An integrated neurobiomechanical model of the mouse to study neural control of locomotion

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1 Introduction

Locomotion is one of the most essential motor behaviors that allows animals to move in and interact with their environment. Although ubiquitous throughout the animal kingdom, it is a complex motor behavior that requires precise coordination of numerous muscles and adaptation of their activities to accommodate to changes in the environment [1]. The underlying neural control of locomotion requires interactions between different levels of the central and peripheral nervous system, the musculoskeletal system, and the environment. Neural networks in the spinal cord generate the rhythm and control the pattern and timing of motorneuron and muscle activation needed for locomotion. These spinal locomotor networks receive signals from the supraspinal centers setting the speed and locomotor task, and integrate sensory afferent feedback signals to adapt to changes in the environment. Recently, by combining molecular genetic approaches, behavioral experiments and computational modeling, substantial progress has been made in decoding the organization and function of the spinal locomotor circuitry and its supraspinal command system. Yet, many mechanisms of how these neural circuitry's interact with each other and how they integrate sensory feedback signals still remain poorly understood.

Computational modeling is an excellent tool to study such complex interactions. Indeed, computational models were instrumental in both, uncovering central neural mechanisms of locomotor control, and investigating the biomechanics of the musculoskeletal system. Here, we combine both approaches to create an integrated neurobiomechanical model. We developed a detailed 3D model of the mouse musculoskeletal system and coupled it with an extended version of our previous neural network model of the spinal locomotor circuitry [2,3].

2 Methods

2.1 Musculoskeletal model

The musculoskeletal system produces the necessary forces based on the inputs from nervous system to generate movement. The full body mouse model has been obtained by a high resolution 3D scan of a mouse skeleton. Figure 1 shows the mouse 3D scan. The model was developed in Blender (Game engine) and is fully articulated.

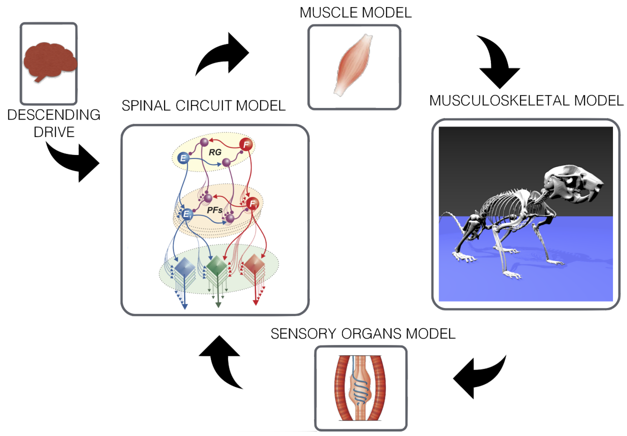

Figure 1: Overview of the closed loop framework to study locomotion

As a preliminary study, we focus here on a reduced hindlimb model. All spinal and forelimb joints were locked.For now, we restricted the the joints to allow movements only in the sagittal plane. Thus, each hind limb consists of four degrees of freedom. Functionally similar groups of muscles were modeled with a single muscle model. Maximal force was summarized across the group and insertion points and moment arms were adjusted to be representative of the set of agnostic muscles. Each degree of freedom is controlled by a pair of antagonist muscles and the metatarsophalangeal joint is passively actuated by a spring and damper. Two bi-articular muscles span over hip-knee and knee-ankle joints. Each muscle is modeled as a Hill-type muscle model based on [4, 5].

