

Modeling the spinal cord neural circuitry controlling cat hindlimb movement during locomotion

D. G. Ivashko¹, B. I. Prilutsky², S. N. Markin¹, J. K. Chapin³, and I. A. Rybak¹

¹*School of Biomedical Engineering, Science and Health Systems, Drexel University,
Philadelphia, PA 19104, USA*

²*Center for Human Movement Studies, Georgia Institute of Technology, Atlanta, GA 30332, USA*

³*Department of Physiology and Pharmacology, SUNY Health Science Center, Brooklyn, NY
11203, USA*

Abstract

We have developed a computational model of the spinal cord neural circuitry that controls locomotor movements of simulated cat hindlimbs. The neural circuitry includes two central pattern generators integrated with reflex circuits. All neurons were modeled in the Hodgkin-Huxley style. The musculoskeletal system includes two three-joint hindlimbs and the trunk. Each hindlimb is actuated by nine one- and two-joint muscles (a Hill-type model). Our simulations allow us to suggest a specific network architecture in the spinal cord and a pattern of feedback connectivities (from Ia, Ib fibers and touch sensors) that provide stable locomotion and realistic patterns of muscle activation and kinematics of limb movements.

Keywords: Spinal cord, Neural control of locomotion, Locomotory CPG, Cat hindlimbs, Musculoskeletal model

1. Introduction

The central nervous system controls locomotion and other automatic movements in a hierarchical fashion. The lower-level controller in the spinal cord generates the motor program for the neuromuscular apparatus. This low-level controller interacts with proprioceptive feedback and receives descending signals from the higher-level (supra-spinal) centers. The higher centers, in turn, may select and initiate the appropriate motor program programs from the

spinal cord's repertoire. The descending commands from supra-spinal centers to spinal interneurons are automatically integrated into the current state of proprioceptive and exteroceptive information [8].

The neuronal circuits in the mammalian spinal cord can generate rhythmic motor patterns that drive locomotor movements even in the absence of descending inputs from higher brain centers and sensory feedback [3,6]. This supports the concept of the *central pattern generator* (CPG), which presumably is located in the spinal cord and generates a basic locomotor rhythm (for review see [5]). According to the contemporary biological view, the CPG is a complex, distributed network of interneurons in the spinal cord integrated into the system of multiple reflex circuits [8]. The basic locomotor pattern, generated by the CPG, provides a coordinated activation of various muscles, which in turn control and coordinate joint movement within and between the limbs. Therefore, locomotion results from a complex interplay between the CPG, reflex circuits and multiple feedback and feedforward modulatory signals. The proprioceptive signals modulate the locomotor rhythm and pattern by providing necessary correction of the locomotor rhythm and pattern to maintain the walking animal in a proper relationship to the environment [14]. They regulate the timing of phase transitions and reinforce the generation of motoneuronal activity during ongoing phases of locomotion [11]. Previous modeling studies have demonstrated that stable and adaptive locomotion involves a global entrainment of the musculoskeletal system to rhythms generated by the CPGs [9,19]. The objective of this work was to develop and analyze a computational model of neural control of locomotion at the spinal cord level using realistic models of the network of neurons, muscles, and limb biomechanics.

2. Model

We have developed a systems model that includes realistic models of neurons and neuronal circuits in the spinal cord as well as a realistic model of the musculoskeletal system. Specifically, we focused on modeling the neural control of the movement of cat hindlimbs during locomotion. Each hindlimb was modeled as a system of three rigid segments

interconnected by three frictionless joints: hip, knee and ankle (Fig. 1A). Two hindlimbs were connected to the common segment (pelvis) whose other end was connected to the trunk segment (Fig. 1A). The distal end of the trunk was held at the constant vertical distance from the ground to compensate for the lack of forelimbs. Each hindlimb was actuated by nine one- and two-joint muscles (Fig. 1B). The dynamics of muscle contraction was described by the Hill/Zajac model [20] that incorporated force-length-velocity properties of the muscles, muscle geometry, and the properties of the tendon. Geometrical parameters characterizing muscle origin and insertion sites were measured in a representative cat. Physiological muscle parameters (optimal fiber length, maximal isometric force, maximum shortening velocity, angle of pennation, resting tendon length, etc. were estimated from the literature [2,16-18]. The dynamics of body (including two legs, pelvis, and trunk) was described by Lagrange equations. The mass-inertia parameters of body segments were calculated using empirical equations by Hoy and Zarnicke [7].

