Interactive report

The intrinsic function of a motor system — from ion channels to networks and behavior

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Accepted 25 October 2000

Abstract

The forebrain, brainstem and spinal cord contribution to the control of locomotion is reviewed in this article. The lamprey is used as an experimental model since it allows a detailed cellular analysis of the neuronal network underlying locomotion. The focus is on cellular mechanisms that are important for the pattern generation, as well as different types of pre- and postsynaptic modulation. This experimental model is bridging the gap between the molecular and cellular level to the network and behavioral level. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Locomotion; Networks; Ion channel; Modulation; Modeling; Behavior

1. Introduction

All vertebrates, without exception, depend on locomotion, which often is the most complex motor behavior performed in a given species. It involves the coordination of a large number of muscles (often more than a hundred), each of which is coordinated in a specific motor pattern repeated within each locomotor cycle. In principle, three different types of control systems are involved (see Fig. 1).

1. The motor system which produces the propulsive movements, be it the leg movements of tetrapods or bipeds, wing movements of birds, or undulatory trunk movements of fish or snakes.
2. The postural motor system, which maintains the appropriate body orientation during ongoing locomotion.
3. The goal directed aspect of the locomotor behavior, which brings the animal to the goal of the locomotor episode, while avoiding all objects that may impede the locomotion. In most cases this is achieved by visuomotor coordination, which in the case of mammals also requires accurate foot placement. Locomotion can also be combined with other motor tasks.

Substantial information is now available concerning the neural subsystems responsible for the equilibrium control [51,21] and for accurate foot placement during locomotion in demanding terrain [22,36]. In this article, however, we will deal only with the neural machinery underlying propulsion.

2. The propulsive neural control system — an overview

The propulsive system generating the stereotypic movements characteristic of locomotion is composed of a supraspinal part, which is responsible for the initiation of locomotion and for maintaining a certain degree of drive to the spinal networks which generate the motor pattern [30–32,37,64], be it swimming, walking or flying (see Fig. 1). The spinal networks are composed of excitatory and inhibitory interneurons which activate the different groups of motoneurones in the appropriate sequence. Stimulation of two areas in the brain stem elicits locomotion by activating the spinal networks [37]. One area is located at the meso-pontine border and referred to as the mesencephalic locomotor region MLR [64] and another area is
Fig. 1. General control strategy for vertebrate locomotion (A). Locomotion is initiated by an increased activity in reticulospinal neurons of the brainstem locomotor center, which activates the central spinal network, which in turn produces the locomotor pattern in close interaction with sensory feedback. With increased activation of the locomotor center, the speed of locomotion will also increase (B). In quadrupeds this also leads to a shift in interlimb coordination, from walk to trot and then to gallop. The basal ganglia exert a tonic inhibitory influence on different motor centers. Once a pattern of motor behavior is selected, the inhibition is released, in this case allowing the locomotor center in the brainstem to be activated. Experimentally, locomotion can also be elicited pharmacologically by administration of excitatory amino acid agonists and by sensory input (C) shows that an asymmetric activation of reticulospinal (RS) neurons gives rise to an asymmetric output in the left (L) and right (R) sides. This will result in a turning movement to one side or the other.
located in the ventral thalamus (lamprey [25]) or a corresponding area in mammals [50,65].

Simple (e.g. 30 Hz) electrical stimulation of the locomotor areas at a certain strength may elicit locomotion by activating the spinal motor pattern generators [37,64,65]. If the stimulation strength is increased (everything else being unchanged), the animal will increase the speed of locomotion (Fig. 1B). In a mammal, the pattern of locomotion may change from slow walking to trot, and finally gallop. In this case the step cycle of each limb will gradually shorten in duration, but in addition the pattern of coordination between the two hind- or forelimbs will change from the strict alternation of walk and trot to the approximate in phase coordination of gallop or bound. In the case of fish swimming, the situation is simpler in that the alternating movements progressively increase in frequency from low to top speed [39]. This type of brainstem–spinal cord organization simplifies the control task for the brain, which only needs to decide when to locomote and the general level of activity, leaving the spinal cord network to faithfully generate the complex pattern of muscle activity required to generate the locomotor movements.

