Neurofunctional plasticity in fraction learning: An fMRI training study

Background: Fractions are known to be difficult for children and adults. Behavioral studies suggest that magnitude processing of fractions can be improved via number line estimation (NLE) trainings, but little is known about the neural correlates of fraction learning.
Method: To examine the neuro-cognitive foundations of fraction learning, behavioral performance and neural correlates were measured before and after a five-day NLE training.
Results: In all evaluation tasks behavioral performance increased after training. We observed a fronto-parietal network associated with number magnitude processing to be recruited in all tasks as indicated by a numerical distance effect. For symbolic fractions, the distance effect on intraparietal activation was only observed after training.
Conclusion: The absence of a distance effect of symbolic fractions before the training could indicate an initially less automatic access to their overall magnitude. NLE training facilitates processing of overall fraction magnitude as indicated by the distance effect in neural activation.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Education, Research group: TUT Game Lab, Computing Sciences, Eberhard-Karls University Tuebingen, Universitätsmedizin Greifswald, Leibniz-Institut für Wissensmedien, Loughborough University, Individual Development and Adaptive Education Center, Université de Paris
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Number of pages: 15
Publication date: 1 Dec 2020
Peer-reviewed: Yes

Publication information

Journal: Trends in Neuroscience and Education
Volume: 21
Article number: 100141
ISSN (Print): 2211-9493
Original language: English
ASJC Scopus subject areas: Neuroscience (miscellaneous), Education, Cognitive Neuroscience, Behavioral Neuroscience
Keywords: Flow experience, fMRI, Fraction processing, Number line estimation training, Numerical distance effect
DOIs:
10.1016/j.tine.2020.100141
Source: Scopus
Source ID: 85090911630
Research output: Contribution to journal › Article › Scientific › peer-review

Assessment of PIV performance in validating CFD models from nasal cavity CBCT scans

Objective: The aim of our study was to investigate how well Particle Image Velocimetry (PIV) measurements could serve Computational Fluid Dynamics (CFD) model validation for nasal airflow.
Material and methods: For the PIV measurements, a silicone model of the nose based on cone beam computed tomography (CBCT) scans of a patient was made. Corresponding CFD calculations were conducted with laminar and two turbulent models (k-ω and k-ω SST).
Results: CFD and PIV results corresponded well in our study. Especially, the correspondence of CFD calculations between the laminar and turbulent models was found to be even stronger. When comparing CFD with PIV, we found that the results were most convergent in the wider parts of the nasal cavities.
Conclusion: PIV measurements in realistically modelled nasal cavities succeed acceptably and CFD calculations produce corresponding results with PIV measurements. Greater model scaling is, however, necessary for better validations with PIV and comparisons of competing CFD models.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Automation Technology and Mechanical Engineering, Clinical Medicine, BioMediTech, Research group: Sensor Technology and Biomeasurements (STB), Tampere University, Tampere University Hospital, Texas Tech University Health Sciences Center at Lubbock, Ear & Sinus Institute, Boston Children’s Hospital
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Number of pages: 9
Publication date: 1 Nov 2020
Peer-reviewed: Yes

Publication information

Journal: Respiratory Physiology and Neurobiology

Volume: 282
Article number: 103508
ISSN (Print): 1569-9048
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Physiology, Pulmonary and Respiratory Medicine
Keywords: 3D silicone modelling, CBCT, CFD, nasal airflow, PIV
DOIs:
10.1016/j.resp.2020.103508
Source: Scopus
Source ID: 85090273511
Research output: Contribution to journal › Article › Scientific › peer-review

Automatic assessment of the myoclonus severity from videos recorded according to standardized Unified Myoclonus Rating Scale protocol and using human pose and body movement analysis

Purpose: Myoclonus in progressive myoclonus epilepsy type 1 (EPM1) patients shows marked variability, which presents a substantial challenge in devising treatment and conducting clinical trials. Consequently, fast and objective myoclonus quantification methods are needed. Methods: Ten video-recorded unified myoclonus rating scale (UMRS) myoclonus with action tests were performed on EPM1 patients who were selected for the development and testing of the automatic myoclonus quantification method. Human pose and body movement analyses of the videos were used to identify body keypoints and further analyze movement smoothness and speed. The automatic myoclonus rating scale (ARMS) was developed. It included the jerk count during movement score and the log dimensionless jerk (LDLJ) score to evaluate changes in the smoothness of movement. Results: The scores obtained with the automatic analyses showed moderate to strong significant correlation with the UMRS myoclonus with action scores. The jerk count of the primary keypoints and the LDLJ scores were effective in the evaluation of the myoclonic jerks during hand movements. They also correlated moderately to strongly with the total UMRS test panel scores (r^2 = 0,77, P = 0,009 for the jerk count score and r^2 = 0,88, P = 0,001 for the LDLJ score). The automatic analyses was weaker in quantification of the neck, trunk, and leg myoclonus. Conclusion: Automatic quantification of myoclonic jerks using human pose and body movement analysis of patients' videos is feasible and was found to be quite consistent with the accepted clinical gold standard quantification method. Based on the results of this study, the automatic analytical method should be further developed and validated to improve myoclonus severity follow-up for EPM1 patients.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Computing Sciences, Research group: Multimedia Research Group - MRG, University Central Hospital Kuopio, Neuro Event Labs Oy (2712284-1), Tampere University Hospital, University of Eastern Finland
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Number of pages: 7
Pages: 72-78
Publication date: 1 Mar 2020
Peer-reviewed: Yes

Publication information
Journal: Seizure
Volume: 76
ISSN (Print): 1059-1311
Original language: English
ASJC Scopus subject areas: Neurology, Clinical Neurology
Keywords: EPM1, Myoclonus, Pose estimation analysis, Unified Myoclonus Rating Scale
DOIs:
10.1016/j.seizure.2020.01.014
Source: Scopus
Source ID: 85078811034
Research output: Contribution to journal › Article › Scientific › peer-review

A Computational Model of Interactions Between Neuronal and Astrocytic Networks: The Role of Astrocytes in the Stability of the Neuronal Firing Rate

Recent research in neuroscience indicates the importance of tripartite synapses and gliotransmission mediated by astrocytes in neuronal system modulation. Although the astrocyte and neuronal network functions are interrelated, they are fundamentally different in their signaling patterns and, possibly, the time scales at which they operate. However, the exact nature of gliotransmission and the effect of the tripartite synapse function at the network level are currently elusive. In this paper, we propose a computational model of interactions between an astrocyte network and a neuron network, starting from tripartite synapses and spanning to a joint network level. Our model focuses on a two-dimensional setup emulating a mixed in vitro neuron-astrocyte cell culture. The model depicts astrocyte-released gliotransmitters exerting opposing effects on the neurons: increasing the release probability of the presynaptic neuron while hyperpolarizing the

post-synaptic one at a longer time scale. We simulated the joint networks with various levels of astrocyte contributions and neuronal activity levels. Our results indicate that astrocytes prolong the burst duration of neurons, while restricting hyperactivity. Thus, in our model, the effect of astrocytes is homeostatic; the firing rate of the network stabilizes to an intermediate level independently of neuronal base activity. Our computational model highlights the plausible roles of astrocytes in interconnected astrocytic and neuronal networks. Our simulations support recent findings in neurons and astrocytes in vivo and in vitro suggesting that astrocytic networks provide a modulatory role in the bursting of the neuronal network.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Research group: Computational Biophysics and Imaging Group, Vrije Universiteit Amsterdam, CNR-ISC, University of Florence, INRIA, CNRS University of Lyon
Contributors: Lenk, K., Satuvuori, E., Lallouette, J., Ladrón-de-Guevara, A., Berry, H., Hyttinen, J. A. K.
Number of pages: 19
Publication date: 22 Jan 2020
Peer-reviewed: Yes

Publication information
Journal: Frontiers in Computational Neuroscience
Volume: 13
Article number: 92
ISSN (Print): 1662-5188
Original language: English
ASJC Scopus subject areas: Neuroscience (miscellaneous), Cellular and Molecular Neuroscience
Keywords: astrocyte, calcium signaling, gliotransmission, network, neuron, simulation
DOIs:
10.3389/fncom.2019.00092

Bibliographical note
INT=bmte,"Satuvuori, Eero"
INT=bmte,"Ladrón-de-Guevara, Antonio"
Source: Scopus
Source ID: 85079035352
Research output: Contribution to journal › Article › Scientific › peer-review

Tidal breathing flow profiles during sleep in wheezing children measured by impedance pneumography
For the first time, impedance pneumography (IP) enables a continuous analysis of the tidal breathing flow volume (TBFV), overnight. We studied how corticosteroid inhalation treatments, sleep stage, and time from sleep onset modify the nocturnal TBFV profiles of children. Seventy children, 1–5 years old and with recurrent wheezing, underwent three, full-night TBFVs recordings at home, using IP. The first recorded one week before ending a 3-months inhaled corticosteroids treatment, and remaining two, 2 and 4 weeks after treatment. TBFV profiles were grouped by hour from sleep onset and estimated sleep stage. Compared with on-medication, the off-medication profiles showed lower volume at exhalation peak flow, earlier interruption of expiration, and less convex middle expiration. The differences in the first two features were significant during non-rapid eye movement (NREM), and the differences in the third were more prominent during REM after 4 h of sleep. These combinations of TBFV features, sleep phase, and sleep time potentially indicate airflow limitation in young children.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research group: Physiological Measurement Systems and Methods Group, BioMediTech, Revenio Research Ltd., Tampere University Hospital
Contributors: Gracia-Tabuenca, J., Seppä, V., Jauhiainen, M., Paassilta, M., Viik, J., Karjalainen, J.
Publication date: 2020
Peer-reviewed: Yes
Early online date: 1 Oct 2019

Publication information
Journal: Respiratory Physiology and Neurobiology
Volume: 271
Article number: 103312
ISSN (Print): 1569-9048
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Physiology, Pulmonary and Respiratory Medicine
Keywords: Impedance pneumography, Lung function, Tidal breathing, Wheezing children

DOIs:
10.1016/j.resp.2019.103312
URLs:
http://urn.fi/URN:NBN:fi:tuni-202004073116. Embargo ended: 1/10/20

Bibliographical note
EXT="Seppä, Ville-Pekka"
dupl=51710383
Source: Scopus
Source ID: 85073034217
Research output: Contribution to journal › Article › Scientific › peer-review

Randomized Multiresolution Scanning in Focal and Fast E/MEG Sensing of Brain Activity with a Variable Depth
We focus on electro-/magnetoencephalography imaging of the neural activity and, in particular, finding a robust estimate for the primary current distribution via the hierarchical Bayesian model (HBM). Our aim is to develop a reasonably fast maximum a posteriori (MAP) estimation technique which would be applicable for both superficial and deep areas without specific a priori knowledge of the number or location of the activity. To enable source distinguishability for any depth, we introduce a randomized multiresolution scanning (RAMUS) approach in which the MAP estimate of the brain activity is varied during the reconstruction process. RAMUS aims to provide a robust and accurate imaging outcome for the whole brain, while maintaining the computational cost on an appropriate level. The inverse gamma (IG) distribution is applied as the primary hyperprior in order to achieve an optimal performance for the deep part of the brain. In this proof-of-the-concept study, we consider the detection of simultaneous thalamic and somatosensory activity via numerically simulated data modeling the 14-20 ms post-stimulus somatosensory evoked potential and field response to electrical wrist stimulation. Both a spherical and realistic model are utilized to analyze the source reconstruction discrepancies. In the numerically examined case, RAMUS was observed to enhance the visibility of deep components and also marginalizing the random effects of the discretization and optimization without a remarkable computation cost. A robust and accurate MAP estimate for the primary current density was obtained in both superficial and deep parts of the brain.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Computing Sciences, Research group: Inverse Problems
Contributors: Rezaei, A., Koulouri, A., Pursiainen, S.
Number of pages: 15
Pages: 161-175
Publication date: 2020
Peer-reviewed: Yes

Publication information
Journal: Brain Topography
Volume: 33
Issue number: 2
ISSN (Print): 0896-0267
Original language: English
ASJC Scopus subject areas: Anatomy, Radiological and Ultrasound Technology, Radiology Nuclear Medicine and imaging , Neurology, Clinical Neurology
Keywords: Brain imaging, Depth reconstruction, EEG and MEG data, Hierarchical Bayesian model, Randomized multiresolution scanning
Electronic versions:
Randomized Multiresolution Scanning in Focal 2020
DOIs:
10.1007/s10548-020-00755-8
URLs:
http://urn.fi/URN:NBN:fi:tuni-202006256224
Source: Scopus
Source ID: 85079741204
Research output: Contribution to journal › Article › Scientific › peer-review

Membrane-Dependent Binding and Entry Mechanism of Dopamine into Its Receptor
Synaptic neurotransmission has recently been proposed to function via either a membrane-independent or a membrane-dependent mechanism, depending on the neurotransmitter type. In the membrane-dependent mechanism, amphipathic neurotransmitters first partition to the lipid headgroup region and then diffuse along the membrane plane to their membrane-buried receptors. However, to date, this mechanism has not been demonstrated for any neurotransmitter-receptor complex. Here, we combined isothermal calorimetry measurements with a diverse set of molecular dynamics simulation methods to investigate the partitioning of an amphipathic neurotransmitter (dopamine) and the mechanism of its

entry into the ligand-binding site. Our results show that the binding of dopamine to its receptor is consistent with the membrane-dependent binding and entry mechanism. Both experimental and simulation results showed that dopamine favors binding to lipid membranes especially in the headgroup region. Moreover, our simulations revealed a ligand-entry pathway from the membrane to the binding site. This pathway passes through a lateral gate between transmembrane alpha-helices 5 and 6 on the membrane-facing side of the protein. All in all, our results demonstrate that dopamine binds to its receptor by a membrane-dependent mechanism, and this is complemented by the more traditional binding mechanism directly through the aqueous phase. The results suggest that the membrane-dependent mechanism is common in other synaptic receptors, too.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research group: Biological Physics and Soft Matter, Physics, University of Helsinki, Universitat Heidelberg , Uniwersytet Jagiellonski w Krakowie, University of Eastern Finland, Turku University Hospital, MEMPHYS, University of Turku
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Number of pages: 11
Pages: 1914–1924
Publication date: 2020
Peer-reviewed: Yes

Publication information
Journal: ACS Chemical Neuroscience
Volume: 11
Issue number: 13
ISSN (Print): 1948-7193
Original language: English
ASJC Scopus subject areas: Biochemistry, Physiology, Cognitive Neuroscience, Cell Biology
Keywords: ligand entry pathway prediction, lipid membrane, molecular dynamics, random acceleration molecular dynamics, synaptic neurotransmission, umbrella sampling
DOIs:
10.1021/acschemneuro.9b00656

Bibliographical note
EXT="Postila, Pekka A."
EXT="Enkavi, Giray"
EXT="Róg, Tomasz"
Source: Scopus
Source ID: 85087135930
Research output: Contribution to journal › Article › Scientific › peer-review

Unique Features of Network Bursts Emerge From the Complex Interplay of Excitatory and Inhibitory Receptors in Rat Neocortical Networks

Spontaneous network activity plays a fundamental role in the formation of functional networks during early development. The landmark of this activity is the recurrent emergence of intensive time-limited network bursts (NBs) rapidly spreading across the entire dissociated culture in vitro. The main excitatory mediators of NBs are glutamatergic alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs) and N-Methyl-D-aspartic-acid receptors (NMDARs) that express fast and slow ion channel kinetics, respectively. The fast inhibition of the activity is mediated through gamma-aminobutyric acid type A receptors ($GABA_A$Rs). Although the AMPAR, NMDAR and $GABA_A$R kinetics have been biophysically characterized in detail at the monosynaptic level in a variety of brain areas, the unique features of NBs emerging from the kinetics and the complex interplay of these receptors are not well understood. The goal of this study is to analyze the contribution of fast $GABA_A$Rs on AMPAR- and NMDAR- mediated spontaneous NB activity in dissociated neonatal rat cortical cultures at 3 weeks in vitro. The networks were probed by both acute and gradual application of each excitatory receptor antagonist and combinations of acute excitatory and inhibitory receptor antagonists. At the same time, the extracellular network-wide activity was recorded with microelectrode arrays (MEAs). We analyzed the characteristic NB measures extracted from NB rate profiles and the distributions of interspike intervals, interburst intervals, and electrode recruitment time as well as the similarity of spatio-temporal patterns of network activity under different receptor antagonists. We show that NBs were rapidly initiated and recruited as well as diversely propagated by AMPARs and temporally and spatially maintained by NMDARs. $GABA_A$Rs reduced the spiking frequency in AMPAR-mediated networks and dampened the termination of NBs in NMDAR-mediated networks as well as slowed down the recruitment of activity in all networks. Finally, we show characteristic super bursts composed of slow NBs with highly repetitive spatio-temporal patterns in gradually AMPAR blocked networks. To the best of our knowledge, this study is the first to unravel in detail how the three main mediators of synaptic transmission uniquely shape the NB characteristics, such as the initiation, maintenance, recruitment and termination of NBs in cortical cell cultures in vitro.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Research group: Computational Neuro Science-CNS
Contributors: Teppola, H., Aćimović, J., Linne, M. L.
Publication date: 6 Sep 2019
Peer-reviewed: Yes

Publication information
Journal: FRONTIERS IN CELLULAR NEUROSCIENCE
Volume: 13
Article number: 377
ISSN (Print): 1662-5102
Ratings:

Scopus rating (2019): CiteScore 5.4 SJR 1.618 SNIP 0.958
Original language: English
ASJC Scopus subject areas: Cellular and Molecular Neuroscience
Keywords: AMPA receptor, cell culture, GABA receptor, microelectrode array, neocortical cells, neuronal network, NMDA receptor, spontaneous network burst activity
Electronic versions:

fncel-13-00377
DOIs:

10.3389/fncel.2019.00377
URLs:

http://urn.fi/URN:NBN:fi:tuni-201910213973
Source: Scopus
Source ID: 85072963878
Research output: Contribution to journal › Article › Scientific › peer-review

Viability of Mouse Retinal Explant Cultures Assessed by Preservation of Functionality and Morphology
Purpose: Retinal explant cultures provide simplified systems where the functions of the retina and the effects of ocular therapies can be studied in an isolated environment. The purpose of this study was to provide insight into long-term preservation of retinal tissue in culture conditions, enable a deeper understanding of the interdependence of retinal morphology and function, and ensure the reliability of the explant technique for prolonged experiments. Methods: Retinal explants from adult mice were cultured as organotypic culture at the air-medium interface for 14 days in vitro (DIV). Retinal functionality was assessed by multielectrode array technique and morphology by immunohistochemical methods at several time points during culture. Results: Retinal explants retained viability for 14 DIV, although with diminishing neuronal activity, progressing neuronal loss, and increasing reactive gliosis. We recorded spontaneous retinal ganglion cell (RGC) activity up to 14 DIV with temporally changing distribution of RGC firing rates. Light responsiveness was measurable from RGCs for 7 DIV and from photoreceptors for 2 DIV. Apoptotic cells were detected beginning at 3 DIV with their density peaking at 7 DIV. The number of RGCs gradually decreased by 70% during 14 DIV. The change was accompanied by the loss of RGC functionality, resulting in 84% loss of electrically active RGCs. Conclusions: Retinal explants provide a valuable tool for studies of retinal functions and development of ocular therapies. However, critical for long-term use, retinal functionality was lost before structural loss, emphasizing a need for both functional and morphologic readouts to determine the overall state of the cultured retina.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research group: Computational Biophysics and Imaging Group, BioMediTech, Tampere University, Tampere University Hospital
Contributors: Alarautalahti, V., Ragauskas, S., Hakkarainen, J. J., Uusitalo-Järvinen, H., Uusitalo, H., Hyttinen, J., Kalesnykas, G., Nymark, S.
Number of pages: 14
Pages: 1914-1927
Publication date: 1 May 2019
Peer-reviewed: Yes

Publication information
Journal: Investigative ophthalmology & visual science
Volume: 60
Issue number: 6
ISSN (Print): 0146-0404
Ratings:

Scopus rating (2019): CiteScore 6.5 SJR 1.789 SNIP 1.295

Original language: English
ASJC Scopus subject areas: Ophthalmology, Sensory Systems, Cellular and Molecular Neuroscience
Electronic versions:

i1552-5783-60-6-1914
DOIs:

10.1167/iovs.18-25156
URLs:

http://urn.fi/URN:NBN:fi:tty-201906111884

Bibliographical note
DUPL=47898722
Source: Scopus
Source ID: 85065551723
Research output: Contribution to journal › Article › Scientific › peer-review

Reduced level of docosahexaenoic acid shifts GPCR neuroreceptors to less ordered membrane regions
G protein-coupled receptors (GPCRs) control cellular signaling and responses. Many of these GPCRs are modulated by cholesterol and polyunsaturated fatty acids (PUFAs) which have been shown to co-exist with saturated lipids in ordered membrane domains. However, the lipid compositions of such domains extracted from the brain cortex tissue of individuals suffering from GPCR-associated neurological disorders show drastically lowered levels of PUFAs. Here, using free energy techniques and multiscale simulations of numerous membrane proteins, we show that the presence of the PUFA DHA helps helical multi-pass proteins such as GPCRs partition into ordered membrane domains. The mechanism is based on hybrid lipids, whose PUFA chains coat the rough protein surface, while the saturated chains face the raft environment, thus minimizing perturbations therein. Our findings suggest that the reduction of GPCR partitioning to their native ordered environments due to PUFA depletion might affect the function of these receptors in numerous neurodegenerative diseases, where the membrane PUFA levels in the brain are decreased. We hope that this work inspires experimental studies on the connection between membrane PUFA levels and GPCR signaling.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, University of Helsinki, Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Universitat Autònoma de Barcelona, University of Texas Health Science Center at Houston, MEMPHYS
Contributors: Javanainen, M., Enkavi, G., Guixà-Gonzaléz, R., Kulig, W., Martinez-Seara, H., Levental, I., Vattulainen, I.
Publication date: 1 May 2019
Peer-reviewed: Yes

Publication information
Journal: PLoS Computational Biology
Volume: 15
Issue number: 5
Article number: e1007033
ISSN (Print): 1553-734X
Ratings:

Scopus rating (2019): CiteScore 7.3 SJR 2.91 SNIP 1.537
Original language: English
ASJC Scopus subject areas: Ecology, Evolution, Behavior and Systematics, Modelling and Simulation, Ecology, Molecular Biology, Genetics, Cellular and Molecular Neuroscience, Computational Theory and Mathematics
Electronic versions:

journal.pcbi.1007033
DOIs:

10.1371/journal.pcbi.1007033
URLs:

http://urn.fi/URN:NBN:fi:tty-201906251906

Bibliographical note
EXT="Martinez-Seara, Hector"
Source: Scopus
Source ID: 85066964975
Research output: Contribution to journal › Article › Scientific › peer-review

Improved EEG source localization with Bayesian uncertainty modelling of unknown skull conductivity

Electroencephalography (EEG) source imaging is an ill-posed inverse problem that requires accurate conductivity modelling of the head tissues, especially the skull. Unfortunately, the conductivity values are difficult to determine in vivo. In this paper, we show that the exact knowledge of the skull conductivity is not always necessary when the Bayesian approximation error (BAE) approach is exploited. In BAE, we first postulate a probability distribution for the skull conductivity that describes our (lack of) knowledge on its value, and model the effects of this uncertainty on EEG recordings with the help of an additive error term in the observation model. Before the Bayesian inference, the likelihood is marginalized over this error term. Thus, in the inversion we estimate only our primary unknown, the source distribution. We quantified the improvements in the source localization when the proposed Bayesian modelling was used in the presence of different skull conductivity errors and levels of measurement noise. Based on the results, BAE was able to improve the source localization accuracy, particularly when the unknown (true) skull conductivity was much lower than the expected standard conductivity value. The source locations that gained the highest improvements were shallow and originally exhibited the largest localization errors. In our case study, the benefits of BAE became negligible when the signal-to-noise ratio dropped to 20 dB.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Mathematics, University of Bath, Institute for Biomagnetism and Biosignalanalysis, University of Münster, Aristotle University of Thessaloniki, Centrum Wiskunde & Informatica, University College London, The University of Auckland, University of Eastern Finland
Contributors: Rimpiläinen, V., Koulouri, A., Lucka, F., Kaipio, J. P., Wolters, C. H.
Number of pages: 9
Pages: 252-260
Publication date: 1 Mar 2019
Peer-reviewed: Yes
Early online date: 6 Dec 2018

Publication information

Journal: NeuroImage
Volume: 188
ISSN (Print): 1053-8119
Ratings:

Scopus rating (2019): CiteScore 10.2 SJR 3.207 SNIP 1.91
Original language: English
ASJC Scopus subject areas: Neurology, Cognitive Neuroscience
Keywords: Bayesian inverse problem, Electroencephalography, Skull conductivity, Source localization, Uncertainty modelling
Electronic versions:

UNMARKED_rimpilainen_20190213. Embargo ended: 15/12/19
DOIs:

10.1016/j.neuroimage.2018.11.058
URLs:

http://urn.fi/URN:NBN:fi:tuni-201910013624. Embargo ended: 15/12/19

Bibliographical note

EXT="Rimpiläinen, Ville"
Source: Scopus
Source ID: 85058408352
Research output: Contribution to journal › Article › Scientific › peer-review

Diffusion tensor imaging and disability progression in multiple sclerosis: A 4-year follow-up study

Objectives: Diffusion tensor imaging (DTI) is sensitive technique to detect widespread changes in water diffusivity in the normal-appearing white matter (NAWM) that appears unaffected in conventional magnetic resonance imaging. We aimed to investigate the prognostic value and stability of DTI indices in the NAWM of the brain in an assessment of disability progression in patients with a relapsing-onset multiple sclerosis (MS). Methods: Forty-six MS patients were studied for DTI indices (fractional anisotropy (FA), mean diffusivity (MD), radial (RD), and axial (AD) diffusivity) in the NAWM of the corpus callosum (CC) and the internal capsule at baseline and at 1 year after. DTI analysis for 10 healthy controls was also performed at baseline. Simultaneously, focal brain lesion volume and atrophy measurements were done at baseline for MS patients. Associations between DTI indices, volumetric measurements, and disability progression over 4 years were studied by multivariate logistic regression analysis. Results: At baseline, most DTI metrics differed significantly between MS patients and healthy controls. There was tendency for associations between baseline DTI indices in the CC and disability progression ($p < 0.05$). Changes in DTI indices over 1 year were observed only in the CC ($p < 0.008$), and those changes were not found to predict clinical worsening over 4 years. Clear-cut association with disability progression was not detected for baseline volumetric measurements. Conclusion: Aberrant diffusivity measures in the NAWM of the CC may provide additional information for individual disability progression over 4 years in MS with the relapsing-onset

disease. CC may be a good target for DTI measurements in monitoring disease activity in MS, and more studies are needed to assess the related prognostic potential.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Faculty of Biomedical Sciences and Engineering, Tampere University Hospital, Department of Radiology, Department of Medical Physics
Contributors: Kolasa, M., Hakulinen, U., Brander, A., Hagman, S., Dastidar, P., Elovaara, I., Sumelahti, M.
Publication date: Jan 2019
Peer-reviewed: Yes
Early online date: 2018

Publication information
Journal: Brain and Behavior
Volume: 9
Issue number: 1
Article number: e01194
ISSN (Print): 2162-3279
Ratings:

Scopus rating (2019): CiteScore 3.2 SJR 0.873 SNIP 0.818
Original language: English
ASJC Scopus subject areas: Behavioral Neuroscience
Keywords: diffusion tensor imaging, longitudinal study, multiple sclerosis
Electronic versions:

Kolasa_et_al-2018-Brain_and_Behavior
DOIs:

10.1002/brb3.1194
URLs:

http://urn.fi/URN:NBN:fi:tty-201901101050

Bibliographical note
EXT="Dastidar, Prasun"
Source: Scopus
Source ID: 85059078902
Research output: Contribution to journal › Article › Scientific › peer-review

A realistic, accurate and fast source modeling approach for the EEG forward problem
The aim of this paper is to advance electroencephalography (EEG) source analysis using finite element method (FEM) head volume conductor models that go beyond the standard three compartment (skin, skull, brain) approach and take brain tissue inhomogeneity (gray and white matter and cerebrospinal fluid) into account. The new approach should enable accurate EEG forward modeling in the thin human cortical structures and, more specifically, in the especially thin cortices in children brain research or in pathological applications. The source model should thus be focal enough to be usable in the thin cortices, but should on the other side be more realistic than the current standard mathematical point dipole. Furthermore, it should be numerically accurate and computationally fast. We propose to achieve the best balance between these demands with a current preserving (divergence conforming) dipolar source model. We develop and investigate a varying number of current preserving source basis elements n (n=1,…,n=5). For validation, we conducted numerical experiments within a multi-layered spherical domain, where an analytical solution exists. We show that the accuracy increases along with the number of basis elements, while focality decreases. The results suggest that the best balance between accuracy and focality in thin cortices is achieved with n=4 (or in extreme cases even n=3) basis functions, while in thicker cortices n=5 is recommended to obtain the highest accuracy. We also compare the current preserving approach to two further FEM source modeling techniques, namely partial integration and St. Venant, and show that the best current preserving source model outperforms the competing methods with regard to overall balance. For all tested approaches, FEM transfer matrices enable high computational speed. We implemented the new EEG forward modeling approaches into the open source duneuro library for forward modeling in bioelectromagnetism to enable its broader use by the brain research community. This library is build upon the DUNE framework for parallel finite elements simulations and integrates with high-level toolboxes like FieldTrip. Additionally, an inversion test has been implemented using the realistic head model to demonstrate and compare the differences between the aforementioned source models.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Mathematics, Signal Processing, Research group: Inverse Problems, University of Münster, University of Eastern Finland, Laboratory of Signal Processing
Contributors: Miinalainen, T., Rezaei, A., Us, D., Nüßing, A., Engwer, C., Wolters, C. H., Pursiainen, S.