The model of the spinal cord neural circuitry has a modular structure. The model of a single Neuronal Module (NM) was constructed as a minimal neural network necessary for the formation of basic reflex circuits and their integration with the central pattern generator (CPG) (Fig. 2A,B). Each NM controls one muscle and contains an α -motoneuron (α -MN), actuating the controlled muscle, and several interneurons, including a Renshaw cell and Ia and Ib interneurons (Fig 2A). Ia and Ib interneurons were included to mediate proprioceptive feedback from of Ia and Ib afferents, respectively (Fig 2B). All neurons were modeled in the Hodgkin-Huxley style (single compartment models) and included the fast sodium, delayed-rectifier potassium, transient potassium-A, high-threshold calcium, calcium-dependent potassium, leakage and synaptic ionic channels. The schematic of reflex circuits was modified from the previous models [1,4] and applied to each antagonistic group of muscles. The synaptic connections within and between the NMs and the structure inputs of Ia and Ib proprioceptive afferents provides the classical stretch reflexes and reciprocal activation of antagonist muscles (Fig 2B).

The neural model of the locomotory CPG (Fig. 3A) was constructed using the hypothesis that each hindlimb is controlled by one complex CPG [10], which in turn is connected with the CPG controlling another hindlimb via a coordinating neural network. The CPG (for each hindlimb) was incorporated into the spinal cord neural circuitry and integrated with the circuits of spinal reflexes via direct synaptic interconnections and through multiple proprioceptive feedbacks.

Because of the paucity of available information on interneuronal connectivities and function in the mammalian spinal cord we utilized information obtained from studies of the homologous, but much better understood respiratory CPG in the medulla. Specifically, we assumed that some general architectural principles and particular neural schematics discovered in studies of the respiratory CPG (e.g. those for phase transitions) might be useful and applicable for the construction of the locomotory CPG (see also [10,14]). With respect to the respiratory CPG, both experimental [13] and modeling [15] studies have demonstrated that, in addition to the “principal” CPG elements (whose activity explicitly defines each phase of the cycle), the CPG may contain special “switching” neural elements that fire during phase transitions and, in fact, produce these transitions via inhibition of the corresponding principal CPG elements. Moreover, we suggest that the switching interneurons operate (fire) under control of various proprioceptive and descending control signals and hence significantly contribute to the shaping of the locomotor pattern (timing of phase transitions, shaping motoneuronal firing bursts, etc.).

Each CPG in our model contains four principal neurons: four principal CPG neurons: pCPG-st, active during the stance phase of locomotion; pCPG-sw, firing during the entire swing phase; pCPG-sw1 and pCPG-sw2 active during the early and late swing phases respectively (Fig. 3A). The locomotor movement is initiated by applying the “descending” drive to all principal CPG neurons. Activation of each principal neuron in the particular phase of the locomotor cycle initiates and supports the firing activity of the corresponding motoneurons within NMs, which in turn actuates the corresponding muscle group (Figs. 2B and 3A).

Activation of the corresponding switching neuron terminates the currently active phase of locomotion and hence produces phase transition. Firing of the switching neurons (and hence the timing of phase transitions) is controlled by proprioceptive feedbacks from the same hindlimb, touch sensors and some contralateral proprioceptive signals (Fig. 3A). The latter, together with the direct neural connections between the CPGs, provides coordination of activities of two CPGs and, therefore, coordination of movements of the hindlimbs (Fig. 3A). The structure and weights of synaptic connections to each switching neurons was manually adjusted to provide stable locomotion. Fig 3B shows activity of all neurons of one CPG during the locomotor cycle.

