

P035-T | Influence of mechanical unloading on the morphofunctional state of the soleus muscle

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During space flights or locomotor pathologies in earth conditions the morphofunctional state of the neuromotor apparatus changes dramatically. One of the main reasons is supposed to be the restriction of support afferentation. In the present work, the morphofunctional state of the m. soleus of rat was evaluated in modeling the restriction of support afferentation of the hind limbs by hanging animals ($n = 7$) by the tail in the upside down position ($\approx 30^\circ$). After 7 days of exposure to the experimental conditions, the isoform composition of titin in the m. soleus and the M-wave parameters were assessed when the sciatic nerve was stimulated. As control data, used data received in the study of intact animals ($n = 5$).

It was found that in m. soleus of rats after seven days of restriction of support afferentation, there is a decrease in the content of titin N2A isoform relative to the content of myosin heavy chains by 25% ($P < 0.05$). The decrease in the relative amount of titin N2A isoform is accompanied by a 3-fold increase in the relative content of T2 fragment ($P < 0.05$), which indicates a change in proteolysis of the titin N2A isoform of titin. With high-frequency stimulation of the sciatic nerve (50 Hz), a significant depression of the M-response was recorded (the decrement was $42 \pm 6\%$, $P < 0.05$), which indicates a decrease in the reliability of synaptic transmission. Thus, the activity of support receptors determines the morphofunctional properties of the motor system. Restriction of support afferentation initiates morphological changes in the rat's soleus muscle, and also leads to impaired neuromuscular transmission.

This work is supported by the Russian Science Foundation under grant 18-75-10027.

P036-T | The model of artificial neural network, allowing the formation of a motor program generator

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The aim of this study was the search of general rules of constructing of the simple neural networks which was capable to form

their own pattern of muscle activity. On the basis of the original software the variants of the neural structures configurations have been tested. These networks can provide the plasticity on the level of conditioning the signals coming from the neural blocks of different functions, which can allow the implementation of the principle of Hebbian plasticity. The principal architecture of dynamic stochastic artificial neural network, provided the facilitation of the execution of the motor program was found.

The present study involved qualitative analysis of neurophysiological data of the principal mechanisms of functioning of relatively simple neural structures. The formal threshold element with formal spike activity without detailed description of the spike shape was chosen as a neuron model. The model of the artificial neural network which provided the simplification of the implementation of the "external" motor program was proposed. The formation of the own pattern generator of muscular activity with the profile of the activity of the prescribed shape for each effectors occurred as a result of repetitions of this motor program. Obtain model allowed us to explain the behaviour of the late responses during frequency stimulation in electrophysiological experiments in situations when performing motor program was familiar to the subject and depended on the context. The described scheme also can explain the necessity of optimal sensory input in restoring pre-existing motor programs, including motor programs after injuries, as well as the necessity of the additional activation or loading for improving of the motor response.

The work supported by RFBR (grant No. 18-44-160032_r_a).

P037-T | Unsupervised learning of activity patterns in the neonatal rat auditory cortex

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Spontaneous activity patterns in the neonatal rat sensory cortex display region-specific features. Here we aimed to compare the spontaneous activity in the auditory (AC) and somatosensory (SC) cortices of P6-7 rats ($N = 7$) using machine learning approach. We developed a method to differentiate one second long patches of activity in AC and SC using convolutional artificial neural networks. We trained the network on the most salient patches of activity to learn characteristic AC and SC waveforms and then applied it to the whole traces of spontaneous activity in both structures. We found that spontaneous activity in AC specifically displayed long-lasting megabursts of the local field potential oscillations in a wide range from theta to gamma frequencies and multiple unit activity lasting for ≥ 7 seconds and occurring at a rate of 40 ± 12 megabursts per hour. The AC

activity also expressed discrete ramp-shaped troughs (sharp potentials, SPs) lasting ~100 ms, some of which occurred within megabursts. SPs were preceded by spiking activity in the inferior colliculus at a delay of 20 ± 4 ms. The current-source density analysis of both AC patterns revealed their main sinks in the cortical layer IV. These findings point on the region-specific organization of activity in the developing cortex and suggest that prior to the onset of hearing the AC activity is largely driven by spontaneous activity at the auditory periphery.

This work was supported by the subsidy allocated to Kazan Federal University for the state assignment № 6.2313.2017/4.6 in the sphere of scientific activities.

P038-T | Prediction of bioisosteric substitutions using the Condensed Reaction Graph approach

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The prediction of bioisosteric substitution for molecule is extremely important and challenging. The replacement is called bioisosteric if activity of molecule is barely influenced. The substitution of potentially toxic fragments by less dangerous can give insight to safe modifications of drugs and/or hit molecules. It also could be used for focused library generation, scaffold hopping or lead optimization.

The approach for prediction of bioisosteric replacements was proposed. It contains 3 steps: (i) bioisosteric rules extraction, (ii) its application for molecules of interest and (iii) filtering results by model, predicting whether substitution is bioisosteric.

149 890 matched molecular pairs (MMP) with known log IC50 values for 12 biological targets was extracted from ChEMBL. Each MMP was considered pseudo-reaction, transforming one molecule into other. Condensed graph of reaction (CGR) approach was used for MMPs representation. CGR is a representation of reaction as a pseudomolecule that has additional to classical (single, double, etc. bonds and charges) features new types as dynamic bonds and/or charges which show changes within transformation. Rules that correspond to substitution of one chemical functionality by the other were automatically extracted for every biological target. Using ISIDA Fragment or descriptors for CGR was calculated. Random Forest (RF) was used to build classification model for every target. If difference in logIC50 was less than 1 substitution was considered bioisosteric. These models were used as a filter for newly generated CGRs to predict if this substitution is bioisosteric.

The approach was tested on one dataset retrospectively. It was shown that application of the approach to a seed molecule generates set of compounds within which compounds with the same type of activities could be found.

This research was funded by the Ministry of education, youth and sport of Czech Republic, agreement NoMSMT-5727/2018-2 and the Ministry of Education and Science of the Russian Federation, agreement No14.587.21.0049.

P039-T | Adverse drug reactions identification in social media posts and electronic health records with neural networks

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Background: Social media posts and electronic health records have become a promising source for detecting adverse drug reactions (ADRs). We introduce a system for automatically detecting of ADRs from natural language texts. The system based on artificial neural networks and consists of two components: named entity recognition (NER) and entity type classification. The NER module aims to extract words and multi-word expressions denoting diseases. Disease type classification is necessary to distinguish drug reactions from drug indications.

Material and methods: The NER module is based on a hybrid Long Short Term Memory (LSTM) and conditional random fields architecture. The classification module is based on Interactive Attention Neural Network (IAN). IAN is the attention-based LSTM network, which takes as an input entity and its context in a sentence. Both entity and context representations interact with each other's attention mechanism to generate the overall representation. Extension of the NER model by the IAN classifier allows to separate the representation of the entity from the context and organize their interaction.

We evaluated the efficiency of the model on CADEC (<https://data.csiro.au>) and MADE (<http://bio-nlp.org/index.php/projects/39-nlp-challenges>) corpora. CADEC corpus consists of user-generated reviews about drugs from askapatient.com forum. MADE corpus contain de-identified electronic health record notes of cancer patients.

Results: We evaluated the model using the F-measure, which is the standard quality metric in natural language processing. The model obtained 76.5% and 72.6% F-measure for ADRs class on the token level for CADEC and MADE corpora respectively.

Conclusions: We present the system for extracting ADRs from texts describing the effects of taking drugs. The high level of obtained results proves the applicability of developed system for this task. A promising future research direction is