA period was from 60ms before APA onset until 60ms before step initiation, and the Step period was from 60ms before step initiation until 140ms after step initiation. Mean muscle activity for each muscle during each time bin was calculated for each trial. These numbers were assembled to form a data matrix, which consisted of 2 time bins x 12 directions x 5 trials = 120 points for each of the 16 each muscles. For display purposes, each muscle's EMG values were initially normalized to the maximum value across all time periods, perturbation directions, and conditions so that each value was between 0 and 1. Tuning curves were generated with respect to step direction in order to examine muscle activity across all 12 perturbation directions in each condition and time bin.

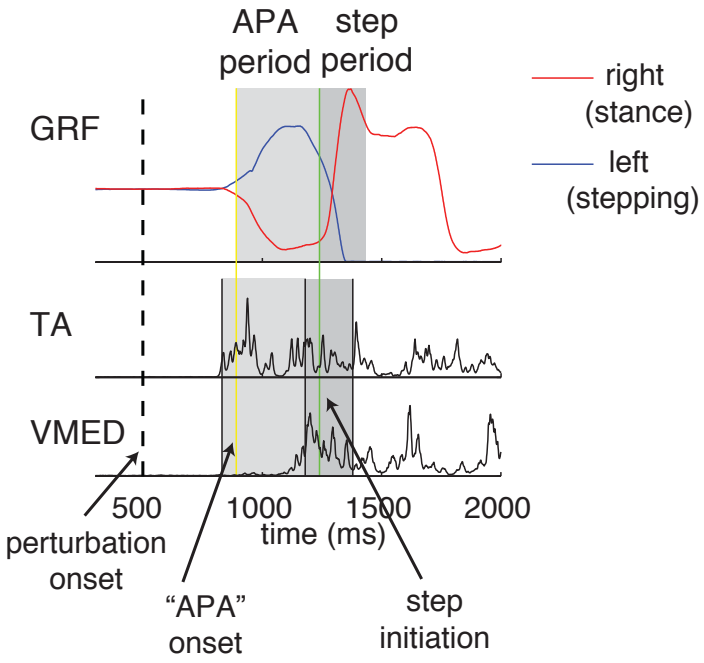


Figure B.1 Example of EMG and GRF during a rightward voluntary step. Vertical dashed line indicates the onset of the light cue, and EMG responses generally occur ~300-400ms after the cue. Shown here are tibialis anterior (TA) and vastus medialis (VMED) from the right (stance) leg. Ground reaction forces under the feet are also shown. EMG activity was averaged during two time periods, the APA period and step period, to generate tuning curves. For EMG analysis, the APA period begins 60ms before APA onset (yellow vertical line) and lasts until 60ms before step initiation (green vertical line). These windows are 60ms earlier than time windows used to analyze forces, to allow for electromechanical delays.

B.3 Results

Voluntary steps in response to a visual cue were initiated later than reactive steps in response to a perturbation, as expected (Figure B.2). Nevertheless, reactive and voluntary steps had similar kinematics. Voluntary steps were slightly longer duration and slightly longer step length than reactive steps, but generally the voluntary steps from the voluntary step out and back condition matched the reactive steps fairly well. The

variability in step locations observed in voluntary steps was similar to that observed in reactive steps.

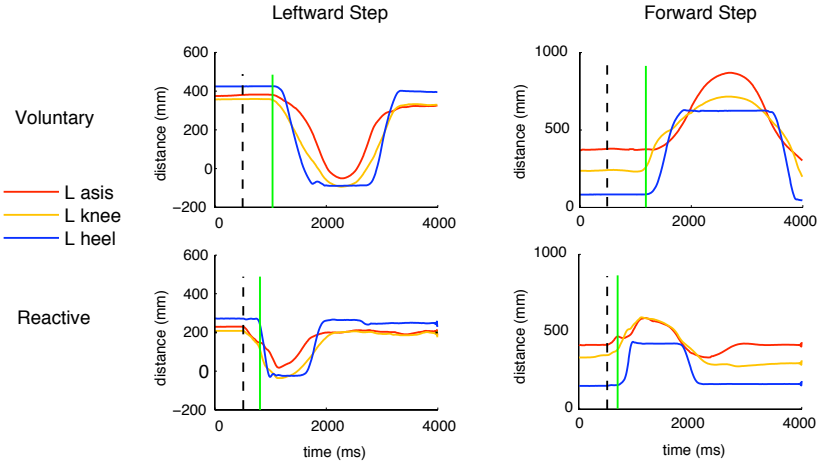


Figure B.2 Step kinematics for reactive and voluntary steps. Shown are the left asis, knee, and heel marker for a leftward step and a forward step in each condition. Although reactive steps are slightly quicker and slightly shorter than voluntary steps, generally the steps are quite similar in distance and duration.