In legged animals, including humans, there is a separate network for each limb that can be further subdivided in network units involved in the control of single joints and groups of muscles [31] (cf. Ref. [66]). The networks for the different limbs can be combined in different ways to produce the different gaits from walk, pace and trot to the different types of gallops.

In all vertebrates, it appears that corresponding brainstem areas are involved in the supraspinal control of locomotion [37] — while the spinal networks have been adapted to the particular type of coordination of a given species. For a number of years, we have chosen to work on a simple experimentally advantageous model, which retains the basic vertebrate features — the lamprey CNS [60,35]. The lamprey, a cyclostome, diverged from the main vertebrate evolutionary line at a stage before elasmobranchs and teleosts, and has since remained comparatively unchanged over more than 400 million years. The brainstem–spinal cord can be maintained in vitro over several days (Fig. 2A), and the motor pattern underlying locomotion can be evoked in the isolated nervous system. This condition has allowed a detailed study of the neural mechanisms of the network underlying locomotion (see Ref. [35]).

3. The lamprey model — forebrain control

Goal-directed locomotion can be elicited by visual or olfactory stimuli [72,73,43]. Afferents from the optic nerve or the olfactory bulb project to the ventral thalamus (VTH in Fig. 2), which in turn projects to and activates reticulospinal neurons [25]. Reticulospinal neurons, in turn, activate spinal cord locomotor networks [48]. An oligosynaptic pathway activated by visual or olfactory stimuli may then elicit behaviorally relevant locomotor activity.

The basal ganglia represent an area that is important for the control of motor behavior. The lamprey basal ganglia appear to be organized in a way similar to that of higher vertebrates [57,58] (Fig. 2). The striatum is comprised of spiny neurons, and contains GABAergic and presumed cholinergic neurons. It has a dense dopaminergic input from an area analogous to the ventral tegmental area, and also 5-HT, enkephalin, galanin, tachykinin and neurotensin inputs (Fig. 2) [57,58,7,5]. Striatal GABAergic neurons project to an area in the ventrolateral pallium (possibly

**Fig. 2.** Forebrain and brainstem structures important for the initiation of locomotion in lamprey. The striatum of the basal ganglia receives dopaminergic, serotonergic, histaminergic and peptidergic inputs, as well as inputs from the thalamus and telencephalon. GABAergic striatal neurons project to the ventrolateral pallium, which in turn sends GABAergic projections to the ventral thalamus. This nucleus also receives olfactory and visual input, and projects to the brainstem where reticulospinal neurons are excited. In addition to this diencephalic locomotor control, the brainstem MLR area also may initiate locomotion by exciting reticulospinal neurons. The brainstem reticulospinal neurons will then in turn activate the spinal locomotor network.
corresponding to the ventral pallidum of mammals). This area, in turn, provides GABAAergic projections to the ventral thalamus. The basal ganglia may then control the output of the ventral thalamus—a type of gate control determining whether, for example, visual or olfactory stimuli should or should not result in locomotor activity [25].

The basal ganglia appear to have a similar overall role in lamprey and mammals including man, since MPTP, a ‘toxin’ which destroys the DA supply to striatum, gives rise to the same general class of symptoms in man and lamprey. In the latter case, locomotor episodes are initiated more rarely, and each episode becomes much briefer. Moreover, the time lag from the initial signs of locomotor initiation to actual effective locomotion is prolonged, and upon cessation of locomotor activity an after-discharge may be present in the trunk muscles [70]. These symptoms concur with the motor symptoms of Parkinson’s disease, which also are produced by MPTP intoxication in primates including man.

