National Research University Higher School of Economics

as a manuscript

Ksenia Volkova

Experimental paradigms and data processing algorithms design in real time cognitive neuroimaging

Dissertation Summary

for the purpose of obtaining

academic degree Doctor of Philosophy in Psychology

Academic Supervisor: PhD Alexei Ossadtchi

Moscow 2021

Publications

- Волкова, К. В., Дагаев, Н. И., Киселёв, А. С., Касумов, В. Р., Александров, М. В., & Осадчий, А. Е. (2017). Интерфейс мозг-компьютер: опыт построения, использования и возможные пути повышения рабочих характеристик. Журнал высшей нервной деятельности им. ИП Павлова, 67(4), 504-520.
- Боброва, Е. В., Решетникова, В. В., Волкова, К. В., & Фролов, А. А. (2017).
 Влияние эмоциональной устойчивости на успешность обучения управлению системой" интерфейс мозг-компьютер". Журнал высшей нервной деятельности им. ИП Павлова, 67(4), 485-492.
- Dagaev, N., Volkova, K., & Ossadtchi, A. (2017). Latent variable method for automatic adaptation to background states in motor imagery BCI. Journal of neural engineering, 15(1), 016004.
- Smetanin, N., Volkova, K., Zabodaev, S., Lebedev, M. A., & Ossadtchi, A. (2018). NFBLab—A versatile software for neurofeedback and brain-computer interface research. Frontiers in neuroinformatics, 12, 100.

GENERAL SUMMARY OF RESEARCH

Current technological developments have greatly contributed to the emergence of a new branch of research in neuroscience, which involves real time interpretation of brain activity measurements in order to generate feedback signal, or produce control commands for external devices (Kohler et al., 2017; Kramer et al., 2019). One of the most relevant tasks in this area is the development of methods that support the operation of brain-computer interfaces (BCIs), systems that provide direct control of external devices based on voluntary modulation of brain activity. BCIs implement an additional channel of information exchange with the external environment, distinct from the natural pathway involving muscles and peripheral nerves (Abdulkader et al., 2015). A complete information exchange channel must be bidirectional and include not only transmission of commands from the brain to controlled external devices (e.g., artificial limbs), but also a feedback loop, providing the brain with information about the current status of these devices in real time (Lebedev, Ossadtchi, 2018).

The primary application of BCIs is providing solutions for motor recovery and communication in people whose motor function had been impaired as a result of injury or illness (Chaudhary et al., 2016). Electroencephalography (EEG) is the most widely used non-invasive brain activity recording technique in such systems (Machado et al., 2010). However, due to the fundamental limitations associated with indirect registration of neuronal activity, the bandwidth of the information channel implemented in such EEG-BCIs is relatively low and does not exceed one bit per second (Mak et al., 2009; Waldert et al., 2016). Therefore, in most cases, EEG-BCIs can decode only a small number of discrete commands. Effective application of BCIs, especially in clinical practice, requires stability, accuracy, and, ultimately, the ability to decode continuous trajectories rather than discrete commands (Mak et al., 2009; Schalk, 2010), which requires at least a tenfold increase in the bandwidth of this communication channel.

Research background for this problem shows that at the early stages of development of EEG-BCI systems, new algorithmic solutions made it possible to achieve significant improvements in system performance (Qin et al., 2004; Wang et al., 2006; Congedo et al., 2013). Recently, however, the use of modern algorithmic approaches, in particular, deep learning solutions, has brought only minor enhancements (Roy et al., 2019). This may indicate the existence of a limit in the task of decoding neural activity, which the research community has recently approached, and which is especially evident in the case of noninvasive BCIs.

Considering this limitation, possible directions of future development in this field include (1) design of interpretable architectures that allow not only to create an efficient decision rule, but also to analyse and interpret the features (Gilpin et al., 2018), and (2) development of methods that employ a priori information, additional to the recorded neural activity samples, to enable further enhancement of decoding capabilities (Gülçehre et al., 2016; Volkova et al., 2017). Examples of a priori knowledge that can be used for this purpose include the information on the physiological substrate of the neural activity modulations used in a particular BCI, known features of the experimental paradigms (Jayaram et al., 2016; Padfield et al., 2019) and the properties of the organism as a whole (Dagaev et al., 2017). Thus, on the one hand, compliance of the used decision rules with physiological principles can be guaranteed, which is especially important when BCI is used for neurorehabilitation purposes. Moreover, it will become possible to use deep architectures to extract new knowledge and discover hidden patterns in experimental data (Baldi, 2012; Alain, Bengio, 2014).

The most radical and effective method of enhancing BCI capabilities is the use of invasive brain activity registration techniques. The data obtained with these methods contains more complete information about motion parameters and can be used, for example, to control complex prostheses with a large number of degrees of freedom (Yanagisawa et al., 2012; Collinger et al., 2013). In particular, the use of invasive

interfaces based on cortical implantation of microelectrode arrays (Kim et al., 2018) has contributed to an increase in degrees of freedom of the controlled device, reported in a number of studies (Hochberg et al. 2012; Collinger et al., 2013; Miranda et al., 2015). However, the use of such interfaces carries risks associated with implantation procedure (Kohler et al., 2017) and is limited to individual patients for whom specialized systems have been developed within the clinical environment (Miranda et al., 2015), and animal studies (Carmena et al., 2003; Velliste et al., 2008). An emerging trend in this field is the use of electrocorticography (ECoG), which involves subdural (under the dura mater) or epidural (over the dura mater) placement of electrodes on the brain surface, without disturbing cortical integrity (Schalk & Leuthardt, 2011).