Number of pages: 12
Pages: 56-67
Publication date: 2019
Peer-reviewed: Yes
Early online date: 28 Aug 2018

Publication information
Journal: NeuroImage
Volume: 184
Issue number: 1
ISSN (Print): 1053-8119
Ratings:

Scopus rating (2019): CiteScore 10.2 SJR 3.207 SNIP 1.91
Original language: English
ASJC Scopus subject areas: Neurology, Cognitive Neuroscience
Keywords: Divergence conforming vector fields, DUNE toolbox, Electroencephalography (EEG), Finite element method (FEM), Focal sources
DOIs:

10.1016/j.neuroimage.2018.08.054
Source: Scopus
Source ID: 85053387965
Research output: Contribution to journal › Article › Scientific › peer-review

Astrocyte lineage cells are essential for functional neuronal differentiation and synapse maturation in human iPSC-derived neural networks

Human astrocytes differ dramatically in cell morphology and gene expression from murine astrocytes. The latter are well known to be of major importance in the formation of neuronal networks by promoting synapse maturation. However, whether human astrocyte lineage cells have a similar role in network formation has not been firmly established. Here, we investigated the impact of human astrocyte lineage cells on the functional maturation of neural networks that were derived from human induced pluripotent stem cells (hiPSCs). Initial in vitro differentiation of hiPSC-derived neural progenitor cells and immature neurons (glia+ cultures) resulted in spontaneously active neural networks as indicated by synchronous neuronal Ca^{2+} transients. Depleting proliferating neural progenitors from these cultures by short-term antimitotic treatment resulted in strongly astrocyte lineage cell-depleted neuronal networks (glia− cultures). Strikingly, in contrast to glia+ cultures, glia− cultures did not exhibit spontaneous network activity. Detailed analysis of the morphological and electrophysiological properties of neurons by patch clamp recordings revealed reduced dendritic arborization in glia− cultures. In addition, a reduced action potential frequency upon current injection in pyramidal-like neurons was observed, whereas the electrical excitability of multipolar neurons was unaltered. Furthermore, we found a reduced dendritic density of PSD95-positive excitatory synapses, and more immature properties of AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) miniature excitatory postsynaptic currents (mEPSCs) in glia− cultures, suggesting that the maturation of glutamatergic synapses depends on the presence of hiPSC-derived astrocyte lineage cells. Intriguingly, addition of the astrocyte-derived synapse maturation inducer cholesterol increased the dendritic density of PSD95-positive excitatory synapses in glia− cultures.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Heinrich Heine University Düsseldorf, Philipps University
Contributors: Klapper, S. D., Garg, P., Dagar, S., Lenk, K., Gottmann, K., Nieweg, K.
Number of pages: 17
Pages: 1893-1909
Publication date: 2019
Peer-reviewed: Yes

Publication information
Journal: Glia
Volume: 67
Issue number: 10
ISSN (Print): 0894-1491
Ratings:

Scopus rating (2019): CiteScore 10 SJR 2.73 SNIP 1.288
Original language: English
ASJC Scopus subject areas: Neurology, Cellular and Molecular Neuroscience
Keywords: human iPSCs, iPSC-derived astrocyte lineage cells, network function, neuronal differentiation, synapse maturation
DOIs:

10.1002/glia.23666
Source: Scopus
Source ID: 85068131634
Research output: Contribution to journal › Article › Scientific › peer-review

Teaching semantics and skills for human-robot collaboration

Recent advances in robotics allow for collaboration between humans and machines in performing tasks at home or in industrial settings without harming the life of the user. While humans can easily adapt to each other and work in team, it is not as trivial for robots. In their case, interaction skills typically come at the cost of extensive programming and teaching. Besides, understanding the semantics of a task is necessary to work efficiently and react to changes in the task execution process. As a result, in order to achieve seamless collaboration, appropriate reasoning, learning skills and interaction capabilities are needed. For us humans, a cornerstone of our communication is language that we use to teach, coordinate and communicate. In this paper we thus propose a system allowing (i) to teach new action semantics based on the already available knowledge and (ii) to use natural language communication to resolve ambiguities that could arise while giving commands to the robot. Reasoning then allows new skills to be performed either autonomously or in collaboration with a human. Teaching occurs through a web application and motions are learned with physical demonstration of the robotic arm. We demonstrate the utility of our system in two scenarios and reflect upon the challenges that it introduces.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Automation Technology and Mechanical Engineering, Research group: Robotics and Automation
Contributors: Angleraud, A., Houbre, Q., Pieters, R.
Number of pages: 12
Pages: 318-329
Publication date: 2019
Peer-reviewed: Yes

Publication information

Journal: Paladyn
Volume: 10
Issue number: 1
ISSN (Print): 2081-4836
Ratings:

Scopus rating (2019): CiteScore 1.4 SJR 0.332 SNIP 0.96
Original language: English
ASJC Scopus subject areas: Human-Computer Interaction, Developmental Neuroscience, Cognitive Neuroscience, Artificial Intelligence, Behavioral Neuroscience
Keywords: cognitive architecture, human-robot interaction, knowledge representation and reasoning, semiotics, symbol grounding
Electronic versions:

[Paladyn Journal of Behavioral Robotics] Teaching semantics and skills for human-robot collaboration
DOIs:

10.1515/pjbr-2019-0025
URLs:

http://urn.fi/URN:NBN:fi:tuni-201910234030
Source: Scopus
Source ID: 85072921192
Research output: Contribution to journal › Article › Scientific › peer-review

Overview of Sources and Characteristics of Nanoparticles in Urban Traffic-Influenced Areas

Atmospheric nanoparticles can be formed either via nucleation in atmosphere or be directly emitted to the atmosphere. In urban areas, several combustion sources (engines, biomass burning, power generation plants) are directly emitting nanoparticles to the atmosphere and, in addition, the gaseous emissions from the same sources can participate to atmospheric nanoparticle formation. This article focuses on the sources and formation of nanoparticles in traffic-influenced environments and reviews current knowledge on composition and characteristics of these nanoparticles. In general, elevated number concentrations of nanoparticles are very typically observed in traffic-influenced environments. Traffic related nanoparticles can originate from combustion process or from non-exhaust related sources such as brake wear. Particles originating from combustion process can be divided to three different sources; 1) primary nanoparticles formed in high temperature, 2) delayed primary particles formed as gaseous compounds nucleate during the cooling and dilution process and 3) secondary nanoparticles formed from gaseous precursors via the atmospheric photochemistry. The nanoparticles observed in roadside environment are a complex mixture of particles from several sources affected by atmospheric processing, local co-pollutants and meteorology.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Research group: The Instrumentation, Emissions, and Atmospheric Aerosols Group, Research area: Aerosol Physics, Finnish Meteorological Institute
Contributors: Rönkkö, T., Timonen, H.
Number of pages: 14
Pages: 15-28
Publication date: 2019
Peer-reviewed: Yes

Publication information
Journal: Journal of Alzheimer's Disease
Volume: 72
Issue number: 1
ISSN (Print): 1387-2877
Ratings:

Scopus rating (2019): CiteScore 6 SJR 1.586 SNIP 1.07
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Clinical Psychology, Geriatrics and Gerontology, Psychiatry and Mental health
Keywords: Air quality, nanoparticles, particle emissions, traffic
Electronic versions:

jad-72-jad190170
DOIs:

10.3233/JAD-190170
URLs:

http://urn.fi/URN:NBN:fi:tuni-201911276343
Source: Scopus
Source ID: 85074397884
Research output: Contribution to journal › Article › Scientific › peer-review

Zeffiro User Interface for Electromagnetic Brain Imaging: a GPU Accelerated FEM Tool for Forward and Inverse Computations in Matlab

This article introduces the Zeffiro interface (ZI) version 2.2 for brain imaging. ZI aims to provide a simple, accessible and multimodal open source platform for finite element method (FEM) based and graphics processing unit (GPU) accelerated forward and inverse computations in the Matlab environment. It allows one to (1) generate a given multi-compartment head model, (2) to evaluate a lead field matrix as well as (3) to invert and analyze a given set of measurements. GPU acceleration is applied in each of the processing stages (1)–(3). In its current configuration, ZI includes forward solvers for electro-/magnetoencephalography (EEG) and linearized electrical impedance tomography (EIT) as well as a set of inverse solvers based on the hierarchical Bayesian model (HBM). We report the results of EEG and EIT inversion tests performed with real and synthetic data, respectively, and demonstrate numerically how the inversion parameters affect the EEG inversion outcome in HBM. The GPU acceleration was found to be essential in the generation of the FE mesh and the LF matrix in order to achieve a reasonable computing time. The code package can be extended in the future based on the directions given in this article.

General information
Publication status: E-pub ahead of print
MoE publication type: A1 Journal article-refereed
Organisations: Computing Sciences, Research group: Inverse Problems
Contributors: He, Q., Rezaei, A., Pursiainen, S.
Number of pages: 14
Publication date: 2019
Peer-reviewed: Yes

Publication information
Journal: Neuroinformatics
ISSN (Print): 1539-2791
Ratings:

Scopus rating (2019): CiteScore 8.2 SJR 1.984 SNIP 2.238
Original language: English
ASJC Scopus subject areas: Software, Neuroscience(all), Information Systems
Keywords: Electrical Impedance Tomography (EIT), Electro-/Magnetoencephalography (EEG/MEG), Finite Element Method (FEM), Hierarchical Bayesian Model (HBM), Matlab Interface
Electronic versions:

He2019_Article_ZeffiroUserInterfaceForElectro
DOIs:
10.1007/s12021-019-09436-9
URLs:
http://urn.fi/URN:NBN:fi:tuni-201911296442
Source: Scopus
Source ID: 85074501520
Research output: Contribution to journal › Article › Scientific › peer-review

Cognitive load and metacognitive confidence extraction from pupillary response

Spontaneous pupillary fluctuations are indicative of the cognitive load imposed while doing a task involving memory resources. However, the fluctuations are also dependent on other factors like lighting conditions, uncertainty or the level of confidence while performing the task and so on. This paper aims to separate various components of pupillary response in order to assess the cognitive load and the confidence with which the task is performed. Hybrid decomposition models using ensemble empirical mode decomposition followed by independent component analysis is found to effectively reconstruct the original signal. The variational Mode Decomposition has been used in order to overcome the limitations imposed by empirical mode decomposition. Results show that variational mode decomposition outperforms existing state-of-the-art methods. Further, we attempted to identify the hidden components of pupillary response during cognitive tasks like mental addition and the anagram test. We obtained F_{score} of 0.67 in the detection of cognitive load and F_{score} of 0.99 for the detection of confidence level from the single channel pupil data.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Signal Processing, Tata Consultancy Services India
Contributors: Gavas, R. D., Tripathy, S. R., Chatterjee, D., Sinha, A.
Number of pages: 10
Pages: 325-334
Publication date: 1 Dec 2018
Peer-reviewed: Yes

Publication information

Journal: Cognitive Systems Research
Volume: 52
ISSN (Print): 1389-0417
Ratings:
Scopus rating (2018): CiteScore 1.7 SJR 0.291 SNIP 1.017
Original language: English
ASJC Scopus subject areas: Experimental and Cognitive Psychology, Cognitive Neuroscience, Artificial Intelligence
Keywords: Cognitive load, Confidence level, EEMD, EMD, Eye tracking, ICA, Pupil size, VMD
DOIs:
10.1016/j.cogsys.2018.07.021
Source: Scopus
Source ID: 85050730185
Research output: Contribution to journal › Article › Scientific › peer-review

Assessment of mutation probabilities of KRAS G12 missense mutants and their long-timescale dynamics by atomistic molecular simulations and Markov state modeling

A mutated KRAS protein is frequently observed in human cancers. Traditionally, the oncogenic properties of KRAS missense mutants at position 12 (G12X) have been considered as equal. Here, by assessing the probabilities of occurrence of all KRAS G12X mutations and KRAS dynamics we show that this assumption does not hold true. Instead, our findings revealed an outstanding mutational bias. We conducted a thorough mutational analysis of KRAS G12X mutations and assessed to what extent the observed mutation frequencies follow a random distribution. Unique tissue-specific frequencies are displayed with specific mutations, especially with G12R, which cannot be explained by random probabilities. To clarify the underlying causes for the nonrandom probabilities, we conducted extensive atomistic molecular dynamics simulations (170 μs) to study the differences of G12X mutations on a molecular level. The simulations revealed an allosteric hydrophobic signaling network in KRAS, and that protein dynamics is altered among the G12X mutants and as such differs from the wild-type and is mutation-specific. The shift in long-timescale conformational dynamics was confirmed with Markov state modeling. A G12X mutation was found to modify KRAS dynamics in an allosteric way, which is especially manifested in the switch regions that are responsible for the effector protein binding. The findings provide a basis to understand better the oncogenic properties of KRAS G12X mutants and the consequences of the observed nonrandom frequencies of specific G12X mutations.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Research group: Biological Physics and Soft Matter, University of Eastern Finland, University Hospital Tuebingen, Eberhard-Karls University Tuebingen, University of Helsinki, MEMPHYS-Center for Biomembrane Physics
Contributors: Pantsar, T., Rissanen, S., Dauch, D., Laitinen, T., Vattulainen, I., Poso, A.
Publication date: 10 Sep 2018
Peer-reviewed: Yes

Publication information
Journal: PLoS Computational Biology
Volume: 14
Issue number: 9
Article number: e1006458
ISSN (Print): 1553-734X
Ratings:

Scopus rating (2018): CiteScore 7.2 SJR 2.949 SNIP 1.408
Original language: English
ASJC Scopus subject areas: Ecology, Evolution, Behavior and Systematics, Modelling and Simulation, Ecology, Molecular Biology, Genetics, Cellular and Molecular Neuroscience, Computational Theory and Mathematics
Electronic versions:

journal.pcbi.1006458-1
DOIs:

10.1371/journal.pcbi.1006458
URLs:

http://urn.fi/URN:NBN:fi:tty-201811012526
Source: Scopus
Source ID: 85054571349
Research output: Contribution to journal › Article › Scientific › peer-review

Improving efficiency in convolutional neural networks with multilinear filters
The excellent performance of deep neural networks has enabled us to solve several automatization problems, opening an era of autonomous devices. However, current deep net architectures are heavy with millions of parameters and require billions of floating point operations. Several works have been developed to compress a pre-trained deep network to reduce memory footprint and, possibly, computation. Instead of compressing a pre-trained network, in this work, we propose a generic neural network layer structure employing multilinear projection as the primary feature extractor. The proposed architecture requires several times less memory as compared to the traditional Convolutional Neural Networks (CNN), while inherits the similar design principles of a CNN. In addition, the proposed architecture is equipped with two computation schemes that enable computation reduction or scalability. Experimental results show the effectiveness of our compact projection that outperforms traditional CNN, while requiring far fewer parameters.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Signal Processing, Aarhus Universitet
Contributors: Tran, D. T., Iosifidis, A., Gabbouj, M.
Number of pages: 12
Pages: 328-339
Publication date: 1 Sep 2018
Peer-reviewed: Yes

Publication information
Journal: Neural Networks
Volume: 105
ISSN (Print): 0893-6080
Ratings:

Scopus rating (2018): CiteScore 13.3 SJR 1.97 SNIP 3.865
Original language: English
ASJC Scopus subject areas: Cognitive Neuroscience, Artificial Intelligence
Keywords: Convolutional neural networks, Multilinear projection, Network compression
DOIs:

10.1016/j.neunet.2018.05.017

Bibliographical note

INT=sgn,"Tran, Dat Thanh"
Source: Scopus
Source ID: 85048580936
Research output: Contribution to journal › Article › Scientific › peer-review

Negatively Charged Gangliosides Promote Membrane Association of Amphipathic Neurotransmitters

Lipophilic neurotransmitters (NTs) such as dopamine are chemical messengers enabling neurotransmission by adhering onto the extracellular surface of the post-synaptic membrane in a synapse, followed by binding to their receptors. Previous studies have shown that the strength of the NT–membrane association is dependent on the lipid composition of the membrane. Negatively charged lipids such as phosphatidylserine, phosphatidylglycerol, and phosphatidic acid have been indicated to promote NT–membrane binding, however these anionic lipids reside almost exclusively in the intracellular leaflet of the post-synaptic membrane instead of the extracellular leaflet facing the synaptic cleft. Meanwhile, the extracellular leaflet is relatively rich in biologically relevant anionic gangliosides such as monosialotetrahexosylganglioside (GM1), yet the role of gangliosides in NT–membrane association is not clear. Here, we explored the role of GM1 in modulating the binding of dopamine and histamine (as amphipathic/cationic NTs) as well as acetylcholine (as a hydrophilic/cationic NT) with the post-synaptic membrane surface. Atomistic molecular dynamics simulations and free energy calculations indicated that GM1 fosters membrane association of histamine and dopamine. For acetylcholine, this effect was not observed. The in silico results suggest that gangliosides form a charge-based vestibule in front of the post-synaptic membrane, attracting amphipathic NTs to the vicinity of the membrane. The results also stress the importance to understand the significance of the structural details of NTs, as exemplified by the GM1–acetylcholine interaction. In a larger context, the NT–membrane adherence, coupled to lateral diffusion in the membrane plane, is proposed to improve neurotransmission efficiency by advancing NT entry into the membrane-embedded ligand-binding sites.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Computational Bioscience Laboratory, University of Jyvaskyla, University of Helsinki, MEMPHYS − Center for Biomembrane Physics
Contributors: Juhola, H., Postila, P. A., Rissanen, S., Lolicato, F., Vattulainen, I., Róg, T.
Number of pages: 10
Pages: 214-223
Publication date: 1 Aug 2018
Peer-reviewed: Yes

Publication information

Journal: Neuroscience
Volume: 384
ISSN (Print): 0306-4522
Ratings:

Scopus rating (2018): CiteScore 6.5 SJR 1.484 SNIP 1.021
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: acetylcholine, cholesterol, dopamine, histamine, molecular dynamics (MD), monosialotetrahexosylganglioside (GM1)
DOIs:

10.1016/j.neuroscience.2018.05.035

Bibliographical note

EXT="Postila, Pekka A."
Source: Scopus
Source ID: 85048589279
Research output: Contribution to journal › Article › Scientific › peer-review

Epileptiform and periodic EEG activities induced by rapid sevoflurane anaesthesia induction

Objectives: The aim of the study was to compare the EEG findings and haemodynamic parameters of adult male patients while undergoing mask induction with sevoflurane anaesthesia with either controlled hyperventilation (CH) or spontaneous breathing (SB). Methods: Twenty male patients, aged 23–52 (mean 42) years were anaesthetized randomly with either spontaneous breathing or mild controlled hyperventilation via mask. EEG was recorded using a full 10–20 electrode set. Results: Anaesthesia induction with high inhaled concentrations of sevoflurane produced several epileptiform and periodic EEG patterns. CH doubled the amount of these EEG patterns compared to SB. Higher heart rate was recorded in the CH group. Conclusions: We describe a high incidence of paroxysmal EEG activity: epileptiform and generalized periodic discharges (GPDs) during rapid sevoflurane in nitrous oxide-oxygen mask induction in hyperventilated male patients. However these activities have no effect to the heart rate or the mean arterial pressure. Significance: The monitoring of GPDs and burst suppression patterns during rapid anaesthesia induction with sevoflurane provides possibility to study the effects of volatile anaesthetics in the healthy brain. In order to analyse the different sources of EEG patterns a wide-band

multichannel EEG recording is necessary.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Faculty of Biomedical Sciences and Engineering, Oulu University Hospital, Department of Clinical Neurophysiology, Central Hospital of Seinäjoki
Contributors: Sonkajärvi, E., Rytky, S., Alahuhta, S., Suominen, K., Kumpulainen, T., Ohtonen, P., Karvonen, E., Jäntti, V.
Number of pages: 8
Pages: 638-645
Publication date: 1 Mar 2018
Peer-reviewed: Yes

Publication information
Journal: Clinical Neurophysiology
Volume: 129
Issue number: 3
ISSN (Print): 1388-2457
Ratings:

Scopus rating (2018): CiteScore 7.1 SJR 1.634 SNIP 1.397
Original language: English
ASJC Scopus subject areas: Sensory Systems, Neurology, Clinical Neurology, Physiology (medical)
Keywords: Anaesthesia, Burst-suppression, EEG, Epileptiform, GPD, Sevoflurane
DOIs:

10.1016/j.clinph.2017.12.037
Source: Scopus
Source ID: 85041455621
Research output: Contribution to journal › Article › Scientific › peer-review

Nonlinear recurrent neural networks for finite-time solution of general time-varying linear matrix equations
In order to solve general time-varying linear matrix equations (LMEs) more efficiently, this paper proposes two nonlinear recurrent neural networks based on two nonlinear activation functions. According to Lyapunov theory, such two nonlinear recurrent neural networks are proved to be convergent within finite-time. Besides, by solving differential equation, the upper bounds of the finite convergence time are determined analytically. Compared with existing recurrent neural networks, the proposed two nonlinear recurrent neural networks have a better convergence property (i.e., the upper bound is lower), and thus the accurate solutions of general time-varying LMEs can be obtained with less time. At last, various different situations have been considered by setting different coefficient matrices of general time-varying LMEs and a great variety of computer simulations (including the application to robot manipulators) have been conducted to validate the better finite-time convergence of the proposed two nonlinear recurrent neural networks.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Signal Processing, Research group: Vision, Jishou University, The Hong Kong Polytechnic University
Contributors: Xiao, L., Liao, B., Li, S., Chen, K.
Number of pages: 12
Pages: 102-113
Publication date: Feb 2018
Peer-reviewed: Yes
Early online date: 2 Dec 2017

Publication information
Journal: Neural Networks
Volume: 98
ISSN (Print): 0893-6080
Ratings:

Scopus rating (2018): CiteScore 13.3 SJR 1.97 SNIP 3.865
Original language: English
ASJC Scopus subject areas: Cognitive Neuroscience, Artificial Intelligence
Keywords: Finite-time convergence, General time-varying linear matrix equations, Nonlinear activation functions, Nonlinear recurrent neural networks
DOIs:

10.1016/j.neunet.2017.11.011
Source: Scopus
Source ID: 85037702750

Research output: Contribution to journal › Article › Scientific › peer-review

A Primal Neural Network for Online Equality-Constrained Quadratic Programming

This paper aims at solving online equality-constrained quadratic programming problem, which is widely encountered in science and engineering, e.g., computer vision and pattern recognition, digital signal processing, and robotics. Recurrent neural networks such as conventional GradientNet and ZhangNet are considered as powerful solvers for such a problem in light of its high computational efficiency and capability of circuit realisation. In this paper, an improved primal recurrent neural network and its electronic implementation are proposed and analysed. Compared to the existing recurrent networks, i.e. GradientNet and ZhangNet, our network can theoretically guarantee superior global exponential convergence. Robustness performance of our such neural model is also analysed under a large model implementation error, with the upper bound of stead-state solution error estimated. Simulation results demonstrate theoretical analysis on the proposed model, which also verify the effectiveness of the proposed model for online equality-constrained quadratic programming.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Signal Processing, Research group: Vision, Shanghai Institute of Ceramics Chinese Academy of Sciences , Institute of Automation Chinese Academy of Sciences
Contributors: Chen, K., Zhang, Z.
Number of pages: 8
Pages: 381–388
Publication date: 2018
Peer-reviewed: Yes

Publication information

Journal: Cognitive Computation
Volume: 10
Issue number: 2
ISSN (Print): 1866-9956
Ratings:

Scopus rating (2018): CiteScore 7.1 SJR 1.06 SNIP 1.965
Original language: English
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Computer Science Applications, Cognitive Neuroscience
Keywords: Global exponential convergence, Online equality-constrained quadratic programming, Recurrent neural networks, Robustness analysis
DOIs:

10.1007/s12559-017-9510-4
Source: Scopus
Source ID: 85030320446
Research output: Contribution to journal › Article › Scientific › peer-review

MetrIntMeas a novel metric for measuring the intelligence of a swarm of cooperating agents

We propose a novel metric called MetrIntMeas (Metric for the Intelligence Measuring) for an accurate and robust measurement of the difficult problem-solving intelligence of a swarm system. The metric allows the classification if a swarm system belongs to the same class with the systems which have a specific reference intelligence value. For proving the efficiency of the proposed metric we realized a case study on a swarm system specialized in solving a NP-hard problem. As an application of the proposed metric, we present the measurement of the swarm systems' evolution in intelligence. We gave a new definition to the intelligent evolving systems. The evolution of intelligent systems can be verified using the proposed MetrIntMeas metric.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Computational Medicine and Statistical Learning Laboratory (CMSL), Research group: Predictive Society and Data Analytics (PSDA), Petru Maior University of Tirgu Mures, Istanbul University
Contributors: Iantovics, L. B., Emmert-Streib, F., Arik, S.
Number of pages: 13
Pages: 17-29
Publication date: 1 Oct 2017
Peer-reviewed: Yes

Publication information

Journal: Cognitive Systems Research
Volume: 45
ISSN (Print): 1389-0417
Ratings:

Scopus rating (2017): CiteScore 2.3 SJR 0.303 SNIP 1.159
Original language: English
ASJC Scopus subject areas: Experimental and Cognitive Psychology, Cognitive Neuroscience, Artificial Intelligence
Keywords: Cognitive system, Collective intelligence, Computational hard problem, Intelligent evolving system, Intelligent system, Measuring machine intelligence
DOIs:

10.1016/j.cogsys.2017.04.006
Source: Scopus
Source ID: 85019885587
Research output: Contribution to journal › Article › Scientific › peer-review

Concerted regulation of npc2 binding to endosomal/lysosomal membranes by bis(monoacylglycero)phosphate and sphingomyelin

Niemann-Pick Protein C2 (npc2) is a small soluble protein critical for cholesterol transport within and from the lysosome and the late endosome. Intriguingly, npc2-mediated cholesterol transport has been shown to be modulated by lipids, yet the molecular mechanism of npc2-membrane interactions has remained elusive. Here, based on an extensive set of atomistic simulations and free energy calculations, we clarify the mechanism and energetics of npc2-membrane binding and characterize the roles of physiologically relevant key lipids associated with the binding process. Our results capture in atomistic detail two competitively favorable membrane binding orientations of npc2 with a low interconversion barrier. The first binding mode (Prone) places the cholesterol binding pocket in direct contact with the membrane and is characterized by membrane insertion of a loop (V59-M60-G61-I62-P63-V64-P65). This mode is associated with cholesterol uptake and release. On the other hand, the second mode (Supine) places the cholesterol binding pocket away from the membrane surface, but has overall higher membrane binding affinity. We determined that bis(monoacylglycero)phosphate (bmp) is specifically required for strong membrane binding in Prone mode, and that it cannot be substituted by other anionic lipids. Meanwhile, sphingomyelin counteracts bmp by hindering Prone mode without affecting Supine mode. Our results provide concrete evidence that lipids modulate npc2-mediated cholesterol transport either by favoring or disfavoring Prone mode and that they impose this by modulating the accessibility of bmp for interacting with npc2. Overall, we provide a mechanism by which npc2-mediated cholesterol transport is controlled by the membrane composition and how npc2-lipid interactions can regulate the transport rate.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Research group: Biological Physics and Soft Matter, University of Helsinki, FIN-00014 University of Helsinki, Minerva Foundation Institute for Medical Research Helsinki, Memphys—Center for Biomembrane Physics, Laboratory of Physics
Contributors: Enkavi, G., Mikkolainen, H., Güngör, B., Ikonen, E., Vattulainen, I.
Publication date: 1 Oct 2017
Peer-reviewed: Yes

Publication information

Journal: PLoS Computational Biology
Volume: 13
Issue number: 10
Article number: e1005831
ISSN (Print): 1553-734X
Ratings:

Scopus rating (2017): CiteScore 7.8 SJR 3.097 SNIP 1.374
Original language: English
ASJC Scopus subject areas: Ecology, Evolution, Behavior and Systematics, Modelling and Simulation, Ecology, Molecular Biology, Genetics, Cellular and Molecular Neuroscience, Computational Theory and Mathematics
Electronic versions:

full text
DOIs:

10.1371/journal.pcbi.1005831
URLs:

http://urn.fi/URN:NBN:fi:tty-201711202175

Bibliographical note

INT=fys,"Mikkolainen, Heikki"
Source: Scopus
Source ID: 85032730334
Research output: Contribution to journal › Article › Scientific › peer-review

Inhibition of Aβ Amyloid Growth and Toxicity by Silybins: The Crucial Role of Stereochemistry

The self-assembling of the amyloid β (Aβ) peptide into neurotoxic aggregates is considered a central event in the pathogenesis of Alzheimer's disease (AD). Based on the "amyloid hypothesis", many efforts have been devoted to designing molecules able to halt disease progression by inhibiting Aβ self-assembly. Here, we combine biophysical (ThT assays, TEM and AFM imaging), biochemical (WB and ESI-MS), and computational (all-atom molecular dynamics) techniques to investigate the capacity of four optically pure components of the natural product silymarin (silybin A, silybin B, 2,3-dehydrosilybin A, 2,3-dehydrosilybin B) to inhibit Aβ aggregation. Despite TEM analysis demonstrated that all the four investigated flavonoids prevent the formation of mature fibrils, ThT assays, WB and AFM investigations showed that only silybin B was able to halt the growth of small-sized protofibrils thus promoting the formation of large, amorphous aggregates. Molecular dynamics (MD) simulations indicated that silybin B interacts mainly with the C-terminal hydrophobic segment ^{35}MVGGVV^{40} of Aβ40. Consequently to silybin B binding, the peptide conformation remains predominantly unstructured along all the simulations. By contrast, silybin A interacts preferentially with the segments ^{17}LVFF^{20} and ^{27}NKGAII^{32} of Aβ40 which shows a high tendency to form bend, turn, and β-sheet conformation in and around these two domains. Both 2,3-dehydrosilybin enantiomers bind preferentially the segment ^{17}LVFF^{20} but lead to the formation of different small-sized, ThT-positive Aβ aggregates. Finally, in vivo studies in a transgenic Caenorhabditis elegans strain expressing human Aβ indicated that silybin B is the most effective of the four compounds in counteracting Aβ proteotoxicity. This study underscores the pivotal role of stereochemistry in determining the neuroprotective potential of silybins and points to silybin B as a promising lead compound for further development in anti-AD therapeutics.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Centro S3, ENEA/CREATE/Università Degli Studi Napoli Federico II, STMicroelectronics, Università degli Studi di Catania, IRCCS-Istituto di Ricerche Farmacologiche Mario Negri
Contributors: Sciacca, M. F., Romanucci, V., Zarrelli, A., Monaco, I., Lolicato, F., Spinella, N., Galati, C., Grasso, G., D'Urso, L., Romeo, M., Diomede, L., Salmona, M., Bongiorno, C., Di Fabio, G., La Rosa, C., Milardi, D.
Number of pages: 12
Pages: 1767-1778
Publication date: 16 Aug 2017
Peer-reviewed: Yes

Publication information

Journal: ACS Chemical Neuroscience
Volume: 8
Issue number: 8
ISSN (Print): 1948-7193
Ratings:

Scopus rating (2017): CiteScore 5.9 SJR 1.442 SNIP 0.991
Original language: English
ASJC Scopus subject areas: Physiology, Biochemistry, Cognitive Neuroscience, Cell Biology
Keywords: Alzheimer's disease, Chiral drugs, natural compounds, neurodegeneration, neuroprotection
DOIs:

10.1021/acschemneuro.7b00110
Source: Scopus
Source ID: 85027418392
Research output: Contribution to journal › Article › Scientific › peer-review

Measures of spike train synchrony for data with multiple time scales

Background Measures of spike train synchrony are widely used in both experimental and computational neuroscience. Time-scale independent and parameter-free measures, such as the ISI-distance, the SPIKE-distance and SPIKE-synchronization, are preferable to time scale parametric measures, since by adapting to the local firing rate they take into account all the time scales of a given dataset. New method In data containing multiple time scales (e.g. regular spiking and bursts) one is typically less interested in the smallest time scales and a more adaptive approach is needed. Here we propose the A-ISI-distance, the A-SPIKE-distance and A-SPIKE-synchronization, which generalize the original measures by considering the local relative to the global time scales. For the A-SPIKE-distance we also introduce a rate-independent extension called the RIA-SPIKE-distance, which focuses specifically on spike timing. Results The adaptive generalizations A-ISI-distance and A-SPIKE-distance allow to disregard spike time differences that are not relevant on a more global scale. A-SPIKE-synchronization does not any longer demand an unreasonably high accuracy for spike doublets and coinciding bursts. Finally, the RIA-SPIKE-distance proves to be independent of rate ratios between spike trains. Comparison with existing methods We find that compared to the original versions the A-ISI-distance and the A-SPIKE-

distance yield improvements for spike trains containing different time scales without exhibiting any unwanted side effects in other examples. A-SPIKE-synchronization matches spikes more efficiently than SPIKE-synchronization. Conclusions With these proposals we have completed the picture, since we now provide adaptive generalized measures that are sensitive to firing rate only (A-ISI-distance), to timing only (ARI-SPIKE-distance), and to both at the same time (A-SPIKE-distance).