4. The lamprey model — brainstem–spinal cord circuitry

By stimulation in the locomotor areas of the lamprey brainstem, locomotor-like activity can thus be elicited in the spinal cord [48]. The alternating segmental burst activity is coordinated along the spinal cord, generally with a rostro-caudal phase lag, which corresponds to the coordination in the swimming lamprey in which an undulatory wave pushes the animal forward through the water (cf. Refs. [29,78]). Also in the isolated spinal cord locomotor coordination can be elicited by elevating the excitability of the spinal cord by administering excitatory amino acid receptor agonists like NMDA, kainate, AMPA, and d-glutamate to the bath [20,38,9] (Fig. 3A, cf. Ref. [59]). Pharmacological analysis has indicated that the network essentially depends on excitatory glutamatergic, and inhibitory glycinergic synaptic transmission [40,8]. In addition, a number of modulatory transmitters modify neuronal and thereby network activity, which will be dealt with separately below.

The spinal cord networks are thus responsible for the motor pattern produced. They are activated from the brainstem via reticulospinal axons (Figs. 2, 3B) that excite spinal excitatory and inhibitory interneurons and motoneurones via both NMDA and AMPA/kainate receptors (cf. Ref. [35]). The reticulospinal system thus drives the spinal cord networks and determines the level of activity in a burst range from 0.2 to 10 Hz. The excitatory spinal interneurons have ipsilateral axons and excite motoneurones and inhibitory interneurons with ipsilateral and contralateral axons [14]. In principle, the ipsilateral excitatory interneurons excite all types of cells on the same side of the spinal cord, while the crossing inhibitory cells provide inhibition of the neurons on the contralateral side (Fig. 3B; Refs. [15,16,13], and unpublished). The network produces one half cycle of excitation in motoneurones and interneurones of one side followed by one half cycle of inhibition when the contralateral side is active [61]. Using biophysically realistic modelling it has been shown that pools of model interneurons, with similar properties to those found experimentally, can produce the alternating motor pattern (see below; Ref. [41]).

5. Importance of cellular properties for the pattern generation

Not only the connectivity but also the membrane properties of different cell types are of critical importance. Calcium currents as well as the activation of calcium dependent potassium channels (KCa) have a key role. The post-spike afterhyperpolarisation is the main determinant of the frequency regulation including frequency adaptation in all network neurons (Fig. 4A; Ref. [26]). During network activity the short range spike frequency adaptation is one important factor. In most cases only a few spikes are generated within each burst. KCa currents are also important in relation to other processes that cause increased Ca2+ levels in the dendrites or cell body. These include the activation of NMDA receptors which give rise to plateau-like depolarizations (Fig. 3B; Ref. [77]). The termination of these plateaus is caused by the activation of KCa currents (Fig. 4B,C), and presumably also by an activation of low voltage activated Ca2+ currents [67]. These lamprey neurons express Ca2+ channels of the N subtype, which are mainly responsible for the activation of KCa channels underlying the afterhyperpolarisation, and for the synaptic release of transmitter [80,23,76,24]. t-channels are less abundant but contribute, however, to the NMDA induced plateau depolarizations.

Low voltage-activated (LVA) calcium channels are also present in network neurons. They are activated when the cells are depolarized from a comparatively hyperpolarized level, and open below the threshold for the action potential. The LVA Ca2+ channels can thus boost the membrane depolarization enabling it to reach the threshold for an action potential. The calcium entry through LVA Ca2+ thus provides a post-inhibitory rebound. This can contribute to the stability of rhythmic network activity [67] since in modelling experiments a blockade of LVA Ca2+ channels may cause a change from a strict reciprocal pattern to more irregular activity. Thus, both LVA Ca2+ channels and voltage-dependent NMDA channels may contribute to burst stability.