Overall, the CPGs in our model operate under regulation of multiple reflex feedbacks. At the same time, they provide control and modulation of reflexes during locomotion. Specifically, co-activation of the Ia internervoneuron and the α -motoneuron in the same NM by the CPG (Fig. 2B) suppressed the classical stretch reflexes for the antagonist muscles in the corresponding phase of locomotion. Moreover, during the extension phase of locomotion, the CPG inhibited the extensor Ib interneuron and hence broke the “classical” negative feedback loop of Ib fibers to the extensor α -motoneurons (Fig. 2B). At the same time, Ib feedback provided excitation of the extensor α -motoneuron via the CPG during the extensor phase of locomotion. Therefore during locomotion the Ib feedback loop to the extensor α -Mn changed from negative to positive, which is consistent with the experimental data [11,12].

3. Model performance. Comparison with experimental data

In order to evaluate the model performance, an experiment was conducted on one adult cat (mass 3 kg) (the methods used were consistent with the American Physiological Society Animal Care Guidelines). The cat was trained to walk on a walkway with two embedded miniature force platforms. Two electronically synchronized high-speed video cameras (60 Hz, Peak Performance Technologies) were placed on both sides of the walkway with their optical axes aligned perpendicular to the plane of progression. The cameras recorded 2D displacements of 28 reflective markers on both sides of the cat’s body. After the experiment, marker

coordinates were digitized and the kinematics and kinetics of cat walking were calculated. A comparison between locomotor variables generated by the model and those recorded experimentally demonstrated a qualitative agreement. The developed model was able to provide the control of stable locomotor movement of the hindlimbs. Figure 4 shows the dynamics of activity of α -motoneurons providing activation of muscles controlling one hindlimb and the corresponding electromyographic activity (EMGs). The latter was similar to the patterns described in the literature [10] with few exceptions (activation of IP and RF was shifted in the cycle and SO became active too early in swing, Fig. 4B). The anterior-posterior component of ground reaction force was negative in the first half and positive in the second half of the stance in both model and experiment (Fig. 5A,B). However, both the anterior-posterior and vertical force components generated by the model in early stance were much higher than the actual forces. The model also demonstrated kinematical patterns (joint angles and stick diagrams) similar to those obtained in the experiment (Figs. 5, 6). In particular, the ankle and knee joints of the model and the cat underwent flexion and then extension in the stance phase. The maximum flexion of these joints occurred in the middle of the swing for both the model and experiment. Hip angles generated by the model and recorded experimentally increased monotonically throughout the stance phase and decreased to the minimum in the swing. The model demonstrated the flexibility necessary for the adaptive adjustment of locomotor movements to characteristics of the environment.

Acknowledgements

This work was supported by ONR (N000140210086) and NSF (0091942) grants to I. A. Rybak, and ONR (N000149810679) and NINDS (NS40543, NS24707) grants to J. K. Chapin. Boris I. Prilutsky was supported by the Center for Human Movement Studies, Georgia Tech, Atlanta.

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Figure legends

Fig. 1. The schematic of musculoskeletal system. **A.** Two 3-joint hindlimbs with pelvis and trunk. **B.** Nine muscles used in the model for control a single hindlimb: IP (iliopsoas); BFA (biceps femoris anterior); RF (rectus femoris); ST (sartorius medial); BFP (biceps femoris posterior); VA (vastii); GA (gastrocnemius); TA (tibialis anterior); SO (soleus).

Fig. 2. Integration of CPG and reflex circuits. **A.** The Neuronal Module (NM) controlling one muscle. **B.** An example of two interconnected NMs, controlling a pair of antagonistic flexor and extensor muscles actuating the same joint.

