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Mathematical methods for multidimensional time series processing in application to real-time electrophysiological signals analysis

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Contents

1 Introduction

1.1 Subject of the study

Mathematical methods for multidimensional time series processing in application to real-time electrophysiological signals analysis are widely used in the field of neuroscience. Such approaches are necessary for the experiments which include the task of instantaneous real-time evaluation of the central nervous system (CNS) activity state. Registration of this activity is usually carried out by using a set of sensors that are sensitive to changes in the electromagnetic field is produced as a result of the CNS work. Examples of such acquisition techniques are electroencephalography (EEG), magnetoencephalography (MEG), electrocorticography (ECoG). In this paper, EEG signals will be considered as basic electrophysiological signals, but the results of this work are equally applicable to MEG and ECoG data analysis. In general, experiments that require an instant evaluation of the CNS state can be presented in the form of a closed-loop system, shown in Fig. 1. Namely: (1) the activity of the participant' CNS is measured in real-time by several sensors, (2) multi-channel signals are processed and some target characteristics of the CNS state are extracted, (3) these characteristics are used to form a stimulus for the subject, or to control the program or an external device. The circuit is closed at the moment when the subject perceives the stimulus or observes (feels) a result of the program/device acting causally dependent on the CNS activity measurements processing.

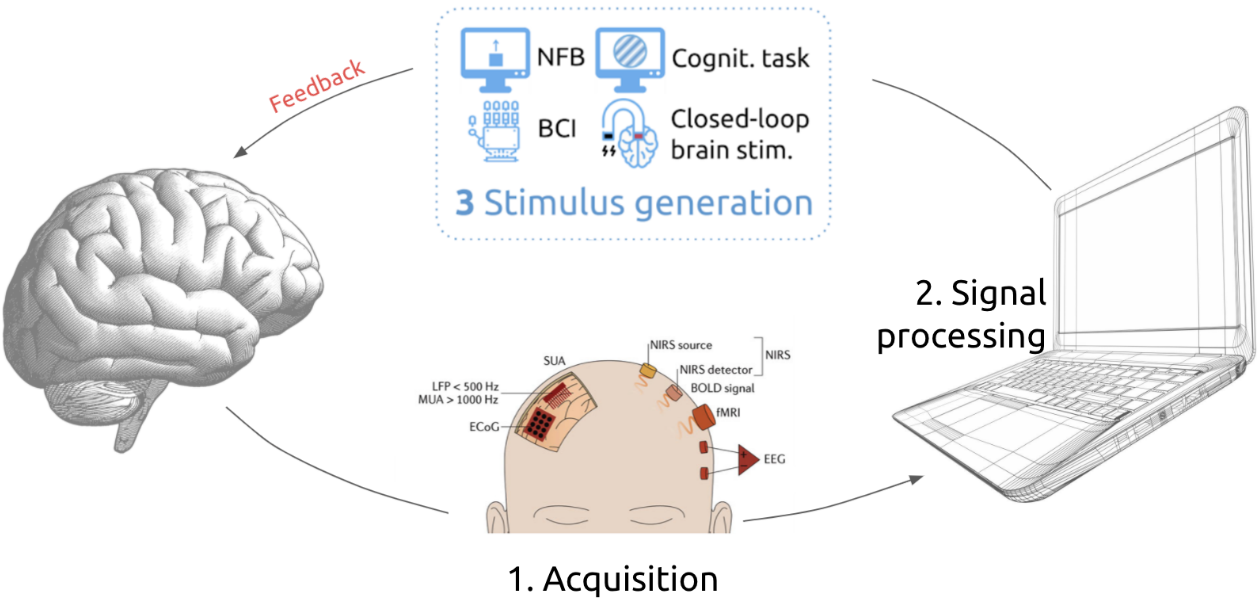

Figure 1: Closed-loop neuroscience paradigms

In the literature, such experimental paradigms are referred to as Closed-loop neuroscience paradigms. Examples of these closed-loop paradigms are:

1. Brain-computer interface (BCI), in which brain activity is used to directly control an

external program or device [1]. This paradigm provides communication with completely paralyzed patients, replaces lost motor function, and facilitates post-stroke neuro-rehabilitation.

2. Neurofeedback (NFB) is a paradigm in which the target characteristics of brain activity are transformed into a visual, auditory, or tactile stimulus interpreted by a participant [2]. The aim of the participant is to hold the stimulus in a certain state, for example, to try to increase the height of the column displayed on the screen, which corresponds to maintaining the target characteristic of brain activity in the desired range. As a result, participants of the NFB session learn to regulate their own CNS activity. This paradigm is used both for the correction of the psychoemotional state, for peak-performance training, as well as for the treatment of a wide range of neurodegenerative diseases, including epilepsy.

3. Stimulation (transcranial magnetic, direct current, alternating current) of brain activity, depending on the current CNS state [3, 4]. In this paradigm, brain activity is monitored in real-time and, a decision is made about the moment when the stimulation is turned on based on the current brain state parameters estimation. Such a setting can be useful for suppressing pathological activity or causing a certain behavioral response, which is used, for example, to suppress tremor in patients with Parkinsonism or reduce the likelihood of epileptic seizure.

4. Behavioral experiments with online monitoring of brain activity, when stimuli or tasks are presented at the moments when the CNS is in a certain state [5]. This kind of paradigm is an alternative to the extensive approach, in which stimuli are presented at random time points, and then at the post-processing stage a researcher selects the trials that correspond to time intervals with the desired type of activity. Using online monitoring allows for a significant reduction of the experiment duration and simplifies results interpretation.

It should be noted that the ways of presenting feedback in these paradigms can vary considerably - from a stimulus displayed on the screen to an electromagnetic pulse or phase synchronization of direct electrical stimulation. However, the signal processing stage is often similar in these paradigms and represents the main **object of the thesis**.

Spatial and temporal filtering are two basic operations used in the processing of a multichannel EEG signal.

Spatial filtering is the reduction of a multidimensional (multichannel) signal to a one-dimensional time series. Such a transformation can be performed trivially, by selecting a single "real" channel (or lead, as it is called in the EEG literature) for subsequent analysis. A more general method involves the formation of a "virtual" channel, which is usually performed by linearly combining several channels into one. This operation is called linear spatial filtering. The one-dimensional time series obtained after the spatial filtering stage will be referred to as the virtual lead signal or virtual sensor signal. The researcher's task is to estimate the coefficients of the spatial filter based on the requirements of the experimental paradigm. It is known that the human brain can be divided into areas based on functional characteristics, for example, the visual system is located in the occipital lobe, motor control refers to the areas near the central gyrus, the frontal cortex is responsible for a range of executive cognitive functions. The purpose of spatial filtering is usually to isolate the activity of the specific brain region. It should also be noted that spatial filtering allows us to switch from EEG-sensors signals to signals from neuronal sources, thereby reducing the volume conductivity effect (projecting a single source signal on multiple sensors), which often makes complicates the direct analysis of sensor data directly.

The spatial filter can be obtained by solving the EEG (MEG or ECoG) inverse problem [6] or by using the spatial decomposition of multichannel electrophysiological data [7]. Currently, a wide range of methods for spatial filter weights estimation has been developed. These methods are mainly used for post-processing of the acquired data. To apply these approaches online, i.e. in real-time and directly during the experiments, it is necessary to create a platform that would allow for a flexible configuration of methods' parameters and the resulting spatial filters. Spatial filtering in the context of closed-loop experiments in comparison with the direct use of data from physical EEG leads allows us to focus on functionally specific sources of neuronal activity, as well as to suppress artifacts and background brain activity. In the case of closed-loop paradigms, spatial filtering can increase the spatial specificity of the feedback signal.

Temporal filtering allows us to select a specific temporal pattern of CNS activity by calculating a sliding window convolution of time samples of a single lead signal. One of the most studied components of neuronal activity are the brain rhythms [8]. The first of the discovered brain rhythms is called alpha rhythm which is an oscillation with a central frequency of 8-12 Hz, discovered by Hans Berger in 1924. For example, the alpha rhythm localized in the occipital lobe reflects the state of the visual cortex of the brain: when the eyes are closed, visual information is not sent to the visual cortex, the power of this rhythm increases, while when the eyes are open, it decreases.

Another important rhythm that is widely used in brain-computer interface paradigms is the sensorimotor rhythm (or mu rhythm), localized in the area of the central sulcus. The central frequency of this rhythm lies in the range of 10-14 Hz and, by analogy with the occipital alpha rhythm, this rhythm reflects the state of the sensorimotor system: in a state of rest and motor inactivity, this rhythm increases, while performing, observing and imagining movements of a certain limb, the amplitude of the rhythm decreases in the areas of representation of this limb in the sensorimotor cortex.

Rhythmic activity can be represented as a narrow-band, frequency-modulated signal, the main characteristics of which are the instantaneous phase and amplitude of the oscillations [9]. According to modern concepts, the difference in amplitudes and the phase of brain rhythms are fundamental parameters associated with the state of the CNS [8, 10]. For closed-loop paradigms, the task is to estimate the instantaneous phase and/or amplitude (envelope) of a narrow-band signal from a raw, in general, broadband signal in real-time. It should be noted that any real-time filtering introduces a delay associated with the causal filtering process. This delay is of a strictly fundamental nature and is a reflection of the Gabor uncertainty principle [11] in the signal processing problems, according to which it is impossible to localize a signal in frequency and time domains with the same accuracy. This delay should not be confused with the technical delay, which consists of the time of data transfer between the acquisition device and the computer, the computing time, and the time of stimulus generation by an executive device, such as a monitor. Usually, with the use of modern software and hardware, technical delays can be minimized and take values significantly lower in comparison with the fundamental delay resulting from the causal time filtering.