In calcium imaging experiments in the spinal cord of the lamprey [3] it was shown that in both soma and dendrites of the network, there is entry of Ca2+ ions during activation (Fig. 5). During an action potential, Ca2+ entry
Fig. 3. (A) In vitro preparation of the lamprey CNS. The isolated brainstem–spinal cord of the lamprey can be maintained alive for several days in an experimental chamber that is kept cold (4–7°C) and continuously perfused with physiological solution. The motor pattern underlying locomotion can be produced by stimulating the brainstem locomotor centers or by adding glutamate receptor agonists to the perfusion medium. The motor activity can be recorded in the ventral roots (motor nerves) that normally activate the musculature on the left (l) and right (r) sides. The activity in single or pairs of cells can be recorded intracellularly with microelectrodes (IC). An intracellular record (IC) of a network neuron with subthreshold membrane potential oscillations is shown above together with the alternating motor activity in the ventral roots on the left and right sides. (B) Locomotor network of the lamprey. Schematic representation of the forebrain, brainstem and spinal components of the neural circuitry that generates rhythmic locomotor activity. All neuron symbols denote populations rather than single cells. The reticulospinal (RS), glutamatergic neurons excite all classes of spinal interneurons and motoneurones. The excitatory interneurons (E) excite all types of spinal neurons on the ipsilateral side, i.e. the inhibitory glycinergic interneurons (I) that cross the midline to inhibit all neuron types on the contralateral side, the lateral interneurons (L) that inhibit I interneurons, and motoneurones (M). The stretch receptor neurons are of two types; one excitatory (SR-E) which excites ipsilateral neurons and one inhibitory (SR-I) which crosses the midline to inhibit contralateral neurons. RS neurons receive excitatory synaptic input from coetaneous afferents (Trigem.), the mesencephalic locomotor region (MLR) and from the ventral thalamus (VTH), which in turn receives input from the basal ganglia.
Fig. 4. Spike frequency regulation, NMDA-plateau potentials and control of burst termination. (A) The amplitude of the slow afterhyperpolarization (sAHP) will determine whether one or several action potentials will occur during the phase of synaptic excitation in locomotor cycle. A large and long-lasting sAHP will make locomotor bursts shorter. (B) Ca\(^{2+}\)-dependent K\(^+\) channels (K\textsubscript{Ca}) not only cause the sAHP but will also promote the termination of NMDA-receptor induced plateau potentials. The control plateau (solid trace) is markedly prolonged in the presence of the K\textsubscript{Ca}-channel blocker apamin (dotted trace). (C) Several different factors contribute to the initiation of the depolarizing phase, its maintenance, and its termination. In addition to the cell through these channels, cause activation of K\textsubscript{Ca}, and thereby a progressive hyperpolarization leading to closure of the NMDA channels. The initiation of the depolarizing phase is facilitated by activation of ipsilateral excitatory stretch receptor neurons (SR-E), while the termination of the depolarized phase is partially a result of activation of contralateral inhibitory stretch receptor neurons (SR-I). Abbreviation: E, excitatory interneuron.
Fig. 5. Imaging of calcium fluctuations in motoneuron dendrites. (A) During network activity, periodic fluctuations in calcium fluorescence could be detected in distal motoneuron dendrites. Pseudocolor images of the same dendritic portion at five different time points. (B) Calcium response in a distal motoneuron dendrite during subthreshold synaptic stimulation, recorded as a fluorescence increase concomitant with a compound EPSP (the latter not shown). Upon blockade of NMDA channels with APV, about 50% of the response remains. (C) Fluorescence measurements of a small region of the dendrite in A. Numbers correspond to images in A. The intra-dendritic calcium level fluctuations are time-locked to the fictive locomotor rhythm, recorded from the ipsilateral ventral root (modified from Ref. [3]).
a significant activation of $K_{Ca}$. This appears, however, not to be the case, since the EPSPs remain at the same amplitude, and they are not modified if amipain-sensitive $K_{Ca}$ channels are blocked [18].

