2020 Virtual Motor Control Workshop

Organized by Peter Thomas and Hillel Chiel (Case Western Reserve University) and
Silvia Daun (University of Cologne)
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(All times are given for the US/Eastern time zone. For Hawaii, subtract 6 hours. For California, subtract 3 hours. For Europe, add 6 hours. For China, add 12 hours.)

Monday 10/26

Moderated by Hillel Chiel

10:00 AM Auke Ijspeert (Biorobotics Laboratory, EPFL, Ecole Polytechnique Fédérale de Lausanne, Switzerland)

Interaction of central and peripheral mechanisms in the spinal cord: lessons from numerical models and robots, from swimming to walking.

The ability to efficiently move in complex environments is a fundamental property both for animals and for robots, and the problem of locomotion and movement control is an area in which neuroscience, biomechanics, and robotics can fruitfully interact. In this talk, I will present how biorobots and numerical models can be used to explore the interplay of the four main components underlying animal locomotion, namely central pattern generators (CPGs), reflexes, descending modulation, and the musculoskeletal system. Going from lamprey to human locomotion, I will present a series of models that tend to show that the respective roles of these components have changed during evolution with a dominant role of CPGs in lamprey and salamander locomotion, and a more important role for sensory feedback and descending modulation in human locomotion. Interesting properties for robot and lower-limb exoskeleton locomotion control will also be discussed

10:30 AM Simon M. Danner (Department of Neurobiology and Anatomy, College of Medicine, Drexel University, Philadelphia, PA)

Spinal circuits for sensorimotor integration during locomotion at different speeds: A computational model

To effectively move in complex and changing environments, animals must control locomotor speed and gait, while precisely coordinating and adapting limb movements to the terrain. The underlying neural control involves dynamic interactions between neural circuits at different levels of the nervous system, biomechanical properties of the musculoskeletal system, and afferent feedback signals from the periphery. Here, we present a computational neuromechanical model of mouse hindlimb locomotion to study the mechanisms of sensorimotor integration and the role of different afferent pathways in the stabilization of locomotion at different speeds and under different environmental conditions. The model closely reproduced characteristics of mouse locomotion at different speeds, while being able to adapt to changes in the environment. With increasing speed, the model exhibited walking, running and hopping gaits. By systematically manipulating feedback gains, we found that feedback pathways serve different roles depending on speed. We suggest that supraspinal control of locomotor speed, besides tonic drive to the rhythm generators and commissural interneurons, includes task-dependent (slow, exploratory, vs. fast, escape-type locomotion) modulation of the gain of sensory afferent pathways to the spinal locomotor circuitry.

11:00 AM Alain Frigon (Neurokinesiology Laboratory, Department of Pharmacology-Physiology, Faculty of Medicine and Health Sciences, Université de Sherbrooke)

Control of locomotor direction and speed by somatosensory feedback

We know that a network of neurons within the spinal cord generates the basic pattern of locomotion, the so-called central pattern generator (CPG). To meet task demands, such as a change in speed or direction, the spinal locomotor CPG receives commands from the brain and from limb afferents. What is the relative contribution of these two control mechanisms in informing the spinal locomotor CPG to change speed and direction? In this presentation, I review the evidence, from the spinal cat model, that the spinal locomotor CPG interacting exclusively with sensory feedback from the limbs can generate full weight bearing hindlimb locomotion, change speed and gait as well as the direction of stepping.

11:30 AM Ilya A Rybak[1], Jessica Ausborn[1], Frederic Bretzner[2]

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On brainstem control of locomotion and steering

