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SYSTEM BIOLOGY AND AGE-RELATED DISEASES

Quasistationary Oscillations in Game-Driven Evolutionary Dynamics

O.S. Vershinina, S.V. Denisov, M.V. Ivanchenko*

Lobachevsky University, Nizhny Novgorod, Russia.
* Presenting e-mail: olya.olya-ver@yandex.ru

Evolutionary game theory is a widely used approach to investigate of the dynamics of cells, living organisms and populations. Much attention is paid to the equilibrium states of biological systems which, however, in real life can be unattainable, as achieving them requires astronomical time. Therefore, we are interested in quasistationary states of the system, where the system rapidly converges to and remains for a long time, before getting into an absorbing state, for example, extinction. Exemplifying in the famous Dawkins` Battle of the Sexes game, we demonstrate that quasistationary distributions can produce much more complex behavior, then the asymptotic ones, that is transient self-sustained oscillations of player numbers and the corresponding non-unimodal probability distribution. Parameters of the quasistationary limit cycle depend on the population size, as well as the absorbtion time.

Diagnosis of Ovarian Cancer Based on Longitudinal Measurements of Multiple Biomarkers

I.P. Mariño[1], M.A. Vázquez[2], O. Blyuss[3], A. Ryan[4] , A. Gentry-Maharaj[4] , J. Kalsi[4], R. Manchanda[4] , I. Jacobs[4] , U. Menon[4] and A. Zaikin[4]*

[1] Universidad Rey Juan Carlos, Madrid, Spain;
[2] Universidad Carlos III de Madrid, Madrid, Spain;
[3] Queen Mary University of London, London, United Kingdom;
[4] University College of London, London, United Kingdom.
* Presenting e-mail: ines.perez@urjc.es

Ovarian cancer remains the fifth most common cause of cancer-related deaths among women, with more than 150,000 annual deceases worldwide. The main problem of this disease is that, usually, it is detected at later stages, for which the survival rates are relatively low. The development of efficient methods for the early detection of the disease could significantly impact on mortality.

Aims

The main objective of this work is to carry out a quantitative study of the performance of two automatic methods for the early detection of ovarian cancer that can exploit longitudinal measurements of multiple biomarkers.

Methods

The study is carried out for a subset of the data [1,2] collected in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS, number ISRCTN22488978; NCT00058032) [3]. The selected dataset included 179 controls (healthy women) and 44 cases (diagnosed women): 35 cases of invasive epithelial ovarian cancer, 3 cases of fallopian tube cancer and 6 cases of peritoneal cancer.
We use statistical analysis techniques, such as the area under the Receiver Operating Characteristic (ROC) curve, for evaluating the performance of two techniques aimed at the classification of subjects as either healthy or suffering from the disease using time-series of multiple biomarkers as inputs. The first method relies on a Bayesian hierarchical model that establishes connections within a set of clinically-interpretable parameters [1,2]. The second technique is a purely discriminative method that employs a recurrent neural network for the binary classification of the inputs.

Results

For the available dataset, the performance of the two detection schemes is similar (the area under ROC curve is 0.98

for the combination of three biomarkers) and the Bayesian approach has the advantage that its outputs (parameters estimates and their uncertainty) can be further analysed by a clinical expert.

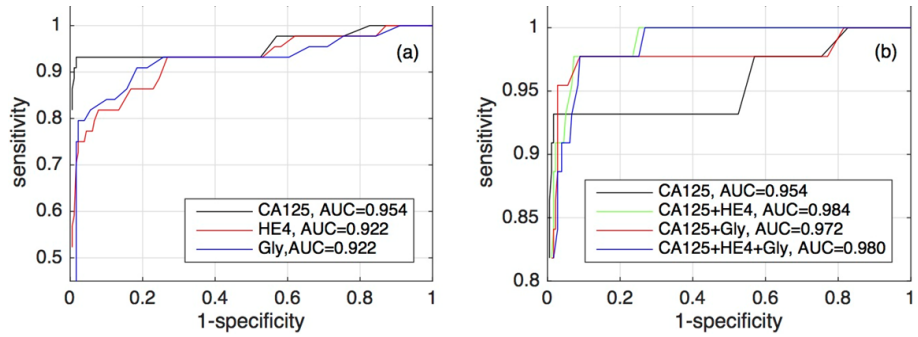

Fig.1. *ROC curves and area under ROC curve (AUC) obtained by the Bayesian Change-point method for different biomarkers: (a) when considering alone CA125, HE4 and glycodelin, (b) when considering different combinations of these three biomarkers.*

Conclusions

The main conclusion of the work is that combining longitudinal time series of different biomarkers can improve the classification of pre-diagnosis samples.

Acknowledgements

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Multiplexing Networks: the Gains and Losses of Synchrony

*M. Ivanchenko**

Lobachevsky University, Nizhny Novgorod, Russia.
* Presenting e-mail: ivanchenko.mv@gmail.com

Inspired by the recent interest in collective dynamics of biological neural networks immersed in the glial cell medium, we investigate the frequency and phase order, i.e., Kuramoto type of synchronization in a multiplex two-layer network of phase oscillators of different time scales and topologies. One of them has a long-range connectivity, exemplified by the Erdos-Renyi random network, and supports both kinds of synchrony. The other is a locally coupled two-dimensional lattice that can reach frequency synchronization but lacks phase order. We find that an indirect but sufficiently strong coupling through the regular layer can induce both phase order in the originally nonsynchronized random layer and global order, even when an isolated regular layer does not manifest it in principle. At the same time,

the route to global synchronization is complex: an initial onset of (partial) synchrony in the regular layer, when its intra- and interlayer coupling is increased, provokes the loss of synchrony even in the originally synchronized random layer. Ultimately, a developed asynchronous dynamics in both layers is abruptly taken over by the global synchrony of both kinds.