Thus, in real-time systems, there is a delay between the occurrence of the target brain activity and the moment when this event is reflected in the feedback signal. Several applications within the closed-loop paradigm require achieving the lowest possible delay, which often leads to a reduction in the quality of rhythmic activity parameters estimations. Depending on the experimental paradigm type, this delay should either be minimized or taken into account during the stimulus generating process to provide the required temporal specificity.

A decrease in temporal specificity leads to low efficiency of the entire paradigm. For example, an increase in the delay between the mental motor initiation and the beginning of the actual program cursor movement in a BCI implementation leads to a decrease in the sense of agency [12]. In the case of the neurofeedback paradigm, analysis of the simulation data [13] shows that the delay or random time offset of the feedback negatively affects the learning rate. Indeed, as we will show, reducing the time delay of the NFB signal presentation leads to an increase in the training efficiency in the neurofeedback paradigm [14]. Thus, the developer of closed-loop systems is faced with the task of reducing the mathematical part of the delay to the fundamentally possible minimum, while maintaining the quality of the envelope or phase estimate. In addition to the classical approaches to this problem [9], there are specialized methods, such as [15, 16]. However, these approaches are heuristics that are difficult in implementation and depend on a large number of parameters with no possibility of explicit control of the system delay parameter.

1.2 Objectives

The suboptimality of the data processing pipeline in the closed-loop paradigm leads to a decrease in the efficiency of various paradigm implementations, making it difficult to apply and limiting the potential capabilities of the paradigm. The main goal of this work is to develop methods and software tools for processing electroencephalographic data for real-time use and aimed at improving the efficiency of implementing closed-loop paradigms.

We should give some comments about the ways of evaluating the effectiveness of the closed-loop paradigm implementations. The effectiveness of the NFB paradigm is generally evaluated by the increase of the target signal during the rest state immediately after training relative to the rest state before training. In addition, one can measure the increase in various behavioral characteristics after the experiment. BCI efficiency can be measured by the accuracy of recognizing the state of the subject brain, the accuracy of the subject's performance in tasks that require control through the BCI, as well as, for example, by questioning the participants to estimate their sense of BCI system control. If the experimental paradigm consists of monitoring and detecting the moments for stimulation, then the effectiveness of the implementation of the data processing pipeline can be evaluated by the accuracy of determining the target states.

In addition, in many experiments, stimulation occurs at random points in time, and then the post-processing stage selects stimuli presented at the target points in time. The correct implementation of algorithms for target states online detection leads to a reduction in the experiment duration since the number of task/stimulus presentations required for analysis is collected faster. Reducing the experiment duration decrease the fatigue of the subject and, as a result, improves the quality of the data obtained. Thus, as a metric of effectiveness in such experiments, we can estimate the reduction in the experiment duration when using online detection in comparison with the classical experiment in which the stimulus is not linked to brain activity.

As noted earlier, the effectiveness of these paradigms implementation largely depends on the accuracy of the method for evaluating the activity of target neuronal sources. Namely, data processing methods should have two key properties: (1) high spatial specificity - high accuracy of target source spatial localization and along with efficient suppression of the background brain activity and external artifacts, (2) high temporal specificity - low delay between the change in the activity of the target neuronal population and the moment when this change appears in the feedback signal.

The thesis is divided into 3 related projects - software, methodological and experimental. The software project is devoted to the development of a platform for design and conducting closed-loop paradigms with the possibility of implementing methods that meet the properties described above (1) and (2). The methodological project is aimed at the direct development of digital filters for low-latency quantification of brain rhythms in real time, corresponding to the property (2). The task of the experimental project is to study the relationship between temporal specificity (property (2)) and the overall efficiency of the closed-loop paradigms implementation.

These projects are united by a common topic "Mathematical methods for multidimensional time series processing in application to real-time electrophysiological signals analysis" and represent a complete study. As a result of the study software and algorithmic tools for processing multichannel EEG signals were developed and their effectiveness was demonstrated in the context of motor imagery BCI and NFB paradigms. Currently, all the developed tools and algorithms are actively used in the research activities of the Center for Bioelectric Interfaces of the Higher School of Economics.

1.3 Main ideas, results and conclusions of the dissertation

As part of the software project, the NFBLab software platform was developed for implementing closed-loop paradigms. This software allows one to: (1) configure the data processing path, including spatial and temporal filtering, including the possibility of individualized settings of filter parameters for recorded functional samples, (2) flexibly form the design of the experiment, namely a sequence of blocks indicating their types and signal processing parameters in each of the blocks, (3) conduct the experiment in a closed-loop paradigm, providing connection, reception, recording and processing of multichannel electrophysiological data, as well as the generation of stimuli with the minimum possible delay in generating the feedback signal. The platform includes a specially developed scripting language that allows us to fully describe the parameters of the signal processing pipeline and the design of an experiment consisting of a sequence of blocks, including the possibility of randomizing their sequence. The developed platform includes both traditional and newly developed data processing methods. Also the platform is used in subsequent projects as the main tool for testing the developed methods and conducting experiments in closed-loop paradigms at the HSE Center for Bioelectric Interfaces.

The methodological project deals with development of a family of methods for the low-latency quantification of the brain rhythms parameters in real-time. The developed approaches make it possible to effectively estimate the envelope and phase of the narrow-band component of a broadband electrophysiological signal. At the same time, the total delay of the processing pipeline is an independent parameter, for every value of which the developed approaches provide optimal accuracy of the estimation of the narrow-band process instantaneous envelope and phase. The design of the developed filters is based on solving the optimization problem of finding a causal complex-valued filter with a finite impulse response (FIR) that approximates a non-causal ideal filter for evaluating an analytical narrow-band signal. In comparison with the standard methods used in closed-loop paradigms [15], the developed methods family provides a lower value of the delay in the envelope and phase estimation while maintaining the accuracy of the estimates. At the same time, the user has the opportunity to explicitly configure the delay-accuracy ratio in the context of a specific application.

The experimental project uses the developed methodology and the software to study the influence of the feedback signal temporal specificity on the effectiveness of the closed-loop paradigms implementation. In particular, we tested the hypothesis about the negative impact of feedback delay on the effectiveness of learning in the NFB paradigm. The experiment included 4 groups of subjects. Subjects from the first three groups were presented with a feedback stimulus with a total delay of 250, 500 and 750 ms. The fourth group of subjects received mock feedback and was used as a control group. According to the results of the experiment, a statistically significant relationship between the efficiency of NFB training and the overall delay of the NFB system was discovered, the smaller the delay of the NFB, the steeper the learning curve was observed and the more expressed the sustained the training effect was.

1.4 Theoretical and practical significance

The NFBLab platform, developed as part of the software project, allows us to design and conduct closed-loop experiments. It is based on the developed file format for signal processing pipeline and experiment design description. The main method of spatial filtering in NFBLab is to create spatial filters based on the decomposition of functional samples recorded during the experiment. In comparison with standard methods based on the solution of the inverse problem citecongedo04, this approach is more individually specific and allows us to select areas of brain activity according to their functional behavior and does not require performing quite time-consuming calculations associated with the evaluation of an individualized direct electromagnetic model and requiring segmentation of the MRI (magnetic resonance imaging) of the subject. However, NFBLab allows the user to take advantage of this generally accepted methodology as well through an efficient interface with the MNE-Python [17] package. The signal processing path uses the mechanism of composite signals, with the help of which it is possible to calculate in real-time measures of the functional interaction of areas of the cerebral cortex. In addition, much attention at the NFBLab development stage was paid to the problem of reducing latency in the signal processing loop. The mathematical delay of the applied methods acts as an independent parameter, whose value is set by the user when designing the signal processing pipeline. There is an opportunity to introduce additional artificial delay for experiments to study the effect of system latency on the effectiveness of the closed-loop paradigm. The software platform also provides the ability to design experiments with an almost arbitrary design, sequence, and duration of blocks, including randomizing their order and using methods for statistical normalization of signals. The developed software is a platform for testing new methods of low-latency estimation of rhythm parameters developed as the part of this thesis. This software platform is an open source project written in python [18] and is currently being developed by a team of developers and users around the world.

The developed NFBLab platform is a unique software that allows the international community to conduct reproducible experiments within the closed-loop paradigm. Moreover, NFBLab provides the ability to flexibly configure the parameters of the signal processing pipeline and create a flexible experimental design. Special attention in this software is paid to monitoring the delay in the signal processing loop. As shown by the authors of this study [14] , such a delay has a significant impact on the effectiveness of training in the neuro-feedback paradigm, and minimizing this delay opens up previously inaccessible opportunities for forming a loop of interaction with the human brain, operating at the speed of the brain itself.