These results thus suggest that the $Ca^{2+}$ entry, due to EPSPs evoked from a reticulospinal axon does not cause a significant $K_{Ca}$ activation. This may be due to either that the $Ca^{2+}$ levels do not reach a sufficiently high concentration to activate local $K_{Ca}$ channels, and/or that $K_{Ca}$ channels are located at some distance from the glutamatergic synapses, where the $Ca^{2+}$ concentration will be too low. These findings suggest that the dendritic processing is more predictable than may otherwise have been case.

The question of whether the amplitude of the locomotor drive potentials in a given neuron represents just the sum of the excitatory and inhibitory input occurring during fictive locomotion, or whether other factors such as voltage dependent processes in the dendrites also contribute to the net membrane potential oscillations have been addressed by Hu et al. ([42], and unpublished observations). In lampreys, the compound QX-314 causes a blockade of Na$^+$ channels present in dendrites, and at a much higher concentration (10-fold) also of $Ca^{2+}$ channels. During fictive locomotion QX-314 was injected through the recording microelectrode. It caused a depression by 20–30% of the peak-to-peak amplitude of the synaptic drive potential (peak EPSP to peak IPSP). The most likely explanation for this depression is that voltage dependent Na$^+$ channels present in dendrites amplify the synaptic excitatory drive potentials recorded in the soma. The contribution of other voltage-dependent processes can, however, not be ruled out. The results show, however, that active properties of dendrites play a significant role.

6. Modulator systems — action on ion channels manifested on the network-behavioral level

In addition to fast ionotropic glutamatergic, glycinergic, and GABAergic actions on the spinal level, there are a number of control mechanisms that act via G-proteins. These include: (1) descending peptidergic (cholecystokinin and peptide YY [5,49,10]) and 5-HTergic [6] pathways, that originate in the brainstem; (2) dorsal root inputs (calcitonin gene related peptide, bombesin, tachykinins, 5-HT; Refs. [74,75,5]); and finally (3) intraspinal systems, for example, bipolar GABAergic and neuropeptide Y containing neurons [4], somatostatin and neurotensin plexa around the lateral edge of the spinal cord [19,11] and intraspinal midline neurons that form a 5-HT, dopamine, and tachykinin-containing plexus [74,75,62,63]. In addition, fast glutamatergic and GABAergic systems can also act via metabotropic receptors (GABA$_B$ [1,17,69]; mGluR I–III [44,45]).

The actions of several of these different modulators have been analyzed in some detail with regard to their molecular, cellular, and overall network effects. Table 1 shows some of the actions mediated by different modulators that act via different receptor subtypes. The leftmost column shows presynaptic actions. In most cases there is a presynaptic inhibitory effect (I), but with regard to tachykinins (substance P-like peptides) synaptic transmission is instead facilitated (F) [53,55]. Presynaptic interactions occur at all levels in the locomotor control system, namely on sensory inputs, inhibitory and excitatory network synapses, and descending reticulospinal axons. Moreover, during locomotor activity there is a phase-dependent gating of synaptic transmission in both interneuronal and sensory axons [1,28], making synaptic transmission more effective in one or other phase of the locomotor cycle. Other modulators (5-HT, dopamine, substance P, mGluR, CCK, PYY) provide a tonic gating of synaptic transmission, for example of glutamatergic synaptic transmission from reticulospinal axons [16,44,2,53,81].

The five middle columns in Table 1 show modulator/receptor-mediated actions on different types of ion channels (Ca$^{2+}$ channel subtypes, K$_{Ca}$, K$^+$, NMDA). It is important to note that the effects are often specific to a given cell type or synapse, and that it is thus unfortunately not possible to extrapolate from one type of neuron to another. For example, GABA$_B$ receptors mediate powerful presynaptic inhibition of sensory and interneuronal axons but not reticulospinal axons [19,1,2]. The converse is true for dopamine, which acts on the latter synapse [79] but not on the sensory level [27]. In addition to different effects at different levels in the spinal cord, modulatory effects are in many cases also neuron- and synapse-specific within the locomotor network itself (see Refs. [53,54]). It is thus imperative that individual network neurons are identified if a satisfactory understanding of network effects is to be achieved.