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Faculty of Biomedical Sciences and Engineering, BioMediTech, Vrije Universiteit Amsterdam, Centro S3, Universitat Pompeu Fabra, Radboud University Nijmegen, Technische Universität Dresden
Contributors: Satuvuori, E., Mulansky, M., Bozanic, N., Malvestio, I., Zeldenrust, F., Lenk, K., Kreuz, T.
Number of pages: 14
Pages: 25-38
Publication date: 1 Aug 2017
Peer-reviewed: Yes

Publication information

Journal: Journal of Neuroscience Methods
Volume: 287
ISSN (Print): 0165-0270
Ratings:

Scopus rating (2017): CiteScore 5.4 SJR 1.242 SNIP 1.028
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Burst, Data analysis, ISI-distance, Spike train distances, SPIKE-distance, SPIKE-synchronization, Time-scale
Electronic versions:

Measures of spike train synchrony for data with multiple time scales
DOIs:

10.1016/j.jneumeth.2017.05.028
URLs:

http://urn.fi/URN:NBN:fi:tty-201707311637
Source: Scopus
Source ID: 85020727117
Research output: Contribution to journal › Article › Scientific › peer-review

Atomistic fingerprint of hyaluronan–CD44 binding

Hyaluronan is a polyanionic, megadalton-scale polysaccharide, which initiates cell signaling by interacting with several receptor proteins including CD44 involved in cell-cell interactions and cell adhesion. Previous studies of the CD44 hyaluronan binding domain have identified multiple widespread residues to be responsible for its recognition capacity. In contrast, the X-ray structural characterization of CD44 has revealed a single binding mode associated with interactions that involve just a fraction of these residues. In this study, we show through atomistic molecular dynamics simulations that hyaluronan can bind CD44 with three topographically different binding modes that in unison define an interaction fingerprint, thus providing a plausible explanation for the disagreement between the earlier studies. Our results confirm that the known crystallographic mode is the strongest of the three binding modes. The other two modes represent metastable configurations that are readily available in the initial stages of the binding, and they are also the most frequently observed modes in our unbiased simulations. We further discuss how CD44, fostered by the weaker binding modes, diffuses along HA when attached. This 1D diffusion combined with the constrained relative orientation of the diffusing proteins is likely to influence the aggregation kinetics of CD44. Importantly, CD44 aggregation has been suggested to be a possible mechanism in CD44-mediated signaling.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Research group: Biological Physics and Soft Matter, University of Helsinki, MEMPHYS - Centre for Biomembrane Physics, University of Southern Denmark, Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
Contributors: Vuorio, J., Vattulainen, I., Martinez-Seara, H.
Publication date: 1 Jul 2017
Peer-reviewed: Yes

Publication information

Journal: PLoS Computational Biology
Volume: 13
Issue number: 7

Article number: e1005663
ISSN (Print): 1553-734X
Ratings:

Scopus rating (2017): CiteScore 7.8 SJR 3.097 SNIP 1.374
Original language: English
ASJC Scopus subject areas: Ecology, Evolution, Behavior and Systematics, Modelling and Simulation, Ecology, Molecular Biology, Genetics, Cellular and Molecular Neuroscience, Computational Theory and Mathematics
Electronic versions:

Atomistic fingerprint of hyaluronan±CD44
DOIs:

10.1371/journal.pcbi.1005663
URLs:

http://urn.fi/URN:NBN:fi:tty-201708291838
Source: Scopus
Source ID: 85026671290
Research output: Contribution to journal › Article › Scientific › peer-review

Calcium Assists Dopamine Release by Preventing Aggregation on the Inner Leaflet of Presynaptic Vesicles
In this study, the dopamine-lipid bilayer interactions were probed with three physiologically relevant ion compositions using atomistic molecular dynamics simulations and free energy calculations. The in silico results indicate that calcium is able to decrease significantly the binding of dopamine to a neutral (zwitterionic) phosphatidylcholine lipid bilayer model mimicking the inner leaflet of a presynaptic vesicle. We argue that the observed calcium-induced effect is likely in crucial role in the neurotransmitter release from the presynaptic vesicles docked in the active zone of nerve terminals. The inner leaflets of presynaptic vesicles, which are responsible for releasing neurotransmitters into the synaptic cleft, are mainly composed of neutral lipids such as phosphatidylcholine and phosphatidylethanolamine. The neutrality of the lipid head group region, enhanced by a low pH level, should limit membrane aggregation of transmitters. In addition, the simulations suggest that the high calcium levels inside presynaptic vesicles prevent even the most lipophilic transmitters such as dopamine from adhering to the inner leaflet surface, thus rendering unhindered neurotransmitter release feasible.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Physics, Research group: Biological Physics and Soft Matter, Structural Bioinformatics Laboratory, Abo Akad Univ, Abo Akademi University, Dept Phys, University of Helsinki, MEMPHYS, University of Southern Denmark
Contributors: Mokkila, S., Postila, P. A., Rissanen, S., Juhola, H., Vattulainen, I., Róg, T.
Number of pages: 9
Pages: 1242-1250
Publication date: 21 Jun 2017
Peer-reviewed: Yes

Publication information
Journal: ACS Chemical Neuroscience
Volume: 8
Issue number: 6
ISSN (Print): 1948-7193
Ratings:

Scopus rating (2017): CiteScore 5.9 SJR 1.442 SNIP 0.991
Original language: English
ASJC Scopus subject areas: Physiology, Biochemistry, Cognitive Neuroscience, Cell Biology
Keywords: binding free energy, dopamine, molecular dynamics simulations, neurotransmitter release, phosphatidylcholine , presynaptic vesicle, Synaptic neurotransmission
DOIs:

10.1021/acschemneuro.6b00395

Bibliographical note
INT=fys,"Mokkila, Sini"
EXT="Postila, Pekka A."
Source: Scopus
Source ID: 85021076435
Research output: Contribution to journal › Article › Scientific › peer-review

CNN-based edge filtering for object proposals
Recent advances in image-based object recognition have exploited object proposals to speed up the detection process by reducing the search space. In this paper, we present a novel idea that utilizes true objectness and semantic image filtering

(retrieved within the convolutional layers of a Convolutional Neural Network) to propose effective region proposals. Information learned in fully convolutional layers is used to reduce the number of proposals and enhance their localization by producing highly accurate bounding boxes. The greatest benefit of our method is that it can be integrated into any existing approach exploiting edge-based objectness to achieve consistently high recall across various intersection over union thresholds. Experiments on PASCAL VOC 2007 and ImageNet datasets demonstrate that our approach improves two existing state-of-the-art models with significantly high margins and pushes the boundaries of object proposal generation.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Signal Processing, Research group: Multimedia Research Group - MRG, Aarhus Universitet
Contributors: Waris, M. A., Iosifidis, A., Gabbouj, M.
Pages: 631-640
Publication date: 2 Jun 2017
Peer-reviewed: Yes

Publication information
Journal: Neurocomputing
Volume: 266
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2017): CiteScore 6.4 SJR 1.073 SNIP 1.56
Original language: English
ASJC Scopus subject areas: Computer Science Applications, Cognitive Neuroscience, Artificial Intelligence
Keywords: Deep learning, Neural networks, Object detection, Object proposals, Region of interest
DOIs:

10.1016/j.neucom.2017.05.071
Source: Scopus
Source ID: 85020766935
Research output: Contribution to journal › Article › Scientific › peer-review

Network-wide adaptive burst detection depicts neuronal activity with improved accuracy
Neuronal networks are often characterized by their spiking and bursting statistics. Previously, we introducedan adaptive burst analysis methodwhich enhances the analysis power for neuronal networks with highly varying firing dynamics. The adaptation is based on single channels analyzing each element of a network separately. Such kind of analysis was adequate for the assessment of local behavior, where the analysis focuses on the neuronal activity in the vicinity of a single electrode. However, the assessment of the whole network may be hampered, if parts of the network are analyzed using different rules. Here, we test how using multiple channels and measurement time points affect adaptive burst detection. The main emphasis is, if network-wide adaptive burst detection can provide new insights into the assessment of network activity. Therefore, we propose a modification to the previously introduced inter-spike interval (ISI) histogram based cumulative moving average (CMA) algorithm to analyze multiple spike trains simultaneously. The network size can be freely defined, e.g., to include all the electrodes in a microelectrode array (MEA) recording. Additionally, the method can be applied on a series of measurements on the same network to pool the data for statistical analysis. Firstly, we apply both the original CMA-algorithm and our proposed network-wide CMA-algorithm on artificial spike trains to investigate how the modification changes the burst detection. Thereafter, we use the algorithms on MEA data of spontaneously active chemically manipulated in vitro rat cortical networks. Moreover, we compare the synchrony of the detected bursts introducing a new burst synchrony measure. Finally, we demonstrate howthe bursting statistics can be used to classify networks by applying k-means clustering to the bursting statistics. The results showthat the proposed network wide adaptive burst detection provides a method to unify the burst definition in the whole network and thus improves the assessment and classification of the neuronal activity, e.g., the effects of different pharmaceuticals. The results indicate that the novel method is adaptive enough to be usable on networks with different dynamics, and it is especially feasible when comparing the behavior of differently spiking networks, for example in developing networks.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Faculty of Biomedical Sciences and Engineering, Pervasive Computing, Research group: Computational Biophysics and Imaging Group, Jyväskylän yliopisto
Contributors: Välkki, I. A., Lenk, K., Mikkonen, J. E., Kapucu, F. E., Hyttinen, J. A.
Publication date: 31 May 2017
Peer-reviewed: Yes

Publication information
Journal: Frontiers in Computational Neuroscience

Volume: 11
Article number: 40
ISSN (Print): 1662-5188
Ratings:
Scopus rating (2017): CiteScore 3.9 SJR 1.08 SNIP 0.832
Original language: English
ASJC Scopus subject areas: Neuroscience (miscellaneous), Cellular and Molecular Neuroscience
Keywords: Burst detection, Burst synchrony, Microelectrode arrays, Network classification, Neuronal networks
Electronic versions:
fncom-11-00040
DOIs:
10.3389/fncom.2017.00040
URLs:
http://urn.fi/URN:NBN:fi:tty-201709061867

Bibliographical note

EXT="Mikkonen, Jarno E."
Source: Scopus
Source ID: 85027575757
Research output: Contribution to journal › Article › Scientific › peer-review

Functional brain segmentation using inter-subject correlation in fMRI

The human brain continuously processes massive amounts of rich sensory information. To better understand such highly complex brain processes, modern neuroimaging studies are increasingly utilizing experimental setups that better mimic daily-life situations. A new exploratory data-analysis approach, functional segmentation inter-subject correlation analysis (FuSeISC), was proposed to facilitate the analysis of functional magnetic resonance (fMRI) data sets collected in these experiments. The method provides a new type of functional segmentation of brain areas, not only characterizing areas that display similar processing across subjects but also areas in which processing across subjects is highly variable. FuSeISC was tested using fMRI data sets collected during traditional block-design stimuli (37 subjects) as well as naturalistic auditory narratives (19 subjects). The method identified spatially local and/or bilaterally symmetric clusters in several cortical areas, many of which are known to be processing the types of stimuli used in the experiments. The method is not only useful for spatial exploration of large fMRI data sets obtained using naturalistic stimuli, but also has other potential applications, such as generation of a functional brain atlases including both lower- and higher-order processing areas. Finally, as a part of FuSeISC, a criterion-based sparsification of the shared nearest-neighbor graph was proposed for detecting clusters in noisy data. In the tests with synthetic data, this technique was superior to well-known clustering methods, such as Ward's method, affinity propagation, and K-means ++. Hum Brain Mapp 38:2643–2665, 2017.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Signal Processing, Department of Mathematical Information Technology, Jyväskylän yliopisto, University of Helsinki, VTT Technical Research Centre of Finland, Aalto University, AI Virtanen Institute for Molecular Sciences, Ita-Suomen yliopisto
Contributors: Kauppi, J., Pajula, J., Niemi, J., Hari, R., Tohka, J.
Number of pages: 23
Pages: 2643-2665
Publication date: 1 May 2017
Peer-reviewed: Yes

Publication information

Journal: Human Brain Mapping
Volume: 38
Issue number: 5
ISSN (Print): 1065-9471
Ratings:
Scopus rating (2017): CiteScore 9.5 SJR 2.664 SNIP 1.413
Original language: English
ASJC Scopus subject areas: Anatomy, Radiological and Ultrasound Technology, Radiology Nuclear Medicine and imaging , Neurology, Clinical Neurology
Keywords: functional magnetic resonance imaging, functional segmentation, Gaussian mixture model, human brain, inter-subject correlation, inter-subject variability, naturalistic stimulation, shared nearest-neighbor graph
DOIs:
10.1002/hbm.23549

Bibliographical note
EXT="Kauppi, Jukka-Pekka"
INT=sgn,"Niemi, Jari"
EXT="Tohka, Jussi"
Source: Scopus
Source ID: 85015094854
Research output: Contribution to journal › Article › Scientific › peer-review

Cell culture chamber with gas supply for prolonged recording of human neuronal cells on microelectrode array
Background Typically, live cell analyses are performed outside an incubator in an ambient air, where the lack of sufficient CO_2 supply results in a fast change of pH and the high evaporation causes concentration drifts in the culture medium. That limits the experiment time for tens of minutes. In many applications, e.g. in neurotoxicity studies, a prolonged measurement of extracellular activity is, however, essential. New method We demonstrate a simple cell culture chamber that enables stable culture conditions during prolonged extracellular recordings on a microelectrode array (MEA) outside an incubator. The proposed chamber consists of a gas permeable silicone structure that enables gas transfer into the chamber. Results We show that the culture chamber supports the growth of the human embryonic stem cell (hESC)-derived neurons both inside and outside an incubator. The structure provides very low evaporation, stable pH and osmolarity, and maintains strong signaling of hESC-derived neuronal networks over three-day MEA experiments. Comparison with existing methods Existing systems are typically complex including continuous perfusion of medium or relatively large amount of gas to supply. The proposed chamber requires only a supply of very low flow rate (1.5 ml/min) of non-humidified 5% CO_2 gas. Utilizing dry gas supply makes the proposed chamber simple to use. Conclusion Using the proposed culture structure on top of MEA, we can maintain hESC-derived neural networks over three days outside an incubator. Technically, the structure requires very low flow rate of dry gas supporting, however, low evaporation and maintaining the pH of the culture.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Faculty of Biomedical Sciences and Engineering, Research area: Microsystems, Research area: Measurement Technology and Process Control
Contributors: Kreutzer, J., Ylä-Outinen, L., Mäki, A., Ristola, M., Narkilahti, S., Kallio, P.
Number of pages: 9
Pages: 27-35
Publication date: 15 Mar 2017
Peer-reviewed: Yes

Publication information
Journal: Journal of Neuroscience Methods
Volume: 280
ISSN (Print): 0165-0270
Ratings:

Scopus rating (2017): CiteScore 5.4 SJR 1.242 SNIP 1.028
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Cell culture environment, Human embryonic stem cells, Long-term culture, MEA, Neuronal cells, Osmolarity, PDMS, pH
Electronic versions:

Manuscript-Kreutzer. Embargo ended: 10/08/18
DOIs:

10.1016/j.jneumeth.2017.01.019
URLs:

http://urn.fi/URN:NBN:fi:tty-201712202441. Embargo ended: 10/08/18
Source: Scopus
Source ID: 85012041450
Research output: Contribution to journal › Article › Scientific › peer-review

Predicting symptom severity in autism spectrum disorder based on cortical thickness measures in agglomerative data
Machine learning approaches have been widely used for the identification of neuropathology from neuroimaging data. However, these approaches require large samples and suffer from the challenges associated with multi-site, multi-protocol data. We propose a novel approach to address these challenges, and demonstrate its usefulness with the Autism Brain Imaging Data Exchange (ABIDE) database. We predict symptom severity based on cortical thickness measurements from 156 individuals with autism spectrum disorder (ASD) from four different sites. The proposed approach consists of two main stages: a domain adaptation stage using partial least squares regression to maximize the consistency of imaging data across sites; and a learning stage combining support vector regression for regional prediction of severity with elastic-net penalized linear regression for integrating regional predictions into a whole-brain severity prediction. The proposed method

performed markedly better than simpler alternatives, better with multi-site than single-site data, and resulted in a considerably higher cross-validated correlation score than has previously been reported in the literature for multi-site data. This demonstration of the utility of the proposed approach for detecting structural brain abnormalities in ASD from the multi-site, multi-protocol ABIDE dataset indicates the potential of designing machine learning methods to meet the challenges of agglomerative data.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Montreal Neurological Institute and Hospital, Universidad Carlos III de Madrid, Instituto de Investigación Sanitaria Gregorio Marañon
Contributors: Moradi, E., Khundrakpam, B., Lewis, J. D., Evans, A. C., Tohka, J.
Pages: 128–141
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: NeuroImage
Volume: 144
Issue number: A
ISSN (Print): 1053-8119
Ratings:

Scopus rating (2017): CiteScore 11.5 SJR 3.679 SNIP 1.814
Original language: English
ASJC Scopus subject areas: Neurology, Cognitive Neuroscience
Keywords: Autism spectrum disorder, Cortical thickness, Domain adaptation, Machine learning, Magnetic resonance imaging
DOIs:

10.1016/j.neuroimage.2016.09.049

Bibliographical note
EXT="Tohka, Jussi"
Source: Scopus
Source ID: 84991258515
Research output: Contribution to journal › Article › Scientific › peer-review

Spinal cord injury induces widespread chronic changes in cerebral white matter
Traumatic spinal cord injuries (SCIs) lead to axonal damage at the trauma site, as well as disconnections within the central nervous system. While the exact mechanisms of the long-term pathophysiological consequences of SCIs are not fully understood, it is known that neuronal damage and degeneration are not limited to the direct proximity of the trauma. Instead, the effects can be detected even in the cerebrum. We examined SCI-induced chronic brain changes with a case-control design using 32 patients and 70 control subjects. Whole-brain white matter (WM) tracts were assessed with diffusion tensor imaging (DTI). In addition, we analysed associations between DTI metrics and several clinical SCI variables. Whole-brain analyses were executed by tract-based spatial statistics (TBSS), with an additional complementary atlas-based analysis (ABA). We observed widespread, statistically significant ($P \leq 0.01$) changes similar to neural degeneration in SCI patients, both in the corticospinal tract (CST) and beyond. In addition, associations between DTI metrics and time since injury were found with TBSS and ABA, implying possible long-term post-injury neural regeneration. Using the ABA approach, we observed a correlation between SCI severity and DTI metrics, indicating a decrease in WM integrity along with patient sensory or motor scores. Our results suggest a widespread neurodegenerative effect of SCI within the cerebrum that is not limited to the motor pathways. Furthermore, DTI-measured WM integrity of chronic SCI patients seemed to improve as time elapsed since injury.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Faculty of Biomedical Sciences and Engineering, Research group: Quantitative medical imaging, Pirkanmaan sairaanhoitopiiri
Contributors: Ilvesmäki, T., Koskinen, E., Brander, A., Luoto, T., Öhman, J., Eskola, H.
Pages: 3637-3647
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: Human Brain Mapping
Volume: 38

Issue number: 7
ISSN (Print): 1065-9471
Ratings:

Scopus rating (2017): CiteScore 9.5 SJR 2.664 SNIP 1.413
Original language: English
ASJC Scopus subject areas: Anatomy, Radiological and Ultrasound Technology, Radiology Nuclear Medicine and imaging , Neurology, Clinical Neurology
Keywords: Cerebrum, Diffusion tensor imaging, Humans, Spinal cord injuries, White matter
DOIs:

10.1002/hbm.23619
Source: Scopus
Source ID: 85018637972
Research output: Contribution to journal › Article › Scientific › peer-review

Advanced boundary electrode modeling for tES and parallel tES/EEG

This paper explores advanced electrode modeling in the context of separate and parallel transcranial electrical stimulation (tES) and electroencephalography (EEG) measurements.We focus on boundary condition based approaches that do not necessitate adding auxiliary elements, e.g. sponges, to the computational domain. In particular, we investigate the complete electrode model (CEM) which incorporates a detailed description of the skin-electrode interface including its contact surface, impedance and normal current distribution. The CEM can be applied for both tES and EEG electrodes which is advantageous when a parallel system is used. In comparison to the CEM, we test two important reduced approaches: the gap model (GAP) and the point electrode model (PEM). We aim to find out the differences of these approaches for a realistic numerical setting based on the stimulation of the auditory cortex. The results obtained suggest, among other things, that GAP and GAP/PEM are sufficiently accurate for the practical application of tES and parallel tES/EEG, respectively. Differences between CEM and GAP were observed mainly in the skin compartment, where only CEM explains the heating effects characteristic to tES.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Mathematics, Research group: Inverse Problems, University of Münster
Contributors: Pursiainen, S., Agsten, B., Wagner, S., Wolters, C. H.
Pages: 37-44
Publication date: 2017
Peer-reviewed: Yes

Publication information

Journal: IEEE Transactions on Neural Systems and Rehabilitation Engineering
Volume: 26
Issue number: 1
ISSN (Print): 1534-4320
Ratings:

Scopus rating (2017): CiteScore 6.7 SJR 1.152 SNIP 2.165
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Biomedical Engineering, Computer Science Applications
Keywords: Boundary conditions, Brain modeling, Complete electrode model (CEM), Computational modeling, Electric potential, Electrodes, Electroencephalography, Electroencephalography (EEG) electrode modeling, Finite element method (FEM)., Skin, Transcranial electrical stimulation (tES)
DOIs:

10.1109/TNSRE.2017.2748930
Source: Scopus
Source ID: 85030762392
Research output: Contribution to journal › Article › Scientific › peer-review

The relationship between recognition memory for emotion-laden words and white matter microstructure in normal older individuals

Functional neuroimaging studies have shown age-related differences in brain activation and connectivity patterns for emotional memory. Previous studies with middle-aged and older adults have reported associations between episodic memory and white matter (WM) microstructure obtained from diffusion tensor imaging, but such studies on emotional memory remain few. To our knowledge, this is the first study to explore associations between WM microstructure as measured by fractional anisotropy (FA) and recognition memory for intentionally encoded positive, negative, and emotionally neutral words using tract-based spatial statistics applied to diffusion tensor imaging images in an elderly sample (44 cognitively intact adults aged 50-79 years). The use of tract-based spatial statistics enables the identification of WM tracts important to emotional memory without a priori assumptions required for region-of-interest approaches that have been used in previous work. The behavioral analyses showed a positivity bias, that is, a preference for positive

words, in recognition memory. No statistically significant associations emerged between FA and memory for negative or neutral words. Controlling for age and memory performance for negative and neutral words, recognition memory for positive words was negatively associated with FA in several projection, association, and commissural tracts in the left hemisphere. This likely reflects the complex interplay between the mnemonic positivity bias, structural WM integrity, and functional brain compensatory mechanisms in older age. Also, the unexpected directionality of the results indicates that the WM microstructural correlates of emotional memory show unique characteristics in normal older individuals.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Electronics and Communications Engineering, BioMediTech
Contributors: Saarela, C., Karrasch, M., Ilvesmäki, T., Parkkola, R., Rinne, J. O., Laine, M.
Number of pages: 5
Pages: 1345-1349
Publication date: 1 Nov 2016
Peer-reviewed: Yes

Publication information
Journal: NeuroReport
Volume: 27
Issue number: 18
ISSN (Print): 0959-4965
Ratings:

Scopus rating (2016): CiteScore 2.5 SJR 0.74 SNIP 0.476
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: diffusion tensor imaging, emotional memory, normal aging, white matter
DOIs:

10.1097/WNR.0000000000000704
Source: Scopus
Source ID: 84995801666
Research output: Contribution to journal › Article › Scientific › peer-review

Effect of rhodopsin phosphorylation on dark adaptation in mouse rods

Rhodopsin is a prototypical G-protein-coupled receptor (GPCR) that is activated when its 11-cis-retinal moiety is photoisomerized to all-trans retinal. This step initiates a cascade of reactions by which rods signal changes in light intensity. Like other GPCRs, rhodopsin is deactivated through receptor phosphorylation and arrestin binding. Full recovery of receptor sensitivity is then achievedwhenrhodopsin is regenerated through a series of steps that return the receptor to its ground state. Here, we show that dephosphorylation of the opsin moiety of rhodopsin is an extremely slow but requisite step in the restoration of the visual pigment to its ground state. We make use of a novel observation: isolated mouse retinae kept in standard media for routine physiologic recordings display blunted dephosphorylation of rhodopsin. Isoelectric focusing followed by Western blot analysis of bleached isolated retinae showed little dephosphorylation of rhodopsin for up to 4 h in darkness, even under conditions when rhodopsin was completely regenerated. Microspectrophotometeric determinations of rhodopsin spectra show that regenerated phospho-rhodopsin has the same molecular photosensitivity as unphosphorylated rhodopsin and that flash responses measured by trans-retinal electroretinogram or single-cell suction electrode recording displayed dark-adapted kinetics. Single quantal responses displayed normal dark-adapted kinetics, but rods were only half as sensitive as those containing exclusively unphosphorylated rhodopsin. We propose a model in which light-exposed retinae contain a mixed population of phosphorylated and unphosphorylated rhodopsin. Moreover, complete dark adaptation can only occur when all rhodopsin has been dephosphorylated, a process that requires >3 h in complete darkness.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Electronics and Communications Engineering, Research group: Computational Biophysics and Imaging Group, Boston University School of Medicine, Keck School of Medicine of USC
Contributors: Berry, J., Frederiksen, R., Yao, Y., Nymark, S., Chen, J., Cornwall, C.
Number of pages: 15
Pages: 6973-6987
Publication date: 29 Jun 2016
Peer-reviewed: Yes

Publication information
Journal: Journal of Neuroscience
Volume: 36

Issue number: 26
ISSN (Print): 0270-6474
Ratings:

Scopus rating (2016): CiteScore 12 SJR 4.849 SNIP 1.617
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Dark adaptation, GPCR, Photoreceptor, Phototransduction, Retina, Rhodopsin
DOIs:

10.1523/JNEUROSCI.3544-15.2016
Source: Scopus
Source ID: 84976512901
Research output: Contribution to journal › Article › Scientific › peer-review

Morphological Differentiation Towards Neuronal Phenotype of SH-SY5Y Neuroblastoma Cells by Estradiol, Retinoic Acid and Cholesterol

Human SH-SY5Y neuroblastoma cells maintain their potential for differentiation and regression in culture conditions. The induction of differentiation could serve as a strategy to inhibit cell proliferation and tumor growth. Previous studies have shown that differentiation of SH-SY5Y cells can be induced by all-trans-retinoic-acid (RA) and cholesterol (CHOL). However, signaling pathways that lead to terminal differentiation of SH-SY5Y cells are still largely unknown. The goal of this study was to examine in the RA and CHOL treated SH-SY5Y cells the additive impacts of estradiol (E_2) and brain-derived neurotrophic factor (BDNF) on cell morphology, cell population growth, synaptic vesicle recycling and presence of neurofilaments. The above features indicate a higher level of neuronal differentiation. Our data show that treatment for 10 days in vitro (DIV) with RA alone or when combined with E_2 (RE) or CHOL (RC), but not when combined with BDNF (RB), significantly ($p < 0.01$) inhibited the cell population growth. Synaptic vesicle recycling, induced by high-K^+ depolarization, was significantly increased in all treatments where RA was included (RE, RC, RB, RCB), and when all agents were added together (RCBE). Specifically, our results show for the first time that E_2 treatment can alone increase synaptic vesicle recycling in SH-SY5Y cells. This work contributes to the understanding of the ways to improve suppression of neuroblastoma cells' population growth by inducing maturation and differentiation.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Research group: Computational Neuro Science-CNS, University of Tampere, St. George's University School of Medicine
Contributors: Teppola, H., Sarkanen, J. R., Jalonen, T. O., Linne, M.
Pages: 731-747
Publication date: 2016
Peer-reviewed: Yes

Publication information

Journal: Neurochemical Research
Volume: 41
Issue number: 4
ISSN (Print): 0364-3190
Ratings:

Scopus rating (2016): CiteScore 4.5 SJR 1.017 SNIP 0.752
Original language: English
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Biochemistry
Keywords: Brain-derived neurotrophic factor, Cholesterol, Differentiation, Estradiol, Retinoic acid, SH-SY5Y
DOIs:

10.1007/s11064-015-1743-6
Source: Scopus
Source ID: 84945586344
Research output: Contribution to journal › Article › Scientific › peer-review

Comparison of Feature Selection Techniques in Machine Learning for Anatomical Brain MRI in Dementia

We present a comparative split-half resampling analysis of various data driven feature selection and classification methods for the whole brain voxel-based classification analysis of anatomical magnetic resonance images. We compared support vector machines (SVMs), with or without filter based feature selection, several embedded feature selection methods and stability selection. While comparisons of the accuracy of various classification methods have been reported previously, the variability of the out-of-training sample classification accuracy and the set of selected features due to independent training and test sets have not been previously addressed in a brain imaging context. We studied two classification problems: 1) Alzheimer's disease (AD) vs. normal control (NC) and 2) mild cognitive impairment (MCI) vs. NC classification. In AD vs. NC classification, the variability in the test accuracy due to the subject sample did not vary between different methods and exceeded the variability due to different classifiers. In MCI vs. NC classification,

particularly with a large training set, embedded feature selection methods outperformed SVM-based ones with the difference in the test accuracy exceeding the test accuracy variability due to the subject sample. The filter and embedded methods produced divergent feature patterns for MCI vs. NC classification that suggests the utility of the embedded feature selection for this problem when linked with the good generalization performance. The stability of the feature sets was strongly correlated with the number of features selected, weakly correlated with the stability of classification accuracy, and uncorrelated with the average classification accuracy.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Research group: Vision, Department of Bioengineering and Aerospace Engineering, Universidad Carlos III de Madrid, Instituto de Investigación Sanitaria Gregorio Marañon
Contributors: Tohka, J., Moradi, E., Huttunen, H., Alzheimer's Disease Neuroimaging Initiative, Alzheimer's Disease Neuroimaging Initiative 2
Number of pages: 18
Pages: 279-296
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Neuroinformatics
Volume: 14
Issue number: 3
ISSN (Print): 1539-2791
Ratings:

Scopus rating (2016): CiteScore 5.4 SJR 1.358 SNIP 1.047
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Information Systems, Software
Keywords: Alzheimer's Disease, Classification, Feature selection, Machine Learning, Magnetic Resonance Imaging, Multivariate pattern analysis
DOIs:

10.1007/s12021-015-9292-3

Bibliographical note
EXT="Tohka, Jussi"
Source: Scopus
Source ID: 84955306208
Research output: Contribution to journal › Article › Scientific › peer-review

How Many Is Enough? Effect of Sample Size in Inter-Subject Correlation Analysis of fMRI
Inter-subject correlation (ISC) is a widely used method for analyzing functional magnetic resonance imaging (fMRI) data acquired during naturalistic stimuli. A challenge in ISC analysis is to define the required sample size in the way that the results are reliable. We studied the effect of the sample size on the reliability of ISC analysis and additionally addressed the following question: How many subjects are needed for the ISC statistics to converge to the ISC statistics obtained using a large sample? The study was realized using a large block design data set of 130 subjects. We performed a split-half resampling based analysis repeatedly sampling two nonoverlapping subsets of 10-65 subjects and comparing the ISC maps between the independent subject sets. Our findings suggested that with 20 subjects, on average, the ISC statistics had converged close to a large sample ISC statistic with 130 subjects. However, the split-half reliability of unthresholded and thresholded ISC maps improved notably when the number of subjects was increased from 20 to 30 or more.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Universidad Carlos III de Madrid
Contributors: Pajula, J., Tohka, J.
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Computational Intelligence and Neuroscience
Volume: 2016
Article number: 2094601
ISSN (Print): 1687-5273
Ratings:

Scopus rating (2016): CiteScore 1.3 SJR 0.295 SNIP 0.89

Original language: English
ASJC Scopus subject areas: Computer Science(all), Mathematics(all), Neuroscience(all)
Electronic versions:

Pajula & Tohka - How Many Is Enough
DOIs:

10.1155/2016/2094601
URLs:

http://urn.fi/URN:NBN:fi:tty-201604293890

Bibliographical note
EXT="Tohka, Jussi"
Source: Scopus
Source ID: 84962632543
Research output: Contribution to journal › Article › Scientific › peer-review