For steps toward the front, back, and right, APAs were present in voluntary steps, as expected (Figure B.3). In rightward voluntary steps, muscle activity preceding the APA onset can be seen during the APA period. TA activation that presumably generates the weight shift characterizing the APA was observed during the APA period in forward and rightward steps, whereas BFLH was active during the APA period in backward steps (Figure B.3). However, for voluntary steps with a leftward component, no APA was observed. Therefore in voluntary leftward steps, subjects were able to push with the stance leg without prior preparatory weight shift or muscle activity.

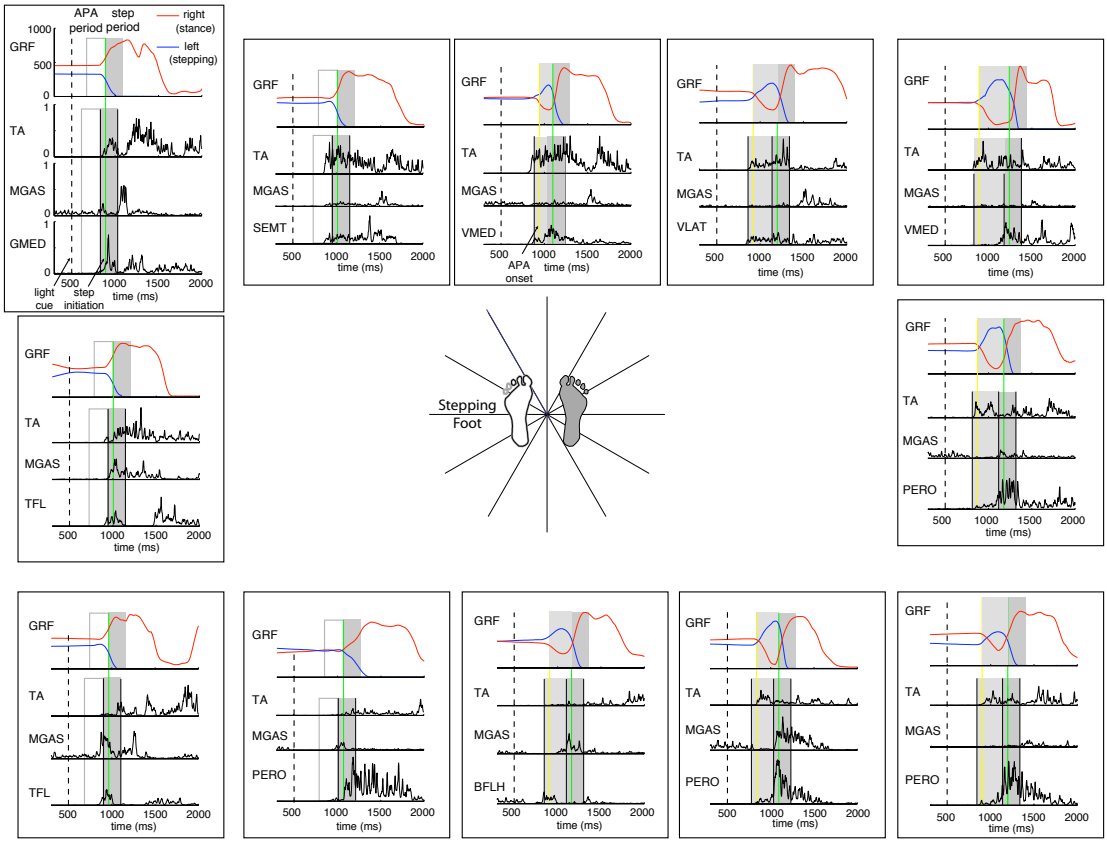


Figure B.3 GRF and EMG during voluntary steps in all 12 directions. The APA period is indicated by light gray shaded box and the step period is indicated by darker gray shaded box. APAs were present in voluntary steps towards the right, front, and back, along with associated muscle activity during the APA period that generates the APA. No APA was observed in leftward voluntary steps.