Fig. 3. The central pattern generator (CPG). **A.** The schematic of neural connections. **B.** Activities of all neurons of the CPG (traces of membrane potentials) during the locomotor cycle. The activity of the touch sensor shown at the bottom to identify the stance phase of locomotion.

Fig. 4. Activation of α -motoneurons (**A**) and integrated EMG (**B**) of the corresponding muscles during a cycle of walking generated by the model. Touch is a feedback signal from the touch receptor which is proportional to the vertical component of the ground reaction force. (The rest of abbreviations are similar to Fig. 1.)

Fig. 5. Comparison between patterns of joint angles and ground reaction forces recorded experimentally (**A**) and generated by the model (**B**). Fx and Fy are anterior-posterior and vertical components of the ground reaction force, respectively.

Fig. 6. Stick-diagrams of one leg (**A** and **A1**) and two legs and the trunk (**B** and **B1**) during walking cycle recorded experimentally in one cat (**A** and **B**) and generated by the model (**A1** and **B1**).

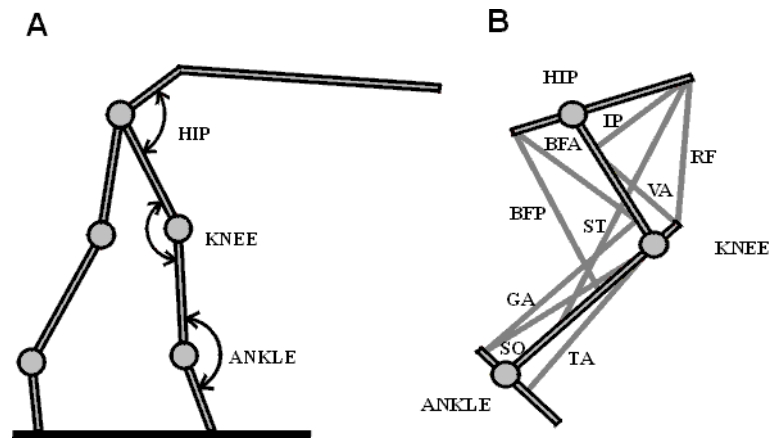


Fig. 1.