Locomotion is a fundamental behavior that allows humans and animals to move in physical space. The spinal cord contains all the circuitry necessary to generate locomotion. This includes rhythm generator (RG) and pattern formation (PF) circuits, controlling movements of each limb and coordinating intralimb muscle activity, as well as commissural and propriospinal neural circuits and pathways, controlling left-right and cervical-lumbar interactions and ensuring interlimb coordination (locomotor gait). These spinal locomotor circuits operate under control of supraspinal centers. The major supraspinal locomotor center - the mesencephalic locomotor region (MLR) - has been identified and includes the cuneiform nucleus (CnF) and the pedunculopontine nucleus (PPN). Optogenetic stimulation of glutamatergic CnF neurons has been shown to initiate locomotion, accelerate locomotor rhythm, and induce speed-dependent locomotor gaits, whereas glutamatergic PPN neurons can induce slow walking gaits and slow down locomotor activity, eventually leading to locomotor arrest. The motor commands of the MLR to spinal locomotor circuits are relayed by multiple nuclei in the pontomedullary reticular formation (PMRF) located within the brainstem. Using mouse genetics, it has been shown that glutamatergic neurons of the lateral paragigantocellular nucleus (LPGi) within PMRF can initiate and accelerate locomotion and may rely on CnF pathways inducing locomotor activity. In turn, some genetically identified glutamatergic neurons of the gigantocellular nucleus (Gi) (also within PMRF) project to the spinal cord and can stop locomotion and induce steering.

Our study focuses on computational modeling of the brainstem control of locomotion and steering based on the above data. We hypothesize that *glutamatergic CnF neurons, acting through LPGi, control locomotor speed and speed-dependent gaits through bilateral descending pathways to spinal RGs and limb-coordinating circuits, whereas glutamatergic PPN neurons, acting unilaterally through Gi, project to PF circuits and motoneurons to control steering.*

The proposed model will extend our current model of spinal circuits and brainstem control of locomotion. Construction and operation of the extended model based on the above hypothesis will be discussed.

12:00 noon Ansgar Büschges (Dept. Animal Physiology, University of Cologne)

Advancing insect walking - fruit flies provide new insights into motor control of leg stepping and interleg coordination during legged locomotion

Presently, it is generally accepted that the neural basis of slow and fast walking in insects is based on differences in the organization of the associated neural networks within the VNC. Unfortunately, most of the contributing studies arise from insect species with highly specialized locomotor systems, e.g. in phasmids that specialized for slow walking and climbing in unpredictable environments, cockroaches that are optimized for high-speed running on flat surfaces, crickets that combine locomotion with communication in searching for a sexual partner, or locusts that can use jumping for spatial translocation. In the past years my lab has started to focus on walking in an insect that spans a broad spectrum of walking speeds from very slow to fast walking. The seminar will present recent basic insights into the organization and operation of neural control walking in the fruit fly, *Drosophila melanogaster*: (i) Fruit flies do not generate distinct gaits, but rather a continuum of interleg coordination patterns that spans the complete range of observed walking speeds between very slow (below 1 BL/s) and high-speed walking (up to 15 BL/s (Wosnitza et al. 2013)). (ii) Interleg coordination is not based on a fixed intersegmental coordination pattern between hemisegmental neural circuits (Berendes et al. 2016), but can be deduced from stability optimization (Szczezecinski et al. 2018). (iii) Walking direction and speed are controlled independently (Bidaye et al. 2014; 2020). (iv) Within the hemisegmental premotor networks single interneurons control individual aspects of leg stepping, e.g. stance phase or the stance-to-swing-transition (Feng et al. 2020, under revision).

Tuesday 10/27

Moderated by Peter Thomas

10:00 AM Hillel Chiel (Department of Biology, Case Western Reserve University)

How a pattern generator can adapt to changing environmental conditions

A classic approach to understanding pattern generators dynamically has been to consider them as limit cycles. However, empirical observations of pattern generators suggest that this viewpoint has significant limitations. In response to changes in mechanical loading, a pattern generator may show very significant alterations in the duration and intensity of specific components of its output, changes that are often hard to capture using classical pattern generator models. We will demonstrate these variations in output using experimental studies of the feeding motor control circuitry in the marine mollusk Aplysia californica, which can show significant and rapid changes in duration, firing frequency and recruitment of motor neurons as an animal attempts to consume large mechanical loads. We will also briefly review some of our studies of a more abstract neuromechanical model based on Aplysia's feeding behavior which suggests a possible neural architecture (stable heteroclinic channels) as the basis for the ability of the pattern generator to use sensory feedback to dwell for long times in particular phases of the pattern, and suggest how this property can allow a pattern generator to be both robust and flexible.