Conversely, in reactive steps towards the front, back, and right, no APAs were observed, as expected (Figure B.4). However, in reactive leftward steps, the swing limb was loaded due to the perturbation and was unloaded prior to the step, resulting in an "APA-like" weight shift and associated muscle activity. No muscle activity was observed during the APA period for most reactive stepping directions, indicating that APA-like weight shifts are passive and due to the perturbation rather than active control. All muscle activity in reactive stepping responses began after the APA onset, and the timing of this muscle activity was consistent with a postural response. The automatic

postural response (APR) has been well-characterized and occurs ~100 ms following the perturbation (Horak and Macpherson 1996), which is consistent with what we observed in reactive stepping responses.

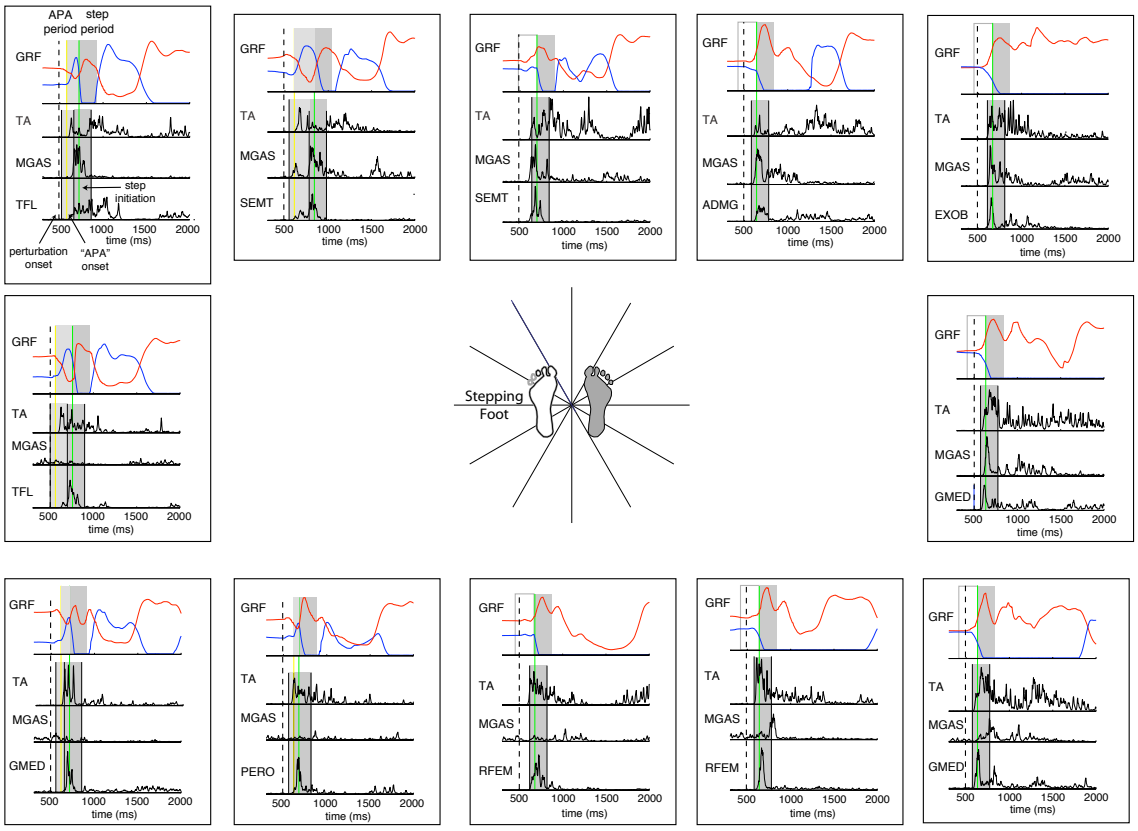


Figure B.4 GRF and EMG during reactive steps in all 12 directions. The APA period is indicated by light gray shaded box and the step period is indicated by darker gray shaded box. No APAs were present in voluntary steps towards the right, front, and back. An "APA-like" weight shift was observed in leftward voluntary steps, due to the platform motion, without associated muscle activity.

