According to the project specifications, the first version of a GPU-based large scale network simulation software package (LSNS) is developed. This simulation environment is currently used for multiscale modeling and consists of:

1) The simulation engine (the core of LSNS package that provides the basic abilities to perform computational simulations of neural networks of Hodgkin-Huxley type neurons). The simulation engine is able to perform for multiscale modeling and computational analysis of cross-level integration of: (a) the intrinsic biophysical properties of single neurons (at the level of ionic channel kinetics, dynamical changes of ionic concentrations, synaptic processes); (b) population properties (synaptic interactions between neurons within populations with random distributions of neuronal parameters); (c) network properties (connectivity and type of synaptic interactions between populations with random distribution of connections), (d) morpho-physiological structure (organization in interacting modules/compartments).

2) The translator <…>.

**Cells model.**

The simulation engine is able to compute the conductance-based single-compartment model of neuron in the Hodgkin–Huxley style. The dynamics of neuronal membrane potential (V) is defined by a set of membrane ionic currents:

(1)

where: is neuronal membrane capacitance are synaptic currents; are currents of ion channels; are pump currents. The ion channels which are implemented by the LSNS core are classified by gating. The current version of LSNS package supports: (i) v*oltage-gated* ion channels open or close depending on the voltage gradient across the membrane, (ii) *other-gated* ion channels <…>; (iii) *ligand-gated* (synapses) ion channels open or close depending on binding of ligands to the channel.

**Implementation of ion channels.**

Ion channels (including ligand-gated ion channels) are implemented according to follow formula:

(2)

where: is maximal conductance; and are gate variables (activation and inactivation); and are power for activation and inactivation, correspondingly; is membrane potential and is reversal potential of the corresponding channels . In general, the gate variables () are described as:

(3)

where is time constant, is steady-state value of correspondent gate variable (activation or inactivation, respectively).

***Voltage-gated ion channels***.

These types of ions channels open or close depending on the membrane potential of the cell and are described as follow:

1) The *generic description* of the gate variable (activation or inactivation) is defined as:

(4)

where is membrane potential, is half-voltage and is slope. The time constants of different subtypes of gate variables are:

1. instant current: ;
2. generic current: ;
3. modified generic current: ;
4. modified generic A-current:

where: , , are time constants; , are half-voltages for time constants; , are slopes for time constants; is threshold.

2) The  *description* of the gate variable (activation or inactivation) is defined as:

,

where: ; is membrane potential; is half-voltage; is slope; are free parameters of either alpha or beta variable. The time constants of different subtypes of gate variables are:

1. instant current:
2. current .

***Other-gated ion channels***

The dynamics of gate variables *for Ca-activated potassium* channels are described according to (3). The steady state for gate variables are:

1. , . The time constants are: or .
2. , ,. The time constants are: or .

The *leak current* approximates the passive properties of the cell and is describes as:

(5)

where is membrane potential and is reversal potential of the leak current.

***Ligand-gated ion channels (synapses)***

Synaptic current for postsynaptic neuron that generated by j-th synapse is calculated as [Ermentrout&Terman, 2010, Destexhe et al., 1994, Destexhe&Mainen, 1994, Destexhe et al., 1998]:

(6)

where: is maximal conductance; is gate variable that characterizes the transmitter release; is the factor that defines how effectively the post-synaptic cell responds to neurotransmitters (=1 for the most synapses, except those the mechanism of synaptic plasticity is implemented); is membrane potential for post-synaptic neuron; is reversal potential for *j*-th synapse.