Compared to microelectrode implantation, electrocorticography constitutes а considerably safer alternative. This method is widely used in clinical practice to localize epileptic foci, identify tumor boundaries and map functionally irreplaceable cortex (Hill et al., 2012). At the same time, ECoG is a promising method for potential BCI implementation due to higher signal stability in long-term compared to intracortical implantation (Shokoueinejad et al., 2019), low noise and high spatial resolution, coverage of a relatively large cortical area (Kellis et al., 2016) and availability of high-frequency activity measurements that reflect local neuronal interactions in the cortex (Schalk & Leuthardt, 2011). Among other factors is a large number of patients who are being monitored using ECoG for their clinical needs and can be potentially involved in related research, without the need to be exposed to additional risks of implantation for that sake.

ECoG signal features such as high spatial resolution, low noise, small number of oculographic and myographic artifacts, as well as the proximity of signal sources in the cortex, make it possible to detect the beginning of the motor act with high accuracy, distinguish the movements of individual fingers, decode the speed and direction of movement, and use a brain-computer interface to control a complex prosthesis hand

(Ball et al. 2009; Kubanek et al. 2009; Yanagisawa et al. 2011; Chestek et al. 2013; Hotson et al. 2016). However, real time decoding of continuous motion, which is part of the endeavor in our work, had not been implemented in the above studies.

The electrodes used to record ECoG signal can also be utilized to conduct current during cortical stimulation, which in some cases is part of the mapping procedure (Ritaccio et al., 2018, Kramer et al., 2019). Thus, ECoG provides opportunities for research and development of methods that, along with evolving implantation technologies, can form a basis for creation of complex, bidirectional brain-computer interfaces. It should be noted that the above conclusions regarding the directions of development of algorithmic aspects of the ECoG are naturally applicable to invasive neural interfaces as well.

In general, the procedure required to set up BCI operation involves setting the parameters of the decoder decision rule for the current user, which allows to ensure the maximum achievable accuracy of such devices. However, improving decoding accuracy requires not only adaptation of the decoding algorithms, but also training the interface user in the operational conditioning framework, using a feedback signal based on performed correct or incorrect actions (Mühl et al., 2014; Hiremath et al., 2015). Simultaneous adaptation of decoding algorithm and BCI user can significantly increase the efficiency of such setup and ensure high performance of the interface within a short learning time (Zander et al., 2011).

The most convincing demonstration of neural interface performance is the real time use of such system. The implementation of real time decoding in clinical setting, which introduces many limitations regrading the setup and the time that can be spent with the patient, requires a combination of methodological and software tools, patient selection methods, and experimental paradigms of user training.

Development of BCI systems, especially based on invasive technologies such as ECoG, involves close interaction between the developing scientists and clinical partners. Patients who are medically implanted with electrodes to localize epileptogenic zones or

map functionally irreplaceable cortical areas are involved in research on the development of invasive neural interfaces. Such cooperation creates opportunities for the design and testing of new clinical procedures that minimize patient risks and improve the quality of medical services. For example, passive intraoperative mapping methods are currently being actively developed (Schalk et al., 2008; Korostenskaja et al., 2015), replacing procedures that require direct electrical cortical stimulation and often result in seizures, critical patient condition and unavoidable change of operating plan. The introduction of safe techniques in clinical centers, as well as the development of new algorithms for signal processing and protocols for presenting relevant functional stimuli to increase the accuracy of cortical mapping and improve the ergonomics of this procedure is another relevant and socially important area of research, closely intertwined with the general direction of neural interface development (Sinkin et al., 2019).

Thus, development of interpretable algorithms for processing multi-channel measurements of brain activity obtained by noninvasive and invasive registration techniques is a **relevant** research direction in the field of neural interfaces. Additionally, these methods can utilize a priori information of the neurophysiology of the processes used for command generation, and take into account the physical properties of recorded signals, gaining the ability to automatically adapt to the changing state of the nervous system and environment. In the task of enhancing the bandwidth of the BCI control channel and ensuring natural control, invasive methods of recording brain activity such as ECoG, are promising. The approaches based on joint iterative interaction between a person and the learning algorithm are relevant for the development of decision rules used in BCI. While it will take at least 5-10 years to create complete bionic prostheses with sensations controlled by signals of brain activity, the results of interaction with clinicians are already bearing fruit in the form of new methods of patient support.

functional cortex in the course of preoperative or intraoperative mapping of patients is a promising and socially important area of research in the field of neural interfaces.

The **purpose** of this study is to improve the technological components of neural interfaces, both invasive and non-invasive, on the basis of physiologically informed approaches to the automated selection of informative features, taking into account the non-stationarity of the user's state, and using electrocorticographic measurements of brain activity in the tasks of real time decoding of movement trajectory. Relevant and socially significant objective of this study is to use the developed experimental procedures for construction and testing of new safe methods of mapping the eloquent cortex of patients during neurosurgical intervention.

Research objectives:

- 1. To develop methods improving the characteristics of non-invasive brain-computer interface based on electroencephalogram (EEG), making use of additional a priori information of the properties of the experimental paradigm and underlying neurophysiological processes.
- 2. To develop and implement experimental paradigms and signal processing techniques for the invasive brain-computer interface based on electrocorticogram (ECoG).
- 3. To implement real time decoding of movement parameters (finger trajectory), for the invasive brain-computer interface based on electrocorticogram (ECoG).
- 4. To implement cortical mapping techniques and compare the mapping results obtained through electrical stimulation and passive functional mapping of the eloquent cortex.