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Comparison of Longitudinal Algorithms for the Early Detection of Ovarian Cancer

*O.B. Blyuss[1] *, V.K. Cherepanova[2], J.F. Timms[3], M. Burnell[3], A. Ryan[3], A. Gentry-Maharaj[3], U. Menon[3], A.A. Zaikin[3,4]*

[1] Wolfson Institute of Preventive Medicine, Queen Mary University of London, UK;
[2] CoMPLEX, University College London, UK;
[3] Institute for Women's Health, University College London, UK;
[4] Department of Mathematics, University College London, UK.
* Presenting e-mail: o.blyuss@qmul.ac.uk

Aims

Ovarian cancer is the leading cause of death from gynaecological cancer among women. Most of women are diagnosed at the late stage where 5-year survival rate is as low as 3%. The only biomarker that is currently used for the ovarian cancer detection is Cancer Antigen 125 (CA125) which goes up when the tumour grows. The conventional cut-off of 35 U/mL that is commonly used is practice doesn't allow early detection of the disease as it doesn't include any information of the deviation from the patients' baselines that could be a sign of the development of cancer. Therefore it is important to find the algorithm that would analyse serial CA125 measurements and allow the detection of ovarian cancer at an early stage.

Methods

In this analysis we compare two established methods, Risk of Ovarian Cancer Algorithm (ROCA) and Parametric Empirical Bayes (PEB) for the analysis of serial measurements of the CA125 with the newly developed method called Method of Mean Trends (MMT) and the conventional CA125 cut-off. The comparison is based on the results of the classification of ovarian cancer cases and healthy patients using the Area under ROC-curve (AUC) as well as the sensitivity at fixed specificity.

Results

All the serial methods performed significantly better than the conventional CA125 cut-off. At a specificity of 89.5%, sensitivities for MMT and PEB were similar to that reported for ROCA.

Conclusions

The results provide clear evidence that serial algorithms are significantly superior to simple cut-offs for ovarian cancer early detection. Further analysis of other advanced techniques for the analysis of serial CA125 measurements such as Recurrent Neural Network is required to see if they could significantly improve those proposed before.

Rigor Mortis-like Process during Organismal Death in *C. elegans*

*Evgeniy R. Galimov[1] *, Rosina E. Pryor[1], Sarah E. Poole[1], Alexandre Benedetto[1,2], Zachary Pincus[3], David Gems[1,4]*

[1] Institute of Healthy Ageing, and Department of Genetics, Evolution and Environment, University College London, London, UK;
[2] Division of Biomedical and Life Sciences, Faculty of Health and Medicine, Lancaster University, Lancaster LA1 4YW, UK;
[3] Department of Genetics and Department of Developmental Biology, Washington University in St. Louis, St. Louis, MO 63110, USA.
* Presenting e-mail: e.galimov@ucl.ac.uk

Summary

In most metazoans ageing is characterized by increase in age-related pathologies which then results in the rise of mortality. Interestingly, while age-related pathologies from mammals to invertebrates have been investigating intensively, organismal death is poorly studied process which also can be a target for medical intervention. We aim to study organismal death in *Caenorhabditis elegans* as a widely used model organism in biomedical research. The process of organismal death model nematode C. *elegans* is accompanied by a calcium-propagated, anterior to posterior (AP) wave of necrosis in the intestine which can be monitored by a burst of blue anthranilate fluorescence (death fluorescence) [1]. In this work we demonstrate that natural or stress-induced death in C. *elegans* is accompanied by transient reduction of body length (death contraction followed by recovery) which immediately precedes death fluorescence. Usage of muscle deficient mutants and direct muscle visualization suggest that death contraction is mediated by muscles. Death contraction typically occurs as an AP wave of body wall muscle contraction, immediately preceded by an AP wave of intramuscular calcium release and followed by an AP wave of death fluorescence. Importantly, the polarity of the two (death contraction and death fluorescence) wave types is strongly correlated, suggesting that death contraction determines death fluorescence. In C. elegans, reduced insulin/IGF-1 signaling (IIS) decreases mortality from severe stress, pathogens, and aging. We report that it also suppresses death contraction, suggesting possible resistance to organismal death. Interestingly, a process similar to death contraction in C. *elegans* is known in higher organisms as rigor mortis which occurs after death. Our results provide an account of the major events in organismal death in C. *elegans* and suggest that, in contrast to mammals, rigor mortis-like process in nematodes is an early event during organismal death which probably promotes it. Critical questions now are: how does senescent pathology trigger rigor mortis-like process and organismal death, and what interventions could prevent them?