One-Class Classification based on Extreme Learning and Geometric Class Information
In this paper, we propose an extreme learning machine (ELM)-based one-class classification method that exploits geometric class information. We formulate the proposed method to exploit data representations in the feature space determined by the network hidden layer outputs, as well as in ELM spaces of arbitrary dimensions. We show that the exploitation of geometric class information enhances performance. We evaluate the proposed approach in publicly available datasets and compare its performance with the recently proposed one-class extreme learning machine algorithm, as well as with standard and recently proposed one-class classifiers. Experimental results show that the proposed method consistently outperforms the remaining approaches.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Aristotle University of Thessaloniki, Aristotle University of Thessaloniki, Department of Informatics
Contributors: Iosifidis, A., Mygdalis, V., Tefas, A., Pitas, I.
Number of pages: 16
Pages: 1-16
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Neural Processing Letters
ISSN (Print): 1370-4621
Ratings:

Scopus rating (2016): CiteScore 2.6 SJR 0.399 SNIP 0.777
Original language: English
ASJC Scopus subject areas: Software, Neuroscience(all), Computer Networks and Communications, Artificial Intelligence
Keywords: Big data, Extreme learning machine, Novelty detection, One-class classification
DOIs:

10.1007/s11063-016-9541-y

Bibliographical note
EXT="Tefas, Anastasios"
Source: Scopus
Source ID: 84982810055
Research output: Contribution to journal › Article › Scientific › peer-review

Severe cerebral white matter lesions in ischemic stroke patients are associated with less time spent at home and early institutionalization
Background: Cerebral white matter lesions are one imaging surrogate for cerebral small vessel disease. These white matter lesions are associated with increased morbidity and mortality in both the general population and ischemic stroke patients. Aims: To investigate whether severe white matter lesions in a cohort of ischemic stroke patients are associated with fewer days spent at home and earlier permanent institutionalization.Methods: We included 391 consecutive patients aged 55-85 years with ischemic stroke admitted to the Helsinki University Central Hospital (the Stroke Aging Memory cohort) with a 21-year follow-up. Hospitalization and nursing home admissions were reviewed from national registers.white matter lesions were rated using magnetic resonance imaging performed three-months poststroke, dichotomized as none-to-moderate and severe. Kaplan-Meier plots log-rank and binary logistic regression (odds ratio) and Cox multivariable proportional hazards model were used to study the association of white matter lesions with days spent at home and the time of permanent institutionalization. Hazards and odds ratio with their 95% confidence intervals are reported.Results: Severe white matter lesions were associated with fewer days spent at home, and more frequent, and earlier permanent

institutionalization (1487 vs. 2354 days; log-rank P <0·001). After adjusting for significant covariates from univariable analyses, severe white matter lesions were associated with fewer days spent at home (odds ratio 1·62; confidence interval 1·16-2·25), permanent institutionalization within five-years (odds ratio 2·29; confidence interval 1·23-4·29), and increased hazards ratio of permanent institutionalization during 21 years of follow-up (1·64; confidence interval 1·119-2·26).Conclusions: After ischemic stroke, patients with severe white matter lesions spend fewer days at home and become permanently institutionalized earlier, especially within the first five-years.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, Tampere University Hospital
Contributors: Sibolt, G., Curtze, S., Melkas, S., Pohjasvaara, T., Kaste, M., Karhunen, P. J., Oksala, N. K. J., Erkinjuntti, T.
Number of pages: 5
Pages: 1192-1196
Publication date: 1 Dec 2015
Peer-reviewed: Yes

Publication information
Journal: INTERNATIONAL JOURNAL OF STROKE
Volume: 10
Issue number: 8
ISSN (Print): 1747-4930
Ratings:

Scopus rating (2015): CiteScore 4.8 SJR 1.558 SNIP 1.32
Original language: English
ASJC Scopus subject areas: Neurology
Keywords: cerebral small vessel disease, institutionalization, ischemic stroke, white matter lesions
DOIs:

10.1111/ijs.12578
URLs:

http://www.scopus.com/inward/record.url?scp=84954382158&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84954382158
Research output: Contribution to journal › Article › Scientific › peer-review

Eustachian tube mucosal inflammation scale validation based on digital video images
Background: The most common cause for Eustachian tube dilatory dysfunction is mucosal inflammation. The aim of this study was to validate a scale for Eustachian tube mucosal inflammation, based on digital video clips obtained during diagnostic rigid endoscopy. Methods: A previously described four-step scale for grading the degree of inflammation of the mucosa of the Eustachian tube lumen was used for this validation study. A tutorial for use of the scale, including static images and 10 second video clips, was presented to 26 clinicians with various levels of experience. Each clinician then reviewed 35 short digital video samples of Eustachian tubes from patients and rated the degree of inflammation. A subset of the clinicians performed a second rating of the same video clips at a subsequent time. Statistical analysis of the ratings provided inter- and intrarater reliability scores. Results: Twenty-six clinicians with various levels of experience rated a total of 35 videos. Thirteen clinicians rated the videos twice. The overall correlation coefficient for the rating of inflammation severity was relatively good (0.74, 95% confidence interval, 0.72-0.76). The intralevel correlation coefficient for intrarater reliability was high (0.86). For those who rated videos twice, the intralevel correlation coefficient improved after the first rating (0.73, to 0.76), but improvement was not statistically significant. Conclusion: The inflammation scale used for Eustachian tube mucosal inflammation is reliable and this scale can be used with a high level of consistency by clinicians with various levels of experience.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Harvard Medical School, Tampere University Hospital, Helsinki University Central Hospital
Contributors: Kivekäs, I., Pöyhönen, L., Aarnisalo, A., Rautiainen, M., Poe, D.
Number of pages: 5
Pages: 1748-1752
Publication date: 1 Dec 2015
Peer-reviewed: Yes

Publication information
Journal: OTOLOGY AND NEUROTOLOGY

Volume: 36
Issue number: 10
ISSN (Print): 1531-7129
Ratings:

Scopus rating (2015): CiteScore 3.3 SJR 1.381 SNIP 1.373
Original language: English
ASJC Scopus subject areas: Otorhinolaryngology, Sensory Systems, Clinical Neurology
Keywords: Dysfunction, Eustachian Tube, Inflammation scale, Video images
DOIs:

10.1097/MAO.0000000000000895
URLs:

http://www.scopus.com/inward/record.url?scp=84955210475&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84955210475
Research output: Contribution to journal › Article › Scientific › peer-review

Elevated levels of soluble CD26 and CD30 in multiple sclerosis

Objective The activation of autoreactive T cells is a major event in the initiation of autoimmune responses in multiple sclerosis (MS). In addition to the T cell receptor stimulation, optimal activation of T cells requires various costimulatory molecules, such as CD26 and CD30, which has not been extensively studied in MS. Our aim was to explore whether the circulating levels of CD26 and CD30 in sera are associated with MS subtypes, inflammatory disease activity and disability in MS patients. Methods The study included 195 participants: 39 relapsing-remitting MS patients, 19 secondary-progressive MS patients, 19 clinically isolated syndrome patients, 58 controls for sCD26 analysis and 60 for sCD30 analysis. The levels of sCD26 and sCD30 in sera were analyzed using enzyme-linked immunosorbent assay, and the levels of interleukin-10, tumor necrosis factor-α and interferon-γ were analyzed with the Luminex assay. Results We observed increased levels of sCD26 and sCD30 in relapsing-remitting MS, secondary-progressive MS, and clinically isolated syndrome patients compared with the controls ($P < 0.05$). Furthermore, elevated levels of sCD30 were noticed in treated relapsing-remitting MS patients than in untreated patients ($P = 0.016$), and also in converted CIS patients than in unconverted patients ($P = 0.009$). Although sCD26 and sCD30 could not associate with clinical measures, such as the disability score or disease activity, the levels of sCD30 correlated positively with interleukin-10 levels ($r = 0.583$, $P < 0.0001$) and sCD26 levels ($r = 0.262$, $P = 0.046$) in MS patients. Conclusion The present results suggest that the elevated levels of sCD30 are associated with the regulatory immune responses predisposing to clinically stable phase of MS.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), ISLAB Laboratory Centre, Turku University Hospital, Helsinki University Central Hospital, Tampere University Hospital
Contributors: Basnyat, P., Natarajan, R., Vistbakka, J., Lehtikangas, M., Airas, L., Matinlauri, I., Elovaara, I., Hagman, S.
Number of pages: 7
Pages: 419-425
Publication date: 1 Nov 2015
Peer-reviewed: Yes

Publication information

Journal: Clinical and Experimental Neuroimmunology
Volume: 6
Issue number: 4
Ratings:

Scopus rating (2015): CiteScore 0.8 SJR 0.289 SNIP 0.221
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Immunology and Microbiology (miscellaneous) , Neuroscience (miscellaneous), Immunology
Keywords: interleukin-10, multiple sclerosis, sCD26, sCD30
DOIs:

10.1111/cen3.12253
URLs:

http://www.scopus.com/inward/record.url?scp=84955169798&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84955169798
Research output: Contribution to journal › Article › Scientific › peer-review

Human anterior thalamic nuclei are involved in emotion-attention interaction

Patients treated with deep brain stimulation (DBS) provide an opportunity to study affective processes in humans with "lesion on demand" at key nodes in the limbic circuitries, such as at the anterior thalamic nuclei (ANT). ANT has been suggested to play a role in emotional control with its connection to the orbitofrontal cortex and the anterior cingulate cortex. However, direct evidence for its role in emotional function in human subjects is lacking. Reported side effects of ANT-DBS in the treatment of refractory epilepsy include depression related symptoms. In line with these mood-related clinical side effects, we have previously reported that stimulating the anterior thalamus increased emotional interference in a visual attention task as indicated by prolonged reaction times due to threat-related emotional distractors. We used event-related potentials to investigate potential attentional mechanism behind this behavioural observation. We hypothesized that ANT-DBS leads to greater attention capture by threat-related distractors. We tested this hypothesis using centro-parietal N2-P3 peak-to-peak amplitude as a measure of allocated attentional resources. Six epileptic patients treated with deep brain stimulation at ANT participated in the study. Electroencephalography was recorded while the patients performed a computer based Executive-Reaction Time test with threat-related emotional distractors. During the task, either ANT or a thalamic control location was stimulated, or the stimulation was turned off. Stimulation of ANT was associated with increased centro-parietal N2-P3 amplitude and increased reaction time in the context of threat-related emotional distractors. We conclude that high frequency electric stimulation of ANT leads to greater attentional capture by emotional stimuli. This is the first study to provide direct evidence from human subjects with on-line electric manipulation of ANT for its role in emotion-attention interaction.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Tampere University Hospital
Contributors: Sun, L., Peräkylä, J., Polvivaara, M., Öhman, J., Peltola, J., Lehtimäki, K., Huhtala, H., Hartikainen, K. M.
Number of pages: 7
Pages: 88-94
Publication date: 1 Nov 2015
Peer-reviewed: Yes

Publication information

Journal: NEUROPSYCHOLOGIA
Volume: 78
ISSN (Print): 0028-3932
Ratings:

Scopus rating (2015): CiteScore 5.9 SJR 2.054 SNIP 1.137
Original language: English
ASJC Scopus subject areas: Experimental and Cognitive Psychology, Arts and Humanities (miscellaneous), Cognitive Neuroscience, Behavioral Neuroscience
Keywords: Anterior thalamic nuclei, Attention, Deep brain stimulation, EEG, Emotion, Epilepsy
DOIs:

10.1016/j.neuropsychologia.2015.10.001
URLs:

http://www.scopus.com/inward/record.url?scp=84943805450&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84943805450
Research output: Contribution to journal › Article › Scientific › peer-review

Building new computational models to support health behavior change and maintenance: new opportunities in behavioral research

Adverse and suboptimal health behaviors and habits are responsible for approximately 40 % of preventable deaths, in addition to their unfavorable effects on quality of life and economics. Our current understanding of human behavior is largely based on static “snapshots” of human behavior, rather than ongoing, dynamic feedback loops of behavior in response to ever-changing biological, social, personal, and environmental states. This paper first discusses how new technologies (i.e., mobile sensors, smartphones, ubiquitous computing, and cloud-enabled processing/computing) and emerging systems modeling techniques enable the development of new, dynamic, and empirical models of human behavior that could facilitate just-in-time adaptive, scalable interventions. The paper then describes concrete steps to the creation of robust dynamic mathematical models of behavior including: (1) establishing “gold standard” measures, (2) the creation of a behavioral ontology for shared language and understanding tools that both enable dynamic theorizing across disciplines, (3) the development of data sharing resources, and (4) facilitating improved sharing of mathematical models and tools to support rapid aggregation of the models. We conclude with the discussion of what might be incorporated into a “knowledge commons,” which could help to bring together these disparate activities into a unified system and structure for organizing knowledge about behavior.

General information

Publication status: Published

MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Research group: Personal Health Informatics-PHI, Research Community on Data-to-Decision (D2D), University of Southern California, Arizona State University, Northeastern University, National Institutes of Health, Bethesda, Northwestern University, Wharton School, University of Pennsylvania, Scientific Institute Hospital San Raffaelle, Valencia Polytechnical University, Columbia University in the City of New York, VTT Technical Research Centre of Finland
Contributors: Spruijt-Metz, D., Hekler, E., Saranummi, N., Intille, S., Korhonen, I., Nilsen, W., Rivera, D. E., Spring, B., Michie, S., Asch, D. A., Sanna, A., Salcedo, V. T., Kukakfa, R., Pavel, M.
Number of pages: 12
Pages: 335-346
Publication date: 17 Sep 2015
Peer-reviewed: Yes

Publication information
Journal: Translational Behavioral Medicine
Volume: 5
Issue number: 3
ISSN (Print): 1869-6716
Ratings:

Scopus rating (2015): CiteScore 3.1 SJR 0.754 SNIP 0.838
Original language: English
ASJC Scopus subject areas: Behavioral Neuroscience, Applied Psychology
Keywords: Computational models of behavior, Connected health, Health-related behavior, Just-in-time adaptive interventions, mHealth, Mobile health, Real-time interventions
DOIs:

10.1007/s13142-015-0324-1

Bibliographical note
EXT="Saranummi, Niilo"
Source: Scopus
Source ID: 84939204163
Research output: Contribution to journal › Article › Scientific › peer-review

DropELM: Fast neural network regularization with Dropout and DropConnect
In this paper, we propose an extension of the Extreme Learning Machine algorithm for Single-hidden Layer Feedforward Neural network training that incorporates Dropout and DropConnect regularization in its optimization process. We show that both types of regularization lead to the same solution for the network output weights calculation, which is adopted by the proposed DropELM network. The proposed algorithm is able to exploit Dropout and DropConnect regularization, without computationally intensive iterative weight tuning. We show that the adoption of such a regularization approach can lead to better solutions for the network output weights. We incorporate the proposed regularization approach in several recently proposed ELM algorithms and show that their performance can be enhanced without requiring much additional computational cost.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Aristotle University of Thessaloniki, Department of Informatics
Contributors: Iosifidis, A., Tefas, A., Pitas, I.
Number of pages: 10
Pages: 57-66
Publication date: 25 Aug 2015
Peer-reviewed: Yes

Publication information
Journal: Neurocomputing
Volume: 162
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2015): CiteScore 4.2 SJR 0.981 SNIP 1.698
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Computer Science Applications, Cognitive Neuroscience
Keywords: DropConnect, Dropout, Extreme Learning Machine, Regularization, Single Hidden Layer Feedforward Networks
DOIs:

10.1016/j.neucom.2015.04.006
URLs:

http://www.scopus.com/inward/record.url?scp=84929271496&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84929271496
Research output: Contribution to journal › Article › Scientific › peer-review

Distance-based human action recognition using optimized class representations

We study distance-based classification of human actions and introduce a new metric learning approach based on logistic discrimination for the determination of a low-dimensional feature space of increased discrimination power. We argue that for effective distance-based classification, both the optimal projection space and the optimal class representation should be determined. We qualitatively and quantitatively illustrate the superiority of the proposed approach to metric learning approaches employing the class mean for class representation. We also introduce extensions of the proposed metric learning approach to allow for richer class representations and to operate in arbitrary-dimensional Hilbert spaces for non-linear feature extraction and classification. Experimental results denote that the performance of the proposed distance-based classification schemes is comparable (or even better) to that of Support Vector Machine classifier (in both the linear and kernel cases) which is currently the standard choice for human action recognition.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Aristotle University of Thessaloniki, Department of Informatics
Contributors: Iosifidis, A., Tefas, A., Pitas, I.
Number of pages: 9
Pages: 47-55
Publication date: 5 Aug 2015
Peer-reviewed: Yes

Publication information

Journal: Neurocomputing
Volume: 161
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2015): CiteScore 4.2 SJR 0.981 SNIP 1.698
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Computer Science Applications, Cognitive Neuroscience
Keywords: Distance-based classification, Optimized class representations
DOIs:

10.1016/j.neucom.2014.10.088
URLs:

http://www.scopus.com/inward/record.url?scp=84929045315&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84929045315
Research output: Contribution to journal › Article › Scientific › peer-review

Evaluation of the different sleep-disordered breathing patterns of the compressed tracheal sound

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Electronics and Communications Engineering, BioMediTech, Tampere University Hospital, Medical Imaging Centre, Department of Clinical Neurophysiology, Medical Imaging Centre and Hospital Pharmacy
Contributors: Tenhunen, M., Huupponen, E., Hasan, J., Heino, O., Himanen, S. L.
Number of pages: 7
Pages: 1557-1563
Publication date: 1 Aug 2015
Peer-reviewed: Yes

Publication information

Journal: Clinical Neurophysiology
Volume: 126

Issue number: 8
ISSN (Print): 1388-2457
Ratings:

Scopus rating (2015): CiteScore 6.4 SJR 1.582 SNIP 1.384
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Neurology, Physiology (medical), Sensory Systems
Keywords: Flow limitation, Oesophageal pressure, Sleep, Sleep-disordered breathing, Tracheal sound
DOIs:

10.1016/j.clinph.2014.11.003

Bibliographical note
EXT="Huupponen, Eero"
Source: Scopus
Source ID: 84937695408
Research output: Contribution to journal › Article › Scientific › peer-review

X-ray microtomographic confirmation of the reliability of CBCT in identifying the scalar location of cochlear implant electrode after round window insertion

Cone-beam computed tomography (CBCT) plays a key role in cochlear implantation in both planning implantation before surgery and quality control during surgery due to the high spatial resolution and convenience of application in the operation theater. We recently designed a novel, highresolution cone-beam acquisition system that has been tested in temporal bones with cochlear implantation to identify the scalar localization of the electrode arrays. The current study aimed to verify the reliability of the experimental CBCT set-up using high-resolution invitro X-ray microtomography (μCT) imaging as a reference. Nine human temporal bones were studied by inserting a straight electrode of a cochlear implant using the round window approach followed by sequential imaging using experimental CBCT and μCT with and without 1% iodine as the contrast agent. In the CBCT images, the electrodes were located in the scala tympani and near the lateral wall in all temporal bones. In the μCT images, the cochlear fine structures, including Reissner's membrane, stria vascularis, spiral ligament, basilar membrane, spiral limbus, osseous spiral lamina, and Rosenthal's canal that hosts the spiral ganglion cells, were clearly delineated; the electrode array avoided the lateral wall of the scala tympani in the hook region and then ran along the lateral wall of the scala tympani without any exception, a feature that was also detected in a temporal bone with ruptures in the basilar and Reissner's membranes. In conclusion, the current invitro μCT imaging system produced high-quality images that could demonstrate the fine cochlear structures faithfully and verify the reliability of a novel experimental CBCT set-up aimed for clinical application in identifying the scalar localization of the electrode array. The straight electrode is safe for cochlear structures with low risk of translocation and is suitable for atraumatic implantation, although a large gap between the contacts and the modiolus exists.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Electronics and Communications Engineering, Research group: Computational Biophysics and Imaging Group, BioMediTech, Integrated Technologies for Tissue Engineering Research (ITTE), Tampere University Hospital, BioMediTech - Institute of Biosciences and Medical Technology, Medical Imaging Centre, University of Tampere , Changhai Hospital, PlanmecaOy
Contributors: Zou, J., Hannula, M., Lehto, K., Feng, H., Lähelmä, J., Aula, A. S., Hyttinen, J., Pyykkö, I.
Number of pages: 7
Pages: 59-65
Publication date: 1 Aug 2015
Peer-reviewed: Yes

Publication information
Journal: Hearing Research
Volume: 326
ISSN (Print): 0378-5955
Ratings:

Scopus rating (2015): CiteScore 5.7 SJR 1.886 SNIP 1.478
Original language: English
ASJC Scopus subject areas: Sensory Systems
DOIs:

10.1016/j.heares.2015.04.005
Source: Scopus
Source ID: 84929459212
Research output: Contribution to journal › Article › Scientific › peer-review

Association between soluble L-selectin and anti-JCV antibodies in natalizumab-treated relapsing-remitting MS patients

Objective In relapsing-remitting MS (RRMS) patients treated with natalizumab, the low level of L-selectin-expressing CD4+ T cells has been associated with the risk of progressive multifocal leukoencephalopathy (PML). In this study, our aim was to correlate the levels of soluble L-selectin and the anti-JCV antibody index in the sera of RRMS patients treated with natalizumab. Methods This study included 99 subjects, including 44 RRMS patients treated with natalizumab, 30 with interferon beta (IFN-β) and 25 healthy controls. The levels of soluble l-selectin (sL-selectin) in sera were measured by ELISA, and the anti-JC Virus (JCV) antibody index was determined by the second-generation ELISA (STRATIFY JCV™ DxSelect™) assay. Results A significant correlation was found between the levels of sL-selectin and anti-JCV antibody indices in sera in the natalizumab-treated patients (r=0.402; p=0.007; n=44), but not in those treated with IFN-β. This correlation became even stronger in JCV seropositive patients treated with natalizumab for longer than 18 months (r=0.529; p=0.043; n=15). Conclusion The results support the hypothesis of sL-selectin being connected to the anti-JCV antibody index values and possibly cellular L-selectin. Measurement of serum sL-selectin should be evaluated further as a potential biomarker for predicting the risk of developing PML.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Tampere, Medical School, Department of Neurology, Helsinki University Central Hospital, Turku University Hospital, Tampere University Hospital
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Number of pages: 5
Pages: 334-338
Publication date: 1 Jul 2015
Peer-reviewed: Yes

Publication information

Journal: Multiple Sclerosis and Related Disorders
Volume: 4
Issue number: 4
ISSN (Print): 2211-0348
Ratings:

Scopus rating (2015): CiteScore 1.8 SJR 0.624 SNIP 0.521
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Neurology, Medicine(all)
Keywords: Anti-JCV antibody index, Biomarkers, Multiple sclerosis, Natalizumab, Progressive multifocal leukoencephalopathy, sL-selectin
DOIs:

10.1016/j.msard.2015.06.008
URLs:

http://www.scopus.com/inward/record.url?scp=84937485577&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84937485577
Research output: Contribution to journal › Article › Scientific › peer-review

The effects of neuron morphology on graph theoretic measures of network connectivity: The analysis of a two-level statistical model

We developed a two-level statistical model that addresses the question of how properties of neurite morphology shape the large-scale network connectivity. We adopted a low-dimensional statistical description of neurites. From the neurite model description we derived the expected number of synapses, node degree, and the effective radius, the maximal distance between two neurons expected to form at least one synapse. We related these quantities to the network connectivity described using standard measures from graph theory, such as motif counts, clustering coefficient, minimal path length, and small-world coefficient. These measures are used in a neuroscience context to study phenomena from synaptic connectivity in the small neuronal networks to large scale functional connectivity in the cortex. For these measures we provide analytical solutions that clearly relate different model properties. Neurites that sparsely cover space lead to a small effective radius. If the effective radius is small compared to the overall neuron size the obtained networks share similarities with the uniform random networks as each neuron connects to a small number of distant neurons. Large neurites with densely packed branches lead to a large effective radius. If this effective radius is large compared to the neuron size, the obtained networks have many local connections. In between these extremes, the networks maximize the variability of connection repertoires. The presented approach connects the properties of neuron morphology with large scale network properties without requiring heavy simulations with many model parameters. The two-steps procedure provides an easier interpretation of the role of each modeled parameter. The model is flexible and each of its components can be further expanded. We identified a range of model parameters that maximizes variability in network connectivity, the property that might affect network capacity to exhibit different dynamical regimes.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research group: Computational Neuro Science-CNS, Department of Signal Processing, University of Oslo
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Publication date: 10 Jun 2015
Peer-reviewed: Yes

Publication information
Journal: Frontiers in Neuroanatomy
Volume: 9
Issue number: June
Article number: 76
ISSN (Print): 1662-5129
Ratings:

Scopus rating (2015): CiteScore 3.7 SJR 1.852 SNIP 0.782
Original language: English
ASJC Scopus subject areas: Anatomy, Neuroscience (miscellaneous), Cellular and Molecular Neuroscience
Keywords: Graph theory, Motifs, Network connectivity, Neurite density field, Neuron morphology, Theoretical model
DOIs:

10.3389/fnana.2015.00076
Source: Scopus
Source ID: 84935865748
Research output: Contribution to journal › Article › Scientific › peer-review

Experiments of the sonification of the sleep electroencephalogram
It is becoming possible to perform sleep recordings at home with equipment targeted for the regular consumers. This alleviates the pressures to increase capacity in sleep clinics. The interpretation of the sleep recordings is not very easy for the laymen and alternative assisting methods should be sought for this. Sonification is a method by which a phenomenon is converted to a sound for human listeners. This paper describes experiments made for the sonification of the electric activity of the brain, the electroencephalography (EEG) for the purpose of recognizing the presence and absence of the necessary refreshing components of sleep, deep sleep and rapid eye movement (REM) sleep. The methods are based on the calculation of features of the EEG signal which are characteristic to the deep and REM sleep as well as wakefulness. The features are converted to amplitude modulation functions of artificial and musical instrument sounds by using mathematical transforms such as Principal Component Analysis and Linear Discriminant Analysis. The results indicate that modulated sinusoidal signals are not appropriate for the sonification of sleep EEG but that modulating the sound of musical instruments could be a viable option for making the recognition of good and bad sleep possible.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Research group: Sleep and Sensory Signal Analysis Group-SSSAG, Instituto Superior Tecnico, Lissabon, Portugal
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Number of pages: 10
Pages: 65-74
Publication date: 11 May 2015
Peer-reviewed: Yes

Publication information
Journal: Finnish Journal of eHealth and eWelfare
Volume: 7
Issue number: 2-3
ISSN (Print): 1798-0798
Original language: English
ASJC Scopus subject areas: Engineering(all), Neuroscience(all)
Keywords: sonification; sleep; electroencephalogram; sleep stage scoring
URLs:

http://ojs.tsv.fi/index.php/stty/article/view/50893
Research output: Contribution to journal › Article › Scientific › peer-review

Standardized evaluation of algorithms for computer-aided diagnosis of dementia based on structural MRI: The CADDementia challenge
Algorithms for computer-aided diagnosis of dementia based on structural MRI have demonstrated high performance in the literature, but are difficult to compare as different data sets and methodology were used for evaluation. In addition, it is unclear how the algorithms would perform on previously unseen data, and thus, how they would perform in clinical

practice when there is no real opportunity to adapt the algorithm to the data at hand. To address these comparability, generalizability and clinical applicability issues, we organized a grand challenge that aimed to objectively compare algorithms based on a clinically representative multi-center data set. Using clinical practice as the starting point, the goal was to reproduce the clinical diagnosis. Therefore, we evaluated algorithms for multi-class classification of three diagnostic groups: patients with probable Alzheimer's disease, patients with mild cognitive impairment and healthy controls. The diagnosis based on clinical criteria was used as reference standard, as it was the best available reference despite its known limitations. For evaluation, a previously unseen test set was used consisting of 354 T1-weighted MRI scans with the diagnoses blinded. Fifteen research teams participated with a total of 29 algorithms. The algorithms were trained on a small training set (n = 30) and optionally on data from other sources (e.g., the Alzheimer's Disease Neuroimaging Initiative, the Australian Imaging Biomarkers and Lifestyle flagship study of aging). The best performing algorithm yielded an accuracy of 63.0% and an area under the receiver-operating-characteristic curve (AUC) of 78.8%. In general, the best performances were achieved using feature extraction based on voxel-based morphometry or a combination of features that included volume, cortical thickness, shape and intensity. The challenge is open for new submissions via the web-based framework: http://caddementia.grand-challenge.org.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Imperial College, London, 24.8.2012, Univ Nacl Colombia, Universidad Nacional de Colombia, Signal Proc & Recognit Grp, Old Domin Univ, Old Dominion University, Vis Lab, Universite' Pierre et Marie Curie, Sorbonne, France, 13.12.2011, Univ Porto, Universidade do Porto, Fac Med, Dept Med Imaging, Delft University of Technology, Univ Reading, University of Reading, Sch Syst Engn, Hosp Sao Joao, Sao Joao Hospital, Dept Neurol, CNRS, Centre National de la Recherche Scientifique (CNRS), Universite de Bordeaux - PRES, Lab Bordelais Rech Informat, PICTURA Res Grp, UMR 5800, Erasmus University Medical Center, VU University Medical Center, Universitats Klinikum Freiburg und Medizinische Fakultat, Universitat Freiburg im Breisgau, Istituto Nazionale Di Fisica Nucleare, Frascati, Universita degli Studi di Bari, Aarhus Universitet, Montreal Neurological Institute and Hospital, Jena University Hospital, Centre d'Analyse et de Traitement des Images (CATI), Universita degli studi Magna Graecia di Catanzaro, Kobenhavns Universitet, MIT Computer Science and Artificial Intelligence Laboratory, Massachusetts General Hospital
Contributors: Bron, E. E., Smits, M., van der Flier, W. M., Vrenken, H., Barkhof, F., Scheltens, P., Papma, J. M., Steketee, R. M. E., Méndez Orellana, C., Meijboom, R., Pinto, M., Meireles, J. R., Garrett, C., Bastos-Leite, A. J., Abdulkadir, A., Ronneberger, O., Amoroso, N., Bellotti, R., Cárdenas-Peña, D., Álvarez-Meza, A. M., Dolph, C. V., Iftekharuddin, K. M., Eskildsen, S. F., Coupé, P., Fonov, V. S., Franke, K., Gaser, C., Ledig, C., Guerrero, R., Tong, T., Gray, K. R., Moradi, E., Tohka, J., Routier, A., Durrleman, S., Sarica, A., Di Fatta, G., Sensi, F., Chincarini, A., Smith, G. M., Stoyanov, Z. V., Sørensen, L., Nielsen, M., Tangaro, S., Inglese, P., Wachinger, C., Reuter, M., van Swieten, J. C., Niessen, W. J., Klein, S.
Number of pages: 18
Pages: 562-579
Publication date: 1 May 2015
Peer-reviewed: Yes

Publication information
Journal: NeuroImage
Volume: 111
ISSN (Print): 1053-8119
Ratings:
Scopus rating (2015): CiteScore 13.1 SJR 4.583 SNIP 1.852
Original language: English
ASJC Scopus subject areas: Cognitive Neuroscience, Neurology
Keywords: Alzheimer's disease, Challenge, Classification, Computer-aided diagnosis, Mild cognitive impairment, Structural MRI
DOIs:
10.1016/j.neuroimage.2015.01.048
Source: WOS
Source ID: 000352224100049
Research output: Contribution to journal › Article › Scientific › peer-review