2.2 Neural model of the spinal locomotor circuits

The spinal locomotor circuits was simulated using 'activity-based' neuron population models. The network organization was adapted from our recent models of central control of locomotor speed and interlimb coordination [2,3,6,7]. These models were based on and validated against a large set of experimental data. Each limb is controlled by two-level central pattern generator, consisting of a rhythm generator (RG) and a pattern formation (PF) level as well as motorneurons and premotor circuits. The RGs generate the locomotor rhythm via persistent sodium currents, neurons

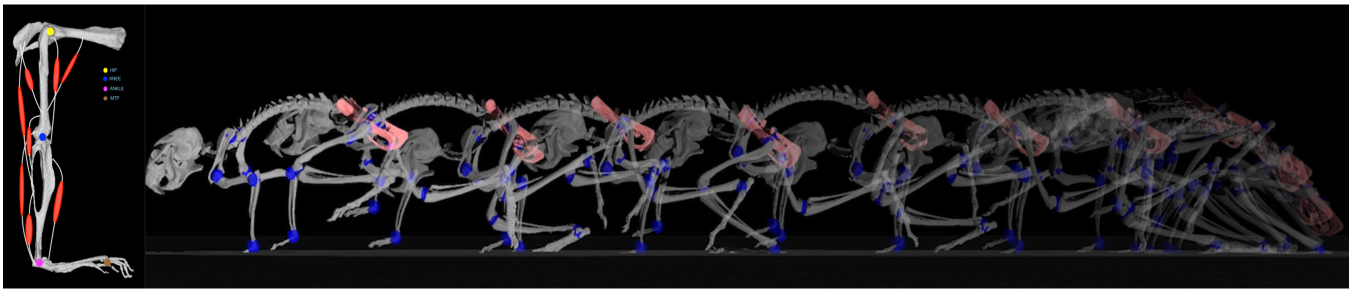

Figure 2: Hind limb muscles and joints (left). A snap shot of the mouse model walking after optimization with feedback.(right)

in PF organize muscle synergies and create muscle-specific motorneuron activation patterns. Commissural interneurons mediate left-right coordination. Brainstem drive acting on the RGs controls oscillation-frequency.

2.3 Sensory model

Sensory afferent feedback signals during locomotion were calculated using the modified regression equations derived by Prochazka [8, 9]. Simulated rigid body dynamics and muscle models were used to evaluate muscle length, velocity and forces, which in turn were used to calculate activities of muscle spindle (velocity-dependent Ia and length-dependent II) and Golgi tendon organs (force-dependent Ib). Cutaneous feedback from the plantar surface of the foot was calculated as a function of vertical ground reaction force and its derivative in time.

2.4 Integrated neurobiomechanical model

Motorneurons were connected to muscles and the calculated afferent feedback was connected to at all levels of the spinal circuitry. At the level of motorneurons, simple reflex pathways were implement, including monosynaptic homonymous Ia excitation, disynaptic reciprocal inhibition and Ib disynaptic inhibition as well as excitation. Feedback interacting with the RG centers can induce or delay phase transitions. Spindle feedback for flexor muscles provided excitation to the flexor center and Ib feedback from the ankle extensors provided excitation to the extensor center.

2.5 Optimization

We used particle swarm optimization to find synaptic weights of the feedback pathways and the PF circuitry distributing the muscle synergies that lead to stable locomotion. The objective function was formulated to maximize distance traveled while minimizing the energy in the muscle excitation space for 20 s of simulation on a surface with changing slopes.

3 Results

The resulting model was able to locomote on a level as well as inclining and declining surfaces. The main gait is characterized by alternating movements of the left and right limbs and shorter stance than swing phase duration's, figure 2. To test the stability of the locomotion, we perturbed the model by applying brief force pulses with randomized directionality to the torso. When afferent feedback connections were removed, the perturbations resulted in a loss of stability and caused the model to fall, yet with afferent feedback the model exhibited a corrective response and continued to locomote.

To probe the function of specific sensory pathways, we manipulated their connection weights and measured the impact on various locomotor parameters.

4 Discussion

The preliminary neurobiomechanical model presented here allowed us to mechanistically study neural interactions and afferent feedback feedback processing on a network level. In the future, this model will provide us with a framework to various aspects of neural control of locomotion. Specifically, the model full quadrupedal locomotion in a 3D environment.

5 Acknowledgments

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