Theoretical and methodological basis for this research included:

- In the field of physiology: current knowledge of the representation and organization of movement planning and execution in the cortex (Johnson et al, 2013; Hiremath et al., 2017; Lee et al., 2018; Kramer et al., 2019 (Kandel et al., 2000; Squire et al., 2012);
- In the field of machine learning: studies considering registration and processing of electrophysiological activity with the purpose of decoding movement parameters (Bishop, 2006; LeCun et al., 2015; Lotte et al., 2007; Lotte et al., 2018; Schalk, Leuthardt, 2011; Anderson et al. 2012; Hotson et al. 2016; Xie et al., 2017);
- In the field of cortical mapping: research addressing sensorimotor cortex stimulation and passive functional mapping with ECoG (Su, Ojemann, 2013; Arya et al., 2018; Tamura et al., 2016; Ritaccio et al., 2018).

In this study, methods such as brain activity registration (EEG, ECoG), brain-computer interface, and machine learning were used.

Empirical basis of the completed research:

- In studies using non-invasive neuroimaging (EEG), the subject sample comprised healthy adults, 21-25 year old, men and women. The research was conducted in the laboratories of the Centre for Cognition and Decision Making at the National Research University Higher School of Economics.
- In studies using invasive neuroimaging (ECoG), the subject sample comprised cognitively preserved patients with epilepsy or neocortex tumors, over 20 years of age, undergoing either implantation of ECoG electrodes or intraoperative

monitoring for the purpose of localization of epileptic activity/tumor boundaries and mapping of the eloquent cortex. The subjects have signed an informed consent to participate in this research. The study was conducted at the Medical Center of Moscow State University of Medicine and Dentistry, which is a clinical partner of the Center for Bioelectric Interfaces of the National Research University Higher School of Economics.

The research was carried out in the following stages:

- 1. Advanced non-invasive motor imagery BCI (MI BCI)
 - a. Development of a method for motor states classification in the EEG-based MI BCI using an automated procedure for selecting physiologically plausible spatial components of the EEG data.
 - b. Development of a method for motor states classification in the EEG-based MI BCI taking into account background components.
- 2. Experimental paradigms and methods for decoding continuous movement kinematics from ECoG signals
 - a. Design and assembly of the experimental setup for stimulus presentation and synchronized recording of continuous movement kinematics and ECoG in clinical environment.
 - b. Development of experimental paradigms and signal processing methods for decoding continuous movement kinematics from ECoG.
- 3. Development of training paradigms to enable rapid subject + machine adaptation and implementation real-time continuous finger movement decoding.
- 4. ECoG-based functional cortex mapping

- a. Development of a passive mapping pipeline and signal processing methods for intraoperative localization of motor speech areas.
- b. Validation of the passive-speech mapping accuracy.

In this study, methods to improve the performance of non-invasive neural interfaces are proposed, making use of a priori physiological information and taking into account changes in the background EEG. The developed methods have been published in leading foreign and local journals (Dagaev et al., 2017; Volkova et al., 2017) and can be implemented in the course of EEG BCI design. Reliability and validity of the results in this part of the study is ensured by the use of statistical analysis, as well as performance indicators of the algorithms obtained from subject test data.

The developed experimental setups, user training paradigms and electrocorticogram signal processing methods **contribute to the experience of invasive ECoG interfaces design** and are **utilized** in the project of the Center for Bioelectric Interfaces of the National Research University Higher School of Economics aiming to implement a bi-directional invasive neural interface with the ability to decode movement parameters in real time and cortical stimulation feedback. Reliability and validity of the results in this part of the study are ensured by performance indicators of the algorithms obtained on the testing data and performance of the designed interface in the task of decoding finger trajectory in real time. Additionally, performance of the obtained methods is confirmed by the fact of ECoG interface functioning in real time. The results obtained by passive mapping of the motor cortex are stable and consistent with those obtained by direct cortical stimulation, which is currently the gold standard of this procedure.

The implemented methods of mapping eloquent speech zones are used in clinical work during brain surgery at the University Clinic of the Yevdokimov Moscow State Medical University. Reliability and validity of the results of the motor speech zones mapping is ensured by comparison with the gold standard using direct cortical electrical stimulation.

The main results:

- 1. Methods utilizing a priori information have been developed to improve the performance of non-invasive BCI. The results show increase in decoding accuracy when using the developed methods in comparison with the basic algorithm
- 2. Experimental setups and paradigms for decoding movement parameters as well as functional mapping of the eloquent cortex have been created. The developed setups have been implemented in the research carried out at the Centre for Bioelectric Interfaces, HSE.
- 3. Finger movement decoding from ECoG has been implemented. An iterative calibration data recording technique has been introduced, enabling real-time decoding of the finger trajectory after less than 0.5 hour of subject training.
- 4. Passive functional mapping procedure of motor speech areas has been implemented. The results obtained by applying the proposed technique are consistent with the results of cortical stimulation.

SUMMARY OF THE TEXT

The **Introduction** contains the description of the research problem and discussion of its relevance, analyzes the development and current state of the research field, formulates goals and objectives of the research, lists the main results of the work, and provides a brief description of the structure of the thesis text.

Chapter 1, **Literature review**, is dedicated to a theoretical review of approaches to decoding motion parameters from the electroencephalogram signal and the implementation of the motor imagery brain-computer interface using invasive and non-invasive brain activity recording techniques.

Section **1.1 Characteristics of BCI systems** contains a description of the brain-computer interface as a system with characteristics that depend on the implementation of each of its elements. BCI components include such parts as the physiological phenomenon which is used to decode the user state, brain activity recording technique, data analysis and signal processing methods that are used for decoding, and the experimental paradigm, including the procedure for recording calibration data and the process of controlling the interface.

Section **1.2 Decoding movement from ECoG signal** provides an overview of studies dedicated to the problem of decoding movement parameters from the electrocorticogram signal. The possibility of decoding various movement characteristics from ECoG signal is discussed, as well as the prospects for using ECoG as a technology for recording brain activity for BCI applications, and the experience in using various experimental paradigms and machine learning algorithms to solve this problem.