10:30 AM Yangyang Wang (Department of Mathematics, University of Iowa)

Variational and phase response analysis for limit cycles with hard boundaries, with applications to neuromechanical control problems

When dynamical systems that produce rhythmic behaviors operate within hard limits, they may exhibit limit cycles with sliding components, that is, closed isolated periodic orbits that make and break contact with a constraint surface. Examples include dynamical systems models of physiological and robotic motor control systems and mechanical stick-slip oscillators. In many rhythmic systems, robustness against external perturbations involves response of both the shape and the timing of the limit cycle trajectory. The existing methods of infinitesimal phase response curve (iPRC) and variational analysis are well established for quantifying changes in timing and shape for smooth systems and have recently been extended to nonsmooth dynamics with transversal crossing boundaries. In this work, we further extend the iPRC method to nonsmooth systems with sliding components and develop a ``local timing response curve'' (lTRC) that is analogous to the iPRC, but measures the local timing sensitivity of a limit cycle within any given local region. Moreover, the classical variational analysis neglects timing information and is restricted to instantaneous perturbations. By defining the ``infinitesimal shape response curve'' (iSRC), we incorporate timing sensitivity of an oscillator to describe the shape response of this oscillator to parametric perturbations. We demonstrate the applications of our methods in a concrete example - a piecewise smooth neuromechanical model of triphasic motor patterns in the feeding apparatus of a marine mollusk which exhibits limit cycles with sliding components in the swallowing mode. We investigate the mechanisms by which sensory feedback generates robust adaptive behavior in response to the sustained perturbation (increased mechanical load) and compare them to the experimental observations.

11:00 AM Jon Rubin (Department of Mathematics, University of Pittsburgh)
Silvia Daun (Heisenbergprofessur für Computational Neuroscience, Zoologisches Institut, Abt. Tierphysiologie, Universität zu Köln)

A computational study of the roles of ascending sensory signals and top-down central control in the entrainment of a locomotor CPG

To generate functional outputs, locomotor control must feature both rhythm generation by CPGs at the level of individual joints and coordination of their rhythmic activities, so that all muscles are activated in an appropriate pattern. I will discuss work to analyze an example of this coordination process in a simplified network model relating to stick insect locomotion. The analysis focuses on how the control system for a single joint in the stick insect leg produces rhythmic output when subjected to ascending sensory signals from other joints in the leg. The model features a half-center oscillator tuned to match some basic experimental observations as the core rhythm generating CPG. While the dynamical features of this CPG, including phase transitions by escape and release, are well understood, we provide novel insights about how these transition mechanisms yield entrainment to the incoming sensory signal, how entrainment can be lost under variation of signal strength and period or other perturbations, how entrainment can be restored by modulation of tonic top-down drive levels, and how these factors impact the duty cycle of the motor output.

Wednesday 10/28

Moderated by Silvia Daun

10:00 AM Zhuojun Yu (Department of Mathematics, Applied Mathematics & Statistics, Case Western Reserve University)

Dynamical consequences of sensory feedback in a half-center oscillator coupled to a simple motor system

We investigate a simple model for motor pattern generation that combines central pattern generator (CPG) dynamics with a sensory feedback (FB) mechanism. Our CPG comprises a half-center oscillator with conductance-based Morris-Lecar model neurons. Output from the CPG drives a push-pull motor system with biomechanics based on experimental data. A sensory feedback conductance from the muscles allows modulation of the CPG activity. We consider parameters under which the isolated CPG system has either ``escape'' or ``release'' dynamics, and we study both inhibitory and excitatory feedback conductances. We find that increasing the FB conductance relative to the CPG conductance makes the system more robust against external perturbations, but more susceptible to internal noise. Conversely, increasing the CPG conductance relative to the FB conductance has the opposite effects. We show that the ``closed-loop'' system, with sensory feedback in place, exhibits a richer repertoire of behaviors than the ``open-loop'' system, with motion determined entirely by the CPG dynamics. Moreover, we show that purely feedback-driven motor patterns, analogous to a chain reflex, occur only in the inhibition-mediated system. Finally, for pattern generation systems with inhibition-mediated sensory feedback, the distinction between escape- and release-mediated CPG mechanisms is diminished. Our observations support an anti-reductionist view of neuro-motor physiology: understanding mechanisms of robust motor control requires studying not only the central pattern generator circuit in isolation, but the intact closed-loop system as a whole.

