Burst dynamics under mixed NMDA and AMPA drive in the models of the lamprey spinal CPG

A. Kozlov[1,2], *A. Lansner*[2], *S. Grillner*[1]

[1] Nobel Institute for Neurophysiology
Dept. of Neuroscience
Karolinska Institute
17177 Stockholm
SWEDEN

[2] Studies of Artificial Neural Systems
Dept. of Numerical Analysis and Computer Science
Royal Institute of Technology
10044 Stockholm
SWEDEN

Abstract

Spinal CPG of lamprey is modeled using chains of nonlinear oscillators. Each oscillator represents a small neuron population capable of bursting under mixed NMDA and AMPA drive. Parameters of the oscillator are derived from detailed conductance-based neuron models. Analysis and simulations of dynamics of a single oscillator, a chain of excitatory oscillators and a chain of two pairs of excitatory and inhibitory oscillators in each segment are done. Roles of asymmetric couplings and additional rostral drive are studied. Conditions for generation of a traveling wave with one cycle per chain length in a realistic frequency range are specified. Results are verified in large-scale spinal cord simulations and correspond to available experimental data.

Present work continues modeling studies of the functions of the lamprey spinal cord and their plausible implementations [1–5] using oscillator models with realistic parameters. We address the problem of generation of oscillations in a wide frequency range by a single segment of the cord and the problem of intersegmental phase lag coordination in chain models of the cord [6,7]. Main building units are nonlinear oscillators representing neurons which are endogenous bursters due to the currents dependent on activation of NMDA receptors and calcium flow. From the technical point of view, the work is characterized by gradual, step-by-step reduction and simplification of detailed conductance-based models of cells and synapses which have been developed earlier. Thus the oscillator model is sufficiently simple for a (limited) mathematical analysis and fast simulations, and still keeps direct correspondences of its parameters and state variables to characteristics measured experimentally.

The oscillator equations comprise leakage, NMDA and AMPA inward currents activated synaptically and from the bath, and KCa outward current. Calcium enters the unit through NMDA channels. A minimal model is determined by a system of ordinary differential equations of 2nd order (for the membrane potential and the intracellular calcium concentration) or 3rd order, if inertia of activation of NMDA synapses is included. It is shown that the unit can oscillate for any level of bath activation of AMPA receptors and sufficiently strong bath activation of NMDA receptors without synaptic self-excitation. Addition of recurrent synaptic couplings with AMPA and NMDA components increases its frequency range. Only drive parameters are varied in simulations.

Two oscillator networks modeling spinal CPG are considered. One having a linear chain of oscillators with excitatory couplings to nearest neighbours and recurrent excitation, E-network, and another one comprising two excitatory chains interacting with each other via two parallel inhibitory chains which provide contralateral inhibition, EI-network. The main function of these networks is to generate a wave of excitation traveling along the chains, with wave length approximately equal to the length of a chain, in wide frequency range (between 1 and 10 Hz).

It is found that the E-network with symmetric couplings generates a forward swimming pattern with the required intersegmental phase lag if an additional drive is applied to the most rostral

segment of the chain. This implements the 'trailing oscillator' hypothesis suggested earlier [8]. There are still no experimental evidences that asymmetry in excitatory couplings should be taken into account.

In contrast, EI-network features prominent descending rostro-caudal asymmetry of contralateral inhibitory connections. It is shown that this asymmetry is sufficient for generation of traveling waves even without extra rostral drive. Results are verified in large-scale simulations as shown on Fig. 1. This network maintains one cycle per chain length for higher frequencies most efficiently. In the low frequency range, additional rostral drive helps to correct the intersegmental phase lag.

In conclusion, chains of endogenous oscillators are shown to possibly underly the swimming pattern generation in the lamprey spinal CPG. Currents depending on activation of NMDA receptors and related calcium dynamics determine the oscillations. Both E- and EI-networks are capable of producing a swimming pattern, with EI-configuration being most efficient.

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