In general, literature review allows us to identify possible areas of development of brain-computer interfaces based on electroencephalogram. Since in the case of non-invasive interfaces, due to the physical properties of signal propagation, the amount of information that can be extracted from the EEG signal is limited, decoding accuracy can be potentially improved by using algorithms that make use of additional information associated with a priori knowledge of the properties of the neurophysiological phenomenon or experimental paradigm that is used. Two developed algorithms based on this principle are presented further in Chapter 2.

At the same time, invasive BCI design based on ECoG is a developing area that is progressing through creation of solutions concerning experimental setups and paradigms, implantation technologies and machine learning algorithms. In addition, the possibility of implementation of sensation by cortical stimulation through implanted electrodes is currently being researched, as one of the opportunities provided by using ECoG recording technique. **Chapters 3-6** of the thesis are devoted to development of experimental setups, implementation of signal processing methods, training paradigms and use of ECoG-based BCI control process.

Chapter 2. Advanced solutions for non-invasive motor BCI imagery describes the implemented non-invasive interface and suggests two methods to improve its performance based on the use of a priori information additional to the recorded signal.

Section **2.1 Motor imagery EEG BCI** describes the implemented BCI that uses EEG for recording brain activity and allows classifying 3-5 states associated with movement execution or imagination. Basic processing pipeline for motor imagery states classification is described, and modifications to this scheme are proposed in the following sections.

Section 2.2 Physiologically relevant CSP topographies selection includes a description of the proposed modification to the common spatial pattern (CSP) method used in the original processing pipeline. The proposed method involves evaluation of the

topographies corresponding to the CSP components from the point of view of their correspondence to the expected picture of the neurophysiological phenomenon that underlies decoding of the states in the motor imagery interface, i.e., modulation of sensorimotor cortex activity in the area of hand movement representation. This physiological assessment can be performed automatically by calculating the fit of each topography to the dipole model. The use of this method helps to prevent overfitting that can happen at the stage of feature extraction in the method of common spatial components, which can be a significant problem, especially when dealing with a limited amount of training data.

Section 2.3 Latent variable method for detection of background components contains a description of the second proposed method to improve the performance of non-invasive interface, developed in collaboration with Nikolai Dagaev. In the proposed method, the Bayesian classification algorithm allows modeling the presence of a background state that is present along the recording of a training sample and the interface control process. Since one of the problems associated with the use of EEG is the non-stationarity of the signal due to both changes in the physical conditions of recording and cognitive states of the user, this solution allows better modeling of signal changes and approaches the idea of neural networks, which are able to model complex patterns in the data.

For both methods, the comparison with the basic algorithm showed improvement in decoding quality (accuracy of state classification). In addition, the use of methods based on a priori known information about the neurophysiological phenomenon used and the experimental paradigm allows to increase the interface stability (robustness).

Chapter **3. Experimental setups for ECoG research** is devoted to the experimental setups designed to conduct research on decoding movement parameters from the ECoG

signal, as well as stimulation through ECoG electrode contacts. Sections of this chapter cover the software and hardware, as well as additional ergonomic solutions developed and used to conduct studies described in the following chapters.

Section **3.1** Synchronous recording of continuous movement and ECoG signal describes the setup implementing the synchronous recording of ECoG signals with a multi-channel amplifier and the parameters of hand movement with a motion capture system. Section **3.2 Realtime movement decoding** covers additional software elements created to implement real-time motion decoding.

Section **3.3 Digitizing tablet input** contains a description of created solutions related to the decoding of fine movements, such as moving a pen across on top of the tablet, as in handwriting.

Sections 3.4 and 3.5 describe the experimental setups created for functional mapping of the eloquent cortex. Section 3.4 Passive functional mapping describes the means of passive cortical mapping through analyzing ECOG signal modulations during motor tasks, perception of tactile and auditory stimuli. Section 3.5 Cortical stimulation mapping describes the hardware and stimulation parameters used for stimulation mapping.

Chapter **4 ECoG signal processing and data analysis methods** contains a description of the methods developed and implemented to perform the decoding of movement parameters from ECoG signal.

Section **4.1 Preprocessing and denoising** describes methods that are used to clean the ECoG signal from artifacts associated with eye movement and epileptic activity.

Section **4.2 Decoding movement parameters using classical and deep learning methods** is dedicated to the methods used to decode motion from the ECoG signal. This section describes classical methods of signal processing, including spatial and temporal filtering, methods used to reduce the dimensionality of the feature vector, the use of linear regression approaches and methods of optimal linear filtering, such as Wiener and Kalman filters. The description of deep learning solutions to the problem of decoding movement parameters, and principles of the analysis of the obtained decision rules for interpretation of the extracted features are discussed further.

Additionally, the problem of decoding movement parameters from electromyogram signal (EMG) is considered. Since it was shown that there is a relationship between EMG and ECoG signals in the sensory cortex, and the movement parameters are represented in the EMG in a more explicit form but can be extracted using the same methods used to process the ECoG signal, the task of decoding motion from the myogram can be used to design algorithms and test systems intended for ECoG decoding.

In chapter **5 Decoding movement from ECoG signal** the details of the implementation of decoding finger movement parameters from the electrocorticogram signal are discussed.

Section **5.1 Offline decoding of finger movement** describes a pilot study carried out in collaboration with the Polenov Institute of Neurosurgery. In this study, parameters of finger movement and ECoG signals were recorded synchronously from a strip of electrodes implanted on top of the cortical surface of the patient to localize the epilepsy focus. The recorded data were divided into training and test samples and used to assess the possibility of decoding finger movement from ECoG signal. A comparative analysis of decoding quality (correlation coefficient between the real movement parameter and its value recovered from the ECoG signal) was obtained for multiple decoding algorithms including both traditional methods of machine learning and deep learning methods based on convolutional neural networks (CNNs). The results of this

comparison demonstrate the advantage of using deep learning methods over traditional methods. The maximum decoding accuracy achieved using deep convolutional neural networks for decoding has reached 0.9 (correlation coefficient between true and recovered from ECOG signal).