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Tactile and Visual Feedback Influence on Operator's Motor Imagery Skill in Brain-Computer Interface

N.A. Grigorev[1], M.V. Lukoyanov[1,2], S.Yu. Gordleeva[1], A.O. Savosenkov[1], A.S. Pimashkin[1], V.B. Kazantsev[1], A.Ya. Kaplan[1,3]*

[1] National Research Lobachevsky State University of Nizhni Novgorod, Nizhni Novgorod, Russia;
[2] Privolzhsky Research Medical University, Nizhni Novgorod, Russia;
[3] Lomonosov Moscow State University, Moscow, Russia.
* Presenting e-mail: na0grigorev@gmail.com

Aims

The aim of the study is to compare the degree of desynchronization of the mu-rhythm in the imagination of movements and the accuracy of the classification of the brain-computer interface (BCI) of motor-imaginary type with three commands (imaginary right/left hand movement and rest) using tactile, visual feedback and no feedback at all.

Methods

Six healthy subjects aged 18-24 years with a leading right arm (median 0.7 points according to the manual asymmetry questionnaire [1]) participated in the study. All subjects previously had no experience being BCI operators. Each subject took part in three experimental sessions with six entries for 10 presentations of each team.

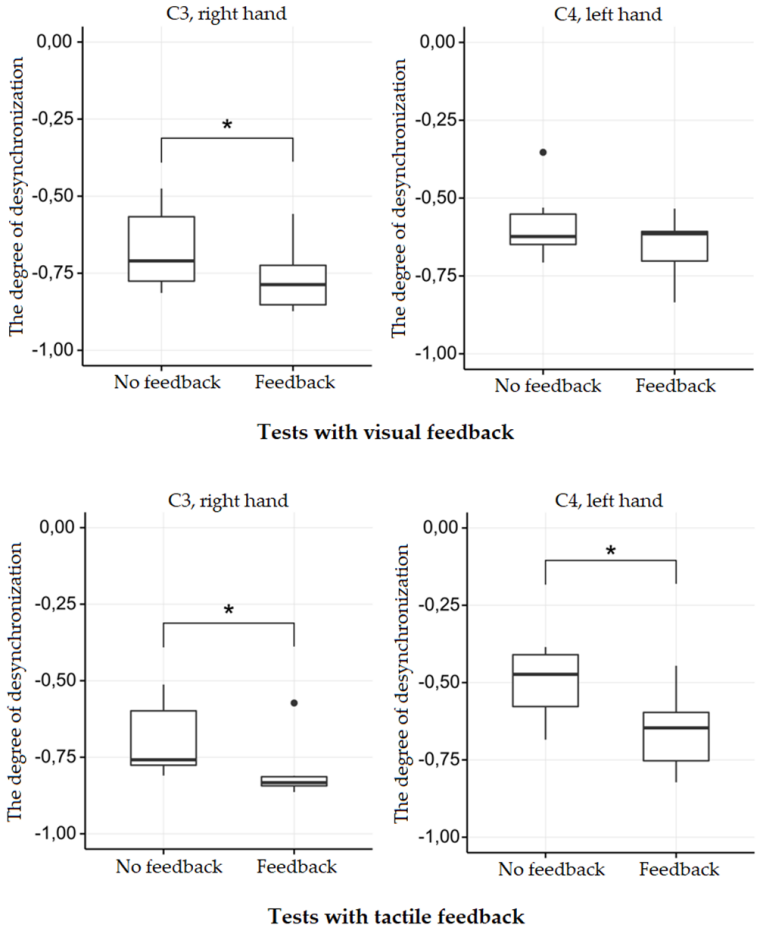

Fig. 1. *Diagram: comparison of the degree of desynchronization in the imagination of hand movements in the BCI circuit with visual feedback, with tactile feedback and no feedback. Statistically significant differences are indicated by an asterisk (Mann-Whitney test P <0.05).*

The EEG was recorded with the NVX-52 electroencephalograph, the signal was recorded from 30 Cl/Ag electrodes, which were installed by the 10-10 system (FT7, FC5, FC3, FC1, FCz, FC2, FC4, FC6, FT8, T7, C5, C3, C1, Cz, C2, C4, C6, T8, TP7, CP5, CP3, CP1, CPz, CP2, CP4, CP6, TP8, P3, P4, POz). The study consisted of three experimental sessions. The training of the participant to perform imaginary movements was carried out in the first session. During the second and third sessions, tests with participants were performed using two types of feedback. In one session only one version of the feedback was provided to the subject and some tests were conducted without feedback as a control. The visual feedback was made as a color filled band on the monitor for correct recognition of the command. Tactile feedback was carried out with the help of vibration motors mounted on the forearms and the back of the neck of operators for signaling successful recognition of EEG patterns of motion representation by the classifier.

Results

Individual results of classification accuracy in three subjects indicate improvement of their skills with BCI using feedback (two of them improved results with a visual feedback, one with a tactile feedback). The accuracy of classification on average for all subjects was not statistically different using visual and tactile feedback relative to control. The desynchronization degree during motor imagery with tactile feedback was significantly lower for both hands for all participants in comparison with their performance using visual feedback (Figure 1).

Conclusion

The results of the classification accuracy analysis suggest that the introduction of tactile feedback into the BCI circuit does not lead to a decrease in the operator's efficiency. Analysis of desynchronization data showed that tactile feedback can lead to more pronounced desynchronization, in comparison with the visual feedback. After training the subject, the presence of the feedback, regardless of its type, does not affect the classification accuracy when working in the BCI. According to the participants reports the presence of the tactile feedback creates for them more comfortable conditions for performing tests while working in the BCI circuit.