The column to the right in Table 1 shows the overall network effects exerted by the different modulator systems. In most cases there is a change in burst frequency when the modulator is applied during ongoing locomotor activity. Intersegmental coordination may also be affected (see for example Ref. [46]), as well as the amplitude and the duration of the bursts within a given locomotor cycle. Since we have a relatively detailed knowledge of how the network functions, the network effects of a modulator can (to some extent) be predicted from its different cellular actions. Extensive biologically relevant mathematical models of the locomotor network have also been developed, based on knowledge of the properties and synaptic connectivity of nerve cells in the network [34,41,68]. In these simulations, known specific modulator-mediated effects on the cellular level can be induced to investigate how these different effects contribute to the overall change in the network output. Thus, by combining detailed experimental analyses of modulator effects at the molecular, cellular, synaptic and network levels, and analyzing this data in computer simulations, we may extend our
Table 1
Spinal modulation involving G-protein-coupled receptors

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<th>Transmitter</th>
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<th>HVA&lt;sub&gt;Ca&lt;/sub&gt;</th>
<th>LVA&lt;sub&gt;Ca&lt;/sub&gt;</th>
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*Metabotropic amino acid, aminergic and peptidergic G-protein-mediated modulation of ion channel, synaptic, cellular and network activity in the lamprey spinal cord. The table summarizes the results of a number of studies (see text as well). The effects of different transmitters and receptors on different targets are listed in the columns on the right. The presynaptic actions can be targeted to sensory afferents, excitatory or inhibitory interneurons and descending reticulospinal axons (see Refs. [1,27,52]). Different transmitters have selective actions on different cellular targets (I indicates presynaptic inhibition and F facilitation). The locomotor network modulates phasically, in each cycle, the synaptic transmission from sensory afferents and interneurons. The modulation of HVA<sub>Ca</sub>, LVA<sub>Ca</sub>, K<sup>+</sup> and NMDA channels is indicated with a downward arrow for depression and an upward arrow for facilitation (cf. Refs. [41,56,63,47]). Again, the effects may be specific to particular cell types. Finally, the effects on the network level have been studied on the background of locomotor activity (arrows relate to locomotion burst frequency), and in related modelling experiments [63,67–69] 5-HT, 5-hydroxytryptamine (serotonin) receptor; D<sub>2</sub>, type 2 dopamine receptor; HVA, high voltage activated; mGluR, metabotropic glutamate receptor; NPY, neuropeptide Y; NT, neurotensin; TK, tachykinin.

understanding of the mechanisms of modulator effects from the molecular to behavioral levels.

7. Modeling on the cellular, network and behavior levels

In order to evaluate the experimental data which indeed is very extensive, it was important to utilize mathematical modelling on a cellular and network level, as an interactive analysis tool. So many interactive processes operate in parallel, at the cell and network level, that it is virtually impossible to intuitively deduce the net outcome. We therefore modeled each type of neuron (Fig. 6A) with voltage dependent Na<sup>+</sup>, K<sup>+</sup> and Ca<sup>2+</sup> currents of different subtypes, using Hodgkin–Huxley formalism [23,67]. Moreover, K<sub>ca</sub> channels activated by the Ca<sup>2+</sup> entry during the action potential are responsible for the post-spike afterhyperpolarisation. The latter is a major determinant of frequency regulation in these cells. Each type of neuron was assigned its specific characteristics with for instance the appropriate input resistance within a certain range. It had five different compartments, axon hillock, soma and three dendritic compartments, each of which could be given different properties. In response to simulated current injections these model neurons behaved as their biological counterparts. They were subsequently equipped with conductance increase EPSPs and IPSPs (Cl<sup>−</sup> equilibrium potential). In addition, voltage dependent NMDA channels were simulated [23,12,71]. The inhibitory synapses were placed closer to the soma and the excitatory ones more distally as indicated by the biology. Subsequently, the inhibitory and excitatory neurons of the network were connected in a way similar to that established experimentally. Simulation of segmental networks driven from the brainstem could produce alternating burst activity in populations of model neurons of each cell type as referred to above (Fig. 6B).