Podocyte apoptosis is prevented by blocking the Toll-like receptor pathway

High serum lipopolysaccharide (LPS) activity in normoalbuminuric patients with type 1 diabetes (T1D) predicts the progression of diabetic nephropathy (DN), but the mechanisms behind this remain unclear. We observed that treatment of cultured human podocytes with sera from normoalbuminuric T1D patients with high LPS activity downregulated 3-phosphoinositide-dependent kinase-1 (PDK1), an activator of the Akt cell survival pathway, and induced apoptosis. Knockdown of PDK1 in cultured human podocytes inhibited antiapoptotic Akt pathway, stimulated proapoptotic p38 MAPK pathway, and increased apoptosis demonstrating an antiapoptotic role for PDK1 in podocytes. Interestingly, PDK1 was downregulated in the glomeruli of diabetic rats and patients with type 2 diabetes before the onset of proteinuria, further

suggesting that reduced expression of PDK1 associates with podocyte injury and development of DN. Treatment of podocytes in vitro and mice in vivo with LPS reduced PDK1 expression and induced apoptosis, which were prevented by inhibiting the Toll-like receptor (TLR) signaling pathway with the immunomodulatory agent GIT27. Our data show that LPS downregulates the cell survival factor PDK1 and induces podocyte apoptosis, and that blocking the TLR pathway with GIT27 may provide a non-nephrotoxic means to prevent the progression of DN.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, Department of Pathology, Laboratory Animal Centre, Helsinki University Central Hospital, Folkhälsan Institute of Genetics, Division of Nephrology, Diabetes and Obesity Research Program, University of Bristol, Baker IDI Heart and Diabetes Institute
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Publication date: 1 May 2015
Peer-reviewed: Yes

Publication information
Journal: CELL DEATH AND DISEASE
Volume: 6
Issue number: 5
Article number: e1752
Original language: English
ASJC Scopus subject areas: Cell Biology, Immunology, Cancer Research, Cellular and Molecular Neuroscience
DOIs:

10.1038/cddis.2015.125
URLs:

http://www.scopus.com/inward/record.url?scp=84940860220&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84940860220
Research output: Contribution to journal › Article › Scientific › peer-review

Analysis of apoptosis-related genes in patients with clinically isolated syndrome and their association with conversion to multiple sclerosis

To analyse whether the expression of apoptotic transcripts is associated with the conversion from clinically isolated syndrome (CIS) to multiple sclerosis (MS). Eleven candidate transcripts belonging to the death receptor pathway, BCL-2, the inflammasome complex and NF-KB family were studied in the nonconverting and converting CIS patients during the four-year follow-up period. Conversion to MS was associated with marked variability in the expression of proapoptotic genes that were linked to TGF-B1 gene levels. The predominant expression of proapoptotic genes in patients with CIS suggests an increased potential to undergo apoptosis with the goal of terminating immune responses and regulating immune system homeostasis.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Tampere, Medical School, Tampere University Hospital, Medical Imaging Centre, School of Management (JKK)
Contributors: Hagman, S., Kolasa, M., Basnyat, P., Helminen, M., Kähönen, M., Dastidar, P., Lehtimäki, T., Elovaara, I.
Number of pages: 6
Pages: 43-48
Publication date: 15 Mar 2015
Peer-reviewed: Yes

Publication information
Journal: JOURNAL OF NEUROIMMUNOLOGY
Volume: 280
ISSN (Print): 0165-5728
Ratings:

Scopus rating (2015): CiteScore 4.5 SJR 1.196 SNIP 0.657
Original language: English
ASJC Scopus subject areas: Immunology and Allergy, Immunology, Neurology, Clinical Neurology
Keywords: Apoptosis, BCL-2, Biomarkers, Clinically isolated syndrome, Multiple sclerosis
DOIs:

10.1016/j.jneuroim.2015.02.006

URLs:

http://www.scopus.com/inward/record.url?scp=84924767384&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84924767384
Research output: Contribution to journal › Article › Scientific › peer-review

Extreme learning machine based supervised subspace learning

This paper proposes a novel method for supervised subspace learning based on Single-hidden Layer Feedforward Neural networks. The proposed method calculates appropriate network target vectors by formulating a Bayesian model exploiting both the labeling information available for the training data and geometric properties of the training data, when represented in the feature space determined by the network's hidden layer outputs. After the calculation of the network target vectors, Extreme Learning Machine-based neural network training is applied and classification is performed using a Nearest Neighbor classifier. Experimental results on publicly available data sets show that the proposed approach consistently outperforms the standard ELM approach, as well as other standard methods.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Department of Signal Processing, Research Community on Data-to-Decision (D2D)
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Number of pages: 7
Pages: 158–164
Publication date: 2015
Peer-reviewed: Yes

Publication information

Journal: Neurocomputing
Volume: 167
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2015): CiteScore 4.2 SJR 0.981 SNIP 1.698
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Computer Science Applications, Cognitive Neuroscience
Keywords: Extreme Learning Machine, Network targets calculation, Supervised subspace learning
DOIs:

10.1016/j.neucom.2015.04.083
Research output: Contribution to journal › Article › Scientific › peer-review

Patient-specific induced pluripotent stem cell—derived RPE cells: Understanding the pathogenesis of retinopathy in long-chain 3-hydroxyacyl-CoA dehydrogenase deiciency

Purpose. Retinopathy is an important manifestation of trifunctional protein (TFP) deficiencies but not of other defects of fatty acid oxidation. The common homozygous mutation in the TFP a-subunit gene HADHA (hydroxyacyl-CoA dehydrogenase), c.1528G>C, affects the long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) activity of TFP and blindness in infancy. The pathogenesis of the retinopathy is unknown. This study aimed to utilize human induced pluripotent stem cell (hiPSC) technology to create a disease model for the disorder, and to derive clues for retinopathy pathogenesis. Methods. We implemented hiPSC technology to generate LCHAD deficiency (LCHADD) patient-specific retinal pigment epithelial (RPE) monolayers. These patient and control RPEs were extensively characterized for function and structure, as well as for lipid composition by mass spectrometry. Results. The hiPSC-derived RPE monolayers of patients and controls were functional, as they both were able to phagocytose the photoreceptor outer segments in vitro. Interestingly, the patient RPEs had intense cytoplasmic neutral lipid accumulation, and lipidomic analysis revealed an increased triglyceride accumulation. Further, patient RPEs were small and irregular in shape, and their tight junctions were disorganized. Their ultratructure showed decreased pigmentation, few melanosomes, and more melanolysosomes. Conclusions. We demonstrate that the RPE cell model reveals novel early pathogenic changes in LCHADD retinopathy, with robust lipid accumulation, inefficient pigmentation that is evident soon after differentiation, and a defect in forming tight junctions inducing apoptosis. We propose that LCHADD-RPEs are an important model for mitochondrial TFP retinopathy, and that their early pathogenic changes contribute to infantile blindness of LCHADD.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: BioMediTech, Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, BioMediTech, VTT Technical Research Centre of Finland, Children’s Hospital, Helsinki University Central Hospital
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Number of pages: 12
Pages: 3371-3382
Publication date: 2015
Peer-reviewed: Yes

Publication information
Journal: Investigative Ophthalmology and Visual Science
Volume: 56
Issue number: 5
ISSN (Print): 0146-0404
Ratings:

Scopus rating (2015): CiteScore 6.2 SJR 2.011 SNIP 1.393
Original language: English
ASJC Scopus subject areas: Ophthalmology, Sensory Systems, Cellular and Molecular Neuroscience
Keywords: Beta oxidation, Mitochondria, Retinal pigment epithelium, Retinopathy
DOIs:

10.1167/iovs.14-14007
URLs:

http://www.scopus.com/inward/record.url?scp=84939639353&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84939639353
Research output: Contribution to journal › Article › Scientific › peer-review

Effects of cytokine activation and oxidative stress on the function of the human embryonic stem cell–derived retinal pigment epithelial cells
PURPOSE. In several retinal complications, such as age-dependent macular degeneration (AMD), oxidative stress is increased and cytokine level is elevated. These are shown to alter the activation and expression of matrix metalloproteinase (MMP) both in human primary and immortalized retinal pigment epithelial (RPE) cells. However, the effects on human embryonic stem cell (hESC)–derived RPE cells remain to be elucidated. METHODS. The mature hESC-RPE cells were exposed to inflammatory cytokines (IFN-γ or TNF-α) for 24 hours or oxidative stress (H_2O_2) for 1 hour. Effects on barrier properties were analyzed with transepithelial electrical resistance (TEER), the expression of MMP-1, MMP-2, MMP-3, MMP-9, collagen I, and collagen IV genes with quantitative RT-PCR, and the expression of MMP- 1 and MMP-3 proteins with Western blot or ELISA, respectively. Also, activation and secretion of MMP-2 and -9 proteins were analyzed with zymography. RESULTS. In normal state, mature hESC-RPE cells expressed MMP-1, -2, -3, and -9 genes in low levels, respectively. Tumor necrosis factor-α increased MMP-1 and -2 gene expression, and H_2O_2 increased MMP-3 and -9 gene expression. Zymography revealed IFN-γ– and TNF-α– induced secretion of MMP-2 and high-molecular-weight species of MMP (HMW MMP), but H_2O_2 decreased their secretion. Furthermore, TNF-α and H_2O_2 significantly decreased barrier properties. CONCLUSIONS. Here, cytokines induced the MMP-1 and -2 gene and protein expression. Also, H_2O_2 induced MMP-3 and -9 gene expression, but not their protein secretion. These data propose that under oxidative stress and cytokine stimuli, mature hESC-RPE cells resemble their native counterpart in the human eye in regard to MMP secretion and expression and could be used to model retinal disorders involving alterations in MMP activity such as AMD, diabetic retinopathy, or proliferative vitreoretinopathy in vitro.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Computer Science Institute, Fimlab Laboratories Ltd
Contributors: Juuti-Uusitalo, K., Nieminen, M., Treumer, F., Ampuja, M., Kallioniemi, A., Klettner, A., Skottman, H.
Number of pages: 10
Pages: 6265-6274
Publication date: 2015
Peer-reviewed: Yes

Publication information
Journal: Investigative Ophthalmology and Visual Science
Volume: 56
Issue number: 11
ISSN (Print): 0146-0404
Ratings:

Scopus rating (2015): CiteScore 6.2 SJR 2.011 SNIP 1.393
Original language: English
ASJC Scopus subject areas: Ophthalmology, Sensory Systems, Cellular and Molecular Neuroscience
Keywords: Matrix metalloproteinase, MMP, Retinal pigment epithelium, Stem cells
DOIs:

10.1167/iovs.15-17333
URLs:

http://www.scopus.com/inward/record.url?scp=84943249379&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84943249379
Research output: Contribution to journal › Article › Scientific › peer-review

Defining the anterior nucleus of the thalamus (ANT) as a deep brain stimulation target in refractory epilepsy: Delineation using 3 T MRI and intraoperative microelectrode recording

Background Deep brain stimulation (DBS) is a minimally invasive and reversible method to treat an increasing number of neurological and psychiatric disorders, including epilepsy. Targeting poorly defined deep structures is based in large degree on stereotactic atlas information, which may be a major source of inconsistent treatment effects. Aim of the study In the present study, we aimed to study whether a recently approved target for epilepsy (anterior nucleus of thalamus, ANT) is visualized in clinically established 3 T MRI and whether ANT is delineated using intraoperative microelectrode recording (MER). We have especially focused on individual variation in the location of ANT in stereotactic space. We also aimed to demonstrate the role of individual variation in interpretation of MER data by projecting samples onto AC-PC (anterior and posterior commissure) and ANT-normalized coordinate systems. Methods Detailed analysis of ANT delineations in 3 T MRI short tau inversion recovery (STIR) images from eight patients undergoing DBS for refractory epilepsy was performed. Coronal and sagittal cross-sectional models of ANT were plotted in the AC-PC coordinate system to study individual variation. A total of 186 MER samples collected from 10 DBS trajectories and 5 patients were analyzed, and the location of each sample was calculated and corrected accordingly to the location of the final DBS electrode and projected to the AC-PC or coordinate system normalized to ANT. Results Most of the key structures in the anatomic atlas around ANT (mammillothalamic tract and external medullary lamina) were identified in STIR images allowing visual delineation of ANT. We observed a high degree of anatomical variation in the location of ANT, and the cross-sectional areas overlapped by study patients decreased in a linear fashion with an increasing number of patients. MER information from 10 individual trajectories correlated with STIR signal characteristics by demonstrating a spike-negative zone, presumably white matter layer, at the lateral aspect of ANT in ANT-normalized coordinate system as predicted by STIR images. However, MER information projected to the AC-PC coordinate system was not able to delineate ANT. Conclusions ANT is delineated in 3 T MRI by visualization of a thin white matter lamina between ANT and other nuclear groups that lack spiking activity. Direct targeting in the anterior thalamic area is superior to indirect targeting due to extensive individual variation in the location of ANT. Without detailed imaging information, however, a single trajectory MER has little localizing value.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Tampere University Hospital, Oulu University Hospital
Contributors: Möttönen, T., Katisko, J., Haapasalo, J., Tähtinen, T., Kiekara, T., Kähärä, V., Peltola, J., Öhman, J., Lehtimäki, K.
Number of pages: 7
Pages: 823-829
Publication date: 2015
Peer-reviewed: Yes

Publication information

Journal: NeuroImage: Clinical
Volume: 7
Ratings:

Scopus rating (2015): CiteScore 4.7 SJR 2.452 SNIP 1.22
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Radiology Nuclear Medicine and imaging, Cognitive Neuroscience, Neurology
Keywords: Anterior nucleus, Deep brain stimulation, Epilepsy, Magnetic resonance imaging, Thalamus
DOIs:

10.1016/j.nicl.2015.03.001
URLs:

http://www.scopus.com/inward/record.url?scp=84926141621&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84926141621
Research output: Contribution to journal › Article › Scientific › peer-review

Regularized extreme learning machine for multi-view semi-supervised action recognition

In this paper, three novel classification algorithms aiming at (semi-)supervised action classification are proposed. Inspired by the effectiveness of discriminant subspace learning techniques and the fast and efficient Extreme Learning Machine (ELM) algorithm for Single-hidden Layer Feedforward Neural networks training, the ELM algorithm is extended by incorporating discrimination criteria in its optimization process, in order to enhance its classification performance. The proposed Discriminant ELM algorithm is extended, by incorporating proper regularization in its optimization process, in order to exploit information appearing in both labeled and unlabeled action instances. An iterative optimization scheme is proposed in order to address multi-view action classification. The proposed classification algorithms are evaluated on three publicly available action recognition databases providing state-of-the-art performance in all the cases.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Aristotle University of Thessaloniki, Department of Informatics
Contributors: Iosifidis, A., Tefas, A., Pitas, I.
Number of pages: 13
Pages: 250-262
Publication date: 5 Dec 2014
Peer-reviewed: Yes

Publication information

Journal: Neurocomputing
Volume: 145
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2014): CiteScore 3.8 SJR 0.875 SNIP 1.709
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Computer Science Applications, Cognitive Neuroscience
Keywords: Extreme learning machine, Multi-view learning, Semi-supervised learning
DOIs:

10.1016/j.neucom.2014.05.036
Source: Scopus
Source ID: 84906935799
Research output: Contribution to journal › Article › Scientific › peer-review

Autoimmunity-related immunological serum markers and survival in a tertiary care cohort of adult patients with epilepsy

We evaluated mortality in relation to a panel of autoimmunity-related immunological serum markers in adult patients with epilepsy (PWE), seen in 1996-1997 at the Department of Neurology, Oulu University Hospital in Finland. Blood samples were drawn from 968 volunteers, and baseline measurements included serum immunoglobulins (IgG, IgA, and IgM), and the following antibodies: anticardiolipin, antinuclear, antimitochondrial, antigliadin (IgA and IgG classes), IgA tissue transglutaminase, and IgA endomysial. Hazard ratios (HR) for all-cause mortality in PWE with abnormal immunological markers relative to 413 patients with normal findings were evaluated with adjustment for confounders during a follow-up of nine years. Borderline statistically significant associations were found only for elevated IgA (HR 2.09, 95% CI 0.99-4.42) and for having two or more abnormal antibody titers (HR 1.58, 95% CI 0.98-2.56). The findings of this exploratory study suggested that elevated serum IgA might be associated with excess mortality in PWE.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Prostate cancer research center (PCRC), Univ of Oulu, UKK Institute Finland, Lundbeck Research USA Inc.
Contributors: Nevalainen, O., Auvinen, A., Ansakorpi, H., Raitanen, J., Isojärvi, J.
Number of pages: 5
Pages: 1675-1679
Publication date: 1 Nov 2014
Peer-reviewed: Yes

Publication information

Journal: EPILEPSY RESEARCH
Volume: 108
Issue number: 9
ISSN (Print): 0920-1211
Ratings:

Scopus rating (2014): CiteScore 3.8 SJR 0.991 SNIP 1

Original language: English
ASJC Scopus subject areas: Neurology, Clinical Neurology
Keywords: Autoantibodies, Endomysial antibodies, Epilepsy, Immunoglobulin A, Mortality
DOIs:

10.1016/j.eplepsyres.2014.08.014
URLs:

http://www.scopus.com/inward/record.url?scp=84907969477&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84907969477
Research output: Contribution to journal › Article › Scientific › peer-review

Immediate effects of deep brain stimulation of anterior thalamic nuclei on executive functions and emotion-attention interaction in humans

Background: Deep brain stimulation (DBS) of anterior thalamic nuclei (ANT) is a novel promising therapeutic method for treating refractory epilepsy. Despite reports of subjective memory impairments and mood disturbances in patients with ANT-DBS, little is known of its effects on cognitive and affective processes. Hypothesis: The anterior thalamus has connections to prefrontal and limbic networks important for cognitive control and emotional reactivity. More specifically, anterior cingulate cortex (ACC), linked with ANT, has been assigned roles related to response inhibition and attention allocation to threat. Thus, we hypothesized ANT-DBS to influence executive functions, particularly response inhibition, and modulate emotional reactivity to threat. Method: Twelve patients having undergone ANT-DBS for intractable epilepsy participated in the study. Patients performed a computer-based executive reaction time (RT) test - that is, a go/no-go visual discrimination task with threat-related emotional distractors and rule switching, while the DBS was switched ON (5/5 mA constant current) and OFF every few minutes. Results: ANT-DBS increased the amount of commission errors - that is, errors where subjects failed to withhold from responding. Furthermore, ANT-DBS slowed RTs in context of threat-related distractors. When stimulation was turned off, threat-related distractors had no distinct effect on RTs. Conclusion: We found immediate objective effects of ANT-DBS on human cognitive control and emotion-attention interaction. We suggest that ANT-DBS compromised response inhibition and enhanced attention allocation to threat due to altered functioning of neural networks that involve the DBS-target, ANT, and the regions connected to it such as ACC. The results highlight the need to consider affective and cognitive side-effects in addition to the therapeutic effect when adjusting stimulation parameters. Furthermore, this study introduces a novel window into cognitive and affective processes by modulating the associative and limbic networks with direct stimulation of key nodes in the thalamus.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Tampere University Hospital, Saint Mary's College of California
Contributors: Hartikainen, K. M., Sun, L., Polvivaara, M., Brause, M., Lehtimäki, K., Haapasalo, J., Möttönen, T., Väyrynen, K., Ogawa, K. H., Öhman, J., Peltola, J.
Number of pages: 11
Pages: 540-550
Publication date: 28 May 2014
Peer-reviewed: Yes

Publication information

Journal: JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY
Volume: 36
Issue number: 5
ISSN (Print): 1380-3395
Ratings:

Scopus rating (2014): CiteScore 4 SJR 1.117 SNIP 1.058
Original language: English
ASJC Scopus subject areas: Clinical Psychology, Neurology, Clinical Neurology
Keywords: Anterior thalamic nuclei, Deep brain stimulation, Emotion, epilepsy, Executive functions
DOIs:

10.1080/13803395.2014.913554
URLs:

http://www.scopus.com/inward/record.url?scp=84901847878&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84901847878
Research output: Contribution to journal › Article › Scientific › peer-review

Comparison of stapedotomy minus prosthesis, circumferential stapes mobilization, and small fenestra stapedotomy for stapes fixation

OBJECTIVE: To compare the outcomes of 3 surgical techniques for primary stapes fixation: stapedotomy minus prosthesis (STAMP), circumferential stapes mobilization (CSM), and small fenestra stapedotomy (SFS). STUDY DESIGN: Retrospective review of 277 primary cases operated for stapes fixation from 1997 to 2007. SETTING: Tertiary academic center. PATIENTS: Consecutive adult and pediatric cases operated for conductive hearing loss because of stapes fixation. INTERVENTIONS: STAMP was performed for otosclerosis limited to the anterior footplate, CSM was conducted for congenital stapes fixation, SFS was performed for more extensive otosclerosis or anatomic contraindications to STAMP/CSM. MAIN OUTCOME MEASURES: Pure-tone audiometry was performed preoperatively and postoperatively (3-6 wk) and the most recent long-term results (≥12 mo). RESULTS: Ninety-nine ears in 90 patients had audiologic follow-up data over 12 months. Sixty-seven ears (68%) underwent SFS, 16 (16%) STAMP, and 16 (16%) CSM. There was significant improvement in average air conduction (AC) thresholds and air-bone gap (ABG) for all techniques. Mean ABG for SFS closed from 29 to 7.1 dB (SD, 6.0), for STAMP from 29 to 3.8 dB (SD, 5.8 dB), and for CSM from 34 to 20 dB (SD, 8.2 dB). AC results were better in the STAMP than in the SFS group, especially in high frequencies. Bone conduction improvements were seen in all groups, highest in STAMP (4.3 dB) and CSM (3.8 dB) groups, but the differences between groups were not statistically significant. CONCLUSION: Satisfactory hearing results were achieved with all the techniques, and STAMP showed better hearing outcomes, especially in high frequencies. CSM is a good option for children and patients in whom it is desirable to avoid a footplate fenestration or prosthesis. CSM and STAMP had significantly higher rates of revision for refixation than SFS.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Ear Nose Throat Department, University of Ottawa, Canada, Harvard Medical School, Electrical Engineering Department, University of California, Los Angeles (UCLA)
Contributors: Acar, G. O., Kivekäs, I., Hanna, B. M., Huang, L., Gopen, Q., Poe, D. S.
Publication date: 2014
Peer-reviewed: Yes

Publication information

Journal: OTOLOGY AND NEUROTOLOGY
Volume: 35
Issue number: 4
ISSN (Print): 1531-7129
Ratings:

Scopus rating (2014): CiteScore 2.9 SJR 1.26 SNIP 1.43
Original language: English
ASJC Scopus subject areas: Otorhinolaryngology, Sensory Systems, Clinical Neurology
Keywords: Circumferential stapes mobilization, Hearing outcome, Otosclerosis, Small fenestra stapedotomy, Stapedotomy minus prosthesis, Stapes fixation
DOIs:

10.1097/MAO.0000000000000280
URLs:

http://www.scopus.com/inward/record.url?scp=84897074438&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84897074438
Research output: Contribution to journal › Article › Scientific › peer-review

Origins and functional consequences of somatic mitochondrial DNA mutations in human cancer

Recent sequencing studies have extensively explored the somatic alterations present in the nuclear genomes of cancers. Although mitochondria control energy metabolism and apoptosis, the origins and impact of cancer-associated mutations in mtDNA are unclear. In this study, we analyzed somatic alterations in mtDNA from 1675 tumors. We identified 1907 somatic substitutions, which exhibited dramatic replicative strand bias, predominantly C > T and A > G on the mitochondrial heavy strand. This strand-asymmetric signature differs from those found in nuclear cancer genomes but matches the inferred germline process shaping primate mtDNA sequence content. A number of mtDNA mutations showed considerable heterogeneity across tumor types. Missense mutations were selectively neutral and often gradually drifted towards homoplasmy over time. In contrast, mutations resulting in protein truncation undergo negative selection and were almost exclusively heteroplasmic. Our findings indicate that the endogenous mutational mechanism has far greater impact than any other external mutagens in mitochondria and is fundamentally linked to mtDNA replication.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Prostate cancer research center (PCRC), Wellcome Trust Sanger Institute, Cambridge University Hospitals NHS Foundation Trust, University of New South Wales (UNSW) Australia, National Cancer Centre, Singapore, Dana-

Farber Cancer Institute, Institute of Cancer Research London, Weatherall Institute of Molecular Medicine, University of Texas, M. D. Anderson Cancer Center, Cancer Genomics Laboratory, Houston, TX, USA, University of Nottingham, National Institute of Environmental Health Sciences, University of North Carolina, Hospital for Sick Children University of Toronto, University of Liverpool, University of Cambridge, Tampere University Hospital, Johns Hopkins University, Royal National Orthopaedic Hospital NHS Trust, Wellcome Trust Centre for Mitochondrial Research
Contributors: Ju, Y. S., Alexandrov, L. B., Gerstung, M., Martincorena, I., Nik-Zainal, S., Ramakrishna, M., Davies, H. R., Papaemmanuil, E., Gundem, G., Shlien, A., Bolli, N., Behjati, S., Tarpey, P. S., Nangalia, J., Massie, C. E., Butler, A. P., Teague, J. W., Vassiliou, G. S., Green, A. R., Du, M. Q., Unnikrishnan, A., Pimanda, J. E., Teh, B. T., Munshi, N., Greaves, M., Vyas, P., El-Naggar, A. K., Santarius, T., Collins, V. P., Grundy, R., Taylor, J. A., Hayes, D. N., Malkin, D., Foster, C. S., Warren, A. Y., Whitaker, H. C., Brewer, D., Eeles, R., Cooper, C., Neal, D., Visakorpi, T., Isaacs, W. B., Bova, G. S., Flanagan, A. M., Futreal, P. A., Lynch, A. G., Chinnery, P. F., McDermott, U., Stratton, M. R., Campbell, P. J.
Publication date: 2014
Peer-reviewed: Yes

Publication information
Journal: eLIFE
Volume: 3
ISSN (Print): 2050-084X
Ratings:

Scopus rating (2014): CiteScore 5.2 SJR 7.888 SNIP 1.633
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Medicine(all), Immunology and Microbiology(all), Biochemistry, Genetics and Molecular Biology(all)
Keywords: cancer genome, evolution, evolutionary biology, genomics, human, mitochondrial DNA, mutational signature, sequencing, somatic mutation
DOIs:

10.7554/eLife.02935
URLs:

http://www.scopus.com/inward/record.url?scp=84994324806&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84994324806
Research output: Contribution to journal › Article › Scientific › peer-review

Learning sparse representations for view-independent human action recognition based on fuzzy distances
In this paper, a method aiming at view-independent human action recognition is presented. Actions are described as series of successive human body poses. Action videos representation is based on fuzzy vector quantization, while action classification is performed by a novel classification algorithm, the so-called Sparsity-based Learning Machine (SbLM), involving two optimization steps. The first one determines a non-linear data mapping to a high-dimensional feature space determined by an l1-minimization process exploiting an overcomplete dictionary formed by the training samples. The second one, involves a training process in order to determine the optimal separating hyperplanes in the resulted high-dimensional feature space. The performance of the proposed human action recognition method is evaluated on two publicly available action recognition databases aiming at different application scenarios.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Aristotle University of Thessaloniki, Department of Informatics
Contributors: Iosifidis, A., Tefas, A., Pitas, I.
Number of pages: 10
Pages: 344-353
Publication date: 9 Dec 2013
Peer-reviewed: Yes

Publication information
Journal: Neurocomputing
Volume: 121
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2013): CiteScore 3.8 SJR 0.817 SNIP 1.915
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Computer Science Applications, Cognitive Neuroscience
Keywords: Action classification, Activity recognition, Fuzzy vector quantization, Sparse data representation
DOIs:

10.1016/j.neucom.2013.05.021

Source: Scopus
Source ID: 84884142409
Research output: Contribution to journal › Article › Scientific › peer-review

Post-stroke depression and depression-executive dysfunction syndrome are associated with recurrence of ischaemic stroke

Background: Depression and depression-executive dysfunction syndrome (DES) are common neuropsychiatric consequences of stroke. We hypothesized that if stroke as a cerebrovascular event causes depression, this so-called post-stroke depression will further increase the risk of recurrent stroke. The objective of the study was to investigate whether patients with post-stroke depression or DES have increased rates of stroke recurrence. Methods: We included 223 patients from the Helsinki Stroke Aging Memory cohort (n = 486) admitted to Helsinki University Central Hospital with a follow-up of 12 years. We included only patients with first-ever ischaemic stroke who were testable for depression and executive dysfunction. For follow-up, national register data were reviewed for all diagnosis codes of ischaemic stroke, survival data and causes of death. Neuropsychological and neuropsychiatric evaluations for depression and executive functions were performed 12-20 weeks after the index stroke. Univariate analysis was performed using χ^2, Mantel-Haenszel, ANOVA, and Kaplan-Meier log rank analyses. A Cox multivariable model with forced entry was used to adjust for stroke risk factors (age, gender, smoking, atrial fibrillation, hypertension, diabetes, peripheral arterial disease, hypercholesterolaemia). Results: The mean time to first recurrent stroke was shorter for the depressed patient group (8.15, 95% CI 7.11-9.19 vs. 9.63, 8.89-10.38 years) and even shorter for patients with DES (7.15, 5.55-8.75 vs. 9.75, 9.09-10.41 years) compared to the remaining groups, respectively. The cumulative risk for recurrent ischaemic stroke in the 12-year follow-up was higher for the depression group (log rank p = 0.04) and for the DES group (log rank p = 0.01) compared to the remaining groups, respectively. Cox multivariable analyses revealed that the older age of the patient (1.05; 1.01-1.08/year), the absence of hypercholesterolaemia (0.24; 0.09-0.59), depression (1.68; 1.07-2.63), and DES (1.95; 1.14-3.33) were all associated with recurrent stroke. Conclusions: Depression and especially DES are associated with a shorter interval to recurrence of ischaemic stroke but executive dysfunction alone is not associated with a more rapid stroke recurrence. Diagnosis and treatment of depressive syndromes should be considered as a part of secondary prevention in patients with ischaemic stroke.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, Tampere University Hospital, Kellokoski Hospital
Contributors: Sibolt, G., Curtze, S., Melkas, S., Pohjasvaara, T., Kaste, M., Karhunen, P. J., Oksala, N. K. J., Vataja, R., Erkinjuntti, T.
Number of pages: 8
Pages: 336-343
Publication date: Dec 2013
Peer-reviewed: Yes

Publication information

Journal: CEREBROVASCULAR DISEASES
Volume: 36
Issue number: 5-6
ISSN (Print): 1015-9770
Ratings:

Scopus rating (2013): CiteScore 5.5 SJR 1.848 SNIP 1.704
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Neurology, Cardiology and Cardiovascular Medicine
Keywords: Executive dysfunction, Ischaemic stroke, Post-stroke depression, Recurrent stroke
DOIs:

10.1159/000355145
URLs:

http://www.scopus.com/inward/record.url?scp=84886733548&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84886733548
Research output: Contribution to journal › Article › Scientific › peer-review

Effects of exogenous alpha-synuclein on stimulated dopamine overflow in dorsal striatum

Alpha-synuclein (α-syn) is mainly a presynaptic protein that has been implicated in Parkinson's disease and various other neurodegenerative disorders. Evidence obtained in knockout mice suggests that α-syn controls plasticity of dopamine (DA) overflow in presynaptic terminals. It is also believed that α-syn spreads and may seed its aggregates from cell to cell. The effects of exogenously applied α-syn on dopaminergic neurotransmission have not been studied. We addressed this issue by microinjecting human α-syn protein into the dorsal striatum of wild-type and α-syn knockout mice and monitoring stimulated DA overflow with constant potential amperometry. The evoked DA overflow was decreased in knockout mice

six days after α-syn microinjection. The maximal velocity of DA re-uptake was reduced in both genotypes. Similar results were not seen when the effects of microinjected α-syn were studied immediately after the treatment, but instead there was a trend toward an increase in both stimulated DA overflow and maximal velocity of DA re-uptake. We conclude that locally applied human α-syn affects DA overflow and the effects depend on the presence of endogenous α-syn.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Ita-Suomen yliopisto, H. Lundbeck A/S
Contributors: Pelkonen, A., Kallunki, P., Yavich, L.
Number of pages: 5
Pages: 141-145
Publication date: 25 Oct 2013
Peer-reviewed: Yes