Section **5.2** Acquisition of online control of ECoG BCI is dedicated to the implementation of an ECoG BCI in which the parameters of finger movement are decoded from the ECoG signal in real time, and the decoded movement is presented to the user as feedback through a three-dimensional hand avatar displayed on the screen. The section describes the data analysis methods and modifications of the experimental paradigm (in particular, the developed iterative procedure of data recording for the training sample), which made it possible to predict the movement coordinate from the ECoG signal with high precision (correlation coefficient between the true and predicted coordinate 0.68 at the end of the iterative training procedure) and to achieve successful decoding of the finger movement in real time. At the end of this section, factors that can affect the representation of movement parameters in the ECoG signal are discussed.

In chapter **6. Mapping of the eloquent cortex** the results of eloquent cortex mapping research using experimental setups described in sections 3.4 and 3.5 are presented.

The first section **6.1 Stimulation mapping of the sensorimotor cortex** describes a study on sensorimotor cortex mapping using cortical stimulation. The mapping procedure involved cortical stimulation via the implanted ECoG electrode contacts using the parameters specified in section 3.5. The mapping was performed in five patients to identify sensory and motor areas and localize the eloquent cortex as part of preoperative monitoring. In addition, the objective was to evaluate the feasibility of the implementation of tactile feedback by means of cortical stimulation that could be used in a bidirectional invasive brain-computer interface.

This section presents maps obtained as a result of observation and processing of responses of the study participants about sensations and motor responses caused by stimulation (based of response tables in Appendix C). The results are consistent with the available information on mixed somatotopy in sensorimotor cortex and the participation of motor and sensory components in the motion. A significant portion of stimuli elicited sensory and motor responses affecting several fingers simultaneously. The responses showed a large variation in the nature of the evoked sensations and the dependence of their intensity, but not their quality on the stimulation parameters for a particular location (a pair of electrodes). Since it is desirable to control both the area of the body in which the sensation occurs and the nature of the sensation in order to implement natural tactile feedback, these results suggest that it is difficult to implement sensation when using ECoG as a signal recording method. However, as discussed at the end of this section, these difficulties can be partially overcome by creating hardware and software setups that can generate more complex (spatially and temporally) stimuli.

The second section of the chapter, **6.2 Stimulation-free mapping**, describes the passive cortical mapping methods that allow to determine the cortical areas involved in a particular task by detecting the ECoG signal modulations associated with the local activation of the cortex during this task.

Section **6.2.1 Comparative analysis of decoding algorithms** compares the performance of methods described in Chapter 4 when applied to the cortical mapping. Here the problem of the eloquent cortex localization is solved by means of the passive mapping method, i.e., identification of channels in which the signal is most strongly modulated during the performance of motor tasks, such as, for example, finger movement. Comparison of the resolution of individual fingers representations, obtained by visualization of 1) the distribution of modulations in the gamma range, 2) decoding accuracy, obtained by creating linear decoders for each ECoG channel, and 3) decoding accuracy of movement parameters from each ECoG channel using a CNN, showed the

advantage of using deep learning solutions compared to classical machine learning methods.

Section **6.2.2 Passive speech mapping** describes the implementation of the procedure for intraoperative mapping of speech zones. Passive speech mapping makes it possible to identify cortical areas involved in speech production by processing ECoG signal recorded at rest and during speech tasks (such as, for example, naming objects or tasks that are presented as stimuli to the patient) by detecting ECoG signal modulations that accompany local cortical activation. In terms of safety, this method has advantages over the traditionally used cortical stimulation mapping, which carries significant risks of causing an epileptic seizure, loss of consciousness, and, as a result, significant complication of the surgery plan.

The study included intraoperative localization of the Broca area using a mobile experimental setup described in section 3.4.3. The section contains the description of the mapping procedure, implemented speech tasks and data processing algorithms. Comparative results of passive and stimulation mapping are presented, and demonstrate the concurrence of the areas involved in speech production localized by these methods. In addition, the proposed mapping procedure was used to localize speech zones in another patient with an ECoG grid implanted for preoperative monitoring. Maps obtained in two consecutive days during the implantation period showed the stability and reproducibility of the proposed method.

In the **conclusion** of the thesis, the results of the conducted research were formulated, along with limitations and prospects for further development of methods, algorithms and experimental paradigms for implementation of brain-computer interfaces.

The **results** of the research include methods to improve the performance of non-invasive BCI, as well as developed experimental setups, paradigms, and data analysis methods for conducting research and creating an ECoG BCI.

In the part of the study devoted to enhancement of the performance of non-invasive EEG BCI, two methods were proposed to improve the decoding accuracy by using a priori information complementary to the recorded brain activity.

Since a significant increase in BCI control channel bandwidth is only possible by employing invasive technologies, further work was focused on studies using ECoG for recording brain activity and concerned with the problem of decoding movement parameters from ECoG. These studies were carried out as part of a project aiming to create a bidirectional ECoG-based BCI.

To accomplish these studies, experimental setups were created that implement the possibility of synchronous recording of ECoG signals and movement parameters, presentation of stimuli and feedback, and realization of passive and stimulation cortical mapping.

To address the problem of movement parameters decoding from ECoG signal, algorithms for data analysis and signal processing were developed and implemented, including both traditional techniques and deep learning methods.