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Astrocyte Regulation of Postsynaptic Cellular Activity in Neuroglial Networks

*A.I. Kalyakulina**

Lobachevsky University, Nizhny Novgorod, Russia.
* Presenting e-mail: kalyakulina.alena@gmail.com

All information received by animals from the environment through the senses is processed in the central nervous system. This complexly organized system coordinates all the animal's actions by temporarily activating various neural networks. Transmission and processing of information at the cellular level of the nervous system occurs due to changes in membrane currents and changes in the membrane potential [1]. Despite the fact that two basic types of cells, neurons and glial cells, form the central nervous system, for a long time neurons were considered as the basic cellular elements involved in the transmission and processing of information. Glial cells were generally regarded as passive cells that provide structural and metabolic support to neurons without participating in the processing of information. However, recent data show that astrocytes can also play an active role in the processing of synaptic information. They are capable of secreting gliotransmitters, which regulate the excitability of neurons and, consequently, detect the ability of glia to coordinate the activity of a neural network [2, 3, 4]. Since one astrocyte can be in contact with a large number of synapses, gliothransmission can facilitate neural synchronization.

In this work, the collective dynamics of postsynaptic neuronal cells connected through a common astrocyte is considered using recently developed model of the basic physiological functions of the tripartite synapse [5]. Nontrivial

changes in neuronal activity observed with an increase in the yield of the gliotransmitter were found, and results were obtained that illustrate the ability of astrocytes to synchronize the membrane potentials of postsynaptic neuronal cells due to a change in the concentration of the two types of gliothransmitters.

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Effect of Motor Imaginary Brain–Computer Interface with Vibro-Tactile Feedback on Corticospinal Excitability in Healthy Adults

M.V. Lukoyanov[1,2], N.A. Grigorev[2], A.O. Savosenkov[2], Y.I. Lotareva[2], S.Y. Gordleeva[2], A.Ya. Kaplan[3]*

[1] Privolzhsky Research Medical University, Nizhny Novgorod, Russia;
[2] Lobachevsky State University, Nizhny Novgorod, Russia;
[3] Lomonosov State University, Moscow, Russia.
* Presenting e-mail: lukoyanovm@gmail.com

The use of motor imaginary brain-computer interfaces (BCI) becomes an increasingly popular approach in the rehabilitation of post-stroke patients [1]. Traditionally, this type of BCI uses either visual feedback in the form of a change in the visual scene on the monitor screen, or the triggering of mechanical devices such as exoskeletons [2]. These types of feedbacks are not always optimal for post-stroke patients. Earlier in our works, the effectiveness of the use of vibro-tactile feedback in motor imaginary BCI was investigated [3]. We have shown that vibro-tactile feedback is not inferior to visual, and under certain conditions, tactile feedback can lead to the greater degree of sensorimotor rhythm desynchronization in subjects, as compared with the visual feedback. It was shown that a greater degree of desynchronization of the sensorimotor rhythm indicates a greater excitability of neurons in the motor cortex [4]. Increased excitability of the motor cortex is a positive factor accelerating the recovery of motor function disorders in post-stroke patients. A more accurate method for assessing the excitability of the motor cortex is an approach based on measuring the amplitude of motor evoked potentials when stimulating the corresponding motor zones with a transcranial magnetic stimulator [5]. In this work, the influence of the use of vibro-tactile feedback in the motor imaginary BCI on corticospinal excitability was studied. To this aim, level of corticospinal excitability, EEG desynchronization, and classification accuracy was compered during working in motor-imaginary BCI with vibro-tactile feedback and without feedback on healthy adults. The level of excitability of motor cortex was evaluated from the change in the amplitude of the motor evoked potentials, recorded by electromyography, with transcranial magnetic stimulation of the corresponding zones of the cerebral cortex. Transcranial magnetic stimulation was carried out under the control of the navigation system on the basis of MR images of the subject, which allowed to achieve precise positioning of the stimulator coil over the selected cortical area.

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Synchronization in Model Neuron-Glial Multiplex Networks: Role of Network Topology

S. Yu. Makovkin, M.V. Ivanchenko, A.A. Zaikin*

Lobachevsky University, Nizhny Novgorod, Russia.
* Presenting e-mail: makovkin@neuro.nnov.ru

We investigate the impact of multiplexing of two layers with different topology on synchronizability. The model is inspired by neural-glial networks in brain, so that the "glial" layer has a local 1D or 2D topology, whereas the "neural" one has a "small-world" connectivity with the tunable rewiring parameter, becoming Erdős–Rényi graph in the limiting case. Interlayer links are mirror and next-neighbor. The dynamical evolution of the oscillator nodes in this multiplex network is given by the coupled Kuramoto model, the frequency ranges between the slower "glial" and faster "neural" layer are order of magnitude different.

Our main findings are: (i) Interaction to the neural layer can induce phase order (non-zero mean-field) in the glial one, absent in the isolated case; (ii) Interlayer coupling leads to desynchronization between the layers; (iii) at large coupling an abrupt transition to system-wide synchrony is observed; (iv) synchronization and desynchronization regions are robust to variations in the rewiring parameter; (v) relaxation time towards an asymptotic distribution of oscillator phases increases sharply at synchronization-desynchronization boundaries.