Publication information
Journal: Neuroscience Letters
Volume: 554
ISSN (Print): 0304-3940
Ratings:

Scopus rating (2013): CiteScore 4 SJR 1.066 SNIP 0.774
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Alpha-synuclein, Constant potential amperometry, Dopamine overflow, Knockout mice, Microinjection
DOIs:

10.1016/j.neulet.2013.08.072
URLs:

http://www.scopus.com/inward/record.url?scp=84884717510&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84884717510
Research output: Contribution to journal › Article › Scientific › peer-review

Transfer learning using a nonparametric sparse topic model
In many domains data items are represented by vectors of counts; count data arises, for example, in bioinformatics or analysis of text documents represented as word count vectors. However, often the amount of data available from an interesting data source is too small to model the data source well. When several data sets are available from related sources, exploiting their similarities by transfer learning can improve the resulting models compared to modeling sources independently. We introduce a Bayesian generative transfer learning model which represents similarity across document collections by sparse sharing of latent topics controlled by an Indian buffet process. Unlike a prominent previous model, hierarchical Dirichlet process (HDP) based multi-task learning, our model decouples topic sharing probability from topic strength, making sharing of low-strength topics easier. In experiments, our model outperforms the HDP approach both on synthetic data and in first of the two case studies on text collections, and achieves similar performance as the HDP approach in the second case study.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Aalto University, deCODE Genetics
Contributors: Faisal, A., Gillberg, J., Leen, G., Peltonen, J.
Number of pages: 14
Pages: 124-137
Publication date: 18 Jul 2013
Peer-reviewed: Yes

Publication information
Journal: Neurocomputing
Volume: 112
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2013): CiteScore 3.8 SJR 0.817 SNIP 1.915
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Computer Science Applications, Cognitive Neuroscience
Keywords: Latent Dirichlet allocation, Nonparametric Bayesian inference, Small sample size, Sparsity, Topic models, Transfer learning
DOIs:

10.1016/j.neucom.2012.12.038
URLs:

http://www.scopus.com/inward/record.url?scp=84877602437&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84877602437
Research output: Contribution to journal › Article › Scientific › peer-review

Mismatch negativity abnormality in traumatic brain injury without macroscopic lesions on conventional MRI

Traumatic brain injury (TBI) causes damage through complex pathophysiological mechanisms. Deficits related to traumatic axonal injury persist in a subset of patients with no macroscopic lesions on conventional MRI. We examined two event-related brain potentials, mismatch negativity (MMN) and P3a, to identify possible electrophysiological anomalies in this subset of TBI patients in comparison with TBI patients with focal abnormalities on MRI/computed tomography and healthy controls. Each group consisted of 10 individuals. A passive oddball paradigm, in which the individuals were instructed to ignore auditory stimuli while watching a silent movie, consisted of non-native speech sounds presented in a random order. Patients with no discernible lesions on conventional MRI showed a significantly augmented amplitude of the brain's involuntary change-detection response MMN, relative to that of the two other groups. In patients with focal neuroradiological abnormalities, this MMN anomaly was not found, whereas the subsequent orientation-related P3a response was significantly enlarged when compared with that of the controls. The present findings demonstrate that MMN is indicative of a functional abnormality in the mechanisms of involuntary attention in chronic TBI patients with normal conventional MRI findings, indexing their increased distractibility associated with the traumatically-induced loss of neural integrity.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, Tampere University Hospital, Helsinki University Central Hospital, Aarhus Universitet
Contributors: Kaipio, M. L., Cheour, M., Öhman, J., Salonen, O., Näätänen, R.
Number of pages: 5
Pages: 440-444
Publication date: 29 May 2013
Peer-reviewed: Yes

Publication information

Journal: NeuroReport
Volume: 24
Issue number: 8
ISSN (Print): 0959-4965
Ratings:

Scopus rating (2013): CiteScore 2.9 SJR 0.92 SNIP 0.542
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Distractibility, Involuntary attention, Mismatch negativity, MRI, P3a, Traumatic axonal injury, Traumatic brain injury
DOIs:

10.1097/WNR.0b013e32836164b4
URLs:

http://www.scopus.com/inward/record.url?scp=84877081041&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84877081041
Research output: Contribution to journal › Article › Scientific › peer-review

Fluorescent probes as a tool for cell population tracking in spontaneously active neural networks derived from human pluripotent stem cells

Applications such as 3D cultures and tissue modelling require cell tracking with non-invasive methods. In this work, the suitability of two fluorescent probes, CellTracker, CT, and long chain carbocyanine dye, DiD, was investigated for long-term culturing of labeled human pluripotent stem cell-derived neural cells. We found that these dyes did not affect the cell viability. However, proliferation was decreased in DiD labeled cell population. With both dyes the labeling was stable up to 4 weeks. CT and DiD labeled cells could be co-cultured and, importantly, these mixed populations had their normal ability to form spontaneous electrical network activity. In conclusion, human neural cells can be successfully labeled with these two fluorescent probes without significantly affecting the cell characteristics. These labeled cells could be utilized further in e.g. building controlled neuronal networks for neurotoxicity screening platforms, combining cells with biomaterials for 3D studies, and graft development.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), NeuroGroup, School of Management (JKK), Pirkanmaan sairaanhoitopiiri
Contributors: Mäkinen, M., Joki, T., Ylä-Outinen, L., Skottman, H., Narkilahti, S., Äänismaa, R.
Number of pages: 9
Pages: 88-96
Publication date: Apr 2013
Peer-reviewed: Yes

Publication information
Journal: Journal of Neuroscience Methods
Volume: 215
Issue number: 1
ISSN (Print): 0165-0270
Ratings:

Scopus rating (2013): CiteScore 4.5 SJR 1.197 SNIP 1.033
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: CellTracker, Co-culture, DiD, Fluorescent probe, Human stem cell derived neural cells, Labeling, Long term
DOIs:

10.1016/j.jneumeth.2013.02.019
URLs:

http://www.scopus.com/inward/record.url?scp=84875797909&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84875797909
Research output: Contribution to journal › Article › Scientific › peer-review

Influence of the experimental design of gene expression studies on the inference of gene regulatory networks: Environmental factors
The inference of gene regulatory networks gained within recent years a considerable interest in the biology and biomedical community. The purpose of this paper is to investigate the influence that environmental conditions can exhibit on the inference performance of network inference algorithms. Specifically, we study five network inference methods, Aracne, BC3NET, CLR, C3NET and MRNET, and compare the results for three different conditions: (I) observational gene expression data: normal environmental condition, (II) interventional gene expression data: growth in rich media, (III) interventional gene expression data: normal environmental condition interrupted by a positive spike-in stimulation. Overall, we find that different statistical inference methods lead to comparable, but condition-specific results. Further, our results suggest that non-steady-state data enhance the inferability of regulatory networks.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Computational Biology and Machine Learning, Queen's University, Belfast, Northern Ireland
Contributors: Emmert-Streib, F.
Publication date: 2013
Peer-reviewed: Yes

Publication information
Journal: PeerJ
Volume: 2013
Issue number: 1
Article number: e10
Ratings:

Scopus rating (2013): CiteScore 0.4
Original language: English
ASJC Scopus subject areas: Agricultural and Biological Sciences(all), Biochemistry, Genetics and Molecular Biology(all), Medicine(all), Neuroscience(all)
Keywords: Experimental design, Gene expression data, Gene regulatory networks, Interventional data, Statistical network inference
DOIs:

10.7717/peerj.10
URLs:

http://www.scopus.com/inward/record.url?scp=84877135982&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84877135982
Research output: Contribution to journal › Article › Scientific › peer-review

Disconnection between periodic leg movements and cortical arousals in spinal cord injury

Objective: In this study we examine the temporal connection between periodic leg movements (PLMs) and cortical arousals, as well as the treatment effect of pramipexole, in a clinical case with spinal cord lesion. Methods: A patient with complete cervical spinal cord injury and PLMs during sleep underwent two baseline sleep recordings, one recording with dopaminergic treatment, and one recording with adaptive servoventilation. Results: The PLMs were temporally dissociated from cortical arousals as well as from respiratory or heart rate events. PLMs were suppressed by pramipexole and persisted after treatment of apnea. Conclusion: The disconnection of PLMs from arousals supports a spinal generator or peripheral trigger mechanism for PLMs. The suppression of movements by a dopamine agonist suggests that its site of action is caudal to the cervical lesion and outside of the brain. Our observation provides significant new knowledge about the pathogenesis of PLMs and warrants studies in larger populations.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Unesta Research Centre, Civic Hospital of Lugano, Tampere University Hospital, Oasi Research Institute (IRCCS)
Contributors: Salminen, A. V., Manconi, M., Rimpilä, V., Luoto, T. M., Koskinen, E., Ferri, R., Öhman, J., Polo, O.
Number of pages: 3
Pages: 1207-1209
Publication date: 2013
Peer-reviewed: Yes

Publication information

Journal: JOURNAL OF CLINICAL SLEEP MEDICINE
Volume: 9
Issue number: 11
ISSN (Print): 1550-9389
Ratings:

Scopus rating (2013): CiteScore 3.9 SJR 0.813 SNIP 1.265
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Pulmonary and Respiratory Medicine, Neurology
Keywords: Case report, Cortical arousal, Dopamine agonist, Periodic leg movements, Sleep apnea, Spinal cord injury
DOIs:

10.5664/jcsm.3174
URLs:

http://www.scopus.com/inward/record.url?scp=84888189303&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84888189303
Research output: Contribution to journal › Article › Scientific › peer-review

Mortality by clinical characteristics in a tertiary care cohort of adult patients with chronic epilepsy

The authors evaluated the contribution of various clinical characteristics to mortality risk and underlying causes of death among all adult patients with epilepsy seen at the Department of Neurology, Oulu University Hospital in Finland during 1996 and 1997. Hazard ratios (HRs) for mortality in 1998-2006 relative to a population-based reference cohort were estimated using Cox modeling, with adjustment for age and gender. The HR for total mortality was 2.66 (95% confidence interval [CI] 2.09-3.39). Infectious etiology of epilepsy (HR 5.77, 95% CI 2.52-13.2) and a seizure frequency of ≥1 per month (HR 4.42, 95% CI 3.00-6.52) related to high risks of death. Cancer (21%), ischemic heart disease (15%), and accidents (12%) caused most of the potential years of life lost. Despite recent advances in treatment of epilepsy and improved seizure control, chronic epilepsy still carries a substantially increased risk of death.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Prostate cancer research center (PCRC), Oulu University Hospital, National Public Health Institute, UKK Institute Finland, Lundbeck Research USA Inc.
Contributors: Nevalainen, O., Auvinen, A., Ansakorpi, H., Artama, M., Raitanen, J., Isojärvi, J.
Publication date: Dec 2012
Peer-reviewed: Yes

Publication information
Journal: EPILEPSIA
Volume: 53
Issue number: 12
ISSN (Print): 0013-9580
Ratings:

Scopus rating (2012): CiteScore 7.3 SJR 2.205 SNIP 1.713
Original language: English
ASJC Scopus subject areas: Neurology, Clinical Neurology
Keywords: Epilepsy, Finland, Mortality, Potential years of life lost, Survival
DOIs:

10.1111/epi.12006
URLs:

http://www.scopus.com/inward/record.url?scp=84870602397&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84870602397
Research output: Contribution to journal › Article › Scientific › peer-review

Extensive white matter changes predict stroke recurrence up to 5 years after a first-ever ischemic stroke

Background: White matter changes (WMCs), a surrogate for small-vessel disease (SVD), have been shown to be associated with a major negative influence on cognition, mood and functioning in daily life. We aimed to investigate whether severe WMCs are a risk factor for recurrent ischemic stroke in a long-term follow-up. Methods: 320 consecutive patients admitted to hospital with a first-ever ischemic stroke were included in the study and followed up for 12 years using extensive national registers. Patients were aged between 55 and 85 years, with a mean age of 70.8 years. WMCs were rated using MRI and stratified into two grades: absent to moderate WMCs versus severe WMCs. Univariate analysis was performed using binary logistic regression analysis, Kaplan-Meier log rank analysis and life table function. To control for factors such as age, education and cardiovascular risk factors, a multivariate Cox regression proportional hazards analysis was made with forced entry. Results: At least one recurrent stroke, nonfatal or fatal, was diagnosed in 76 (23.8%) patients at 5 years and in 127 (39.7%) patients at 12 years. In univariate analysis, only advancing age was associated with WMCs. The cumulative 5-year recurrence risk was 24.5% [95% confidence interval (95% CI) 23.8-25.2] for patients with absent to moderate WMCs and 39.1% (95% CI 38.1-40.1) for patients with severe WMCs. The cumulative 12-year recurrence risk was 48.1% (95% CI 45.5-50.7) for patients with absent to moderate WMCs and 60.9% (95% CI 56.7-65.1) for patients with severe WMCs. In Cox regression proportional hazards analysis, independent predictors of recurrent stroke at 5 years were severe WMCs [hazard ratio (HR) 1.80, 95% CI 1.11-2.95], atrial fibrillation (HR 1.81, 95% CI 1.09-3.02), hypertension (HR 1.69, 95% CI 1.05-2.71) and peripheral arterial disease (HR 1.89, 95% CI 1.06-3.38). At 12 years, only increasing age remained as an independent predictor (HR 1.04, 95% CI 1.02-1.07). In receiver operating characteristic analysis, the area under the curve for severe WMCs was 0.58 (95% CI 0.51-0.65) for the prediction of stroke recurrence within 5 years. Conclusions: In our well-defined cohort of poststroke patients, the presence of severe WMCs was an indicator of stroke recurrence up to 5 years after a first-ever ischemic stroke. WMCs can be considered as an SVD marker that summarizes the effects of several classical risk factors on the small-vessel brain network and therefore can be used as a score for risk stratification of stroke recurrence. Our findings further underline the poor long-term prognosis of cerebral SVD.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, School of Management (JKK)
Contributors: Melkas, S., Sibolt, G., Oksala, N. K. J., Putaala, J., Pohjasvaara, T., Kaste, M., Karhunen, P. J., Erkinjuntti, T.
Number of pages: 8
Pages: 191-198
Publication date: Oct 2012
Peer-reviewed: Yes

Publication information
Journal: CEREBROVASCULAR DISEASES
Volume: 34
Issue number: 3
ISSN (Print): 1015-9770
Ratings:

Scopus rating (2012): CiteScore 5.7 SJR 1.723 SNIP 1.325
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Neurology, Cardiology and Cardiovascular Medicine
Keywords: Recurrent stroke, Vascular risk factors, White matter changes

DOIs:
10.1159/000341404
URLs:
http://www.scopus.com/inward/record.url?scp=84866500043&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84866500043
Research output: Contribution to journal › Article › Scientific › peer-review

Melatonin pathway genes are associated with progressive subtypes and disability status in multiple sclerosis among Finnish patients

In this study we investigated the relationship between melatonin pathway and multiple sclerosis (MS) in a high-risk Finnish population by studying the single nucleotide polymorphisms (SNPs) in the genes coding for critical enzymes and receptors involved in the melatonin pathway. A total of 590 subjects (193 MS patients and 397 healthy controls) were genotyped for seven SNPs in four genes including tryptophan hydroxylases (TPH)1 and 2, arylalkylamine N-acetyltransferase (AANAT) and melatonin receptor 1B (MTNR1B). An overrepresentation of T allele carriers of a functional polymorphism (G-703T, rs4570625) in the promoter region of TPH2 gene was observed in the progressive MS subtypes. The haplotype rs4570625-rs10506645TT of TPH2 gene was associated with the risk of severe disability in primary progressive MS (PPMS), while haplotype rs4570625-rs10506645TC appeared to be protective against disability in secondary progressive MS (SPMS). In the MTNR1B gene, the haplotype rs10830963-rs4753426GC was associated with the risk of SPMS, whereas another haplotype rs10830963-rs4753426GT showed an association with the risk of PPMS. These data showing the association of polymorphisms in the TPH2 and MTNR1B genes with the progressive subtypes of MS and disability suggest dysregulation in melatonin pathway. Melatonin pathway seems to be involved in disease progression, and therefore its potential effects in overcoming MS-related neurodegeneration may be worth evaluating in future clinical trials.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Helsinki, Kanta-Häme Central Hospital, Tampere University Hospital
Contributors: Natarajan, R., Einarsdottir, E., Riutta, A., Hagman, S., Raunio, M., Mononen, N., Lehtimäki, T., Elovaara, I.
Number of pages: 5
Pages: 106-110
Publication date: 15 Sep 2012
Peer-reviewed: Yes

Publication information

Journal: JOURNAL OF NEUROIMMUNOLOGY
Volume: 250
Issue number: 1-2
ISSN (Print): 0165-5728
Ratings:
Scopus rating (2012): CiteScore 5.7 SJR 1.277 SNIP 0.883
Original language: English
ASJC Scopus subject areas: Immunology, Clinical Neurology, Immunology and Allergy, Neurology
Keywords: Expanded Disability Status Scale (EDSS), Melatonin pathway genes, MTNR1B, Multiple sclerosis, Single nucleotide polymorphisms (SNPs), TPH2
DOIs:
10.1016/j.jneuroim.2012.05.014
URLs:
http://www.scopus.com/inward/record.url?scp=84864838067&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84864838067
Research output: Contribution to journal › Article › Scientific › peer-review

Neuroprotective effect of RO-20-1724-a phosphodiesterase4 inhibitor against intracerebroventricular streptozotocin induced cognitive deficit and oxidative stress in rats

Cyclic nucleotides viz cGMP and cAMP are known to play an important role in learning and memory processes. Enhancement of cyclic nucleotide signalling through inhibition of phosphodiesterases (PDEs) has been reported to be beneficial in several neurodegenerative disorders associated with cognitive decline. The present study was undertaken to investigate the effect of RO-20-1724-a PDE4 inhibitor on streptozotocin (STZ) induced experimental sporadic dementia of Alzheimer's type. The STZ was injected twice intracerebroventrically (3 mg/kg i.c.v.) on alternate days (day 1 and day 3) in rats. The STZ injected rats were treated with RO-20-1724 (125, 250 and 500 μg/kg i.p.) for 21 days following first i.c.v. STZ administration. Learning and memory in rats were assessed by passive avoidance [PA (days 14 and 15)] and Morris water maze [MWM (days 17, 18, 19, 20 and 21)] following first i.c.v. STZ administration. On day 22 rat cerebral homogenate was used for all the biochemical estimations. The pharmacological inhibition of PDE4 by RO-20-1724

significantly attenuated STZ induced cognitive deficit and oxidative stress. RO-20-1724 was found to not only improve learning and memory in MWM and PA paradigms but also restore STZ induced elevation in cholinesterase activity. Further, RO-20-1724 significantly reduced malondialdehyde and nitrite levels, and restored the glutathione levels indicating attenuation of oxidative stress. Current data complement previous studies by providing evidence for a subset of cognition enhancing effects after PDE4 inhibition. The observed beneficial effects of RO-20-1724 in spatial memory may be due to its ability to restore cholinergic functions and possibly through its antioxidant mechanisms.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Computational Science X (CompX), Neuropharmacology Div., ISF College of Pharmacy
Contributors: Sharma, V., Bala, A., Deshmukh, R., Bedi, K. L., Sharma, P. L.
Number of pages: 7
Pages: 239-245
Publication date: Apr 2012
Peer-reviewed: Yes

Publication information
Journal: PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
Volume: 101
Issue number: 2
ISSN (Print): 0091-3057
Ratings:

Scopus rating (2012): CiteScore 4.7 SJR 1.197 SNIP 0.913
Original language: English
ASJC Scopus subject areas: Biochemistry, Clinical Biochemistry, Pharmacology, Toxicology, Behavioral Neuroscience, Biological Psychiatry
Keywords: Alzheimer's disease, Cognitive dysfunction, Oxidative stress, Phosphodiesterase4, RO-20-1724, Streptozotocin
DOIs:

10.1016/j.pbb.2012.01.004
URLs:

http://www.scopus.com/inward/record.url?scp=84857569798&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84857569798
Research output: Contribution to journal › Article › Scientific › peer-review

Inhibition of Casein kinase-2 induces p53-dependent cell cycle arrest and sensitizes glioblastoma cells to tumor necrosis factor (TNFα)-induced apoptosis through SIRT1 inhibition
Glioblastoma multiforme (GBM) are resistant to TNFα-induced apoptosis and blockade of TNFα-induced NF-κB activation sensitizes glioma cells to apoptosis. As Casein kinase-2 (CK2) induces aberrant NF-κB activation and as we observed elevated CK2 levels in GBM tumors, we investigated the potential of CK2 inhibitors (CK2-Is)-DRB and Apigenin in sensitizing glioma cells to TNFα-induced apoptosis. CK2-Is and CK2 small interfering RNA (siRNA) reduced glioma cell viability, inhibited TNFα-mediated NF-κB activation, and sensitized cell to TNFα-induced apoptosis. Importantly, CK2-Is activated p53 function in wild-type but not in p53 mutant cells. Activation of p53 function involved its increased transcriptional activation, DNA-binding ability, increased expression of p53 target genes associated with cell cycle progression and apoptosis. Moreover, CK2-Is decreased telomerase activity and increased senescence in a p53-dependent manner. Apoptotic gene profiling indicated that CK2-Is differentially affect p53 and TNFα targets in p53 wild-type and mutant glioma cells. CK2-I decreased MDM2-p53 association and p53 ubiquitination to enhance p53 levels. Interestingly, CK2-Is downregulated SIRT1 activity and over-expression of SIRT1 decreased p53 transcriptional activity and rescued cells from CK2-I-induced apoptosis. This ability of CK2-Is to sensitize glioma to TNFα-induced death via multiple mechanisms involving abrogation of NF-κB activation, reactivation of wild-type p53 function and SIRT1 inhibition warrants investigation.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Computational Science X (CompX), National Brain Research Centre, Paras Hospitals
Contributors: Dixit, D., Sharma, V., Ghosh, S., Mehta, V. S., Sen, E.
Publication date: Feb 2012
Peer-reviewed: Yes

Publication information
Journal: CELL DEATH AND DISEASE
Volume: 3

Issue number: 2
Article number: e271
Original language: English
ASJC Scopus subject areas: Cancer Research, Cell Biology, Immunology, Medicine(all), Cellular and Molecular Neuroscience
Keywords: Casein kinase-2, Glioblastoma, NF-κB, p53, TNFα
DOIs:
10.1038/cddis.2012.10
URLs:
http://www.scopus.com/inward/record.url?scp=84857852626&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84857852626
Research output: Contribution to journal › Article › Scientific › peer-review

Cortical spreading depression in alpha-synuclein knockout mice

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Ita-Suomen yliopisto
Contributors: Pelkonen, A., Yavich, L.
Number of pages: 4
Pages: 81-84
Publication date: Jan 2012
Peer-reviewed: Yes

Publication information
Journal: SYNAPSE
Volume: 66
Issue number: 1
ISSN (Print): 0887-4476
Ratings:
Scopus rating (2012): CiteScore 5 SJR 1.331 SNIP 0.754
Original language: English
ASJC Scopus subject areas: Cellular and Molecular Neuroscience
Keywords: Alpha-synuclein, Cortical spreading depression, Direct current recording, Knockout mice
DOIs:
10.1002/syn.20980
URLs:
http://www.scopus.com/inward/record.url?scp=81555214098&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 81555214098
Research output: Contribution to journal › Article › Scientific › peer-review

The effect of different text presentation formats on eye movement metrics in reading
Eye movement data were collected and analyzed from 16 participants while they read text from a computer screen. Several text presentation formats were compared, including sentences as part of a full paragraph, sentences presented one by one, sentences presented in chunks of at most 30 characters at a predefined rate, and line-by-line presentation fitting the width of the computer screen. The goal of the experiment was to study how these different text presentation modes affect eye movement metrics (fixation duration, fixations per minute, regressions, etc.). One-way repeated measures ANOVA revealed that differences in presentation format have a significant effect on fixation duration, number of fixations per minute, and number of regressions.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Augmented Human Activities (AHA)
Contributors: Sharmin, S., Špakov, O., Räihä, K. J.
Publication date: 2012
Peer-reviewed: Yes

Publication information
Journal: JOURNAL OF EYE MOVEMENT RESEARCH
Volume: 5

Issue number: 3
Article number: 3
Original language: English
ASJC Scopus subject areas: Ophthalmology, Sensory Systems
Keywords: Eye movements, Fixation count, Fixation duration, Reading, Regressions, Text presentation format
URLs:

http://www.scopus.com/inward/record.url?scp=84879365477&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84879365477
Research output: Contribution to journal › Article › Scientific › peer-review

COX-2 regulates the proliferation of glioma stem like cells

Cancer stem-like cells (CSCs) possessing features of neural precursor cells (NPC) influence initiation, recurrence and chemoresistance of glioblastoma multiforme (GBM). As inflammation is crucial for glioblastoma progression we investigated the effect of chronic IL-1β treatment on CSCs derived from glioblastoma cell line U87MG. Exposure to IL-1β for 10 days increased (i) accumulation of 8-OHdG - a key biomarker of oxidative DNA damage; (ii) DNA damage response (DDR) indicators γH2AX, ATM and DNA-PK; (iii) nuclear and cytoplasmic p53 and COX-2 levels and (iv) interaction between COX-2 and p53. Despite upregulating p53 expression IL-1β had no effect on cell cycle progression, apoptosis or self renewal capacity of CSCs. COX-2 inhibitor Celecoxib reduced self renewal capacity and increased apoptosis of both control and IL-1β treated CSCs. Therefore the ability of COX-2 to regulate proliferation of CSCs irrespective of exposure to IL-1β, warrants further investigation of COX-2 as a potential anti-glioma target.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Computational Science X (CompX), National Brain Research Centre
Contributors: Sharma, V., Dixit, D., Ghosh, S., Sen, E.
Number of pages: 5
Pages: 567-571
Publication date: Oct 2011
Peer-reviewed: Yes

Publication information

Journal: NEUROCHEMISTRY INTERNATIONAL
Volume: 59
Issue number: 5
ISSN (Print): 0197-0186
Ratings:

Scopus rating (2011): CiteScore 5.4 SJR 1.283 SNIP 0.852
Original language: English
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Cell Biology
Keywords: COX-2, Glioblastoma, IL-1β, p53
DOIs:

10.1016/j.neuint.2011.06.018
URLs:

http://www.scopus.com/inward/record.url?scp=80052927442&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 80052927442
Research output: Contribution to journal › Article › Scientific › peer-review

Pathway analysis of expression data: Deciphering functional building blocks of complex diseases

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Prostate cancer research center (PCRC), Computational Biology and Machine Learning Lab., Faculty of Medicine, Health and Life Sciences, Queen's University, Belfast, Northern Ireland, University of Arkansas for Medical Sciences
Contributors: Emmert-Streib, F., Glazko, G. V.
Publication date: May 2011
Peer-reviewed: Yes

Publication information

Journal: PLoS Computational Biology

Volume: 7
Issue number: 5
Article number: e1002053
ISSN (Print): 1553-734X
Ratings:

Scopus rating (2011): CiteScore 8.1 SJR 3.613 SNIP 1.636
Original language: English
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Ecology, Molecular Biology, Genetics, Ecology, Evolution, Behavior and Systematics, Modelling and Simulation, Computational Theory and Mathematics
DOIs:

10.1371/journal.pcbi.1002053
URLs:

http://www.scopus.com/inward/record.url?scp=79958152651&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 79958152651
Research output: Contribution to journal › Article › Scientific › peer-review

Disease-associated inflammatory biomarker profiles in blood in different subtypes of multiple sclerosis: Prospective clinical and MRI follow-up study

To identify biomarkers of disease activity and progression in multiple sclerosis (MS), we analyzed the serum profiles of cytokines, chemokines and apoptotic molecules in different subtypes of MS including clinically isolated syndrome (CIS) and correlated their levels with clinical and volumetric MRI findings obtained over a one-year follow up. Upregulated levels of apoptotic sFas molecule were found in MS patients with a worsening EDSS score and an accumulation of hypointense lesions in MRI. In such patients, the levels of MIF appeared to be higher than in non-progressing patients. In addition, increased levels of serum TNF-α and CCL2 were found especially in primary progressive MS (PPMS). These observations suggest that serum Fas and MIF are candidate biomarkers of neurological worsening related to progressive neurodegeneration, while serum TNF-α and CCL2 reflect the presence of inflammatory responses in PPMS.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), University of Tampere, Medical School, Tampere University Hospital, Medical Imaging Centre
Contributors: Hagman, S., Raunio, M., Rossi, M., Dastidar, P., Elovaara, I.
Number of pages: 7
Pages: 141-147
Publication date: May 2011
Peer-reviewed: Yes

Publication information

Journal: JOURNAL OF NEUROIMMUNOLOGY
Volume: 234
Issue number: 1-2
ISSN (Print): 0165-5728
Ratings:

Scopus rating (2011): CiteScore 5.4 SJR 1.271 SNIP 0.876
Original language: English
ASJC Scopus subject areas: Immunology, Clinical Neurology, Immunology and Allergy, Neurology
Keywords: Apoptosis, Biomarkers, Chemokines, Cytokines, Expanded disability status scale, Magnetic resonance imaging , Multiple sclerosis
DOIs:

10.1016/j.jneuroim.2011.02.009
URLs:

http://www.scopus.com/inward/record.url?scp=79955673049&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 79955673049
Research output: Contribution to journal › Article › Scientific › peer-review

Mesopic background lights enhance dark-adapted cone ERG flash responses in the intact mouse retina: A possible role for gap junctional decoupling

The cone-driven flash responses of mouse electroretinogram (ERG) increase as much as twofold over the course of several minutes during adaptation to a rod-compressing background light. The origins of this phenomenon were investigated in the present work by recording preflash-isolated (M-)cone flash responses ex vivo in darkness and during application of various steady background lights. In this protocol, the cone stimulating flash was preceded by a preflash that

maintains rods under saturation (hyperpolarized) to allow selective stimulation of the cones at varying background light levels. The light-induced growth was found to represent true enhancement of cone flash responses with respect to their darkadapted state. It developed within minutes, and its overall magnitude was a graded function of the background light intensity. The threshold intensity of cone response growth was observed with lights in the low mesopic luminance region, at which rod responses are partly compressed. Maximal effect was reached at intensities sufficient to suppress ~90% of the rod responses. Light-induced enhancement of the cone photoresponses was not sensitive to antagonists and agonists of glutamatergic transmission. However, applying gap junction blockers to the dark-adapted retina produced qualitatively similar changes in the cone flash responses as did background light and prevented further growth during subsequent light-adaptation. These results are consistent with the idea that cone ERG photoresponses are suppressed in the dark-adapted mouse retina by gap junctional coupling between rods and cones. This coupling would then be gradually and reversibly removed by mesopic background lights, allowing larger functional range for the cone light responses.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Aalto University, Department of Biomedical Engineering and Computational Science
Contributors: Heikkinen, H., Vinberg, F., Nymark, S., Koskelainen, A.
Number of pages: 10
Pages: 2309-2318
Publication date: May 2011
Peer-reviewed: Yes

Publication information
Journal: Journal of Neurophysiology
Volume: 105
Issue number: 5
ISSN (Print): 0022-3077
Ratings:

Scopus rating (2011): CiteScore 5.9 SJR 2.848 SNIP 1.209
Original language: English
ASJC Scopus subject areas: Physiology, Neuroscience(all)
Keywords: Electroretinogram, Light adaptation, Photoreceptor, Retina, Rod-cone coupling
DOIs:

10.1152/jn.00536.2010
URLs:

http://www.scopus.com/inward/record.url?scp=79956275463&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 79956275463
Research output: Contribution to journal › Article › Scientific › peer-review

Cost-effectiveness of decompressive craniectomy in non-traumatic neurological emergencies
Background: Decompressive craniectomy is used regularly in traumatic brain injury (TBI) and malignant middle cerebral artery infarction. Its benefits for other causes of non-traumatic brain swelling, if any, are unclear, especially after a devastating primary event. Methods: We evaluated the outcomes as well as treatment costs of all emergency decompressive craniectomies performed between the 2000 and 2006 in a single institution to lower intractable intracranial pressure, excluding the standard indications TBI and malignant middle cerebral infarction. The health-related quality of life (HRQoL) was evaluated on the Euroqol (EQ-5D) scale, and cost of a quality-adjusted life year (QALY) calculated. Results: The overall 3-year mortality rate was 62% for subarachnoid haemorrhage (SAH, 29 patients) and 31% for other neurological emergencies (13 patients). Patients with SAH were on average 13years older than the other indications mean. Of the non-survivors, 45% died within a month and 95% within 1year. Median EQ-5D index values were poor (0.15 for SAH and 0.62 for the other emergencies, versus 0.85 for the normal population), but of the survivors, 73% and 89% were able to live at home. The cost of neurosurgical treatment for one QALY was 11000€ for SAH and 2000€ for other emergencies. Conclusion: Mortality after non-traumatic neurological emergencies leading to decompressive craniectomy was high, and the HRQoL index of the survivors was poor. Most survivors were, however, able to live at home, and the cost of neurosurgical treatment for a QALY gained was acceptable.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Päijät-Häme Central Hospital, Tampere University Hospital, Helsinki University Central Hospital
Contributors: Malmivaara, K., Ohman, J., Kivisaari, R., Hernesniemi, J., Siironen, J.
Number of pages: 8
Pages: 402-409

Publication date: Mar 2011
Peer-reviewed: Yes

Publication information
Journal: European Journal of Neurology
Volume: 18
Issue number: 3
ISSN (Print): 1351-5101
Ratings:

Scopus rating (2011): CiteScore 6.3 SJR 1.547 SNIP 1.368
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Neurology
Keywords: Decompressive craniectomy, Intensive care, Quality of life, Subarachnoid haemorrhage, Surgery
DOIs:

10.1111/j.1468-1331.2010.03162.x
URLs:

http://www.scopus.com/inward/record.url?scp=79951666249&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 79951666249
Research output: Contribution to journal › Article › Scientific › peer-review

Fault tolerant machine learning for nanoscale cognitive radio
We introduce a machine learning-based classifier that identifies free radio channels for cognitive radio. The architecture is designed for nanoscale implementation, under nanoscale implementation constraints; we do not describe all physical details but believe future physical implementation to be feasible. The system uses analog computation and consists of cyclostationary feature extraction and a radial basis function network for classification. We describe a model for nanoscale faults in the system, and simulate experimental performance and fault tolerance in recognizing WLAN signals, under different levels of noise and computational errors. The system performs well under expected non-ideal manufacturing and operating conditions.