The main purpose of the part of the study devoted to the development of invasive ECoG research was to implement movement decoding in real time. In order to assess the possibility of decoding finger movement parameters from ECoG, a study dedicated to offline decoding of movement parameters from synchronously recorded ECoG signal was conducted. The results of this study allowed to compare the decoding quality achieved using different algorithms and eventually demonstrated the advantage of using deep learning solutions for this task. The use of deep learning algorithms and the

proposed paradigm of iterative user training allowed to implement real-time decoding of finger movement.

Additionally, possibility of using cortical stimulation through ECoG electrodes to implement artificial tactile feedback during interface control was assessed as a part of the project on bidirectional ECoG BCI design. The results of the stimulation mapping were also used to localize the eloquent cortex in the preoperative mapping. Another clinical application of the created mapping capabilities was the implementation of intraoperative passive mapping of speech function representation.

The main **limitation** of the conducted research in the field of development of invasive interfaces is the number of subjects, which is limited by the number of patients with clinical needs for implantation of ECoG electrodes for preoperative monitoring. In the part of the study dedicated to the implementation of real time decoding, the performance of the designed system is ensured by evaluating the quality of decoding during online control sessions, so the number of subjects in this case does not hinder the assessment of the obtained result. Nevertheless, to perform a statistical comparison of different experimental paradigms and factors that may affect the learning of the interface use, it is necessary to sample a sufficient number of patients who can be divided into groups with different conditions, which at this stage is not possible due to reasons such as individual grid positions in each patient. While the development of long-term implantation technology is likely to increase the amount of data over time and provide new opportunities for research in this area, experience with both invasive and non-invasive interfaces suggests that system setup and operation will remain individual for a particular user.

The **prospects** for the development of ideas discussed in this work include several directions.

First of all, the characteristics of both invasive and non-invasive brain-computer interfaces can be improved by developing machine learning algorithms capable of modeling complex patterns in data, extracting maximum amount of information related to the representation of movement parameters.

As it was shown in the part of the thesis devoted to enhancement of the characteristics of non-invasive interface, improving decoding accuracy is possible by using a priori information on the physiology of the process or on the experimental paradigm. Also promising is the use of deep learning algorithms which automatically extract features and model patterns in the data at different levels of complexity, as well as provide additional capabilities, such as extracting information from unannotated data, or the use of transfer learning.

In addition, an important feature of methods used to decode user state in BCI is their interpretability. At the same time, due to the automatic nature of the feature selection in deep learning methods, interpretability is considered to be a weakness of such algorithms. The development of methods that allow to interpret the features extracted by these algorithms is another relevant direction in this area.

Another area of development is the design of paradigms for learning and controlling BCI. While for non-invasive BCIs, there are many studies on factors that can affect the speed and quality of user interface adaptation, in the case of invasive interfaces, this area is not yet developed due to the limited number of subjects. At the same time, the paradigm that is used during calibration and control determines the information that is contained in the measured ECoG signal, and thus the possible decoding accuracy.

Finally, the use of invasive interfaces can be enhanced by creating artificial sensation, which requires the development of an individualized dictionary to generate feedback through cortical stimulation with ECoG electrodes. While the results of this thesis show the limitations of standard protocols, the possibilities of stimulation can be expanded by designing new hardware and software capabilities to generate more complex stimuli, including dynamic spatial and temporal patterns of stimulation.

The conducted research contributes to the field of BCI development, offering solutions related to both algorithmic and behavioral aspects of interface design, as well as expanding experience in the field of invasive ECoG-based interfaces through new results on real-time movement decoding and stimulation. The developed experimental setups, paradigms and data analysis methods are being used in the research that is continuing as a part of the project at the Center for Bioelectric Interfaces of the National Research University Higher School of Economics, aiming to implement an invasive bidirectional brain-computer interface. This project is the first and only research on the subject of invasive interfaces being conducted in Russia.

Literature

Abdulkader, S. N., Atia, A., & Mostafa, M. S. M. (2015). Brain computer interfacing: Applications and challenges. Egyptian Informatics Journal, 16(2), 213-230.

Anderson, N. R., Blakely, T., Schalk, G., Leuthardt, E. C., & Moran, D. W. (2012). Electrocorticographic (ECoG) correlates of human arm movements. Experimental brain research, 223(1), 1-10.

Arya, R., Horn, P. S., & Crone, N. E. (2018). ECoG high-gamma modulation versus electrical stimulation for presurgical language mapping. Epilepsy & Behavior, 79, 26-33.

Bishop, C. M. (2006). Pattern recognition and machine learning. springer.

Bleichner, M. G., Freudenburg, Z. V., Jansma, J. M., Aarnoutse, E. J., Vansteensel, M. J., & Ramsey, N. F. (2016). Give me a sign: decoding four complex hand gestures based on high-density ECoG. Brain Structure and Function, 221(1), 203-216.

Brunner, P., Ritaccio, A. L., Lynch, T. M., Emrich, J. F., Wilson, J. A., Williams, J. C., ... & Schalk, G. (2009). A practical procedure for real-time functional mapping of eloquent cortex using electrocorticographic signals in humans. Epilepsy & Behavior, 15(3), 278-286.

Carmena, J. M., Lebedev, M. A., Crist, R. E., O'Doherty, J. E., Santucci, D. M., Dimitrov, D. F., ... & Nicolelis, M. A. (2003). Learning to control a brain-machine interface for reaching and grasping by primates. PLoS biology, 1(2), e42.

Ball, T., Schulze-Bonhage, A., Aertsen, A., & Mehring, C. (2009). Differential representation of arm movement direction in relation to cortical anatomy and function. Journal of neural engineering, 6(1), 016006.

Chaudhary, U., Birbaumer, N., & Ramos-Murguialday, A. (2016). Brain–computer interfaces for communication and rehabilitation. Nature Reviews Neurology, 12(9), 513.