Testing EEG-Based Motor Imagery Brain-Computer Interface with Tactile Feedback in People after Stroke

A.O. Savosenkov[1], N.A. Grigorev[1], M.V. Lukoyanov[1,2], S.Y. Gordleeva[1]*

[1] National Research Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia;
[2] Privolzhsky Research Medical University, Nizhny Novgorod, Russia.
* Presenting e-mail: andrey.savosenkov@gmail.com

Aims

The aim of the study is to determine the possibility of patients after stroke to work in the EEG-based motor imagiry brain-computer interface with vibrotactile feedback. Determination of differences in the success of the mental representation of hand movement (estimated by the degree of desynchronization of the μ-rhythm) in patients with stem and hemispheric ischemic stroke.

Methods

Of the 30 patients examined during the study, 11 people met the criteria for inclusion in the study, 5 of them gave informed consent for participation in the study. Of these 5 patients (2 men and 3 women, mean age 66.4 ± 6.48), lacunar stroke was localized in 1 person in the inferior parts of the temporal lobe, 3 in the region of the pons, 1 in the basal ganglia on right. In the course of this work, a neurological and neuropsychological examination of the patient was performed to assess the severity of his condition and the degree of dysfunction opposite to the stroke of the hand. At the next stage, in preparation for EEG recording, the technique of representing movements was explained to select the subjects most comfortable for themselves (finger movement, rotation in the wrist joint, or capturing the object), focusing on the presentation of tactile sensations [1]. The depth of depression of the μ-rhythm was checked for imaginary movement with the right / left hand. We have carried out evaluated the degree of retention of the mental image of motion on the basis of EEG recording using vibrotactile feedback for each patient.

Results

Previous studies have shown that desynchronization of the μ-rhythm in the left hemisphere of the brain, exceeding the value of 50%, occurs with real movement, and also with successful reproduction from memory of arbitrary actions in both the right and left arm. In the right hemisphere, the desynchronization of the μ-rhythm on the EEG exceeding 50% is detected only when the movements reproduction from memory in the left hand. Thus, desynchronization of the μ-rhythm in the left hemisphere, exceeding the value of 50%, can be used as an indicator of the success of an attempt to represent the motion of both the left and right hands [2].

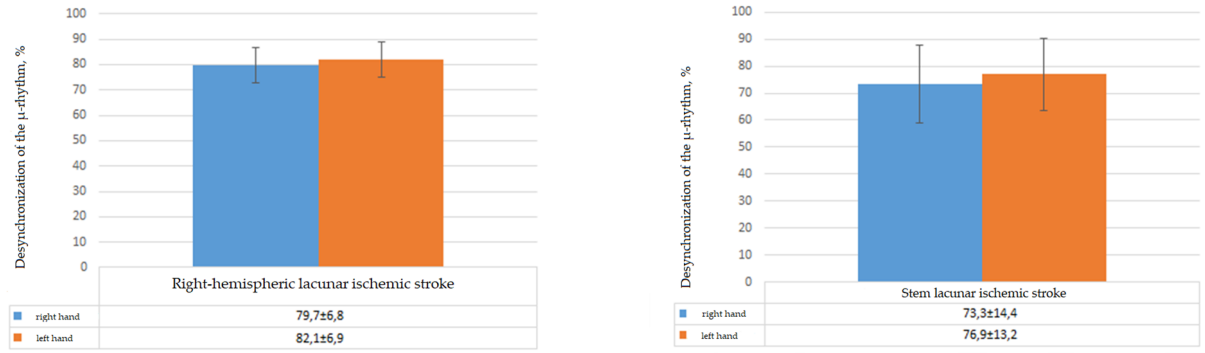

Fig. 1. *The maximum percentage (%) of desynchronization of μ -rhythm on the EEG in the left hemisphere of the brain with a mental representation of movement in the right arm and left arm in patients with a stem and right-hemispheric ischemic stroke*

Conclusion

The results of the analysis indicate that the success of the mental reproduction of movements (determined by the degree of desynchronization of the μ-rhythm on the EEG during the task) in both the right and left arm is lower when the localization of ischemia in the brain stem, rather than in cerebral hemisphere.

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Detection of Spatiotemporal Calcium Activity in Astrocytes

*M.I. Krivonosov**

Lobachevsky University, Nizhny Novgorod, Russia.
* Presenting e-mail: mike_live@mail.ru

Number of glial cells roughly equals to number of neurons in the adult mammalian brain. Astrocytes are the primary neuronal structural and trophic supportive elements. They are organized into complex astrocytes networks and extend fine processes that interact intimately with synapses. The interaction of astrocytes and neurons plays an important role in the functioning of neural networks. In response to neuronal activity astrocytes can release gliotransmitters, which modulate the synaptic transmission and excitability of neurons. The release of gliotransmitters is affected by intracellular calcium Ca^{2+} in astrocytes. The roles that astrocytic calcium elevations play in modulation of neuronal activity have been intensely researched in recent years.

In this work we study spatiotemporal dynamics of calcium events in individual astrocytes, the key problem is developing stable algorithms for recognizing calcium events.

Video stream of calcium imaging of hippocampal slices recorded in laboratory for the analysis of calcium activity. In each pixel the intensity of the fluorescent colorant binding to Ca^{2+} is proportional to the amount of calcium.

We analyze Ca^{2+} events which were defined as spatiotemporally interconnected transient Ca^{2+} increases. Using such analysis in single astrocytes in culture and in slices we verify that areas and durations of Ca^{2+} events follow power law distributions. Varying threshold of noise assumption which specify significance of calcium signal revealed that there is a wide interval for which the power law is applicable. It is found that calcium events are not separate spatiotemporal entities, which puts forth the problem of - the propagation of calcium fronts. This is addressed by an algorithm for detecting the velocity field of the fronts of calcium events.