General information
Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Research Community on Data-to-Decision (D2D), Aalto University, Nokia
Contributors: Pajarinen, J., Peltonen, J., Uusitalo, M. A.
Number of pages: 12
Pages: 753-764
Publication date: Feb 2011
Peer-reviewed: Yes

Publication information
Journal: Neurocomputing
Volume: 74
Issue number: 5
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2011): CiteScore 4.2 SJR 0.898 SNIP 1.793
Original language: English
ASJC Scopus subject areas: Computer Science Applications, Cognitive Neuroscience, Artificial Intelligence
Keywords: Cognitive radio, Fault tolerance, Nanoelectronics, Nanotechnology, Radial basis function network
DOIs:

10.1016/j.neucom.2010.10.007
URLs:

http://www.scopus.com/inward/record.url?scp=78650719880&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 78650719880
Research output: Contribution to journal › Article › Scientific › peer-review

Neuromuscular pathology in mice lacking alpha-synuclein
This work was undertaken in order to study the possible role of alpha-synuclein in the function of the neuro-muscular junction in skeletal muscles. Repeated stimulation of skeletal muscle motor neurons revealed signs of neuromuscular pathology in alpha-synuclein null mutated (C57Bl/6JOlaHsd) and knockout (B6;129X1-Snca^{tm1Rosl}/J) mice. This stimulation produced repetitive compound muscle action potentials in both lines of alpha-synuclein deficient mice. Muscle strength and muscle coordination during ambulation were unaffected, though motor learning was slower in alpha-synuclein

deficient mice in the Rotarod test. We conclude that alpha-synuclein may play a role in acetylcholine compartmentalization at the neuromuscular junction, and in the fine control of activity of skeletal muscles.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Integrated Technologies for Tissue Engineering Research (ITTE), Ita-Suomen yliopisto
Contributors: Pelkonen, A., Yavich, L.
Number of pages: 4
Pages: 350-353
Publication date: 10 Jan 2011
Peer-reviewed: Yes

Publication information

Journal: Neuroscience Letters
Volume: 487
Issue number: 3
ISSN (Print): 0304-3940
Ratings:

Scopus rating (2011): CiteScore 3.9 SJR 1.032 SNIP 0.759
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Alpha-synuclein, Electromyography, Knockout mice, Neuromuscular junction, Skeletal muscles
DOIs:

10.1016/j.neulet.2010.10.054
URLs:

http://www.scopus.com/inward/record.url?scp=78650518172&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 78650518172
Research output: Contribution to journal › Article › Scientific › peer-review

Influence of the neural network topology on the learning dynamics

We study the influence of the topology of a neural network on its learning dynamics. The network topology can be controlled by one parameter p_{rw} to convert the topology from regular to random in a continuous way [D.J. Watts and S.H. Strogatz, Collective dynamics of small-world networks, Nature 393 (1998) 440-442]. As test problem, which requires a recurrent network, we choose the problem of timing to be learned by the network, that means to connect a predefined input neuron with a output neuron in exactly T_f time steps. We analyze the learning dynamics for different parameters numerically by counting the number of paths within the network which are available for solving the problem. Our results show, that there are parameter values for which either a regular, small-world or random network gives the best performance depending strongly on the choice for the predefined input and output neurons.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: Stowers Institute for Medical Research, Institut für Theoretische Physik, University of Bremen
Contributors: Emmert-Streib, F.
Number of pages: 4
Pages: 1179-1182
Publication date: May 2006
Peer-reviewed: Yes

Publication information

Journal: Neurocomputing
Volume: 69
Issue number: 10-12
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2006): SJR 0.475 SNIP 1.052
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Cellular and Molecular Neuroscience
Keywords: Learning dynamics, Neural network, Small-world network
DOIs:

10.1016/j.neucom.2005.12.070
URLs:

http://www.scopus.com/inward/record.url?scp=33646117248&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 33646117248
Research output: Contribution to journal › Article › Scientific › peer-review

A constrained HMM-based approach to the estimation of perceptual switching dynamics in pigeons

We describe a method for the analysis of behavioural data from experiments on perception of bistable stimuli in pigeons. The approach is based on a Hidden Markov Model (HMM) with additional linear factorial constraints for which a modified Baum-Welch algorithm is derived. It allows the estimation of the perceptual switching events, which might directly relate to transitions between states of activation of corresponding neural populations. From the resulting time series, characteristics of the underlying perceptual dynamics can be estimated. We also demonstrate that-inspite of the Markov assumption-the method can reveal certain non-Markovian contributions to the dynamics.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: University of Bremen, Center for Cognitive Sciences
Contributors: Otterpohl, J. R., Emmert-Streib, F., Pawelzik, K.
Number of pages: 7
Pages: 1495-1501
Publication date: Jun 2001
Peer-reviewed: Yes

Publication information

Journal: Neurocomputing
Volume: 38-40
ISSN (Print): 0925-2312
Ratings:

Scopus rating (2001): SJR 0.418 SNIP 0.643
Original language: English
ASJC Scopus subject areas: Artificial Intelligence, Cellular and Molecular Neuroscience
Keywords: bistable perception, constrained hidden Markov model, renewal process, pigeons, estimation, HIDDEN MARKOV-MODELS
DOIs:

10.1016/S0925-2312(01)00511-2
URLs:

http://www.scopus.com/inward/record.url?scp=0035383916&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 0035383916
Research output: Contribution to journal › Article › Scientific › peer-review

Erratum: Extracting the dynamics of perceptual switching from 'noisy' behaviour: An application of hidden Markov modelling to pecking data from pigeons (Journal of Physiology Paris (2000) 94:5-6 (555-567) PII: S0928425700010950)

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: University of Bremen, Institute of Theoretical Neurophysics
Contributors: Otterpohl, J. R., Haynes, J. D., Emmert-Streib, F., Vetter, G., Pawelzik, K.
Number of pages: 1
Pages: 497
Publication date: 2001
Peer-reviewed: Yes

Publication information

Journal: Journal of Physiology: Paris
Volume: 95
Issue number: 1-6
ISSN (Print): 0928-4257
Ratings:

Scopus rating (2001): SJR 0.625 SNIP 0.51
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Physiology (medical)

DOIs:
10.1016/S0928-4257(01)00091-2
URLs:
http://www.scopus.com/inward/record.url?scp=0034750325&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 0034750325
Research output: Contribution to journal › Article › Scientific › peer-review

Extracting the dynamics of perceptual switching from 'noisy' behaviour: An application of hidden Markov modelling to pecking data from pigeons

When studying animal perception, one normally has the chance of localizing perceptual events in time, that is via behavioural responses time-locked to the stimuli. With multistable stimuli, however, perceptual changes occur despite stationary stimulation. Here, the challenge is to infer these not directly observable perceptual states indirectly from the behavioural data. This estimation is complicated by the fact that an animal's performance is contaminated by errors. We propose a two-step approach to overcome this difficulty: First, one sets up a generative, stochastic model of the behavioural time series based on the relevant parameters, including the probability of errors. Second, one performs a model-based maximum-likelihood estimation on the data in order to extract the non-observable perceptual state transitions. We illustrate this methodology for data from experiments on perception of bistable apparent motion in pigeons. The observed behavioural time series is analysed and explained by a combination of a Markovian perceptual dynamics with a renewal process that governs the motor response. We propose a hidden Markov model in which non-observable states represent both the perceptual states and the states of the renewal process of the motor dynamics, while the observable states account for overt pecking performance. Showing that this constitutes an appropriate phenomenological model of the time series of observable pecking events, we use it subsequently to obtain an estimate of the internal (and thus covert) perceptual reversals. These may directly correspond to changes in the activity of mutually inhibitory populations of motion selective neurones tuned to orthogonal directions.

General information

Publication status: Published
MoE publication type: A1 Journal article-refereed
Organisations: University of Bremen, Institute of Theoretical Neurophysics
Contributors: Otterpohl, J. R., Haynes, J. D., Emmert-Streib, F., Vetter, G., Pawelzik, K.
Number of pages: 13
Pages: 555-567
Publication date: 2000
Peer-reviewed: Yes

Publication information

Journal: Journal of Physiology: Paris
Volume: 94
Issue number: 5-6
ISSN (Print): 0928-4257
Ratings:
Scopus rating (2000): SJR 0.544 SNIP 0.383
Original language: English
ASJC Scopus subject areas: Neuroscience(all), Physiology (medical)
Keywords: Apparent motion, Bistable perception, Hidden Markov model, Pigeons, Renewal process
DOIs:
10.1016/S0928-4257(00)01095-0
Source: Scopus
Source ID: 0034486059
Research output: Contribution to journal › Article › Scientific › peer-review

Salivary cortisol reactivity to psychological stressors in infancy: A meta-analysis

Measurement of salivary cortisol is a practical and non-invasive tool for studying stress reactivity to various types of stressors even in young infants. Whereas studies using physical stressors during the first months of life have found robust cortisol responses to painful stimuli, research with older infants using psychological stressors (e.g., parental separation) has produced mixed findings, limiting our understanding of potential developmental changes in cortisol reactivity across infancy. In the present study, we used meta-analysis to systematically investigate whether psychological stressor paradigms are associated with measurable cortisol responses in infants under 18 months of age and whether the magnitude of the responses is moderated by the type of psychological stressor (i.e., separation, frustration, novelty, or disruption of parental interaction), infant age, and other potential moderators. Across 47 studies (N = 4095, age range: 3–18 months), we found that commonly used psychological stressor paradigms are associated with a small (Hedges' g = .11) increase in salivary cortisol levels in typically developing infants. Stressor type moderated the effect sizes, and when effect sizes in each category were analyzed separately, only the separation studies were associated with a consistent increase in cortisol following the stressor. Age did not moderate the effect sizes either in the full set of studies or within the

separate stressor types. These meta-analytic results indicate that the normative cortisol response to psychological stressors across infancy is small and emphasize the need for standardized stressor paradigms to assess cortisol responses systematically across infancy.

General information
Publication status: Published
MoE publication type: A2 Review article in a scientific journal
Organisations: Education, Human Information Processing Laboratory
Contributors: Puhakka, I. J., Peltola, M. J.
Publication date: 1 May 2020
Peer-reviewed: Yes

Publication information
Journal: PSYCHONEUROENDOCRINOLOGY
Volume: 115
Article number: 104603
ISSN (Print): 0306-4530
Original language: English
ASJC Scopus subject areas: Endocrinology, Diabetes and Metabolism, Endocrinology, Endocrine and Autonomic Systems , Psychiatry and Mental health, Biological Psychiatry
Keywords: Cortisol, Infant, Meta-Analysis, Saliva, Stressor
DOIs:

10.1016/j.psyneuen.2020.104603
Source: Scopus
Source ID: 85081216139
Research output: Contribution to journal › Review Article › Scientific › peer-review

From in silico astrocyte cell models to neuron-astrocyte network models: A review
The idea that astrocytes may be active partners in synaptic information processing has recently emerged from abundant experimental reports. Because of their spatial proximity to neurons and their bidirectional communication with them, astrocytes are now considered as an important third element of the synapse. Astrocytes integrate and process synaptic information and by doing so generate cytosolic calcium signals that are believed to reflect neuronal transmitter release. Moreover, they regulate neuronal information transmission by releasing gliotransmitters into the synaptic cleft affecting both pre- and postsynaptic receptors. Concurrent with the first experimental reports of the astrocytic impact on neural network dynamics, computational models describing astrocytic functions have been developed. In this review, we give an overview over the published computational models of astrocytic functions, from single-cell dynamics to the tripartite synapse level and network models of astrocytes and neurons.

General information
Publication status: Published
MoE publication type: A2 Review article in a scientific journal
Organisations: Research group: Computational Biophysics and Imaging Group, Faculty of Biomedical Sciences and Engineering, BioMediTech, Bernstein Center for Computational Neuroscience, University of Lyon
Contributors: Oschmann, F., Berry, H., Obermayer, K., Lenk, K.
Pages: 76-84
Publication date: 2018
Peer-reviewed: Yes
Early online date: 8 Feb 2017

Publication information
Journal: BRAIN RESEARCH BULLETIN
Volume: 136
ISSN (Print): 0361-9230
Ratings:

Scopus rating (2018): CiteScore 4.8 SJR 1.073 SNIP 0.922
Original language: English
ASJC Scopus subject areas: Neuroscience(all)
Keywords: Astrocyte, In silico, Network, Neuron, Simulation, Tripartite synapse
DOIs:

10.1016/j.brainresbull.2017.01.027
Source: Scopus
Source ID: 85011990201
Research output: Contribution to journal › Review Article › Scientific › peer-review

Advances in Human Stem Cell-Derived Neuronal Cell Culturing and Analysis

This chapter provides an overview of the current stage of human in vitro functional neuronal cultures, their biological application areas, and modalities to analyze their behavior. During the last 10 years, this research area has changed from being practically non-existent to one that is facing high expectations. Here, we present a case study as a comprehensive short history of this process based on extensive studies conducted at NeuroGroup (University of Tampere) and Computational Biophysics and Imaging Group (Tampere University of Technology), ranging from the differentiation and culturing of human pluripotent stem cell (hPSC)-derived neuronal networks to their electrophysiological analysis. After an introduction to neuronal differentiation in hPSCs, we review our work on their functionality and approaches for extending cultures from 2D to 3D systems. Thereafter, we discuss our target applications in neuronal developmental modeling, toxicology, drug screening, and disease modeling. The development of signal analysis methods was required due to the unique functional and developmental properties of hPSC-derived neuronal cells and networks, which separate them from their much-used rodent counterparts. Accordingly, a line of microelectrode array (MEA) signal analysis methods was developed. This work included the development of action potential spike detection methods, entropy-based methods and additional methods for burst detection and quantification, joint analysis of spikes and bursts to analyze the spike waveform compositions of bursts, assessment methods for network synchronization, and computational simulations of synapses and neuronal networks.

General information

Publication status: Published
MoE publication type: A3 Part of a book or another research book
Organisations: Research group: Computational Biophysics and Imaging Group, BioMediTech, NeuroGroup, Danish Research Institute of Translational Neuroscience - DANDRITE, Aarhus Universitet, Department of Biomedicine, Tampere University
Contributors: Ylä-Outinen, L., Tanskanen, J. M., Kapucu, F. E., Hyysalo, A., Hyttinen, J. A., Narkilahti, S.
Number of pages: 31
Pages: 299-329
Publication date: 2019

Host publication information

Title of host publication: In Vitro Neuronal Networks : From Culturing Methods to Neuro-Technological Applications
Publisher: Springer New York LLC
ISBN (Print): 978-3-030-11134-2
ISBN (Electronic): 978-3-030-11135-9

Publication series

Name: Advances in Neurobiology
Volume: 22
ISSN (Print): 2190-5215
ASJC Scopus subject areas: Biochemistry, Neurology, Developmental Neuroscience, Cellular and Molecular Neuroscience
Keywords: Human neurons, Human pluripotent stem cells, Microelectrode arrays, Signal analysis
DOIs:
10.1007/978-3-030-11135-9_13
URLs:
http://urn.fi/URN:NBN:fi:tuni-201911266288. Embargo ends: 10/05/21

Bibliographical note

EXT="Ylä-Outinen, Laura"
EXT="Kapucu, Fikret E."
Source: Scopus
Source ID: 85065845190
Research output: Chapter in Book/Report/Conference proceeding › Chapter › Scientific › peer-review

Deep audio-visual saliency: Baseline model and data

This paper introduces a conceptually simple and effective Deep Audio-Visual Embedding for dynamic saliency prediction dubbed "DAVE" in conjunction with our efforts towards building an Audio-Visual Eye-tracking corpus named "AVE". Despite existing a strong relation between auditory and visual cues for guiding gaze during perception, video saliency models only consider visual cues and neglect the auditory information that is ubiquitous in dynamic scenes. Here, we propose a baseline deep audio-visual saliency model for multi-modal saliency prediction in the wild. Thus the proposed model is intentionally designed to be simple. A video baseline model is also developed on the same architecture to assess effectiveness of the audio-visual models on a fair basis. We demonstrate that audio-visual saliency model outperforms the video saliency models. The data and code are available at https://hrtavakoli.github.io/AVE/and https://github.com/hrtavakoli/DAVE.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Computing Sciences, Nokia, Aalto University
Contributors: Tavakoli, H. R., Borji, A., Kannala, J., Rahtu, E.
Publication date: 6 Feb 2020

Host publication information
Title of host publication: Proceedings ETRA 2020 Short Papers - ACM Symposium on Eye Tracking Research and Applications, ETRA 2020
Publisher: ACM
Editor: Spencer, S. N.
Article number: 3
ISBN (Electronic): 9781450371346
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: Audio-Visual Saliency, Deep Learning, Dynamic Visual Attention
DOIs:

10.1145/3379156.3391337

Bibliographical note
EXT="Tavakoli, Hamed Rezazadegan"
Source: Scopus
Source ID: 85085734752
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Human-robot interactive learning architecture using ontologies and symbol manipulation
Robotic systems developed for support can provide assistance in various ways. However, regardless of the service provided, the quality of user interaction is key to adoption by the general public. Simple communication difficulties, such as terminological differences, can make or break the acceptance of robots. In this work we take into account these difficulties in communication between a human and a robot. We propose a system that allows to handle unknown concepts through symbol manipulation based on natural language interactions. In addition, ontologies are used as a convenient way to store the knowledge and reason about it. To demonstrate the use of our system, two scenarios are described and tested with a Care-O-Bot 4. The experiments show that confusions and difficulties in communication can effectively be resolved through symbol manipulation.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Automation Technology and Mechanical Engineering, Aalto University
Contributors: Angleraud, A., Houbre, Q., Kyrki, V., Pieters, R.
Number of pages: 6
Pages: 384-389
Publication date: 6 Nov 2018

Host publication information
Title of host publication: RO-MAN 2018 - 27th IEEE International Symposium on Robot and Human Interactive Communication : August 27-31, 2018, Nanjing, China.
Publisher: IEEE
ISBN (Print): 978-1-5386-7981-4
ISBN (Electronic): 9781538679807

Publication series
Name: IEEE RO-MAN
ISSN (Print): 1944-9445
ISSN (Electronic): 1944-9437
ASJC Scopus subject areas: Human-Computer Interaction, Cognitive Neuroscience, Communication, Artificial Intelligence
Electronic versions:

roman2018_Angleraud
DOIs:

10.1109/ROMAN.2018.8525580
URLs:

http://urn.fi/URN:NBN:fi:tuni-201912136859

Bibliographical note
jufoid=72047

Source: Scopus
Source ID: 85058077478
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Automatic objective thresholding to detect neuronal action potentials

In this paper, we introduce a fully objective method to set thresholds (THs) for neuronal action potential spike detection from extracellular field potential signals. Although several more sophisticated methods exist, thresholding is still the most used spike detection method. In general, it is employed by setting a TH as per convention or operator decision, and without considering either the undetected or spurious spikes. Here, we demonstrate with both simulations and real microelectrode measurement data that our method can fully automatically and objectively yield THs comparable to those set by an expert operator. A Matlab function implementation of the method is described, and provided freely in Matlab Central File Exchange.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Electronics and Communications Engineering, Research group: Computational Biophysics and Imaging Group, Department of Pervasive Computing, BioMediTech
Contributors: Tanskanen, J. M., Kapucu, F. E., Välkki, I., Hyttinen, J. A.
Number of pages: 5
Pages: 662-666
Publication date: 29 Aug 2016

Host publication information

Title of host publication: Proceedings of 2016 24th European Signal Processing Conference (EUSIPCO)
ISBN (Print): 978-1-5090-1891-8
ISBN (Electronic): 978-0-9928-6265-7
ASJC Scopus subject areas: Signal Processing, Neuroscience(all)
Keywords: Neuronal action potential, Thresholding, Spike detection, Microelectrode array, Electric field potential
Electronic versions:

EUSIPCO2016_Tanskanen
DOIs:

10.1109/EUSIPCO.2016.7760331
URLs:

http://urn.fi/URN:NBN:fi:tty-201612124857
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Whole-cell morphological properties of neurons constrain the nonrandom features of network connectivity

We addressed the principles of micro-level organization of neuronal circuits and explored how the neuronal morphology constrains this organization. Several studies have demonstrated the non-trivial properties of the network connectivity using in vitro recordings from multiple neurons [1, 2, 3], yet it is unclear to what extent this structure reflects reorganization caused by synaptic plasticity, and what is imposed by the morphological constraints. Two recent articles explored this issue using the simulated neural circuits and demonstrated the specific structural properties in those circuits [4, 5].We analyzed a model that emphasizes the role of single-cell morphology, a homogeneous population of neurons in a planar space without boundaries. Each neuron is composed of two displaced neurite fields defined on the limited support. A neurite field describes the likelihood of finding a neurite segment at a certain point in the plane. Using a proximity criterion (Peters' rule) the expected number of potential synapses is estimated between each pair of neurons. Alternatively, this number can be estimated from the realistic morphology of a simulated neuron, or from the morphologies reconstructed from in vitro/in vivo recordings. The number of potential synapses depends on the axon-dendrite distance, which leads to a definition of the expected radius. An axon-dendrite pair that is expected to form at least one synapse must be on a distance not larger than the effective radius. All considered statistical measures of network connectivity are expressed as the functions of the effective radius normalized with the neuron size. In this study, we considered the standard graph theoretic measures of network connectivity, the motif counts, clustering coefficient, path length, and small-world coefficient. It has been demonstrated that they have a significant impact on the population activity in simulated networks [6].Changing the normalized effective radius from small (<0.3) to big (>10) we vary the network properties between the two extremes. For the small values of the effective radius, the networks favor unidirectional connections and sparse local connectivity. The clustering coefficient and the path length are similar to those obtained in uniform random networks, i.e. in the networks independent of topology. For the large values of the effective radius, the local connectivity is dense with the majority of bidirectional connections. As the normalized effective radius increases, the clustering coefficient increases towards the values obtained for the networks with dominant local connectivity, while the path length remains close to the one of the uniform random networks. The normalized effective radius on the interval 1-2, provides the biggest variability of connectivity patterns and the optimized properties relevant for the information transfer.Conclusions: We present a theoretical framework that relates neuromorphology with the connectivity in neuronal circuits, and that can be solved analytically. The normalized effective radius was found to be the key morphological property that dominantly affects considered connectivity measures. By tuning it we can obtain the networks with the biggest variability of local connectivity

patterns. At the same time, those networks acquire the key characteristics of the small-world networks, known to optimize the information transfer.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Faculty of Biomedical Sciences and Engineering
Contributors: Acimovic, J., Mäki-Marttunen, T. M., Linne, M.
Number of pages: 1
Pages: P:O7
Publication date: 4 Dec 2015

Host publication information
Title of host publication: 24th Annual Computational Neuroscience Meeting: CNS*2015
Volume: 16 (Suppl 1)
Place of publication: Prague
Publisher: BioMed Central
Editors: Cymbalyuk, G., Burkitt, A.
Article number: O7
ASJC Scopus subject areas: Neuroscience (miscellaneous), Signal Processing
Keywords: network connectivity, clustering coefficient, effective radius, neuronal circuit, connectivity pattern, morphology, dendrites, Neurite density field, neurites
URLs:

https://bmcneurosci.biomedcentral.com/articles/supplements/volume-16-supplement-1
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Real-time hidden gaze point correction
The accuracy of gaze point estimation is one of the main limiting factors in developing applications that utilize gaze input. The existing gaze point correction methods either do not support real-time interaction or imply restrictions on gazecontrolled tasks and object screen locations. We hypothesize that when gaze points can be reliably correlated with object screen locations, it is possible to gather and leverage this information for improving the accuracy of gaze pointing. We propose an algorithm that uses a growing pool of such collected correlations between gaze points and objects for real-time hidden gaze point correction. We tested this algorithm assuming that any point inside of a rectangular object has equal probability to be hit by gaze. We collected real data in a user study to simulate pointing at targets of small (80px) size. The results showed that our algorithm can significantly improve the hit rate especially in pointing at middle-sized targets. The proposed method is real-time, person- and taskindependent and is applicable for arbitrary located objects.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA)
Contributors: Špakov, O., Gizatdinova, Y.
Number of pages: 4
Pages: 291-294
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the Symposium on Eye Tracking Research and Applications, ETRA 2014
Publisher: Association for Computing Machinery
ISBN (Print): 9781450327510
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: Accuracy correction, Algorithms, Cumulative distribution function, Eye tracking, Gaze point, Pointing
DOIs:

10.1145/2578153.2578200
URLs:

http://www.scopus.com/inward/record.url?scp=84899672400&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84899672400
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

TraQuMe: A tool for measuring the gaze tracking quality
Consistent measuring and reporting of gaze data quality is important in research that involves eye trackers. We have developed TraQuMe: a generic system to evaluate the gaze data quality. The quality measurement is fast and the interpretation of the results is aided by graphical output. Numeric data is saved for reporting of aggregate metrics for the

whole experiment. We tested TraQuMe in the context of a novel hidden calibration procedure that we developed to aid in experiments where participants should not know that their gaze is being tracked. The quality of tracking data after the hidden calibration procedure was very close to that obtained with the Tobii's T60 trackers built-in 2 point, 5 point and 9 point calibrations.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA), School of Management (JKK)
Contributors: Akkil, D., Isokoski, P., Kangas, J., Rantala, J., Raisamo, R.
Number of pages: 4
Pages: 327-330
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the Symposium on Eye Tracking Research and Applications, ETRA 2014
Publisher: Association for Computing Machinery
ISBN (Print): 9781450327510
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: Gaze interaction, Gaze tracking
DOIs:

10.1145/2578153.2578192
URLs:

http://www.scopus.com/inward/record.url?scp=84899688722&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84899688722
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Look and lean: Accurate head-assisted eye pointing
Compared to the mouse, eye pointing is inaccurate. As a consequence, small objects are difficult to point by gaze alone. We suggest using a combination of eye pointing and subtle head movements to achieve accurate hands-free pointing in a conventional desktop computing environment. For tracking the head movements, we exploited information of the eye position in the eye tracker's camera view. We conducted a series of three experiments to study the potential caveats and benefits of using head movements to adjust gaze cursor position. Results showed that head-assisted eye pointing significantly improves the pointing accuracy without a negative impact on the pointing time. In some cases participants were able to point almost 3 times closer to the target's center, compared to the eye pointing alone (7 vs. 19 pixels). We conclude that head assisted eye pointing is a comfortable and potentially very efficient alternative for other assisting methods in the eye pointing, such as zooming.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA)
Contributors: Špakov, O., Isokoski, P., Majaranta, P.
Number of pages: 8
Pages: 35-42
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the Symposium on Eye Tracking Research and Applications, ETRA 2014
Publisher: Association for Computing Machinery
ISBN (Print): 9781450327510
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: Eye tracking, Gaze input, Head movements, Pointing
DOIs:

10.1145/2578153.2578157
URLs:

http://www.scopus.com/inward/record.url?scp=84899691537&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84899691537
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Haptic feedback to gaze events

Eye tracking input often relies on visual and auditory feedback. Haptic feedback offers a previously unused alternative to these established methods. We describe a study to determine the natu-ral time limits for haptic feedback to gazing events. The target is to determine how much time we can use to evaluate the user gazed object and decide if we are going to give the user a haptic notification on that object or not. The results indicate that it is best to get feedback faster than in 250 milliseconds from the start of fixation of an object. Longer delay leads to increase in incorrect associations between objects and the feedback. Delays longer than 500 milliseconds were confusing for the user.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA), School of Management (JKK)
Contributors: Kangas, J., Rantala, J., Majaranta, P., Isokoski, P., Raisamo, R.
Number of pages: 8
Pages: 11-18
Publication date: 2014

Host publication information

Title of host publication: Proceedings of the Symposium on Eye Tracking Research and Applications, ETRA 2014
Publisher: Association for Computing Machinery
ISBN (Print): 9781450327510
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: Gaze interaction, Gaze tracking, Haptic feedback
DOIs:

10.1145/2578153.2578154
URLs:

http://www.scopus.com/inward/record.url?scp=84899691269&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84899691269
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

On the effect of network structure and synaptic mechanisms on sustained bursting activity

The sustained activity in recurrent networks has been under wide computational examination in studies concerning, e.g., working memory and epilepsy. Synaptic and cellular mechanisms for sustained activity have been reviewed in [1], and the optimal structural features for sustained activity have been sought for in [2]. In this work, we analyze the effect of network structure and synaptic mechanisms on the sustained high-frequency network-wide activity, i.e., sustained network bursts. In more detail, we assess the degree to which the neuronal activity can be maintained by changing fine details of network structure, given a certain set of synaptic mechanisms (e.g., short-term plasticity).