This was made possible with the help of a family of low-latency methods developed in this study for estimation of brain rhythmic activity parameters, which allow reducing the delay of the feedback signal while maintaining the quality of the estimation in comparison with classical methods. The approaches from the proposed family allow us to take into account the nonstationarity of the brain rhythm signal, and also have the ability to adapt to an arbitrary form of the signal spectrum. In addition, the new methods allow you to explicitly control the delay of the signal processing pipeline, which is an independent parameter of the methods. Thus, the proposed methods can be used as the main approaches for instantaneous estimation of the phase or envelope of the target rhythmic activity in a wide range of closed-loop paradigms, in which minimizing the delay is a critical requirement. The author of this thesis demonstrated that the proposed family of methods provides a lower delay and a higher accuracy of estimating the parameters of the brain rhythms [19] than the existing approaches [15]. Increasing the temporal specificity allows us to significantly increase the efficiency of the implementation of these experimental paradigms.

The project to study the effect of feedback temporal specificity on the effectiveness of the implementation of closed-loop paradigms is the first attempt to systematically study this phenomenon in the neuro-feedback paradigm. Previously, the effect of delayed sensory feedback on learning effectiveness has been confirmed in a wide range of behavioral studies. For example, back in 1948, Grice showed that the effectiveness of learning in the task of discriminating complex visual patterns significantly depends on the delay of the feedback signal [20]. The paper [21] shows that the behavioral correlates of learning deteriorate, with an unknown delay in presenting the feedback. Increasing the feedback delay significantly worsens the sense of involvement and reduces the sense of authorship while controlling external devices using the brain-computer interface [12], which is essentially one of the implementations of the closed-loop paradigm. However, in almost all implementations of neuro-feedback paradigms, insufficient attention has been paid to monitoring the value of the delay parameter when presenting a feedback signal. This study is an attempt to develop a feedback methodology with an explicitly controlled delay in the presentation of the feedback signal. The prerequisites for the need for such work were obtained earlier.

A recent study, [22], examined changes in the temporal structure of the EEG caused by NFB. The alpha rhythm of the EEG was recorded on the parietal lead P4, and the average power of this signal was presented to the subjects through visual feedback. The task of the subject was to increase the level of the average power of the alpha rhythm. Analysis of episodes of high-power alpha rhythm showed that the subjects could not modulate the amplitude of the rhythm or the duration of maintaining a state of high-amplitude alpha rhythm. Instead, the increase in the average power of the alpha rhythm in the session was achieved solely by increasing the specific number of episodes of entering the target state, characterized by a high value of the instantaneous amplitude of the alpha oscillation. As a result, it was hypothesized that to increase the efficiency of the NFB, instead of using the average power of the rhythm over the entire time interval, episodes of entering the state of high synchronization of the alpha rhythm should be considered as discrete events. The importance of the discrete component in the interpretation of neuronal activity was also demonstrated in citeshin17, where the authors showed that the number of beta-rhythm spindles per unit time (not the amplitude or duration) determines the effectiveness of performing a motor task. In accordance with the results obtained, it can be concluded that the beginning and end of entering the target state are specifically significant events, the reinforcement of the reproduction of which can lead to a more specific training in the NFB paradigm. Given that the characteristic length of alpha activity bursts is in the range of 200-300 ms, we can suggest the importance of time specificity as one of the factors influencing the effectiveness of the implementation of the NFB paradigm. The software and signal processing methodology developed in this paper allowed us to conduct the world's first systematic study [14], which confirmed the exceptional importance of the feedback delay on the effectiveness of training in the NFB paradigm.

1.5 The author's contribution to the study

The author of this study is the main developer of the NFBLab [23] platform. A family of low-latency algorithms was formulated and investigated by the author of [24]. In the experimental study [14], the author provided methodological and technical support for the NFB system, and also took an active part in processing the results of the experiment. The results of this work are described in three articles published in the international Q1 (WoS core collection) journals. In two papers the author is the first author, in the third article his contribution is equal to the contribution of the first author.

1.6 Publications and approbation of the work

1.7 First-tier publications

1. Nikolai Smetanin, Ksenia Volkova, Stanislav Zabodaev, Mikhail A. Lebedev, and Alexei Ossadtchi. NFBLab—a versatile software for neurofeedback and brain-computer interface research. Frontiers in Neuroinformatics, 12, December 2018.

2. Nikolai Smetanin, Anastasia Belinskaya, Mikhail Lebedev, and Alexei Ossadtchi. Digital filters for low-latency quantification of brain rhythms in real time. Journal of Neural Engineering, 17(4):046022, August 2020.

3. Anastasiia Belinskaia, Nikolai Smetanin, Mikhail Lebedev, and Alexei Ossadtchi. Short-delay neurofeedback facilitates training of the parietal alpha rhythm. Journal of Neural Engineering, 17(6):066012, December 2020.

Conferences

1. Limitless: Augmenting brain function, Lausanne, Switzerland, October 19-21, 2018 Report: "Augmenting the brain with temporarily-structured neurofeedback". Ossadtchi A. E., Smetanin N. M., Volkova K. V. Lebedev M. A.

2. Cell-NERF Symposium: Neurotechnologies, Leuven, Belgium, September 29 – October 02, 2018 Report: "Online and offline modulation of sensorimotor components following focal vibration". Bulgakova V. O., Smetanin N. M., Volkova K. V., Ossadtchi A. E.

3. International Conference Neurocomputer Interface: Science and Practice, Samara, Russia, November 11-12, 2018 Report: "Towards zero-latency neurofeedback". Ossadtchi A. E., Smetanin N. M., Belinskaya A. A.

4. 5th Annual Conference of the USSR Brain Codes: Control and Perception, Moscow, Russia, November 29-30, 2018 Report: "Towards zero-latency neural feedback". Ossadtchi A. E., Smetanin N. M., Belinskaya A. A.

5. Skolkovo robotics Forum, Russia, Moscow, April 16, 2019 Report: "Brain-computer interfaces: decoding walking". Lebedev M. A., Smetanin N. M.

6. OHBM Annual Meeting, Rome, Italy, 09-13 June 2019 Report: "From low-latency to predictive neurofeedback: methods and feasibility check". Smetanin N. M., OssadtchiA. E.

7. OHBM Annual Meeting, Rome, Italy, 09-13 June 2019 Report: "The effect of feedback latency on the effectiveness of training in the neurofeedback paradigm". Belinskaya A. A., Smetanin N. M., Ossadtchi A. E.

8. The Second Neuroadaptive Technology Conference NAT 2019, Liverpool, United Kingdom The Second Neuroadaptive Technology Conference NAT 2019, July 16 – 18, 2019 “Different effects of neurofeedback latency on the incident rate, amplitude and duration of alpha-bursts”. Smetanin N. M., Belinskaya A. A., Ossadtchi A. E. - the third prize for the best report.

9. International Conference Neurocomputer Interface: Science and Practice, Samara, Russia, 02-05 November 2019 Report: "Software Platform for MEG-Based Neurofeedback Training". Smetanin N. M., Osadchy A. E.

10. International Conference Neurocomputer Interface: Science and Practice, Samara, Russia, 02-05 November 2019 Report: "Foot motor imaging triggered locomotion in exoskeleton: first results with paraplegic patients". Smetanin N. M., Kuznetsova A. A., Ossadtchi A. E.

11. Open Project Workshop #CNBR_Open, Skolkovo Innovation Center, Moscow, Russia, February 12, 2020 Open lecture and demonstration: "Demystifying brain-computer interfaces". Alexey Ossadtchi, Nikolai Smetanin.

Patents and copyrights

1. Invention. RU 2713110 C1. A method for estimating the differences in the power of the oscillatory components of electroencephalogram signals in psychophysiological states based on quantile analysis. 03.02.2020

2. Software. RU 2020613238. Cognigraph. 12.03.2020

3. Software. RU 2020618826. Software implementation of the paradigm of low-latency neurofeedback with visual stimulation based on the registration of the human electroencephalogram "Low-latency NFB". 05.08.2020

4. Software. RU2018611760. Software for training in the neurofeedback paradigm. 06.02.2018

2 Content of the work

2.1 NFBLab - a platform for conducting closed loop experiments

This section provides a summary of the published work [24], which gives a detailed description of the developed NFBLab software. At the early stages of developing this software, the main task was to support experiments in the neurofeedback paradigm, taking into account the reproducibility and flexibility of the signal processing pipeline and the experimental design. However, as the development progressed, this platform turned into a full-fledged software that allows us to implement a wide range of closed-loop paradigms.

Purpose and properties of the platform To implement closed-loop paradigms in practice, various software solutions are used that implement connection to an EEG / MEG device, processing of the received multi-channel data in order to suppress artifacts and isolate the target signal, followed by presenting the feedback signal via one of the human sensory modalities, or using such a signal to control external devices. One of such solutions is the NFBLab software developed by the authors, which is briefly described in this part of the thesis. NFBLab can be described as a software for conducting experiments in closed-loop paradigms based on the standard and original low-latency algorithms for processing multichannel bioelectric signals. The key features of this software are:

- support for low-latency connection to the majority of currently common EEG / MEG devices via a protocol based on the Lab Streaming Layer socket technology [25]; item the presence of an internal pseudo-language that allows us to implement flexible configuration of the experiment script using xml-pseudo-code, which provides reproducibility and automatic documentation of the experiments performed, and allows us to automate the experimental procedure.