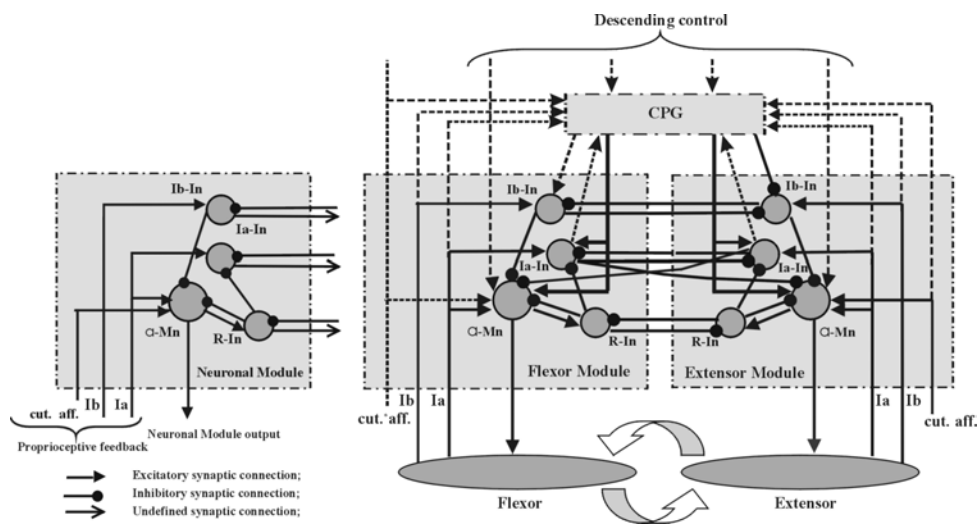


Fig. 2

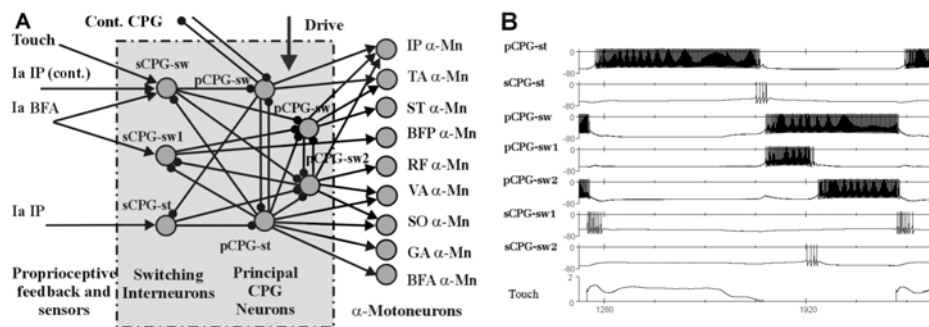


Fig. 3.

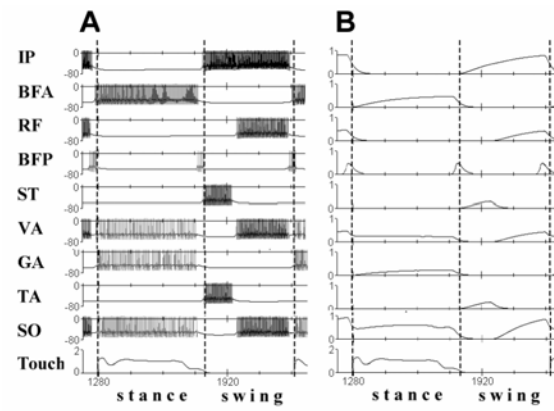


Fig. 4.

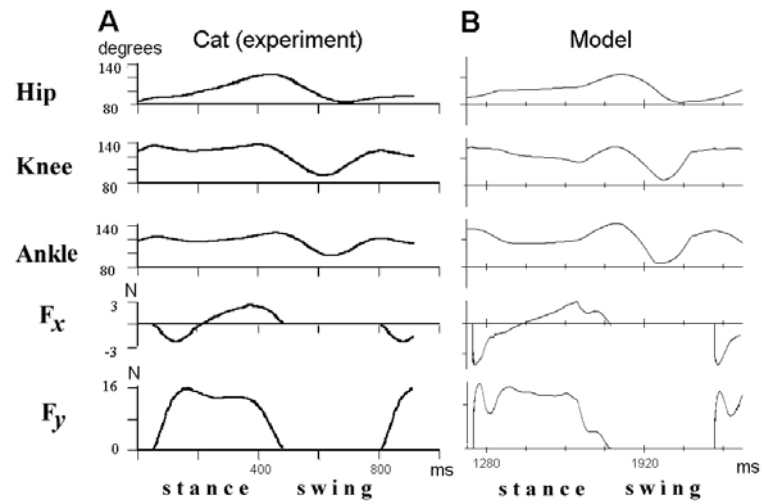


Fig. 5.

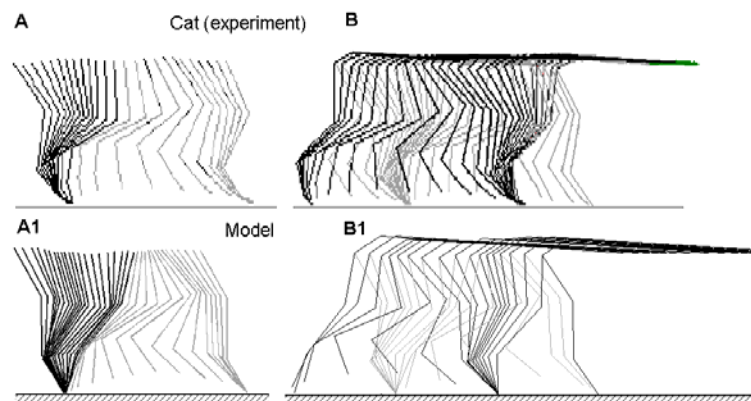


Fig. 6.