10:30 AM Paul S. Katz (Department of Biology, Neuroscience and Behavior Graduate Program, University of Massachusetts Amherst)

Distinct neural circuit architectures underlying homologous behaviors in nudibranch molluscs

It has been posited that different circuit configurations can produce the same output. A real life instantiation of this occurs in the central pattern generators (CPGs) underlying swimming in nudibranch molluscs. In particular, two species, *Melibe leonine* and *Dendronotus iris* have homologous swimming behaviors produced by CPGs composed of homologous neurons. Yet the synaptic connective of those CPGs, the mechanisms underlying the production of rhythmic bursting, and the roles played by individual neurons differ. Using dynamic clamp, we rewired the circuitry of one species to resemble that of another species and demonstrated that both configurations are capable of producing rhythmic activity in the same species. We also found that a neuron that is a member of the CPG in one species serves as an extrinsic neuromodulatory that activates the CPG in the other species. Thus, although the behavior has been conserved, the roles of neurons and the neural mechanisms that produce the behavior have diverged.

11:00 AM Boris I. Prilutsky (School of Biological Sciences, Georgia Institute of Technology)

Atypical patterns of locomotor activity in the cat: Role of CPG and motion-related sensory feedback

Locomotor rhythmic activity in cats has several typical features, including reciprocal activation of flexors and extensors and synergistic activation within flexors and extensors across the entire leg. Previous studies (Smith et al. 1985, 1998) have identified several rhythmic behaviors – downslope walking and paw shake, in which these typical activity patterns break down. During downslope walking, one-joint hip extensors are silent throughout the entire locomotor cycle, while hindlimb flexors demonstrate swing- and stance-related activity bursts. During paw shake, anterior and posterior hindlimb muscles demonstrate reciprocal activity irrespective of their anatomical flexor or extensor function. We investigated the contributions of spinal CPG and motion-related sensory feedback to these atypical activity patterns by using muscle synergy analyses of recorded EMG activity and by neuromechanical simulations of slope walking and paw shake in the cat. The obtained results demonstrate that the two identified flexor synergies and one of three extensor synergies are shared among level, upslope and downslope walking and thus are likely generated by spinal CPG. The two unique extensor synergies during downslope walking appear to arise from supraspinal inputs rather than from hindlimb motion-related sensory feedback. Neuromechanical simulations suggest that spinal CPG and hindlimb somatosensory feedback alone cannot explain motor patterns of upslope walking and additional supraspinal excitatory input to extensors is needed. Neuromechanical simulations of paw shake show that the reciprocal activity of anterior and posterior muscles can be explained by an alternating activity of CPG flexor and extensor half-centers and motion-related sensory feedback from muscles stretched by passive joint interaction moments.

Thursday 10/29

Moderated by Peter Thomas

10:00 AM Yaroslav Molkov (Georgia State University)