The neurons in our study are modeled as point-neurons that are activated by noisy fluctuations of the membrane potential. Given strong enough recurrent excitatory connections, the spontaneous firing extends to a network-wide sustained activity. Experimental in vitro data (e.g., [3]) show that this emergent activity dies out and restarts spontaneously in dissociated cultures. Several mechanisms have been suggested for ceasing the sustained activity, namely, the delayed activation of the inhibitory population, depletion of glutamatergic resources, and synchronization of the excitatory population [1,4]. The main focus of this work lies on the latter two mechanisms. We employ the integrate-and-fire neuron model with short-term depression [4] for deriving the main results. We also use a more biophysically realistic integrate-and-fire model that combines different synaptic currents, e.g., AMPA and NMDA [5], and a yet more detailed Hodgkin-Huxley-based model [6] to confirm our results. We consider four essentially different classes of network structure: 1) an Erdős-Rényi type of random network 2) a locally connected network, 3) a random network with high occurrence of directed loops of length 6, and 4) a random network with high number of triples of nodes constituting a feed-forward loop. The in-degree distribution of all networks is kept fixed in order to ensure that the networks are comparable.

Our results reveal links between the network excitability and the network structure. In purely excitatory networks with short-term depression, the amount of activity is increased with the synaptic strength, first from spontaneous tonic firing to spontaneous network-wide bursting activity and finally to long or ceaseless bursts. We show that the range of values of synaptic strength for observing one of these three modes depends on the choice of network structure. The networks with a high number of feed-forward loops show an increased ability to cease the burst in the regime of high synaptic strength, whereas the networks with a high number of 6-loops require lower synaptic strength in order to express ceaseless bursting activity. We calculate the parameter ranges of the named three modes of activity for several variations of synaptic currents. We also study the effect of an inhibitory subpopulation on the three modes. The results are discussed in comparison to "superbursts" that can be observed in dissociated cultures [7]. Our results could help in identifying structures that promote sustained bursting activity and further the understanding of contribution of different synaptic mechanisms.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Faculty of Biomedical Sciences and Engineering
Contributors: Mäki-Marttunen, T. M., Acimovic, J., Ruohonen, K. P., Linne, M.
Number of pages: 1
Pages: P247
Publication date: 8 Jul 2013

Host publication information
Title of host publication: Twenty Second Annual Computational Neuroscience Meeting: CNS*2013
Volume: Volume 14 Suppl 1
Place of publication: Paris, France
Publisher: BioMed Central
Editors: Cymbalyuk, G., Prinz, A.
ASJC Scopus subject areas: Neuroscience (miscellaneous), Signal Processing
Keywords: Computational neuroscience, Neuronal networks, Neuronal network activity, Hodgkin-Huxley model neuron, synapses, spontaneous activity, integrate-and-fire model neuron, structure-function relation
URLs:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3704507/
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

In silico study on structure and dynamics in bursting neuronal networks
In vitro cell cultures have been widely used as a model system for studying neuronal development and electroresponsiveness in the absence of in vivo regulation. These networks are characterized by population bursts that vary largely in both frequency and shape (Wagenaar et al., BMC Neurosci. 2000). In this work we study the interplay of structure and activity in simulated spontaneously bursting networks. The computational approach is useful due to the difficulty of gaining enough control on the structure in in vitro experiments, although promising attempts are being made in cultured neuronal networks (Wheeler, Proc. IEEE 2010). Recently, the effect of network structure on activity has been analyzed through, e.g., the degree distribution width (Roxin, Front. Comp. Neurosci. 2011) and occurrence of second-order connections (Zhao et al. 2011, Front. Comp. Neurosci. 2011). In the present work we apply a set of graph measures to a wide set of different networks in order to determine which of the structural measures are relevant in the prediction of the bursting network activity. The network activity is quantified using standard measures such as number of bursts and burst duration.
We use two neuron models that are applicable to small (N=100) spontaneously bursting networks, namely, an integrate-and-fire model with short-term plasticity (Tsodyks et al., J. Neurosci. 2000) and a more detailed point-neuron model with four ionic and three synaptic currents (Golomb et al., J. Neurophysiol. 2006). We show that when the in-degree is sharp (binomial), the network activity is best predicted by using the clustering coefficient of the underlying graph. By contrast, when a broad in-degree is used (power-law), the maximum eigenvalue of the connectivity matrix becomes dominant in predicting the network activity. The results are consistent across the two neuron models. In our work the neurons are identical by their features, and no input is applied to the network, and hence all statistical difference between the compared networks is caused by the network structure and the network structure only.
The obtained results shed light on the relevance of different aspects of structure. In in vivo applications the full connectome is rarely accessible, but estimates of certain structural measures may be assessed indirectly (Vlachos et al., PLoS Comp. Biol. 2012). Extracting the structure-function relationship in neuronal networks may have implication on both the way experiments are conducted and on how biologically inspired artificial intelligence will be designed in the future.

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Computational Neuro Science-CNS, Department of Signal Processing, Research group: Computational Neuro Science-CNS
Contributors: Mäki-Marttunen, T. M., Acimovic, J., Ruohonen, K. P., Linne, M.
Number of pages: 1
Publication date: 13 Oct 2012

Host publication information
Title of host publication: Neuroscience 2012; 42nd Annual Meeting, New Orleans, USA, October 14-18, 2012
Publisher: Society for Neuroscience (SfN)
Article number: 300.26/DDD70
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Neuroscience (miscellaneous), Applied Mathematics
URLs:

http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=11797e11-d125-4e7e-b77e-b19fd7d32528&cKey=34320433-3c96-47d0-97cc-fa64305a073f&mKey=%7b70007181-01C9-4DE9-A0A2-EEBFA14CD9F1%7d

Significance of graph theoretic measures in predicting neuronal network activity

One of the most prominent patterns of activity observed in developing cortical neuronal networks in vitro is network-wide spontaneous bursting (Wagenaar et al. 2005). In this work, we study computationally the spontaneous emergence of bursts and the effect of network structure on burst shape and frequency. Recent computational structure-function approaches show the effect of, e.g., second-order connections (Zhao et al. 2011) and degree distribution widths (Roxin 2011) on activity patterns. We aim to study a wider set of graph-theoretical measures using networks with identical in-degree distributions. We apply a biophysically plausible point-neuron model of a cortical cell (Golomb et al. 2006). The model network consists of a small (N=100) number of neurons, both excitatory pyramidal neurons and inhibitory interneurons. A model of short-term depression (Golomb and Amitai 1997) is used for glutamatergic synapses. The activity simulation is run over a wide set of classes of network structure. To quantify the structure of the network, we consider graph theoretical measures such as clustering coefficient, geodesic path length, node-betweenness and occurrence of different motifs. We restrict to unweighted bidirectional graph representation, hence the synaptic weights between the neurons are uniform. We study the significance of different graph theoretic measures using a prediction framework: How well can a bursting property, such as burst duration or frequency, be estimated using various measures of structure as attributes? We show that the prediction of bursting properties is improved by taking one or more of the aforementioned measures as prediction attributes. It is best improved when the prediction is based on the clustering coefficient or occurrence of the most highly connected motifs. We confirm the results using a noise-driven LIF model with short-term depression (Tsodyks et al. 2000). We conclude that the significance of measures of clustering is prominent compared to other measures of structure.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Signal Processing, Faculty of Biomedical Sciences and Engineering, Research group: Computational Neuro Science-CNS, Research group: Computational Neuro Science-CNS
Contributors: Mäki-Marttunen, T. M., Acimovic, J., Ruohonen, K. P., Linne, M.
Number of pages: 1
Pages: 55-55
Publication date: 23 Feb 2012

Host publication information

Title of host publication: Proceedings of The 9th annual Computational and Systems Neuroscience meeting (COSYNE 2012)
Place of publication: Salt Lake City
Article number: I-15
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Neuroscience (miscellaneous), Applied Mathematics
URLs:

http://cosyne.org/cosyne12/Cosyne2012_program_book.pdf

Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Gaze gestures or dwell-based interaction?

The two cardinal problems recognized with gaze-based interaction techniques are: how to avoid unintentional commands, and how to overcome the limited accuracy of eye tracking. Gaze gestures are a relatively new technique for giving commands, which has the potential to overcome these problems. We present a study that compares gaze gestures with dwell selection as an interaction technique. The study involved 12 participants and was performed in the context of using an actual application. The participants gave commands to a 3D immersive game using gaze gestures and dwell icons. We found that gaze gestures are not only a feasible means of issuing commands in the course of game play, but they also exhibited performance that was at least as good as or better than dwell selections. The gesture condition produced less than half of the errors when compared with the dwell condition. The study shows that gestures provide a robust alternative to dwell-based interaction with the reliance on positional accuracy being substantially reduced.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA), De Montfort University
Contributors: Hyrskykari, A., Istance, H., Vickers, S.
Number of pages: 4
Pages: 229-232
Publication date: 2012

Host publication information

Title of host publication: Proceedings - ETRA 2012: Eye Tracking Research and Applications Symposium
ISBN (Print): 9781450312257

ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: assistive input devices, eye tracking, gaze and gaming, gaze gestures, physically disabled user groups
DOIs:

10.1145/2168556.2168602
URLs:

http://www.scopus.com/inward/record.url?scp=84862671730&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84862671730
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Comparison of eye movement filters used in HCI

We compared various real-time filters designed to denoise eye movements from low-sampling devices. Most of the filters found in literature were implemented and tested on data gathered in a previous study. An improvement was proposed for one of the filters. Parameters of each filter were adjusted to ensure their best performance. Four estimation parameters were proposed as criteria for comparison. The output from the filters was compared against two idealized signals (the signals denoised offline). The study revealed that FIR filters with triangular or Gaussian kernel (weighting) functions and parameters dependent on signal state show the best performance.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA)
Contributors: Špakov, O.
Number of pages: 4
Pages: 281-284
Publication date: 2012

Host publication information

Title of host publication: Proceedings - ETRA 2012: Eye Tracking Research and Applications Symposium
ISBN (Print): 9781450312257
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: algorithms, eye tracking, filters, gaze, smoothing
DOIs:

10.1145/2168556.2168616
URLs:

http://www.scopus.com/inward/record.url?scp=84862667279&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84862667279
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Simple gaze gestures and the closure of the eyes as an interaction technique

We created a set of gaze gestures that utilize the following three elements: simple one-segment gestures, off-screen space, and the closure of the eyes. These gestures are to be used as the moving tool in a gaze-only controlled drawing application. We tested our gaze gestures with 24 participants and analyzed the gesture durations, the accuracy of the stops, and the gesture performance. We found that the difference in gesture durations between short and long gestures was so small that there is no need to choose between them. The stops made by closing both eyes were accurate, and the input method worked well for this purpose. With some adjustments and with the possibility for personal settings, the gesture performance and the accuracy of the stops can become even better.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA)
Contributors: Heikkilä, H., Räihä, K. J.
Number of pages: 8
Pages: 147-154
Publication date: 2012

Host publication information

Title of host publication: Proceedings - ETRA 2012: Eye Tracking Research and Applications Symposium
ISBN (Print): 9781450312257
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems

Keywords: closure of both eyes, eye tracking, gaze control, gaze gestures, gaze-based interaction, off-screen space
DOIs:

10.1145/2168556.2168579
URLs:

http://www.scopus.com/inward/record.url?scp=84862701036&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84862701036
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

The validity of using non-representative users in gaze communication research

Gaze-based interaction techniques have been investigated for the last two decades, and in many cases the evaluation of these has been based on trials with able-bodied users and conventional usability criteria, mainly speed and accuracy. The target user group of many of the gaze-based techniques investigated is, however, people with different types of physical disabilities. We present the outcomes of two studies that compare the performance of two groups of participants with a type of physical disability (one being cerebral palsy and the other muscular dystrophy) with that of a control group of able-bodied participants doing a task using a particular gaze interaction technique. One study used a task based on dwell-time selection, and the other used a task based on gaze gestures. In both studies, the groups of participants with physical disabilities performed significantly worse than the able-bodied control participants. We question the ecological validity of research into gaze interaction intended for people with physical disabilities that only uses able-bodied participants in evaluation studies without any testing using members of the target user population.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Augmented Human Activities (AHA), De Montfort University
Contributors: Istance, H., Vickers, S., Hyrskykari, A.
Number of pages: 4
Pages: 233-236
Publication date: 2012

Host publication information

Title of host publication: Proceedings - ETRA 2012: Eye Tracking Research and Applications Symposium
ISBN (Print): 9781450312257
ASJC Scopus subject areas: Computer Vision and Pattern Recognition, Human-Computer Interaction, Ophthalmology, Sensory Systems
Keywords: assistive input devices, eye tracking, gaze communication, physically disabled user groups, representative users
DOIs:

10.1145/2168556.2168603
URLs:

http://www.scopus.com/inward/record.url?scp=84862702657&partnerID=8YFLogxK (Link to publication in Scopus)
Source: Scopus
Source ID: 84862702657
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Emergence of global and local structural features during development of neuronal networks

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Faculty of Biomedical Sciences and Engineering
Contributors: Acimovic, J.
Publication date: 6 Jun 2011

Host publication information

Title of host publication: Proceedings of the Eighth International Workshop on Computational Systems Biology, WCSB 2011, June 6-8, 2011, Zürich, Switzerland
Place of publication: Tampere
Publisher: TICSP

Publication series

Name: TICSP Series
Publisher: Tampere International Center for Signal Processing
Volume: 57

ASJC Scopus subject areas: Signal Processing, Cellular and Molecular Neuroscience, Neuroscience (miscellaneous)
Keywords: morphology, connectivity, complex networks, neurite, dendritic structure
URLs:

https://iris.unimore.it/retrieve/handle/11380/699320/40887/WCSB_villanibarbieriserra_final_TICSP.pdf
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Effects of structure on spontaneous activity in simulated neuronal networks

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Signal Processing, BioMediTech, Research group: Computational Neuro Science-CNS, Faculty of Biomedical Sciences and Engineering, Department of Mathematics, Research group: Computational Neuro Science-CNS
Contributors: Mäki-Marttunen, T., Acimovic, J., Ruohonen, K., Linne, M.
Publication date: 11 Apr 2011

Host publication information
Title of host publication: Proceedings of Mathematical Neuroscience (ICMS 2011), April 11-13, 2011, Edinburgh, Scotland
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Neuroscience (miscellaneous), Applied Mathematics, Signal Processing
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Computational study of structural changes in neuronal networks during growth: a model of dissociated neocortical cultures
Networks of neurons possess distinct structural organization that constraints generated activity patterns, and consequently, the functions of the system. The emergence of the network structure can be understood by studying the rules that govern growth of neurons and their self-organization into neuronal circuits. We analyze these rules using a computational model of growth developed for dissociated neocortical cultures. Compared to the growth in vivo, the cultures represent simplified two dimensional systems that still possess the intrinsic properties of single neurons although they lack the natural extracellular environment present in vivo. This setup provides a possibility to address in depth the selected mechanisms that affect neuronal growth. The collected structural data (through staining and microscopy) and electrophysiological data (using microelectrode arrays) facilitate validation of computational models. Neuronal growth in dissociated cultures has been examined in several studies in order to access the role of activity in network development [6],[7] or to extract the structural changes during growth from the recorded activity and identify the significant time points in network development [4]. In addition, two simulators of neuronal growth were recently published to aid the development of computational models [3],[9]. Their performance, in context of modeling neocortical cultures, is compared in [1].

The analyzed model consists of two types on neurons, most commonly observed in the neocortical cultures, the pyramidal cells and the nonpyramidal GABAergic cells, placed in a dish-like space with the density of cells corresponding to the experimental values. The phenomenological model that takes into account growth of every neurite is constructed using the description from the literature [3],[8]. It is compared to the model that defines only the overall shape of each neuritic field. We examine the critical time point in network development, i.e. the emergence of fully connected networks [2],[4], which is dependent on the overall growth speed of neurites. The local structural features are accessed using the frequency of motifs in networks [2],[5]. Local connectivity patterns, captured by the motif counts, depend on the shape of neurites and distribution of synaptic contacts along neurites. The goal of this study is to analyze model dynamics through evaluation of the proposed measures. The dependence on model parameters is examined in details, particularly, whether small variations in parameter values significantly affect both measures of network structure. The obtained conclusions are compared to the experimental findings from the literature [4, 5].

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Signal Processing, Research group: Computational Neuro Science-CNS, Research group: Algebraic and Algorithmic Methods in Signal Processing AAMSP, Research group: Computational Systems Biology
Contributors: Acimovic, J., Mäki-Marttunen, T., Linne, M.
Number of pages: 1
Pages: P203
Publication date: 2011

Host publication information
Title of host publication: Twentieth Annual Computational Neuroscience Meeting: CNS*2011
Volume: 12 (Suppl 1)
Place of publication: Stockholm
Publisher: BioMed Central
Editors: Fellous, J., Prinz, A.

Article number: P203

Publication series
Name: Annual Computational Neuroscience Meeting CNS
Publisher: BioMed Central
Volume: 12
ISSN (Print): 1471-2202
ASJC Scopus subject areas: Neuroscience (miscellaneous)
Keywords: computational model, pyramidal cell, synaptic contact, network development, neuronal circuit
DOIs:
10.1186/1471-2202-12-S1-P203

Bibliographical note
ei ut-numeroa 12.10.2013
Contribution: organisation=sgn,FACT1=1
Source: researchoutputwizard
Source ID: 5648
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Computational modeling of growth in cortial cultures using the NETMORPH simulation tool

Spontaneously developing cortical cultures represent a convenient experimental model system to study the growth and maturation of neurons and neuronal networks. Different microscopical techniques in combination with cell staining provide a possibility to monitor the morphological changes of neurons as well as synaptogenesis. We study the growth in cortical cultures through mathematical models and numerical simulations, using a recently published simulator NETMORPH (Koene et al. 2009). The construction of the simulator is based on the extensive studies of neuron growth in vitro and the statistical description of relevant phenomena, such as neurite elongation rate, elongation direction, and neurite branching (van Pelt & Uylings 2005). The precise dynamics of biophysical processes involved in growth is not included, but only the statistical description of morphology. The obtained model thus has moderate complexity, with relatively low number of model parameters. Single neuron descriptions are incorporated into the computational model of neuronal cultures, consisting of around 10000 neurons, in (Koene et al. 2009). In our study we focus on the first two weeks in vitro. At the beginning of simulations neurons are disconnected, and the first synapses are formed until the end of first week in vitro. The number of synapses per cell progressively increases until the end of second week in vitro. The range of relevant model parameters is first constrained in accordance with the experimental evidences. This parameter space is systematically sampled and the statistics describing the networks of neurons at the end of the first and second week in vitro is obtained through simulations. The relevant network parameters are adopted from graph theory. Each neuron soma represents a node in the graph, and a synapse formed between a dendrite of one and the axon of another neuron represents an edge in the graph. The number of synapses between two neurons can be described as a weight of the corresponding edge. The graph measures, including in- and out-degree distributions and statistics of motifs (Milo et al. 2002), are then extracted. Our preliminary study demonstrates how precisely these parameters describe the network structure during growth. Here, we are further analyzing how the single cell growth parameters, for example the probability of branching, reflect on the network structure. Finally, the obtained results are compared to the experimental evidence describing the distribution of potential synapses developed in cortical cultures (Ichikawa et al. 1993).

General information
Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Department of Signal Processing, Research group: Algebraic and Algorithmic Methods in Signal Processing AAMSP, Research group: Computational Systems Biology
Contributors: Acimovic, J., Mäki-Marttunen, T., Linne, M.
Pages: 2 p
Publication date: 2010

Host publication information
Title of host publication: Neuroscience 2010, 40th Annual Meeting, San Diego, USA, 13-17 November 2010
ASJC Scopus subject areas: Neuroscience (miscellaneous), Signal Processing
Keywords: computational model, morphology, neurite structure, connectivity, structured connectivity
URLs:
http://www.abstractsonline.com/Plan/ViewAbstract.aspx?mID=2554&sKey=f3ce95ee-02ad-4c1f-8871-c673e6f6e717&cKey=e0908b3a-79fb-45f5-84d2-dcdbba7b8b26&mKey=e5d5c83f-ce2d-4d71-9dd6-fc7231e090fb

Bibliographical note
Contribution: organisation=sgn,FACT1=1
Source: researchoutputwizard
Source ID: 7616
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Computational tools for assessing the properties of 2D neural cell cultures

Neurons cultured in vitro provide a particularly promising experimental system for the analysis of properties, such as information coding, transmission, and learning, that are conventionally associated with biological neural networks. In these systems, isolated cells are placed on top of a recording plate (microelectrode array, MEA), where they spontaneously develop a random connectivity structure. Typical cultures consist of several thousands of neurons and the connectivity density varies from very low at the beginning of an experimental trial to high in mature cultures. In the absence of external stimuli, a culture exhibits a typical pattern of spontaneous activity, alternating intervals of slow spiking and bursting with the transition intervals of increasing activity. Spontaneous activity recorded in the cultures of rat cortical cells is described in [1, 2] and an explanation of the phenomena is proposed in [3]. The behavior in the presence of external stimuli is also reported in the literature, for example, the adaptation exhibited in the presence of frequent and rare stimuli is assessed experimentally and through a computational model in [4]. The present work is related to the previously reported study [3] in which an image-processing algorithm is used to detect some structural parameters of cell cultures. A typical result from this study is illustrated in Figure 1. The original image of cultured cells on top of recording plate is shown in panel A, one of its segments in B, and the result of the applied algorithm in C. The blue pattern on panel C corresponds to cells. This approach, in general, enables automated estimation of parameters like the number of cells, or the average density of connections between the cells. Here, we propose a computational model based on the study in [3]. The neural network model is composed of leaky integrate-and-fire neurons, connected in a recurrent network as shown in panel D. The network is fed with the quantitative information about the structure of the cell cultures. Such model, although approximate, captures well the essential properties of the topologies observed in cultures. The presented model is used to reproduce and analyze network behavior observed in the absence of external stimuli. The structural parameters are estimated in different phases of development to closely relate them to the observed behavior. The relation between the network topology and behavior is systematically examined throughout this study.

General information

Publication status: Published
MoE publication type: A4 Article in a conference publication
Organisations: Faculty of Biomedical Sciences and Engineering
Contributors: Acimovic, J., Teppola, H., Selinummi, J. J., Linne, M.
Number of pages: 1
Pages: P170
Publication date: 13 Jul 2009

Host publication information

Title of host publication: Eighteenth Annual Computational Neuroscience Meeting: CNS*2009
Volume: 10 (Suppl 1)
Place of publication: Berlin
Publisher: BioMed Central
Editor: Johnson, D.
Article number: P170
ASJC Scopus subject areas: Neuroscience (miscellaneous), Signal Processing
Keywords: external stimulus, spontaneous activity, connectivity structure, microelectrode array, recurrent network
URLs:

https://bmcneurosci.biomedcentral.com/articles/10.1186/1471-2202-10-S1-P170
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Assessment of respiratory effort during sleep with noninvasive techniques

General information

Publication status: Published
MoE publication type: B1 Article in a scientific magazine
Organisations: Department of Electronics and Communications Engineering, BioMediTech, Department of Clinical Neurophysiology, Department of Medical Physics, Tampere University Hospital, Pirkanmaa Hospital District, University of Tampere
Contributors: Tenhunen, M., Hasan, J., Himanen, S. L.
Number of pages: 2
Pages: 103-104
Publication date: 1 Dec 2015
Peer-reviewed: No

Publication information

Journal: Sleep Medicine Reviews
Volume: 24
ISSN (Print): 1087-0792
Ratings:

Scopus rating (2015): CiteScore 15.4 SJR 3.399 SNIP 3.309
Original language: English
ASJC Scopus subject areas: Clinical Neurology, Physiology (medical), Pulmonary and Respiratory Medicine, Neurology
DOIs:

10.1016/j.smrv.2015.08.010
Source: Scopus
Source ID: 84944583589
Research output: Contribution to journal › Article › Scientific

Effects of local structure of neuronal networks on spiking activity in silico

The structure of the neuronal network, including synaptic connectivity, is the basis for information transfer in the network. Various graph-theoretic measures such as degree distribution, mean geodesic path length, clustering coefficient and motif distribution exist for analysing the structure of networks [1], and each of them captures only one perspective of the properties that are crucial regarding the activity in the network. In this work, we vary the local structure of neuronal networks and observe changes in their activity in silico, i.e. in simulations where the activity of single neurons and their interaction is modeled. The local structure is analysed through the occurrence of different motifs, i.e. different patterns of connectivity. The effect of motifs on network dynamics has been widely studied in different types of networks: from the stability point of view in networks with unspecified dynamics [2], in artificial neural networks [3], and from synchronization point of view in spiking neuronal networks [4]. Our work focuses on noise-driven neuronal networks, where the activity can be characterised by spike trains of neurons in the network, and particularly by the bursting behaviour of the network.

To study the local structure of networks we consider the occurrences of three separate connectivity patterns: (1) the bidirectional edges, (2) the loops of three nodes, and (3) the feed-forward motifs of triples of nodes. Networks with one of these three local connectivity patterns promoted are generated – we abbreviate these networks (L1), (L2) and (L3). In addition, different distance-dependent networks are generated, including networks with ring topology (RT) and biologically plausible topology, obtained by the NETMORPH [5] simulator (NM). All networks except for NM have binomially distributed in-degree, as is the case with the random networks (RN) that are widely used in neuronal activity simulations. Small illustrations of these network structures are shown in Figure Figure1.1. Neuronal activity in these types of networks of size N=100 is simulated using the model presented in [6]. The simulations show a difference in the activity of these networks. Preliminary results indicate, that network bursts occur more frequently in distance dependent networks RT and NM, especially in RT. Accordingly, the overall spiking frequency is high in these networks, but also in L3 networks.

General information

Publication status: Published
MoE publication type: Not Eligible
Organisations: Department of Signal Processing, Faculty of Biomedical Sciences and Engineering, Research group: Computational Neuro Science-CNS, Department of Mathematics, Research group: Computational Neuro Science-CNS
Contributors: Mäki-Marttunen, T. M., Acimovic, J., Ruohonen, K. P., Linne, M.
Number of pages: 1
Pages: P202
Publication date: 18 Jul 2011

Host publication information

Title of host publication: Twentieth Annual Computational Neuroscience Meeting: CNS*2011
Volume: 12 (Suppl 1)
Place of publication: Stockholm
Publisher: BioMed Central
Editors: Fellous, J., Prinz, A.
ASJC Scopus subject areas: Neuroscience (miscellaneous), Cellular and Molecular Neuroscience, Signal Processing
Keywords: spiking neuronal network, structure, complex networks
URLs:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3240304/
Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

Data-driven study of synchronous population activity in generic spiking neuronal networks: How much do we capture using the minimal model for the considered phenomena?

General information

Publication status: Published
Organisations: Faculty of Biomedical Sciences and Engineering
Contributors: Acimovic, J., Teppola, H., Mäki-Marttunen, T. M., Linne, M.
Number of pages: 1
Pages: 68-69
Publication date: 29 Oct 2018

Peer-reviewed: Yes

Publication information
Journal: BMC Neuroscience
Volume: 19
Issue number: Suppl 2
ISSN (Print): 1471-2202
Ratings:
Scopus rating (2018): CiteScore 4 SJR 1.017 SNIP 0.831
Original language: English
ASJC Scopus subject areas: Neuroscience (miscellaneous), Signal Processing
Keywords: spiking neuronal network, neuronal activity, spontaneous activity, data-driven computational model, model fitting, short-term synaptic dynamics
Research output: Contribution to journal › Meeting Abstract › Scientific › peer-review

Improvement of computational efficiency of a biochemical plasticity model

Multi-scale models in neuroscience typically integrate detailed biophysical neurobiological phenomena from molecular level up to network and system levels. Such models are very challenging to simulate despite the availability of massively parallel computing systems. Model Order Reduction (MOR) is an established method in engineering sciences, such as control theory. MOR is used in improving computational efficiency of simulations of large-scale and complex nonlinear mathematical models. In this study the dimension of a nonlinear mathematical model of plasticity in the brain is reduced using mathematical MORmethods.

Traditionally, models are simplified by eliminating variables, such as molecular entities and ionic currents, from the system. Additionally, assumptions of the system behavior can be made, for example regarding the steady state of the chemical reactions. However, the current trend in neuroscience is incorporating multiple physical scales of the brain in simulations. Comprehensive models with full system dynamics are needed in order to increase understanding of different mechanisms in one brain area. Thus the elimination approach is not suitable for the consequent analysis of neural phenomena.

The loss of information typically induced by eliminating variables of the system can be avoided by mathematical MOR methods that strive to approximate the entire system with a smaller number of dimensions compared to the original system. Here, the effectiveness of MOR in approximating the behavior of all the variables in the original system by simulating a model with a radically reduced dimension, is demonstrated.

In the present work, mathematical MOR is applied in the context of an experimentally verified signaling pathway model of plasticity (Kim et al., PLoS Comp. Biol., 2013). This nonlinear chemical equation based model describes the biochemical calcium signaling steps required for plasticity and learning in the subcortical area of the brain. In addition to nonlinear characteristics, the model includes time-dependent terms which pose an additional challenge both computational efficiency and reduction wise.

The MOR method employed in this study is Proper Orthogonal Decomposition with Discrete Empirical Interpolation Method (POD+DEIM), a subspace projection method for reducing the dimensionality of nonlinear systems (Chaturantabut et al., SIAM, 2010). By applying these methods, the simulation time of the model is radically shortened. However, our preliminary studies show approximation error if the model is simulated for a very long time. The tolerated amount of approximation error depends on the final application of the model. Based on these promising results, POD+DEIM is recommended for dimensionality reduction in computational neuroscience.

In summary, the reduced order model consumes a considerably smaller amount of computational resources than the original model, while maintaining a low root mean square error between the variables in the original and reduced models. This was achieved by simulating the system dynamics in a lower dimensional subspace without losing any of the variables from the model. The results presented here are novel as mathematical MOR has not been studied in neuroscience without linearisation of the mathematical model and never in the context of the model presented here.

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General information
Publication status: Published
Organisations: Faculty of Biomedical Sciences and Engineering, Mathematics, Research group: Computer Science and Applied Logics, Research group: Computational Neuro Science-CNS
Contributors: Lehtimäki, M., Paunonen, L., Linne, M.
Pages: 66-66
Publication date: 29 Sep 2018
Peer-reviewed: Yes

Publication information
Journal: BMC Neuroscience
Volume: 19
Issue number: Suppl 2
Article number: P130
ISSN (Print): 1471-2202
Ratings:

Scopus rating (2018): CiteScore 4 SJR 1.017 SNIP 0.831
Original language: English
ASJC Scopus subject areas: Neuroscience (miscellaneous)
Keywords: Computational neuroscience, Control theory, Plasticity
DOIs:

10.1186/s12868-018-0452-x#Sec613
Research output: Contribution to journal › Meeting Abstract › Scientific › peer-review

Data-driven study of synchronous popula on ac vity in generic spiking neuronal networks: How much do we capture using the minimal model for the considered phenomena?

General information
Publication status: Published
Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Computational Neuro Science-CNS, Research group: Computational Neuro Science-CNS
Contributors: Acimovic, J., Teppola, H., Mäki-Marttunen, T. M., Linne, M.
Publication date: 20 Sep 2018
Peer-reviewed: Unknown
Event: Paper presented at Brain and Mind Symposium 2018, Helsinki, Finland.
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Neuroscience (miscellaneous), Signal Processing
URLs:

https://www.helsinki.fi/sites/default/files/atoms/files/bm_sympo_posters.pdf
Research output: Other conference contribution › Paper, poster or abstract › Scientific

Neural networks, cell cultures and some older work on data analysis.

General information
Publication status: Published
Organisations: Faculty of Biomedical Sciences and Engineering
Contributors: Acimovic, J.
Publication date: 15 Jun 2009
Peer-reviewed: Unknown
Event: Paper presented at Okinawa Computational Neuroscience Course 2009, Japan.
ASJC Scopus subject areas: Cellular and Molecular Neuroscience, Neuroscience (miscellaneous), Modelling and Simulation, Signal Processing, Human-Computer Interaction
Keywords: computational neuroscience, spiking networks, complex networks, cortical networks, brain-machine interfaces
Research output: Other conference contribution › Paper, poster or abstract › Scientific