The developed algorithm can be used in various biological setups, where time-lapse imaging would produce spatially structured and dynamically changing events.

Acknowledgements

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Network Epigenetic Classifiers for Cancer

*I.I. Yusipov**

Lobachevsky University, Nizhny Novgorod, Russia.
* Presenting e-mail: yusipov.igor@gmail.com

Recently, it has been demonstrated that gene specific measures of DNA methylation, such as mean, variance, and alike reflect cancer-related changes and enable differentiation between normal and tumor tissue samples. We go beyond a single or a few gene classifiers, seeking for integrative signatures of cancer in methylation data. We employ the parenclictic network approach, where pairwise gene methylation anomalies are taken as connectivities between respective gene network nodes. The artificial network constructed in this way, obtains footprints of differential cancer methylation, and allows to derive genome-wide network markers.

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Contour Integration and Noise-Induced Synchronization in the Visual Cortex

E. Ullner[1], C. Korndörfer[2], J. García-Ojalvo[3] and G. Pipa[2]*

[1] University of Aberdeen, Aberdeen, UK;
[2] University of Osnabrück, Osnabrück, Germany;
[3] Universitat Pompeu Fabra, Barcelona, Spain.
* Presenting e-mail: e.ullner@abdn.ac.uk

Visual stimuli can evoke synchronous responses at visual cortex sites up to several mm apart [1] and the strength of this synchrony varies with geometrical stimulus features such as spatial continuity [2, 3] or similarity of orientation [4]. Interpretations of these results have been conflicting: Such varying synchronous responses are either seen as an (inconsequential) epiphenomenon of cortical connectivity [5], or as evidence for a synchrony-based mechanism that supports the grouping of separate stimulus components [6, 7].

We propose a mechanism of origin as well as possible functional role of spike synchrony as it occurs across a range of species during perceptions of continuous visual shapes [8]. Here, we understand "synchrony" as the average degree of zero time-lag synchrony of some set of measured cells, that is simply the extent to which these cells fire simultaneously. This phenomenon of spike synchrony has sparked a long-standing debate on the nature of temporal organization in cortical networks. One prominent view, underpinned by many computational models, is that it reveals a synchrony-based mechanism for the binding or grouping of separate stimulus components. However, the dynamics predicted by commonly discussed (continuous, rate-based) oscillator models are difficult to relate to the (pulsed, spiking) cortical synaptic connections most likely involved. Here, we resolve this mismatch by showing that excitatory, chemically pulse-coupled spiking networks operating in a noisy environment can directly produce spike synchrony variations as observed. Notably, the associated network dynamics suggest a view of synchronous respons-

es not in terms of the integration of separate stimulus components, but in terms of the quick recognition of familiar input patterns.

We investigate networks of coupled excitable two-dimensional Izhikevich spiking neuron model [9] or alternatively of excitable FitzHuge-Nagumo neurons, capturing the essential neuronal features of excitable systems: stable fixpoint at rest, excitation threshold, fast but delayed response to a supra-threshold perturbation and refractoriness. The neurons receive synaptic input that mediates the lateral coupling in the network and the input from upstream connections. We model the synaptic current as nonlinear pulse coupling via chemical synapses. Upstream connections, responsible for delivering external, random input to the network, can be either excitatory or inhibitory. The random upstream spikes occur independent of each other across time and space with the spike events following a Poisson distribution with a certain rate and represent the external stimulus of the network. Different stimulus patterns, i.e. different choices of input-receiving cells, lead to different degrees of average zero time lag synchrony among these cells, depending on the lateral connections between them. Stimuli activating cells connected by short paths expressed stronger zero-lag synchrony in the firing of these cells than more scattered stimuli. Synchrony differences between different stimuli are distinguishable after a few spikes.

In cortical synchrony experiments only a few (multi-)electrode recording sites are usually set and stay fixed throughout the various stimulus presentations. Implementing such a setup into our in silico experiments we fix the cells for recording and vary the cells receiving upstream stimuli. We find that two fixed, small groups of cells fire with increased synchrony if a stimulus activates cells on the direct path between those groups. The more parts of the stimulus pattern fall on the path between measured locations, the stronger their synchrony. Switching all inputs to the region between measured groups from off to on produces the clearest change in synchrony.

The synchronization effect is related to the Noise-Enhanced Phase Synchronization in excitable media [10]. We verified the robustness of our findings against regular and random lateral networks, various rates of the excitatory and inhibitory Poissonian upstream spike sequences, and different lateral and upstream synaptic conductances.

Our suggestion is that coherent visual stimuli are marked by increased spike synchrony because these stimuli activate well-connected subsets of an excitable network.

