***Bernstein Prize Nomination: Sten Grillner***

Sten Grillner is Professor at the Karolinska Institute since 1975 and is a member of the National Academy of Science (US), Institute of Medicine (US), and several other academies and his awards include The Kavli Prize in Neuroscience (2008). He was Secretary General for IBRO (2013-2015) and was President for FENS 2010-2012.

Sten Grillner is one of the world's foremost neurophysiologists whose lifetime scientific career has been devoted to understanding the modular network organization underlying fundamental aspects of motor control. Grillner's initial work defined the basic organisation of the mammalian locomotor system. He was able to demonstrate that mammals, like the cat, were able to generate well-coordinated locomotor movements of the hindlimbs after a low thoracic spinal transection, using a complex pattern of muscle activity that in great detail corresponded to that of the intact animal. An extensive series of studies led to the conclusion that the basic substrate for generating locomotor movements resided in the spinal cord, a finding that much later led to the adoption of training programs for patients with spinal cord injury.

The actual motor pattern of locomotion Grillner subsequently showed to be generated by a central pattern generating network (CPG) in the spinal cord that could provide the detailed motor pattern (not only alternation) even without sensory feedback. On the other hand, the CPG was shown to be complemented by a well-organized sensory control system signalling the position of the limb (hip), thereby contributing to the stance-swing reversal. With his interest in the control of locomotion, Grillner spent the spring of 1971 in Moscow interacting in particular with G.N. Orlovski and Mark Shik but also with Viktor Gurfinkel and the researchers in I.M. Gelfand´s “Laboratory for Application of Mathematical Methods in Biology”. This laboratory was inspired by the thoughts of Bernstein and his memory was very much alive (please see attached Autobiography).

To address the next level question - the molecular, cellular and synaptic design of the neuronal circuitry – another major undertaking was to develop a simpler vertebrate model (lamprey). The different network interneurons, their synaptic interaction (transmitters, receptor subtypes), and their membrane properties (ion channel subtypes expressed) were identified. The palette of different subtypes of ion channels expressed in different neurones was found to be of critical importance for network function. Through an interaction between detailed multi-faceted experimentation and large scale modelling with biophysically realistic numbers of Hodgkin-Huxley neurons, it proved possible to understand the operation of this entire motor control system of the lamprey in exquisite detail.

Currently Sten Grillner is working again on a next level question - the neural mechanisms underlying selection of behaviour using the lamprey as a model, with a primary focus on the role of the basal ganglia. A detailed analysis of the connectivity within the different parts of the basal ganglia including the dopamine system and the habenulae demonstrates that it is conserved in considerable detail. Furthermore, transmitters, receptor subtypes, and membrane properties, are also maintained from lamprey to mammals. Moreover, movements can be elicited by stimulation of the lamprey pallium (cortex) and the projection pattern of the pallial neurons to the basal ganglia, brainstem and spinal cord is virtually identical to that of mammals. The inference is that the forebrain design, with regard to pallium, the basal ganglia and related structures as well as the brainstem – spinal cord organisation, evolved very early in vertebrate evolution, and has been conserved over 500 million years, when the lamprey line of evolution diverged from that leading up to mammals including man. With regard to the motor system the lamprey CNS thus can be regarded as a blueprint of that of mammals. In short, Sten Grillner has unravelled intrinsic functions of microcircuits generating locomotor movements at the brainstem–spinal cord level, the midbrain control mechanisms for steering, and the forebrain mechanisms underlying selection of behavior. His research extends from ion channels and synapses to network mechanisms utilizing a multitude of techniques. On the basis of detailed experimentation, he has successfully modeled the networks underlying locomotion including steering and posture. Since receiving early inspiration from the Moscow school as a post-doc, Sten Grillner and his research stands as an example, par excellence, of a multi-level approach to motor control that no doubt stems from the spirit of Nikolai Alexandrovich Bernstein. In the opinion of this nominator, Grillner, though a humble man, would not only be honored by the Bernstein Prize, but also enhance the profile of the award and the International Society of Motor Control.