- the ability to change the experiment scenario by editing xml pseudocode or using a graphical interface, as well as graphical programming interface; item the presence of an interface for conducting the experiment, including an interactive module for forming a signal processing pipeline based on the functional samples and a range of spatiotemporal decomposition methods commonly used in the field;

- the ability to play back the completed experiment; item the ability to visualize the extracted target signals, as well as the presence of a software interface for connecting third-party programs to the extracted signals for presenting the feedback, controlling external devices, and games; item the ability to flexibly configure the experimental design as a sequence of experimental blocks, a mechanism for randomizing the sequence of experimental blocks and generating a mock feedback signal for conducting scientific experiments using control groups

- availability of implemented new proprietary algorithms for low-latency estimation of the instantaneous power of narrow-band signals [19]
- open source in Python, cross-platform interface

NFBLab Analogs The most popular projects for real-time EEG experiments that are currently being developed and supported are OpenVIBE [26] and BCI2000 [27]. The scope of these platforms is experiments with the use of various paradigms for processing and visualizing biosignals in real time. Unlike OpenVIBE and BCI2000, NFBLab not only allows us to configure target signal extraction paths of limited complexity, but also contains a module for controlling the entire experiment and switches, repeats, and randomizes experimental blocks automatically. Also, in contrast to the listed platforms, the NFBLab project uses an individualized and most spatially specific approach - the method of functional sample decomposition - as the main method for designing spatial filters. Also, NFBLab has implemented methods that increase the temporal specificity of the data processing pipeline. In addition, NFBLab is distributed as open source software written in Python [18], which allows advanced users to implement new protocols and signal processing modules as well as involves further development of the project by the efforts of the global community.

Architecture NFBLab consists of three main modules. The first module "Experiment protocol editor" allows us to create an experiment scenario. The resulting design includes a description of the signal processing pipelines, virtual leads, target signals, as well as the parameters for calculating the feedback signal for each of the experimental blocks and the sequence of these blocks, including the randomization scheme and the parameters of the normalization statistics. The design of the experiment is represented in the pseudocode form and is stored in an .xml file that can be loaded for further reuse and conducting a stereotyped experiment. The second module "Experiment module" is launched at the start of the experiment, processes and displays raw and target signals in real time, calculated in accordance according to the signal processing pielines described in the xml pseudocode, controls the sequence of blocks, and also presents various kinds of stimuli. The third module, the "Data-driven filter designer", is an interactive module for editing the properties of the signal processing pipeline and constructing spatiotemporal filters based on the analysis of recorded data. To do so the module exploits recorded data frequency analysis and spatial decomposition by various methods (see sections 4.1 and 6.3 in [24]).As a rule, this module is executed directly during the experiment, suspends the work of the previous module, and serves to create individualized signal processing pipeline and update the xml pseudocode of the experiment. Data is received from the EEG / MEG device using the Lab streaming layer (LSL) or FieldTripBuffer (FTB) technologies (see Section 3.1 in [24]). The recorded experimental data, including all target signals calculated based on the signal processing paths described in the xml pseudocode, is saved to an hdf5 file (see section 6.2 in [24]). Also, the target signals calculated in real time are sent to the LSL Outlet for communication with external programs/devices (see Section 3.1 of the in [24]). The module communication scheme is shown in Figure 2A. For a more detailed description of the modules, see the article [24].

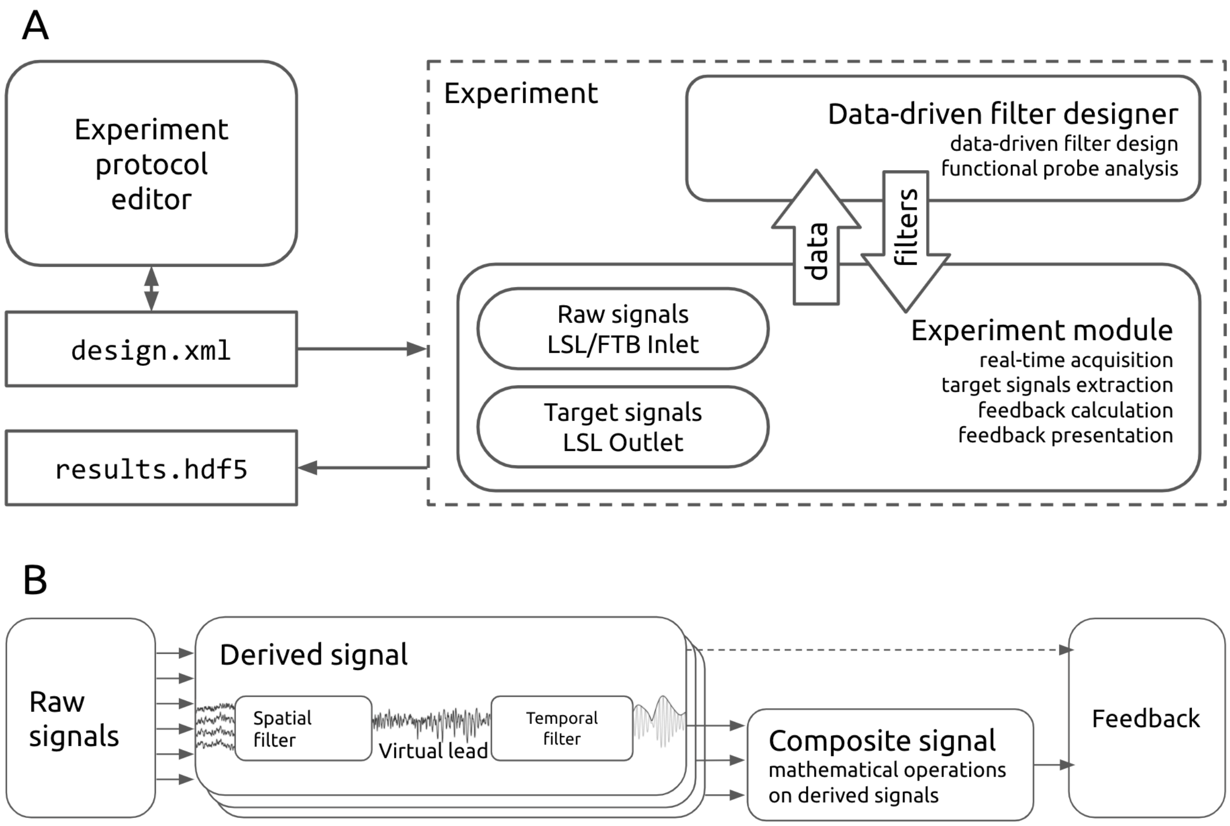

Figure 2: The communication scheme of the main modules in NFBLab (A) and the signal processing stages (B)

Signal processing in NFBLab NFBLab implements the ability to process raw encephalographic signals in real time, calculate virtual leads, filter them in a given frequency range, and then evaluate the instantaneous power of brain rhythms (target signals) and arbitrary functions of target signals specified by a mathematical expression (composite signals). Figure 2B schematically shows the main stages of target/composite signal extraction.

The virtual lead formed using a vector of linear combination coefficients can be trivial and consist of all zeros except for one position in which the unit coefficient is located. In this case, the virtual lead matches the actual real lead from the electrode with the number corresponding to the position of the unit coefficient of the weight vector. Calculating the linear combination with the weights obtained from, for example, solution the inverse problem and corresponding to a certain row of the inverse operator will give a virtual lead that reflects activity of the corresponding cortical region. An alternative method for finding weights for forming a virtual lead can be the use of functional samples in combination with mathematical methods of multidimensional signal processing to isolate projections of maximum contrast or maximum power. In any case, when calculating the virtual lead, weight coefficients are used for spatial selection of the component by anatomical or functional feature. Often, components that are distinguished by a functional feature also have spatial specificity. Therefore, the calculation of the virtual lead in terms of filtering can be called spatial filtering.

More formally, spatial filtering is expressed by the following relation: $y[t] = \mathbf{w}^T\mathbf{x}[t]$, where $\mathbf{x}[t]$ is a vector column of multichannel measurements at time t, $y[t]$ is the value of the signal on the virtual lead at time t, $\mathbf{w}$ is a vector column of spatial filter coefficients, the number of elements of which is equal to the number of recording channels. The spatial filter can be represented as the product of two components $\mathbf{w} = \mathbf{Ru}$. The rejection matrix $\mathbf{R}$ is usually an projection matrix and is used to detach from some pattern of physiological activity (for example, to exclude eye artifacts). The column vector $\mathbf{u}$ acts in the opposite way to $\mathbf{R}$ and serves to highlight the required activity, forming a virtual lead signal. A range of spatial decomposition methods is used to find the rejection matrices and spatial filters in NFBLab:

1. The ICA (Independent Component Analysis) method is used to decompose the signal into independent components and to isolate and remove various kinds of artifacts [28].

2. The CSP (Common Spatial Pattern) method allows us to select components with the maximum signal power ratio for two windows (for example, the first window may correspond to the first half of the recording, in which the subjects eyes are closed, the second - with open eyes). The key part of the algorithm is the solution of the generalized eigenvalue problem [29].