The burst range produced by the segmental network model could cover the normal biological frequency range. The properties of the NMDA channels were found to be of particular importance for maintaining regular burst activity in a lower frequency range. Including low voltage activated Ca<sup>2+</sup> channels in the network model could also promote a more distinct burst pattern [76,41,71,67]. By
Fig. 6. Mathematical modelling of the lamprey locomotor network—simulations at neuronal, network and behavioral levels. (A) Neurons of the network were simulated in a realistic fashion, with the different voltage-dependent (Na⁺, K⁺, Ca²⁺), Ca²⁺-dependent K⁺ channels, and ligand-gated channels (AMPA/kainate, NMDA, glycine). Action potentials with early and late afterhyperpolarisation (AHP), and spike frequency adaptation, can be simulated, together with postsynaptic potentials occurring in different compartments. (B) Simulation of the segmental network using a pool of excitatory (E) and inhibitory (I) interneurons and lateral (L) interneurons. The activity is driven by excitatory reticulospinal neurons (R). Activity on the left and right sides alternates. (C) Pattern of intersegmental coordination, produced by a simulated network of 60 segments. This circuitry will produce a rostro-caudal phase lag along the simulated spinal cord, and this lag can be reversed if the excitability is increased in the caudal end, which results in backward locomotion. (D) Simulation of actual swimming movements using a neuro-mechanical model. Frames show steady-state swimming at 4 Hz, resulting from tonic excitation of the network, with the model lamprey moving forwards at a speed of 0.73 m/s. Time interval between frames is 50 ms (modified from Ref. [35]).

Simulating a number of segments along the spinal cord, an intersegmental lag from rostral to caudal could be produced (Fig. 6C; Refs. [35,41]). The simulations show that with the available information on interneurons and their connectivity and membrane properties we can largely account for the output of the locomotor network, at least to a first approximation.

Ekeberg et al. [23] simulated the visco-elastic properties of the muscle segments along the spinal cord and constructed a mechanical model of the body controlled by a neuronal network similar to the one just described. By also including the viscous properties of water, the simulated lamprey could be made to swim through the simulated water with seemingly normal movements (Fig. 6D). Moreover, by increasing the activity of the reticulospinal drive signals unilaterally, the ‘simulated animal’ could be made to turn left or right. A further elaboration of the segmental network model and the myotome into a ventral and a dorsal compartment, has allowed a separate control of these two parts, and thereby swimming movements with a superimposed steering in 3-D [23] (see Ref. [33]).

8. Concluding remarks

In this brief review we have presented a model system for studying the cellular bases of motor behavior. We now have acquired a fairly extensive knowledge of the networks in the brainstem—spinal cord that generate the stereotypic motor pattern characteristic of locomotion. The interaction between cellular properties and the connectivity configurations is critical for the pattern generation. A great variety of aminergic and peptidergic transmitters target specific ion channels or other molecules and thereby...
modify cellular properties in a given way that in turn will produce changes in network activity. We can thus now bridge from the molecular to the behavioral level.

An understanding of neuronal microcircuits, like the locomotor CPG or cortical columns, is one major requirement for us to be able to utilize the extensive progress at the molecular and cellular levels towards a better understanding of neuronal systems and the cellular bases of behavior. The progress until 2010 hopefully will make us bridge this gap, which currently in most experimental models appears insurmountable.

Acknowledgements

Support from the Swedish MRC (3026), the Science Research Council and the Wallenberg Foundation is gratefully acknowledged.

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