Dmitry G. Ivashko received his M.S. in Applied Mathematics and Ph.D. in Physical and Mathematical Sciences from Moscow Institute of Physics and Technology (Russia) in 1993 and 1999 respectively. In 1996-1997 he was a junior researcher at the Computing Center of the Russian Academy of Sciences (Moscow). From 1997 to 2001 he was a research assistant in the Department of Theoretical Mechanics at Moscow Institute of Physics and Technology. From 2001 he is a postdoctoral researcher in Ilya Rybak's group at the School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, PA. His research interests include nonlinear control systems, mathematical modeling, biomechanics and control of locomotion.



Boris I. Prilutsky received his B.S. in Physical Education from Central Institute of Physical Culture, Moscow and in Applied Mathematics and Mechanics from Moscow Institute of Electronic Engineering in 1978 and 1987, respectively, and Ph.D. in Biology and Biomechanics from Research Institute of Traumatology and Orthopedics, Riga, in 1990. From 1978 to 1992 he was a research scientist and a lecturer at the Biomechanics Laboratory and the Department of Biomechanics of Central Institute of Physical Culture in Moscow. He was a postdoctoral fellow at the Department of Kinesiology of University of Calgary, Canada in 1992-1995 and the Department of Health and Performance Sciences of Georgia Institute of Technology, Atlanta, GA, USA in 1995-1998. He is currently a senior research scientist at the Center for Human Movement Studies at Georgia Institute of Technology, Atlanta, GA. Dr. Prilutsky is a member of the American Association for the Advancement of Science, the American Society of Biomechanics (Young Scientist Award, 1995), International Society of Biomechanics, and the Society for Neuroscience. His research interests include biomechanics and neuromuscular control of movement.



Sergey N. Markin received his M.S. in Radiophysics and Ph.D. in Computer Science from Rostov State University (Russia) in 1992 and 1997 respectively. From 1992 to 2000 he was a research scientist in AB Kogan Research Institute for Neurocybernetics at Rostov State University. In 1998-1999 he was a visiting scientist in the Center for Artificial Vision Research at Korea University in Seoul. From 2000 he is a postdoctoral researcher at Drexel University (Philadelphia, PA). He is currently conducting research in groups of Ilya Rybak and Simon Gizster. His research interests include modeling of neural network, neural control, visual perception and biologically inspired robotics.



John K. Chapin received his Ph.D. in Physiology from the University of Rochester in 1979. He has held faculty positions at the University of Texas Southwestern Health Science Center and the Medical College of Pennsylvania and is currently Professor of Physiology and Pharmacology at the SUNY Downstate Medical College in Brooklyn, New York. He is an expert in somatosensory and motor functions of the CNS. He has also developed techniques for large-scale simultaneous multi-neuron recording in the motor system and the use of these recorded motor command signals to control robotic devices.



Ilya A. Rybak received his Ph.D. in Biophysics from St. Petersburg University in 1988. In 1977-1991 he was a senior researcher and head of the lab for Neural Network Modeling in Vision Research in AB Kogan Research Institute for Neurocybernetics at Rostov State University (Russia). In 1992 he received "The Best Paper Award" from "Neurocomputing" for his work on neural network model of visual perception. In 1993-1998 he was a visiting scientist at the Central Research Department at the DuPont Company. He is currently a Research Professor at the School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, PA. His scientific interests include computational modeling of biological neurons and neural networks with a research focus on neural control of respiration and locomotion, visual perception, biologically inspired robotics and brain-machine interfaces.