3. In the SSD (Spacio-Spectral Decomposition) method, the decomposition also obtained by solving a generalized eigenvalue problem. This method allows us to isolate components with the maximum signal power ratio for two different frequency bands (the central band and two flankers), which allows us to isolate narrow-band oscillator components [30]

As a rule, the researcher is interested in tracking the dynamics of brain's rhythmic activity, which is reflected in the EEG in the form of a narrow-band random process. Brain rhythms have characteristic frequencies and the next element of the signal processing pipeline is the digital frequency filter, whose coefficients are calculated based on the user-specified frequency band and the filter order. The rhythmic activity of the brain is non-stationary, and can be characterized as a sequence of bursts [31]. The instantaneous power of such activity is described by the envelope of a narrow-band process, calculated, for example, using the Hilbert transform. Thus, the next element of the signal processing path is the estimation of the signal envelope. In addition to the classical approaches, NFBLab implements a new method for estimating the envelope of a narrow-band process, published in [19] and described in the next section of this document. The new envelope estimation method reduces the latency of the feedback signal presentation while maintaining the envelope estimation accuracy. As a result of the described actions, the target signal is obtained, which is a sequence of values that reflects the instantaneous signal power in the virtual lead in a given frequency band.

Such signals will be called Derived signals and is supported by a certain structure in the XML file. The properties of the signal filters used can be determined in the Experiment Design module before the experiment starts, or they can be changed based on the recorded functional samples in the interactive module "Data-driven filter designer" during the experiment. In addition, for advanced users, it is possible to easily edit the text of the XML file.

Often, the feedback signal is formed as the ratio of narrow-band components power of a pair of real or virtual leads. NFBLab implements the Composite signal class, which is defined as an arbitrary mathematical function of two target signals. The type of function is set by the experimenter. For example, to build a training protocol that determines the ratio of the frontal beta rhythm to the occipital alpha rhythm, you need to create two Derived signals corresponding to the frontal beta rhythm and the occipital alpha rhythm, and then create a Composite signal that combines two Derived signals using the division function. In addition to calculating an arbitrary mathematical functions, the mechanism of composite signals allows us to calculate in real time estimates of the functional relationship of the cerebral cortex areas corresponding to a pair of virtual leads.

The experiment scenario usually consists of several blocks. In accordance with the NFBLab ideology, the signal and stimulus settings remain unchanged throughout the block. At the end of each block, the recorded data is added to the HDF5 file with the results and, as a rule, one or more events from the following list are triggered and processed: updating the z-score statistics of the signal (using mean and standard deviation or maximum and minimum value), which are then used to standardize or normalize the feedback signal; launching an interactive Data-driven filter designer to change or create filters for target signals based on previously recorded functional samples; pausing the experiment by sending an audio signal signaling the end of the block.

The experiment blocks differ in the type of visualization. This section describes the main blocks - Baseline and Feedback. The Baseline block consists of presenting a text message with instructions for the subject. Such blocks are usually needed to record the states of the subject, for example, to record the background state, the state with closed eyes, motor states, as well as to collect data used further by the filter design module or to update the z-score statistics of target signals. In the Feedback block, the NFB stimulus is visualized and presented. In addition to presenting a real NFB signal, this block has the ability to generate a mock signal from previously recorded data during the current experiment or from other experiments. The main use of this feature is to conduct experiments in the control group. If necessary, the visualization types can be extended using the LSL interface to connect external visualization programs to the extracted target signals in real time. At the same time, however, it is necessary to take into account the additional delay of the order of tens milliseconds introduced by the LSL interface.

The experiment scenario is formed from a set of customized blocks in the form of a sequence (see the example in Figure 7 in [24]). A subset of blocks (or all blocks) can be added to Blocks group, within which it is possible to repeat and shuffle blocks. At the end of each block, it is possible to implement one or more of the events described in the previous section. Examples of experiments and XML scripts can be found in section 8 in [24].

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2.2 Digital filters for low-latency quantification of brain rhythms in real time

Problem statement An important characteristic of real-time signal processing methods is the temporal resolution and the delay of the processing pipeline. As described in the introduction, low temporal specificity can be the reason for the low efficiency of the closed-loop paradigms implementation and low efficiency of neurofeedback therapy in particular. The present work is aimed at solving the problem of temporal specificity. Modern software solutions that implement a feedback loop and are used both in the clinic (BrainMaster, NeuroRT Training, Cygnet, etc.) and for research (OpenVibe, BCI2000) allow us to evaluate the power of oscillatory brain activities with a delay exceeding 500 ms. This delay is measured from the moment the EEG data is received to the moment the signal is transmitted to the NFB stimulus visualization module. An additional delay of about 100 ms occurs due to technical reasons, namely, due to the process of transmission between the EEG-device and PC and due to the time spent on generating a stimulus with an executive device, such as a monitor. Thus, the total latency of the operating system usually exceeds 600 ms. Due to the presence of such a delay, stimulation in closed-loop paradigms can occur at times when the target activity pattern has already passed. For example, such a pattern of activity as a short burst in the alpha range (8-14 Hz) lasts about 200-300 ms. To detect this type of activity, it is necessary to reduce the delay of the closed-loop system to at least 100-200 ms. This research, conducted as the part of the thesis, is devoted to the development of methods for estimating the instantaneous amplitude and phase of narrow-band signals from real-time recorded EEG/MEG. Detailed results of the work are published in [19] and are given in the appendix **??**.

From the viewpoint of the computer that receives and processes the EEG, the signal coming from the electroencephalograph is a multi-channel time series with a given sampling frequency, for example, equal to $f_s = 500$ Hz. The first stage of EEG processing is the conversion of a multichannel signal to a single-channel form by spatial filtering. Without limiting generality, we will assume that the input to the developed algorithm receives a single-channel signal $x[n]$. Next, a single-channel signal $x[n]$ can be represented as the sum of two signals:

$$x[n] = s[n] + \eta[n]$$

, where $s[n]$ is the target narrow-band signal whose power and phase need to be estimated, and $\eta[n]$ is the broadband noise whose influence on the estimate of the power of interest needs to be minimized. In such a model, it is assumed that all irrelevant narrow-band sources are filtered out in advance with negligible signal distortion in the target frequency range. For example, noise sources of 50Hz or 60Hz associated with interference from the electrical network can be filtered out by notch or comb filters without significant signal distortion in the spectral range of interest, for example, alpha rhythm. Irrelevant neuronal sources, muscle-related sources, and general background EEG noise with a spectrum of the $1/f$-shape form the noise broadband component $\eta[n]$ of the signal x[n].

Further, $s[n]$ can be transformed into a complex-valued analytical signal using the Hilbert transform. The resulting signal $y[n]$ is represented as:

$$y[n] = a[n]e^{j\phi[n]}$$

where $a[n]$ is the instantaneous signal amplitude (the square root of the instantaneous power), $\phi[n]$ is the instantaneous phase, and j is the imaginary unit. The estimate of $a[n]$ and $\phi[n]$ for known values of $y[n]$ is obtained by calculating the absolute value and angle of the complex number $y[n]$, namely:

$$a[n] = (Re(y[n])^2 + Im(y[n])^2)^{\frac{1}{2}}$$

$$\phi[n] = arctg(y[n]/x[n])$$

, $Re(y[n])$ - the real part of $y[n]$, $Im(y[n])$ - the imaginary part of $y[n]$.

It should be noted that the operations of calculating the absolute value and argument of the analytical signal do not introduce an additional fundamental delay in the processing pipeline, since they are calculated for each moment of time using the signal values only at current moment of time. However, calculating the Hilbert transform at the point n‘ ideally requires an infinite window centered around the point n‘ on the time axis. Using the classical approximation of filters with infinite impulse response, it is possible to present the calculation of the Hilbert transform as a convolution of the signal and the finite impulse response of the Hilbert filter. However, such an approximation involves non-causal processing, requiring knowledge of the input values of $s[n]$ for n both from the past with respect to the current time value ($n < n$‘) and values from the future ($n > n$‘) to evaluate the transformed signal at time

n‘. This transform cannot be performed in real-time. However, the use of such an algorithm for a known complete EEG record allows us to extract the envelope $a[n]$ and the phase $\phi[n]$, which will be called the ideal envelope and the ideal phase, with the exception of the values at the edges of the corresponding record.

Thus, the problem of this section is formulated as the construction of a causal algorithm that estimates the amplitude $a[n]$ and the phase $\phi[n]$ in real-time on a single-channel signal $x[n]$. In this case, one of the parameters of the developed method should be the explicitly specified method delay D. The best method is the one that allows, with a decrease in the parameter D, to evaluate $a[n]$ and $\phi[n]$ in real-time with the best possible quality, which will be defined below.

Existing methods The classical method (hereinafter referred to as *rect*) for estimating the instantaneous power is a method based on the amplitude demodulation of the signal and is similar to the principle of the simplest radio receiver working, which detects the amplitude modulated signal [9]. This method involves three consecutive steps: narrow-band filtering in a given range,"rectification" of the narrow-band signal (calculating the absolute value), and smoothing the signal with a low-pass filter (LPF). The output of this algorithm is an estimate of the instantaneous amplitude $a[n]$. The delay of this algorithm consists of the delays of the narrow-band filter and the low-pass filter. In the case when symmetric filters with a finite impulse response (FIR) are used as filters, this delay is half the sum of the filter response lengths. In this paper, filters with symmetric FIR are used as filters. The length N_1 of the narrow-band filter response and the delay value D are used as parameters. Accordingly, the length N_2 of the low-pass filter response can be determined from the values of the desired total delay D and length N_1 of the first filter FIR as:

$$N_2 = 2D - N_1$$

The second method (hereinafter referred to as *hilb*) is based on the Hilbert window transformation. In this case, the signal is processed locally using the sliding window method of length N_3. The last sample inside the window corresponds to the last received sample of $x[n]$. For each new window, the recorded signal is filtered in the narrow-band range with zero phase, then the narrow-band signal is replaced by its analytical form using the Hilbert transform. The absolute value of the analytical signal at a point that is D samples before from the window end is an estimate of the instantaneous amplitude with a delay of D samples. Thus, the parameters of the method are the values D and N_3. It should be noted that this method is affected by transients at the window boundaries.