Chestek, C. A., Gilja, V., Blabe, C. H., Foster, B. L., Shenoy, K. V., Parvizi, J., & Henderson, J. M. (2013). Hand posture classification using electrocorticography signals in the gamma band over human sensorimotor brain areas. Journal of neural engineering, 10(2), 026002.

Collinger, J. L., Wodlinger, B., Downey, J. E., Wang, W., Tyler-Kabara, E. C., Weber, D. J., ... & Schwartz, A. B. (2013). High-performance neuroprosthetic control by an individual with tetraplegia. The Lancet, 381(9866), 557-564.

Cronin, J. A., Wu, J., Collins, K. L., Sarma, D., Rao, R. P., Ojemann, J. G., & Olson, J. D. (2016). Task-specific somatosensory feedback via cortical stimulation in humans. IEEE transactions on haptics, 9(4), 515-522.

Dagaev N., Volkova K. and Ossadtchi A. Latent variable method for automatic adaptation to background states in motor imagery BCI. J Neural Eng. 2017 Jul 18. doi: 10.1088/1741-2552/aa8065.

Graimann, B., Huggins, J. E., Schlogl, A., Levine, S. P., & Pfurtscheller, G. (2003). Detection of movement-related patterns in ongoing single-channel electrocorticogram. IEEE Transactions on neural systems and rehabilitation engineering, 11(3), 276-281.

Hill, N. J., Gupta, D., Brunner, P., Gunduz, A., Adamo, M. A., Ritaccio, A., & Schalk, G. (2012). Recording human electrocorticographic (ECoG) signals for neuroscientific research and real-time functional cortical mapping. JoVE (Journal of Visualized Experiments), (64), e3993.

Hiremath, S. V., Tyler-Kabara, E. C., Wheeler, J. J., Moran, D. W., Gaunt, R. A., Collinger, J. L., ... & Wang, W. (2017). Human perception of electrical stimulation on the surface of somatosensory cortex. PloS one, 12(5), e0176020.

Hochberg, L. R., Serruya, M. D., Friehs, G. M., Mukand, J. A., Saleh, M., Caplan, A. H., ... & Donoghue, J. P. (2006). Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature, 442(7099), 164.

Hotson, G., Fifer, M. S., Acharya, S., Benz, H. L., Anderson, W. S., Thakor, N. V., & Crone, N. E. (2014). Coarse electrocorticographic decoding of ipsilateral reach in patients with brain lesions. PloS one, 9(12), e115236.

Hotson, G., McMullen, D. P., Fifer, M. S., Johannes, M. S., Katyal, K. D., Para, M. P., ... & Crone, N. E. (2016). Individual finger control of a modular prosthetic limb using high-density electrocorticography in a human subject. Journal of neural engineering, 13(2), 026017.

Jayaram, V., Alamgir, M., Altun, Y., Scholkopf, B., & Grosse-Wentrup, M. (2016). Transfer learning in brain-computer interfaces. IEEE Computational Intelligence Magazine, 11(1), 20-31.

Johnson, L. A., Wander, J. D., Sarma, D., Su, D. K., Fetz, E. E., & Ojemann, J. G. (2013). Direct electrical stimulation of the somatosensory cortex in humans using electrocorticography electrodes: a qualitative and quantitative report. Journal of neural engineering, 10(3), 036021.

Kandel, E. R. Schwartz, J. H. & Jessell T. M. (Eds.). (2000). Principles of neural science (Vol. 4, pp. 1227-1246). Department of Biochemistry and Molecular Biophysics, New York: McGraw-hill.

Kellis, S., Sorensen, L., Darvas, F., Sayres, C., O'Neill III, K., Brown, R. B., ... & Greger, B. (2016). Multi-scale analysis of neural activity in humans: Implications for micro-scale electrocorticography. Clinical Neurophysiology, 127(1), 591-601.

Kim, G., Kim, K., Lee, E., An, T., Choi, W., Lim, G., & Shin, J. (2018). Recent progress on microelectrodes in neural interfaces. Materials, 11(10), 1995.

Kohler, F., Gkogkidis, C. A., Bentler, C., Wang, X., Gierthmuehlen, M., Fischer, J., ... & Ball, T. (2017). Closed-loop interaction with the cerebral cortex: a review of wireless implant technology. Brain-Computer Interfaces, 4(3), 146-154.

Korostenskaja, M., Kamada, K., Guger, C., Salinas, C. M., Westerveld, M., Castillo, E. M., ... & Elsayed, M. (2015). Electrocorticography-based real-time functional mapping for pediatric epilepsy surgery. Journal of Pediatric Epilepsy, 4(04), 184-206.

Kramer, D. R., Kellis, S., Barbaro, M., Salas, M. A., Nune, G., Liu, C. Y., ... & Lee,
B. (2019). Technical considerations for generating somatosensation via cortical stimulation in a closed-loop sensory/motor brain-computer interface system in humans.
Journal of Clinical Neuroscience, 63, 116-121.

Kubanek, J. O. J. W. G. S. J., Miller, K. J., Ojemann, J. G., Wolpaw, J. R., & Schalk, G. (2009). Decoding flexion of individual fingers using electrocorticographic signals in humans. Journal of neural engineering, 6(6), 066001.

LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. nature, 521(7553), 436-444.

Lee, B., Kramer, D., Armenta Salas, M., Kellis, S., Brown, D., Dobreva, T., ... & Andersen, R. A. (2018). Engineering artificial somatosensation through cortical stimulation in humans. Frontiers in systems neuroscience, 12, 24.