Further, differences in the function of the stance leg in the generation of reactive and voluntary steps were evident in the different muscle tuning curves associated with stepping. During the APA period, different muscles are used in reactive and voluntary steps (Figure B.5). In voluntary stepping, muscle activity during the APA period

generates an APA. However, in reactive stepping, muscle activity in the APA period represents a postural response, since it occurs after APA onset. During the step period, opposite muscles were activated during voluntary and reactive steps for steps in the anterior/posterior directions. For example, VMED was activated for forward voluntary steps and backward reactive steps (Figure B.5). In voluntary steps, the stance leg generates the propulsion needed for the step, whereas in reactive steps, the stance leg acts as a brake to stop the momentum caused by the perturbation. But, in medial/lateral directions, the same muscles were activated during voluntary and reactive steps, because the stance leg generates propulsion in both of these conditions.

B.4 Discussion

We propose a new role for the APA to set the state of the system to perform a movement. In rightward voluntary steps, the APA is necessary to shift the CoM toward the stance leg, supporting the CoM during the step. This suggests that the APA functions to change the initial state of the system. By contrast, in leftward steps, there is no need to shift the CoM rightward towards the stance leg because the overall goal is to step leftward. For leftward voluntary steps, APAs may not be necessary because the body is in the correct state to perform the movement.

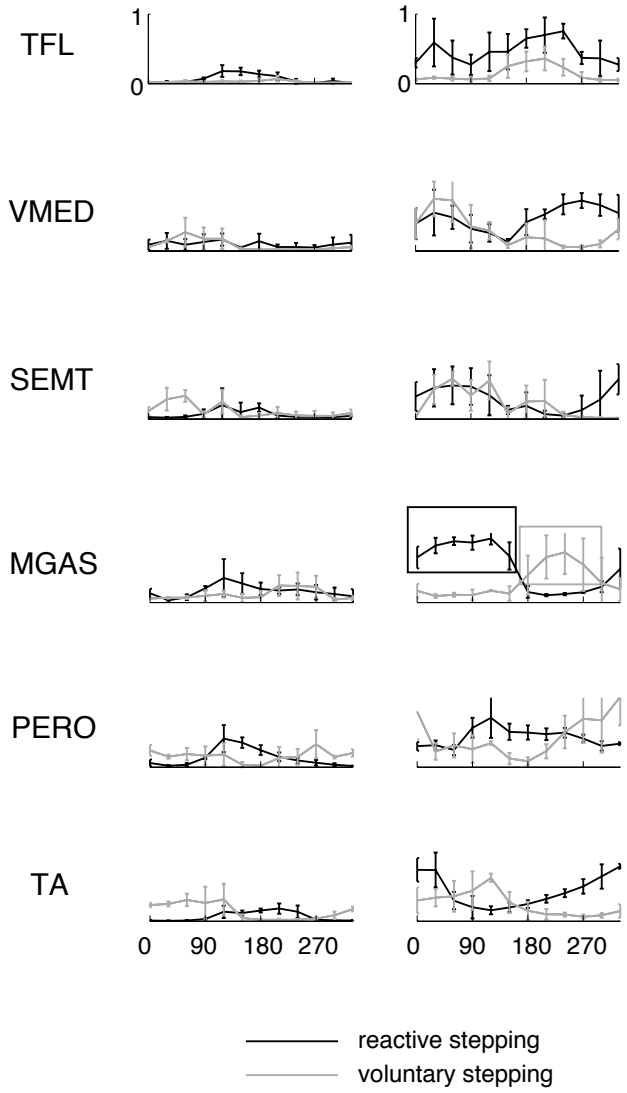


Figure B.5 Muscle tuning curves during reactive stepping (black) and voluntary stepping (gray) during the APA period and step period. Shown are the mean tuning curves ± standard deviations for 5 trials of each perturbation direction for each condition.

Therefore the presence or absence of APAs may not be specific to voluntary or reactive steps but rather reflects the required task dynamics. The prepatory action (braking or propulsing) is setting up a biomechanical condition (state) that allows for a step in a particular direction. Perhaps voluntary and reactive steps are similar, despite

differences in their initiation and execution, because they have particular biomechanical goals that have to be achieved in order to take a step.

The next step will be to examine the muscle synergies used during voluntary steps to determine if similar neural mechanisms for muscle coordination are used in voluntary and reactive stepping. Our results from Chapter 4 showed a common pool of muscle synergies was robustly recruited across various motor tasks such as walking and posture responses. Therefore, I expect to see similar muscle synergies used during the Step period to push the CoM away from the starting position in both reactive stepping and voluntary stepping. Furthermore, the same set of muscle synergies may be used to direct the CoM during anticipatory movements voluntary stepping conditions.

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VITA

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