There are also several modifications of the method described above, which are actively used in closed-loop paradigms when there is a need for accurate real-time phase estimation [32, 33]. One of these methods proposed in [15] is the method based on autoregressive correction of boundary effects. This method, hereinafter referred to as *ffiltar*, is designed to estimate the phase with zero delay $D = 0$. In this paper, the estimation of the envelope at time $D = 0$ was also used for comparison. Methods similar to the *ffiltar* method are also currently appearing, but using more complex predictive models. Examples of such methods are [16, 34].

Developed methods family The proposed new algorithm for estimating the parameters of the brain rhythmic activity of the brain is based on the following idea. Let f_s denote the sampling rate of the recording device. The transition from the broadband signal $x[n]$ to the analytical narrow-band signal $y[n]$ with an additional delay of D samples is represented as a linear stationary system with a complex-valued frequency impolse response (cFIR). The cFIR is determined in the interval from $-\pi$ to π, such that for the frequencies ω from range $2\pi f_1/f_s$ to $2\pi f_2/f_s$ it takes values equal to $e^{-j\omega D}$ and is equal to 0 outside this range, including for the negative frequency range from $-2\pi f_2/f_s$ to $-2\pi f_1/f_s$. The frequencies f_1 and f_2 are measured in Hertz (Hz) and determine the width of the narrow-band signal spectrum. This system will be referred to as the ideal detector of a narrow-band analytical signal with a delay of D.

This system can be approximated by a causal system with the FIR. For this purpose, it is possible to use the criterion of the minimum sum of squares of the difference between the frequency response of an ideal narrow-band analytical signal detecor with a delay of D and its causal FIR approximation. The solution of the optimization problem leads to the following statement: the FIR of the approximating system $b[n]$ is obtained from the ideal frequency response using the inverse discrete Fourier transform. The parameters of the method are N_t - the length of the FIR and N_f - the number of discrete frequencies in the Fourier transform. If $N_f > N_t$ then $x[n]$ is padded with zeros. For nonnegative delays D , such a solution, with proper formulation of the *hilb* method, coincides with the proposed method. Negative delays make it possible to predict the signal into the future by $|D|$ samples. As a result, the evaluation of the analytical signal is obtained by convolution $y[n] = b[n] * x[n]$. The absolute value and angle of the resulting complex-valued signal is an estimate of the instantaneous amplitude and phase of the desired narrow-band signal. The resulting envelope (amplitude) and phase detector is denoted as *cfir*.

Further, various modifications of the optimization problem can be proposed that increase the accuracy of the designed narrow-band envelope and phase detector. For example, it is possible to take into account the spectral features of the individual signal of the subject. Adding the amplitude spectrum of the signal to the optimization problem as weights allows us to formulate the objective function in accordance with the criterion of the weighted sum of least squares and obtain an individual filter for each subject. This method is designated as the *wcfir* method. It is also possible to search for filter coefficients using an optimization problem formulated in the time domain, which makes it possible to take into account the non-stationarity of the signal of neuronal activity and use adaptive approaches based on the recursive least squares (RLS) method. A method with time domain optimization is denoted as *tcfir*. It should be noted that the *wcfir* and *tcfir* methods require pre-recording a small EEG/MEG segment to determine the signal spectrum and adjust the filter parameters. The length of the pre-recording depends on the brain rhythm used. The minimum length is the segment necessary to accurately determine the central frequency of the rhythm and containing a sufficient number of bursts of rhythmic activity. For example, based on practice, one or two minutes of recording is enough to determine the individualized central frequency of the alpha rhythm. A detailed description of the developed algorithms is given in [19] and in the appendix **??**.

Method comparison To check the quality of the developed algorithms and compare them with existing approaches, the following metrics were used. To assess the quality of the envelope estimatation for the delay D, the correlation coefficient was used to compare the estimate $\hat{a[n]}$ and the ideal envelope $a[n]$ shifted by D samples.

$$r_a = \frac{\sum_{n \in \mathcal{N}_a} (a[n-D] - m_a)(\hat{a}[n] - m_{\hat{a}})}{\sqrt{\sum_{n \in \mathcal{N}_a} (a[n-D] - m_a)^2} \sqrt{\sum_{n \in \mathcal{N}_a} (\hat{a}[n] - m_{\hat{a}})^2}} \tag{1}$$

Similarly, to verify the quality of phase reconstruction, the bias b_ϕ and the standard deviation σ_ϕ of the phase estimate $\hat{\phi}[n]$ were calculated relative to the ideal phase at time points $\mathcal{N}_\phi = \{n : n \in \mathcal{N}_a,\ sign(\hat{\phi}[n]) > sign(\hat{\phi}[n-1])\}$ when $\hat{\phi}[n]$ crossed the value 0 (zero phase detection):

$$b_\phi = \frac{1}{|\mathcal{N}_\phi|} \sum_{n \in \mathcal{N}_\phi} \phi[n-D] \tag{2}$$

$$\sigma_\phi = \sqrt{\frac{1}{|\mathcal{N}_\phi| - 1} \sum_{n \in \mathcal{N}_\phi} (\phi[n-D] - b_\phi)^2} \tag{3}$$

As the signals on which the algorithm was tested, a sample of EEG recordings was used. Namely 2 minutes of rest state with open eyes for 10 subjects. The recording was carried out on 32 channels EEG system of the standard 10-20 montage scheme with referents A1-A2. Sampling frequency of 500 Hz was used. Measurement was recorded by an electroencephalograph Neurovisor 136 (OOO “Medical Computer Systems”). Only the P4 channel was used for the analysis. The idial envelope and phase were estimated as the envelope and phase of the filtered rhythm in the range of 8-12 Hz.

The quality of the algorithm was evaluated separately for each record, as well as separately for each delay D from a set of values from -100 to 250 ms in increments of 50 ms. Each recording was divided into two parts of 2 minutes. For each algorithm the first half of the record was used to search the parameters, at which the maximum metrics values are reached. For the found optimal parameters, the metrics value was calculated in the second half of the record. The last value was used as an the quality estimation of the algorithms. This approach allows us to guarantee for each of the methods that the optimal parameters are selected among the possible parameters, while it evaluates the quality on an independent test set of data. Table 1 of the appendix **??** shows a grid of parameter values used for optimization.

In the figure 3 the results of the algorithms quality evaluation are presented. For each value of the delay, a 95% confidence interval is specified, calculated by the bootstrap method with 1000 iterations according to the statistic "average value for a sample of EEG records".

As expected, the accuracy of the envelope estimation (fig 3A) improves when the delay parameter D is increased. The *rect* method demonstrates the most rapidly decreasing quality of the envelope estimation with a decrease in the delay parameter. For delays of less than 150 ms, this method becomes difficult to use due to the poor quality of the envelope estimation. The family of methods developed in this paper allows us to better preserve quality with reduced latency, while the *wcfir* method shows the best result at each point. The envelope estimation for the *ffiltar* method is only available for zero delay. The quality of the envelope at this point is comparable to proposed complex-valued filters. However, it should be noted that this method requires calculating the parameters of the AR model at each step and setting additional parameters, the optimal values of which may change throughout the experiment. Thus, this method is more time-consuming to use, more expensive in terms of the number of calculations, depends on a large number of parameters and does not allow you to adjust the delay parameter, which significantly complicates the use of this approach in closed-loop paradigms that require a quick quantification of the brain rhythmic activity parameters.

The phase estimation accuracy metrics are shown in panels B, C, and D. For non-negative delays, the bias b_ϕ and the absolute bias value behave similarly for all methods and do not exceed 5. As for the standard deviation of the phase, complex-valued filters show a better value of this metric compared to the *ffiltar* method.

The effect of the signal-to-noise ratio (SNR) on the accuracy of the envelope and phase reconstruction was also analyzed (Fig. 4 in [19]). A detailed description of the results can be found in [19] and in the appendix **??**. Here we only note that the estimation quality improves with the growth of SNR for all methods. At the same time, the new developed methods demonstrate better robustness to noise.