Let suppose that and , are equal for N synapses (*j* = 1…N), then

(7)

According to (7) the total synaptic current for postsynaptic neuron for all similar synapses (*j* = 1..N) is calculating as:

(8)

The current version of the package is supported three types of synapses which are:

1. *Weighted sum* synapse*.*

The neural transmitter release for this type of synapse is modeled as weighted sum of all input signals for the synapse, and can be written as:

(9)

where: is rate of transmitter release; and are weight of connection and input signal between post-synaptic neuron and non-spiking element of the network (like drive, output, feedback, etc). The total synaptic current for all similar synapses can be written then as:

10

1. *Instant* synapse*.*

The simplest model of transmitter release at *j*-th synapse between post- and pre- synaptic non-spiking neuron is modeling by sigmoid function and is described as follow:

(11)

where: – rate of transmitter release; - weight of connection for *j*-th synapse between post- and pre- synaptic neurons; – the membrane potential of presynaptic neuron; and are half-voltage and slope for instant synapse. The total synaptic current for instant synapses is:

where: (12)

1. *Pulse model* of synapse.

The model of transmitter release for pulse synapse is written as recurrence equation for -th integration step:

(13)

where: - integration step; T - time constant; – rate of transmitter release; - weight of connection for *j*-th synapse between post- and pre- synaptic neurons; – Dirac function (which is equal to 1 then spike is generated by presynaptic neuron or 0 otherwise); – the membrane potential of presynaptic neuron; =0. The total synaptic current then can be written as:

(14)

The equations (10, 12 and 14) could be rewritten as linear recurrence equation as follow:

(15)

where: is rate of transmitter release; =0; for pulse model of the synapse or 0 otherwise; or or for

The mechanism for synaptic plasticity that involves the NMDA receptors is also implemented in the current version of LSNS package. The synaptic current for *NMDA synapse* is calculated similar to equation (7) [Destexhe&Mainen, 1994, Ermentrout&Terman, 2010] where: represents the magnesium block and is calculating as: . The model of transmitter release () is described similar to the model of transmitter release for AMPA/GABA(a) synapses (see. 13, 14 ) [Destexhe et al., 1994, Destexhe&Mainen, 1994, Destexhe et al., 1998].

**Implementation of ions dynamics**.

Reversal potential (E = RT/Fz\*ln[Out]/[In])

Dynamics:

Ca-ions

Na-ions

Network units

a) drives;

b) outputs;

c) feedbacks.

Biomechanics

a) muscles;

b) arm model.

**References**

1. G.B. Ermentrout and D.H. Terman, Mathematical Foundations of Neuroscience, Interdisciplinary Applied Mathematics 35, DOI 10.1007/978-0-387-87708-27, Springer Science+Business Media, LLC 2010
2. Destexhe, A., and Mainen, Z.F. Synthesis of Models for Excitable Membranes, Synaptic Transmission and Neuromodulation Using a Common Kinetic Formalism. Journal Of Computational Neuroscience, 1, 195-230, 1994
3. Destexhe, A., Mainen, Z.F. and Sejnowski, T.J. An efficient method for computing synaptic conductances based on a kinetic model of receptor binding Neural Computation 6: 10-14, 1994.
4. Destexhe, A., Mainen, Z.F. and Sejnowski, T.J. Kinetic models of synaptic transmission. In: Methods in Neuronal Modeling (2nd edition; edited by Koch, C. and Segev, I.), MIT press, Cambridge, 1998, pp. 1-25
5. Destexhe, A. and Sejnowski, T.J. G-protein activation kinetics and spill-over of GABA may account for differences between inhibitory responses in the hippocampus and thalamus. Proc. Natl. Acad. Sci. USA 92: 9515-9519, 1995.
6. Destexhe, A., Bal, T., McCormick, D.A. and Sejnowski, T.J. Ionic mechanisms underlying synchronized oscillations and propagating waves in a model of ferret thalamic slices. Journal of Neurophysiology 76: 2049-2070, 1996.
7. X.-J. Wang, J. Tegne, C. Constantinidis, and P. S. Goldman-Rakic Division of labor among distinct subtypes of inhibitory neurons in a cortical microcircuit of working memory. PNAS, V101, No 5, 1368 –1373, 2004