Complicated relationships between respiration, heart beat and blood pressure

Coupling of the respiratory and the cardiovascular systems is reciprocal. This interaction is more evident in the effect of the respiration on the cardiovascular system rather than vice versa. For example, the first described property of cardiorespiratory coupling (CRC) was the respiratory sinus arrhythmia (RSA), which is respiratory modulation of heart rate (HR) with HR increasing during inspiration and decreasing during expiration. Another well-known effect of respiration on the cardio-vascular system is Traube-Hering (TH) Waves, which are observed as the respiratory modulation of arterial pressure. The reciprocal manifestation of CRC is cardio-ventilatory coupling (CVC), which refers to the cardiovascular system driving changes in the respiratory system. Experimentally, CVC manifests itself by the onset of inspiration occurring at a preferential latency following the last heartbeat in expiration. In the first part of this presentation I will talk about respiratory modulation of the cardiovascular system and try to answer the question whether the RSA and TH waves have the same underlying mechanism. To do that we analyzed respiratory, electrocardiogram, and blood pressure traces from healthy, supine male subjects during resting and slow deep breathing (SDB), and recovery. Across all conditions, blood pressure and heart rate (HR) were modulated with respiration and the amplitude of both RSA and TH waves increased during SDB. The data were deconstructed using a simple mathematical model of blood pressure. Interestingly, the amplitude of the TH waves could be captured by only HR modulation in the model. However, RSA alone did not accurately predict the timing of TH waves relative to the respiratory cycle. Adding respiratory modulation of pulse pressure (PP) to the model corrected the phase shift showing the expected pattern of blood pressure. This indicates that short-term variability of blood pressure referred to as TH waves has at least two independent mechanisms whose interaction forms their pattern: RSA and respiratory-driven changes in PP. The second part of the talk is about CVC. We hypothesized that the heartbeat, via baroreceptor activation modulating brainstem expiratory neuronal activity, delays the initiation of inspiration. In supine male subjects, we analyzed ventilation and electrocardiogram. In in situ rodent preparations, we recorded brainstem activity in response to pulses of perfusion pressure. In humans, the latency between heartbeats and onset of inspiration was consistent across different breathing patterns. In in situ preparations, a transient pressure pulse during expiration increased neuronal activity in a subpopulation of expiratory neurons normally active during post-inspiration; thus, delaying the next inspiration. We applied a well-established respiratory network model to interpret these data. In the model, baroreceptor input to post-inspiratory neurons accounted for the effect. These studies are consistent with baroreflex activation modulating respiration through a pauci-synaptic circuit from baroreceptors to the post-inspiratory population of neurons in the brainstem respiratory network.

10:30 AM Mette Olufsen (Department of Mathematics, North Carolina State University)

Using model data and model-based analysis to understand emergence 0.1Hz oscillations in patients with Postural Orthostatic Tachycardia (POTS)

Postural Orthostatic Tachycardia Syndrome (POTS) is associated with the onset of tachycardia upon postural change. A positive diagnosis is made if Heart Rate (HR) increases more than 30 bpm (40 bpm in patients aged 12-19 years) upon either a head-up tilt (HUT) or active standing test. This study uses signal processing and mathematical modeling to examine the emergence of 0.1 Hz oscillations in systolic arterial blood pressure (SBP) and HR signals characterizing the baroreflex in control and POTS patients. Results analyzing the signals show that the amplitude of the 0.1 Hz oscillations is higher in POTS patients and that the phase response between the two signals is shorter ($p < 0.005$). These markers were subsequently used in a systems-level differential equations model understanding under what conditions 0.1 Hz oscillations emerge. We found that oscillations emerge by increasing sensitivity of heart rate control and that by also modulating control of peripheral vascular resistance it is possible to generate oscillations in 0.1 Hz frequency interval.

11:00 AM Carter Johnson (Department of Mathematics, University of California at Davis)

Neuromechanical Mechanisms of Gait Adaptation in *C. Elegans*: The Relative Roles of Neural and Mechanical Coupling

Understanding principles of neurolocomotion requires the synthesis of neural activity, sensory feedback, and biomechanics. The nematode *C. elegans* is an ideal model organism for studying locomotion in an integrated neuromechanical setting because its nervous system is well characterized and its forward swimming gait adapts to the surrounding fluid using sensory feedback. However, it is not understood how the gait emerges from mechanical forces, neuronal coupling, and sensory feedback mechanisms. Here, an integrated neuromechanical model of *C. elegans* forward locomotion is developed and analyzed. The model captures the experimentally observed gait adaptation over a wide range of parameters, provided that the muscle response to input from the nervous system is faster than the body response to changes in internal and external forces. The model is analyzed using the theory of weakly coupled oscillators to identify the relative roles of body mechanics, neural coupling, and proprioceptive coupling in coordinating the undulatory gait. The analysis shows that the wavelength of body undulations is set by the relative strengths of these three coupling forms. The model suggests that the experimentally observed decrease in wavelength in response to increasing fluid viscosity is the result of an increase in the relative strength of mechanical coupling, which promotes a short wavelength.

Joint work with Tim Lewis and Bob Guy.