In addition, the applicability analysis of the developed approaches in discrete paradigms

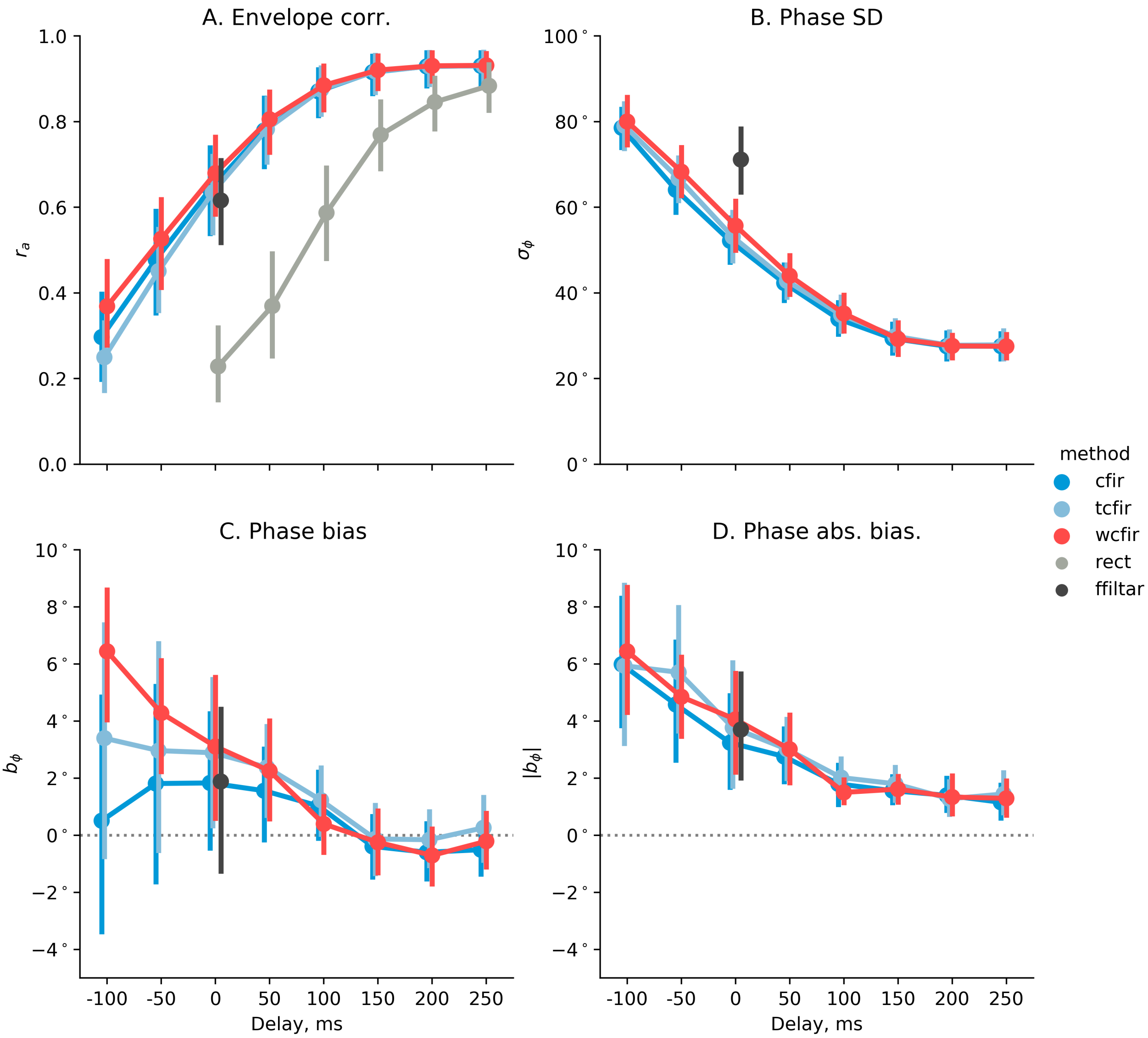

Figure 3: Envelope and phase estimation quality metrics for different methods and at different delays

was performed. The start of brain activity stimulation (for example, using transcranial magnetic stimulation) is tied to the moments when a certain envelope threshold is exceeded (Fig. 5 in [19]), for example, 95% percentile. The analysis showed that for zero delay, the developed methods allow to achieve 75% accuracy of detection of such moments.

2.3 Short-delay neurofeedback facilitates training of the parietal alpha rhythm

This part of the thesis describes an experiment in which participants were trained in the NFB paradigm. The NFB paradigm was implemented using the software platform described in the first part of the thesis (see section refnfblab), and the signal processing methods developed within the second thesis project described in section 2.2. The aim of the experiment was to test the hypothesis about the effect of the NFB system delay on the effectiveness of participants training to control target brain activity. A detailed description of the experiment and the results obtained is described in [14] and in the appendix **??**.

EEG recordings were made using an electroencephalograph Neurovisor 136 (LLC "MCS") with a sampling frequency of 500 Hz, a reference A1-A2 and an AFz ground electrode. The alpha-rhythm envelope on the P4 channel was used as a feedback signal. The envelope was estimated using the *cfire* method described in the appendix **??**. The protocol of the experiment consisted of the following parts:

1. Pre-recording of functional samples and configuring the NFB signal using an interactive module individual data-driven filter design. For this purpose, the blocks Close – a rest state with closed eyes lasting 1 minute and Open – a rest state with open eyes lasting 1 minute were recorded. Based on the recorded data, a spatial rejection filter was formed that removes oculomotor artifacts, and the individual frequency range of the alpha rhythm of the subject was selected.

2. Recording of the rest state before the training in the NFB paradigm with a duration of 2 minutes

3. Recording of the NFB session – 15 blocks of 2 minutes with breaks of 15 seconds. The window displayed a reinforcing stimulus in the form of a circle, the roughness of the border of which was regulated by the NFB signal. The subject task was to make the boundary of the circle as smooth as possible, which corresponds to the maximum value of the target signal, which reinforces the state with a high average power of the parietal alpha oscillation.

4. Recording of the resting state after the training in the NFB paradigm with a duration of 2 minutes

The participants were divided into 4 groups. In the first group (FB0), the extracted NFB signal was visualized without additional delays. In group 2 (FB 250) and 3 (FB500), an additional delay of 250ms and 500ms was introduced, respectively. Groups 2 and 3 correspond to the delay of standard NFB systems, while group 1 corresponds to the low-latency NFB system developed within the project. Group 4 (FBMock) was a control group that used a mock feedback signal generated from the recording files of groups 1-3.

The participants of the experiment were trained to control the power of the parietal alpha rhythm. The average power of the reinforced signal, depending on the NFB session block number, is shown in Figure 4. As can be seen from the figure, an increase in the reinforced feedback signal was observed in each of the groups. At the same time, the learning rate in the FB0 group was the highest.

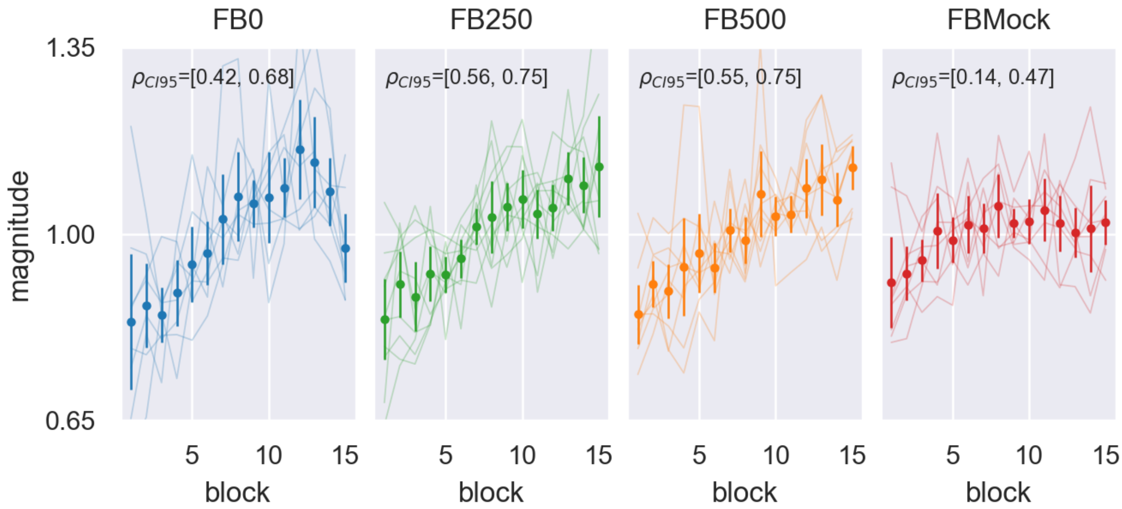

Figure 4: Average power of the reinforced signal depending on the NFB session block number

In addition, detailed analysis of changes in characteristics of the alpha-rhythm was performed. Such characteristics are the number of bursts per unit time, the length and amplitude of alpha-bursts. It was demonstrated that along with the increase in the power of the rhythm in the groups with real feedback, the number of bursts per unit time increases compared to the control group. The amplitude and length of the bursts remained unchanged. The increase in the number of bursts in the F0 group was statistically significantly higher than that recorded in the FB500 group.

We also analyzed the effect of NFB training on the activity of the alpha-rhythm at rest state before and after training. For this purpose, the relative increase in power, as well as the number, duration, and amplitude of bursts at rest after the NFB session, compared to the same subject' state before the session, was estimated. This comparison showed that in the group with minimal delay, there was a significant increase in the power and number of bursts of the reinforced alpha rhythm. In addition, it was shown that the increase in the number of bursts of rhythmic activity after the experiment is inversely proportional to the delay with which the feedback was presented (Fig. The full description of the experimental paradigm and the results are presented in the article [14].