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Spatiotemporal Evolution of Cortical Spreading Depression Simulated with Refractory Period Effect

Shangbin Chen[1] and Bing Li[2]*

[1] School of Engineering Sciences, Huazhong University of Science and Technology-Wuhan National Laboratory for Optoelectronics, Wuhan, China;
[2] Department of Biomedical Engineering, Huazhong University of Science and Technology, Wuhan, Hubei, China.
* Presenting e-mail: sbchen@mail.hust.edu.cn

Cortical spreading depression (CSD) is an enigma of pathophysiological phenomenon, which underlies some neurological disorders, such as migraine, epilepsy and stroke. Previous experiments revealed that the spatiotemporal evolution (including amplitude, speed, extent and pattern) of a series CSD waves is time-varying. To better interpret the observations, we have applied a 2D reaction-diffusion equation with recovery term to study the spatiotemporal evolution of CSD in the current work. By modulating the recovery rate (i.e. mimicking the effect of refractory period) from CSD in the modeled cortex, the simulated successive CSD waves were present with different spatiotemporal evolutions, either bypassing some areas or propagating slowly in these areas. In addition, spiral CSD waves could also be induced in case of the transiently altered recovery rate, i.e. block release from the absolute refractory period. In another parallel simualation study, we simulated that continuous injection of KCl solution can induce repetitive CSD

waves. The first CSD wave often has a larger amplitude and faster velocity than those of the succeeding secondary waves. If the induction interval is long enough for recovery, a series of CSD waves would have the same profile as the first one. In the relative refractory period, an early stimulation might lead to a late initiation of CSD, i.e., "haste makes waste". The amplitude and velocity of CSD waves were found increasing with the initiation interval and asymptotic to those of the first CSD wave. These results suggested that the propagation dynamics of CSD waves is modulated by the relative refractory period. The refractory period is critical for preventing undesirable CSD waves. This modelling work is helpful to interpret the mechanisms of CSD propagation.

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Ovarian Cancer Applied to Ovarian Cancer Prediction

Harry J Whitwell [1], Oleg Blyuss[2], Usha Menon[3], Peter DiMaggio[1], John F. Timms[3], Alexey Zaikin[3,4]*

[1] Chemical Engineering, Imperial College London, UK;
[2] Wolfson Institute for Preventative Medicine, Queen Mary University of London, UK;
[3] Institute for Women's Health, University College London, UK;
[4] Department of Mathematics, University College London, UK.
* Presenting e-mail: h.whitwell@imperial.ac.uk

Prediction and diagnosis of complex disease may not always be possible with a small number of biomarkers. Modern 'omics' technologies make it possible to cheaply and quantitatively assay hundreds of molecules generating large amounts of data from individual samples. In this study, we describe a parenclitic network-based approach to disease classification using a synthetic data set modelled on data from the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) and serological assay data from a nested set of samples from the same study. This

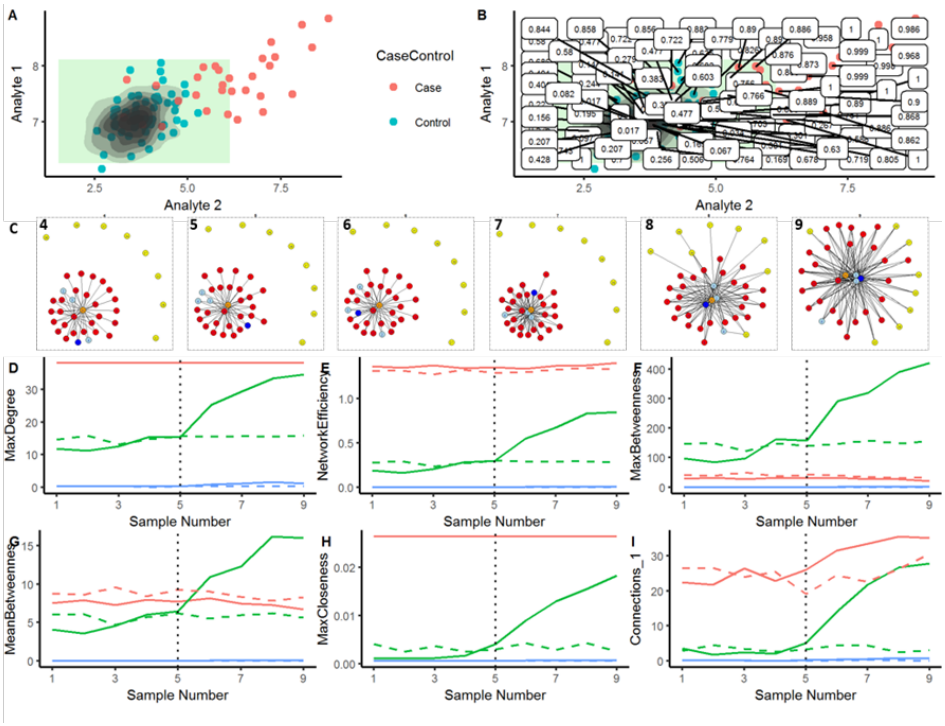

Fig.1. ***A*** *Great 2-dimensional kernel density map of an individual for all pairs of analytes.* ***B*** *Quantify difference of individual from a control cohort.* ***C*** *Construct [parenclitic] network of the differing analytes.* ***D*** *Use network topologies to construct predictive models.*

approach allows us to integrate quantitative proteomic and categorical metadata into a single network, and then use network topologies to construct logistic regression models for disease classification. In this study of ovarian cancer, comprising of 30 controls and cases with samples taken <14 months to diagnosis (n = 30) and/or >34 months to diagnosis (n = 29), we were able to classify cases with a sensitivity of 80.3% within 14 months of diagnosis and 18.9% in samples exceeding 34 months to diagnosis at a specificity of 98%. Furthermore, we use the networks to make observations about proteins within the cohort and identify GZMH and FGFBP1 as changing in cases (in relation to controls) at time points most distal to diagnosis. We conclude that network-based approaches may offer a solution to the problem of complex disease classification that can be used in personalised medicine and to describe the underlying biology of cancer progression at a system level.