Leuthardt, E. C., Miller, K. J., Schalk, G., Rao, R. P., & Ojemann, J. G. (2006). Electrocorticography-based brain computer interface-the Seattle experience. IEEE Transactions on Neural Systems and Rehabilitation Engineering, 14(2), 194-198.

Lotte, F., Congedo, M., Lécuyer, A., Lamarche, F., & Arnaldi, B. (2007). A review of classification algorithms for EEG-based brain–computer interfaces. Journal of neural engineering, 4(2), R1.

Lotte, F., Bougrain, L., Cichocki, A., Clerc, M., Congedo, M., Rakotomamonjy, A., & Yger, F. (2018). A review of classification algorithms for EEG-based brain–computer interfaces: a 10 year update. Journal of neural engineering, 15(3), 031005.

Machado, S., Araújo, F., Paes, F., Velasques, B., Cunha, M., Budde, H., ... & Piedade, R. (2010). EEG-based brain-computer interfaces: an overview of basic concepts and clinical applications in neurorehabilitation. Reviews in the Neurosciences, 21(6), 451-468.

Mak, J. N., & Wolpaw, J. R. (2009). Clinical applications of brain-computer interfaces: current state and future prospects. IEEE reviews in biomedical engineering, 2, 187-199.

Miller, K. J., Leuthardt, E. C., Schalk, G., Rao, R. P., Anderson, N. R., Moran, D. W., ... & Ojemann, J. G. (2007). Spectral changes in cortical surface potentials during motor movement. Journal of Neuroscience, 27(9), 2424-2432.

Miranda, R. A., Casebeer, W. D., Hein, A. M., Judy, J. W., Krotkov, E. P., Laabs, T. L., ... & Weber, D. J. (2015). DARPA-funded efforts in the development of novel brain–computer interface technologies. Journal of neuroscience methods, 244, 52-67.

Padfield, N., Zabalza, J., Zhao, H., Masero, V., & Ren, J. (2019). EEG-based brain-computer interfaces using motor-imagery: Techniques and challenges. Sensors, 19(6), 1423.

Pistohl, T., Schulze-Bonhage, A., Aertsen, A., Mehring, C., & Ball, T. (2012). Decoding natural grasp types from human ECoG. Neuroimage, 59(1), 248-260.

Ritaccio, A. L., Brunner, P., & Schalk, G. (2018). Electrical Stimulation Mapping of the Brain: Basic Principles and Emerging Alternatives. Journal of clinical neurophysiology: official publication of the American Electroencephalographic Society, 35(2), 86-97.

Satow, T., Matsuhashi, M., Ikeda, A., Yamamoto, J., Takayama, M., Begum, T., ... & Hashimoto, N. (2003). Distinct cortical areas for motor preparation and execution in human identified by Bereitschaftspotential recording and ECoG-EMG coherence analysis. Clinical neurophysiology, 114(7), 1259-1264.

Schalk, G., Miller, K. J., Anderson, N. R., Wilson, J. A., Smyth, M. D., Ojemann, J. G., ... & Leuthardt, E. C. (2008). Two-dimensional movement control using electrocorticographic signals in humans. Journal of neural engineering, 5(1), 75.

Schalk, G. (2010). Can electrocorticography (ECoG) support robust and powerful brain-computer interfaces?. Frontiers in neuroengineering, 3, 9.

Schalk, G., & Leuthardt, E. C. (2011). Brain-computer interfaces using electrocorticographic signals. IEEE reviews in biomedical engineering, 4, 140-154.

Schalk, G., Leuthardt, E. C., Brunner, P., Ojemann, J. G., Gerhardt, L. A., & Wolpaw, J. R. (2008). Real-time detection of event-related brain activity. Neuroimage, 43(2), 245-249.

Squire, L., Berg, D., Bloom, F. E., Du Lac, S., Ghosh, A., & Spitzer, N. C. (Eds.). (2012). Fundamental neuroscience. Academic Press.

Su, D. K., & Ojemann, J. G. (2013). Electrocorticographic sensorimotor mapping. Clinical neurophysiology: official journal of the International Federation of Clinical Neurophysiology, 124(6), 1044.

Tamura, Y., Ogawa, H., Kapeller, C., Prueckl, R., Takeuchi, F., Anei, R., ... & Kamada, K. (2016). Passive language mapping combining real-time oscillation analysis with cortico-cortical evoked potentials for awake craniotomy. Journal of neurosurgery, 125(6), 1580-1588.

Velliste, M., Perel, S., Spalding, M. C., Whitford, A. S., & Schwartz, A. B. (2008). Cortical control of a prosthetic arm for self-feeding. Nature, 453(7198), 1098. Waldert, S. (2016). Invasive vs. non-invasive neuronal signals for brain-machine interfaces: will one prevail?. Frontiers in neuroscience, 10, 295.

Wang, W., Collinger, J. L., Degenhart, A. D., Tyler-Kabara, E. C., Schwartz, A. B., Moran, D. W., ... & Kelly, J. W. (2013). An electrocorticographic brain interface in an individual with tetraplegia. PloS one, 8(2), e55344.

Xie, Ziqian, Odelia Schwartz, and Abhishek Prasad (2017). "Decoding of finger trajectory from ECoG using Deep Learning". In: Journal of neural engineering.

Yanagisawa, T., Hirata, M., Saitoh, Y., Goto, T., Kishima, H., Fukuma, R., ... & Yoshimine, T. (2011). Real-time control of a prosthetic hand using human electrocorticography signals. Journal of neurosurgery, 114(6), 1715-1722.

Yanagisawa, T., Hirata, M., Saitoh, Y., Kishima, H., Matsushita, K., Goto, T., ... & Yoshimine, T. (2012). Electrocorticographic control of a prosthetic arm in paralyzed patients. Annals of neurology, 71(3), 353-361.