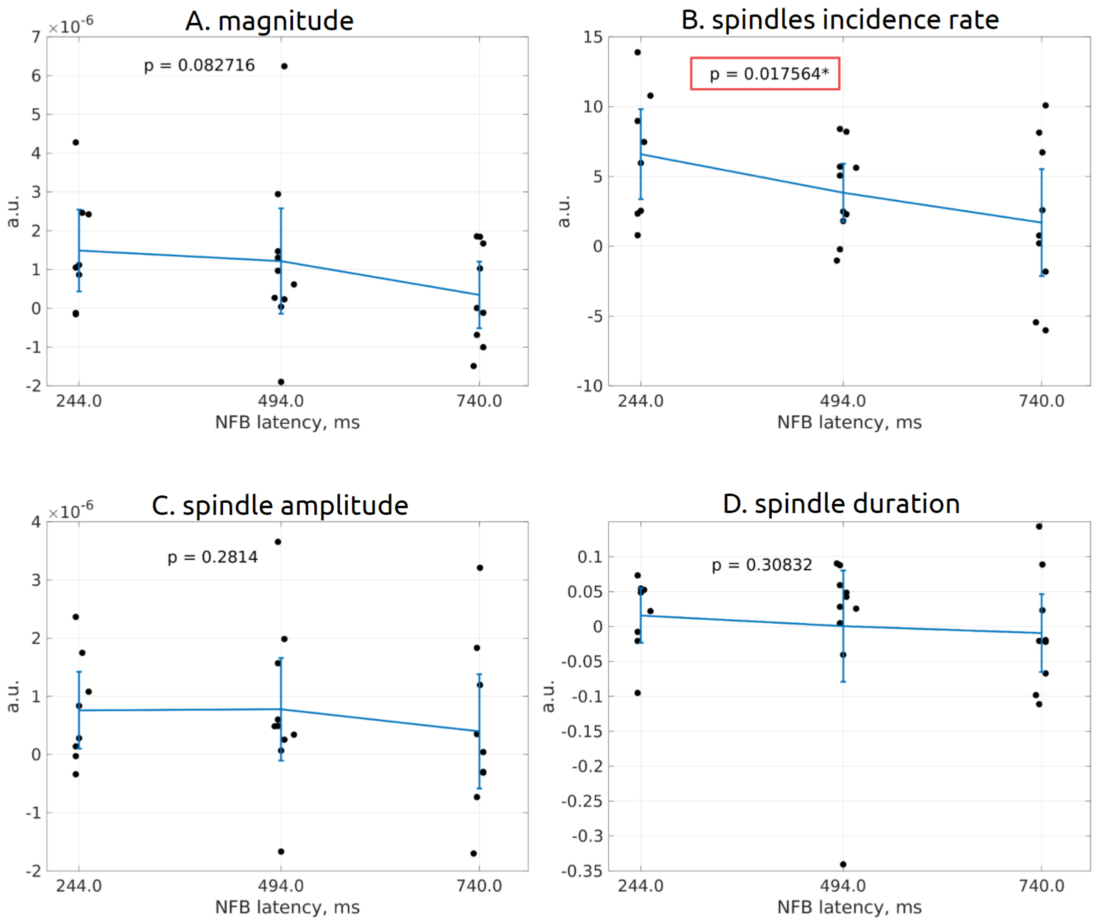

Figure 5: The dependence of the gain (OY axis) of the magnitude (A) of the alpha rhythm, as well as the number (B), amplitude (C), and length (D) of the bursts with the total delay of the NFB system (OX axis)

3 Conclusion

Closed-loop paradigms are an important tool for studying the central nervous system, allowing you to change the experimental parameters, depending on the current state of neuronal activity. A distinctive feature of such paradigms is the need to use electrophysiological signal processing techniques that operate in real-time. At the same time, the developer of systems that implement one of the closed-loop paradigms is tasked with creating a signal processing pipeline that provides accurate extraction of target signals.

As follows from the experimental project of the thesis, the delay parameter of the NFB system has a critical effect on the NFB training efficiency. The development and application of new low-latency methods, thus, can improve the efficiency of the NFB. Within the framework of the methodological project, a family of methods for low-latency quantification of brain rhythms phase and envelope was proposed. The developed methods combine simplicity and high-performance characteristics compared to the approaches currently used. The low-latency estimation of the parameters of the brain rhythmic activity, achieved using these methods, opens up new opportunities for interaction with the brain within the closed-loop paradigms, in which an artificially formed feedback loop runs at a speed comparable to the processes occurring in the central nervous system. Such a scenario will allow us to launch implicit mechanisms of brain plasticity, both aimed at normalizing its work, and allowing us to develop a new generation of devices for interacting with the brain. For example, in devices that implement the augmented intelligence paradigm, information can be presented at times corresponding to certain states of the brain, which guarantees more efficient processing, better memorization, and receptivity to exteroceptive information.

Also, for the design of highly effective closed-loop paradigms, qualitatively new software is required, compared to that used for conducting in the standard paradigm, which implies a stereotypical repetition of the stimulus material, independent of the subject neuronal activity. Such software, on the one hand, should be sufficiently flexible and allow for easy changes in experimental paradigms, and on the other hand, it should have the necessary functionality that implements the main components of EEG/MEG signal processing.

An example of such software is the NFBLab platform developed within the framework of the thesis, which allows us to design and conduct experiments in a closed-loop paradigm. The platform, on the one hand, contains a number of necessary components that allow you to minimize the care about the details of receiving and processing EEG data. On the other hand, the software is distributed with open source and users interested in implementing specific signal processing techniques have the opportunity to independently implement them in accordance with the required NFBLab interface. We hope that the low-latency methods developed in this paper and the NFBLab platform, with its broad compatibility and flexibility in setting experimental parameters, can become the basis for closed-loop paradigms.

3.1 List of results submitted to the defense

We will list the main results obtained, which are achieved in this thesis and are submitted for defense:

1. The NFBLab software platform has been developed for implementing a wide range of experiments in the closed-loop paradigm. The NFBLab [24] software allows us to: configure the data processing pipeline, set the design of the experiment, conduct the experiment in a closed-loop paradigm, providing connection, acquisition, recording and processing of multichannel electrophysiological data, as well as generating stimuli. The platform includes

both classical and newly developed methods of data processing and estimation of brain rhythms parameters. The program was tested in real experiments with BCI and NFB paradigms. This result has practical significance in the research of closed-loop paradigms and is constantly used in the projects of the HSE Center for Bioelectric Interfaces. A detailed description of NFBLab can be found in [24], the software code is available in the [18] project repository.

2. A family of low-latency methods for estimating the instantaneous amplitude and phase of rhythmic brain activity in real time has been developed. This family is based on the approximation of a non-causal ideal system for evaluating a narrow-band analytical signal using a causal complex-valued filter with a finite impulse response. Three filters from the proposed family are investigated: (1) a method with optimization in the frequency domain, (2) in the frequency domain with the use of individualized spectral weights, (3) in the time domain, including the possibility of using adaptive algorithms based on the principle of recursive least squares (RLS). The family of methods allows us to estimate the parameters of rhythms with minimal delay while maintaining the maximum quality of estimates. In comparison with the currently available methods, the developed family allows us to reduce the delay of the envelope and phase estimation while maintaining the quality of the estimation. The paper is published in [19].

3. An experimental study of the visual feedback delay on the effectiveness of learning in the NFB paradigm was conducted. As a result, a significant effect of the delay in the presentation of the feedback signal was revealed both on the learning rate in the neurofeedback paradigm and on the increase in the number of bursts of rhythmic activity observed in post-experimental data. A significant negative correlation was found between the delay value and the increase in the number of alpha bursts. The work is published in [14].

In general, the conducted research represents a complete cycle of works that form the instrumental and phenomenological basis of a new direction of low-latency neurofeedback. The results clearly demonstrate the importance of taking into account the delay in the presentation of the feedback signal, as one of the key factors affecting the intensity of plastic changes and determining the effectiveness of interaction with the brain. The developed new algorithmic solutions provide access to the area of low delays in the formation of a feedback loop based on the brain rhytms parameters, which for the first time opens up the possibility of direct non-invasive interaction with the brain at the natural speed of neuronal processes. The developed software platform is an ergonomic tool for prototyping high-performance implementations of closed-loop paradigms and can be applied in both research and clinical applications.

3.2 Further research

The developed family of methods described in the section refcfir assumes that the spectrum of the noise component in the frequency range of a narrow-band signal has a negligible amplitude. However, in real problems with a large signal-to-noise ratio, such an assumption may give an inaccurate result of estimating the envelope and phase. Thus, it is necessary to develop approaches that are able to separate the noise and the useful signal in the target frequency band. One possible solution to this problem is to take into account the dynamic characteristics of brain rhythms and apply appropriate models of target oscillatory activity. For example, a dynamic model of an oscillator in discrete time can be used at the prediction step of Kalman and Bayesian filters. The oscillatory time series obtained in this way will allow us to reconstruct the directly unobservable target signal, its envelope, and phase. In the near future, it is planned to conduct a systematic study of these methods in application to the problem of low-latency filtering. Preliminary results, which are not included in this thesis, demonstrate an increase in the performance characteristics of ideomotor interfaces constructed using the brain rhythmic activity, evaluated using explicit dynamic filtering based on the rhythm model as a frequency-modulated signal.

The developed algorithms, together with the NFBLab platform, are an ergonomic environment for conducting reproducible experiments on the study of closed-loop paradigms with low latency. At the moment, together with colleagues from the Center for Bioelectric Interfaces of the Higher School of Economics, further experimental studies of low-latency NFB are being conducted . In addition, it is planned to conduct a number of clinical studies, including on a population of patients with pharmacoresistant epilepsy, in order to develop a tool for reducing the frequency of epileptic seizures using high-performance training in the neuro-feedback paradigm, aimed at increasing the average power of the sensorimotor rhythm.

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