Time-Lapse Imaging for Calcium Activityanalysis in Astrocytes with Automatic Video Processing

V.D. Kustikova[1], M.I. Krivonosov[2], P.A. Denisov[2], A.A. Zaikin[3], M.V. Ivanchenko[2], I.B. Meyerov[2], and A.V. Semyanov[4]*

[1] Lobachevsky State University of Nizhni Novgorod, Nizhni Novgorod, Russian Federation;
[2] Lobachevsky State University of Nizhni Novgorod, Nizhni Novgorod, Russian Federation;
[3] Department of Mathematics and Institute for Women's Health, University College London, London, United Kingdom;
[4] Shemyakin-Ovchinnikov Institute of bioorganic chemistry, Moscow, Russian Federation.
* Presenting e-mail: valentina.kustikova@itmm.unn.ru

Fluorescent imaging is the main approach to study calcium activity in astrocytes and, more general, their role in cognitive brain functioning. Calcium signaling produces complex spatio-temporal patterns in time-lapse recordings, putting forth a challenging problem of an automated video processing and analysis [1 – 6]. Existing solutions have a number of limitations, in particular, specific data origin, lack of source code availability, and require delicate tuning of method parameters.

To overcome the existing problems, we developed a method for detecting calcium activity in a sequence of astrocyte images based on the sliding window approach, applied to the variation of pixel intensity relative to the fluorescence baseline level [7]. The general scheme of the method is similar to that described in [8]. The novelty consists in the procedure of determining the noise parameters on the input data, as well as in the iterative procedure of estimating the fluorescence baseline level.

In result, we identified much longer in time and more structurally complex calcium events, than previously demonstrated, sometimes, extending over all observation time.

The developed software implementation of the method is publicly available [9].

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Comparison of Two Methods of Identification of Characteristic Features for the Brain-Machine Interface Classifier of the Motor-Imaginary Type with Vibrotactile Feedback Systems on Patients with Post-Stroke Brain Damage

*Yu.A. Lotareva**

Lobachevsky State University of Nizhni Novgorod, Nizhni Novgorod, Russian Federation;
* Presenting e-mail: lotarevaj@gmail.com

The technology of brain-computer interfaces allows a person by mental efforts to form specific EEG patterns that are translated into commands for external executive devices. Thus, a person is given the opportunity to manage these devices and the ability to communicate with the outside world without the help of nerves and muscles, using only his brain. Qualitative processing and classification of EEG signals is one of the components of successful implementation of such projects. Improving productivity and increasing the accuracy of classifiers are necessary for the further development of the field of brain-computer interfaces. In this article, a comparison was made between two methods of isolating characteristic features for the brain-computer interface of the motor-imaginary type.

Methodology

The study involved 4 patients (2 males and 2 females, mean age 66.4 ± 6.48) whose lacunar stroke was localized in 1 person in the deep sections of the right temporal lobe, in 2 people - in the field of the variolium bridge, in 1 - in the basal ganglia on the right. The subjects were explained the technique of representing the movements and suggested the choice of the most comfortable for themselves movement: flexion of fingers, rotation in the wrist joint or capture of the object, placing emphasis on the presentation of tactile sensations. The depth of depression of the μ-rhythm was checked for imaginary movement with the right / left hand. The classifier analyzed the segments of the record length of 500 ms, and after each such segment the classifier gave an answer about the correctness of the performance of the mental task and the subject was given a vibration feedback length of 200 ms. Classification occurs every 500 ms, then suspended for 200 ms to feed feedback.

In the first method, to isolate the signs that are significant for the classification of EEG patterns, the signal was filtered in the 6 - 16 Hz band with the subsequent calculation of the individual spatial CSP filter (Koles, et al., 1990).

In the second method, after transformation of the spatial domain of the signal, each channel was analyzed separately in the spectral domain. For each of the two compared states, the probability density of each spectral component in the range 7-30 Hz was restored (for this we used the Fourier expansion with a rectangular window function of width 1 s with a shift of 0.1 s) The obtained densities of each component were compared for two patterns of classified states with the calculation of the overlap area. The index, equal to 100% minus the overlap area (in fractions of the total area under the probability density curve), was called ERDd. Four spatial-spectral traits with the highest ERDd indicators were used to train the classifier.

The classification was carried out using a linear discriminant analysis method. As an indicator of the accuracy of classification, the probability of a correct classification was used, calculated as the ratio of correctly classified tasks to the total number of tasks.

Results

At the first stage of the experiment, for all 4 subjects the maximum desynchronization was observed at C3 and/or C4 electrodes in the range from 11 to 14 Hz and exceeded the level of 50%. On this basis, all subjects were considered successfully mastered the technique of imaginary movements and were are allowed to test the work of the BCI with feedback.

patient	1 method,%	2 method,%
1	50 ±28,7	66,7 ±7,3
2	71,7 ±18,4	81,6 ±5,8
3	76,7 ±9,7	78,3 ±2,9
4	70 ±20	78,6 ±3,2
average	67,5 ±15	76,7 ±5,8

Table 1. *Accuracy of the classification using two methods of distinguishing characteristic features (mean ± standard deviation).*

As a result of the experiment, the second method of isolating traits was more effective than the first. On average, the classification accuracy increased by 10%. Only in one of four patients the classification accuracy increased insignificantly, while in others the efficiency of the classifier increased noticeably.