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BI’17 Abstracts

(Main Conference)

Cognitive and Computational Foundations of Brain Science

Construct Individual Cerebral Cortex Functional Map Based on Fast Marching Algorithm

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Abstract. Background: The human brain atlas is the foundation of understanding brain structure and function. The typical anatomical atlas is mainly based on brain morphometry which can't ensure the consistency of structure and function, and is also hard to cover individual functional differences especially in cerebral cortex. Thus, in recent years, functional atlas for individuals, that has captured neuroscientists' great attention due to its unique advantages, is essential not only for identifying the unique functional organization of individual brain, but also to explore individual variation in behavior and cognition. In this study, a novel propagation approach is proposed to accurately parcellate whole cerebral cortex at the individual level by using resting-state functional magnetic resonance image (Rs-fMRI). In addition, some evaluation methods are proposed to assess the consistency and validity of identifying functional regions in individual. Subject: Imaging data from 200 healthy adults are obtained from Human Connectome Project (HCP), which includes resting state fMRI of two 00days (Day 1 and Day 2) and 7 task-evoked fMRI. Methods: First, the cerebral cortex is divided into two hemispheres, and then inner surfaces of cerebral cortex are reconstructed and normalized into structural atlas separately. Rs-fMRI and task-evoked fMRI signals are mapped on to vertices of surface in the original space. Then, N-Cut method is performed on the surface to parcellate atlas surface into small functional homogeneous regions based on averaged Rs-fMRI connectivities between vertices. When this functional atlas is applied to individual, a propagation approach is performed to identify the edge of each functional regions based on individual Rs-fMRI data. A new evaluation criterion, similarity of cluster (SC coefficient), is defined as measuring how similar that voxel is to voxels in its own cluster compared to voxels in the neighbor cluster. The SC coefficient is applied to examine whether the parcellation results could be extended to the data on task-related fMRI. Finally, the Dice coefficient is used for estimating the cluster homogeneity and reproducibility. Result: Functional networks mapped by this method effectively capture the variability across subjects. The parcellation results have demonstrated the high consistency between Day 1 and Day 2 (for all ROI, Dice > 0.72). The curve of SC coefficient shows an accordant tendency across different tasks. Besides, with the number of regions increasing, the SC coefficient sharply increases at first and then slowly decreases. The turn point of SC coefficient is approximately located in region=1800. In summary, the results have demonstrated that the validity of propagation method across subjects, time and data types, which may provide a new insight for the development of functional map at the individual level and cluster validity criteria.

Keywords: resting-state, fMRI, functional connectivity, parcellation

Sparse Bayesian Approach for Spatiotemporal Independent EEG Source Imaging

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Abstract. Analyzing broad and strongly overlapping far-field scalp projections of underlying spatially distinct locally-synchronous cortical field activities has long posed a challenge for cognitive neuroscience researchers. Even the accurate forward solution was obtained, the source localization problem is still highly underdetermined if multiple sources contribute to the EEG recordings. To attack the indeterminate nature of the EEG source analysis problem, some constraints were usually applied. The linear regulation‐based methods, for instance, minimum-norm estimators (MNE), low resolution tomography (LORETA), etc., drive solutions to smoothness, whereas parametric dipole fitting and Sparse Bayesian Learning (SBL) algorithms drive source to an opposite direction, sparsity.

Here, we propose a new source imaging method whose goal is to obtain more physiologically realistic solutions to the EEG inverse problem by combining a priori knowledge about nature and structure of brain sources, including spatiotemporal independence, sparsity, spatial compactness and local smoothness. Unlike conventional two-stage independent component analysis (ICA), the approach is proposed to concurrently identify both the spatial source distribution of each cortical source and its event-related dynamics. A correlation-variance model which decomposes the covariance matrix into the multiplication of a correlation coefficient matrix is used to describe the local tendency toward synchronization of neural activities at nearby dipoles in the source space. The performance of the proposed method is evaluated qualitatively by using experimental and simulated EEG data. The experimental data were collected from sixteen subjects in a self performance-monitoring and -inhibition emotional stop-signal paradigm (ESSP). The results included spatiotemporal ICA component processes in visual, motor, frontal and anterior cingulate cortical areas.

Keywords: EEG, source localization, spatiotemporal independent component analysis

Research on the Measurement of Neurochemical and Neurophysiological Signals in Monkeys Using a Dual-mode Detection System

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Abstract. The communications between the neurons are inherently neurophysiological and neurochemical in nature. Neurons communicate based on dual-mode signals, that is, neurochemical signal and neurophysiological signal. In order to understand the mechanisms of central nervous system diseases, a means to record the neurochemical and neurophysiological signals synchronously in the monkey brain becomes an urgent demand [1-2]. In our work, a dual-mode detection system, which comprised High precision detecting apparatus and Implantable microelectrode array (MEA) probe, was developed. The High precision detecting apparatus consisted of electrochemical potentiostat, electrophysiological amplifier and signal analysis software. The Implantable MEA probe was fabricated and modified by the methods reported previously [2]. Briefly, the microelectrode array fabricated using silicon on insulator substrates by Micro-Electro-Mechanical System (MEMS) technique and electroplated with the Pt-black nano-particles to reduce the impedance of the electrode; and each site of the microelectrode was modified by nafion for detecting dopamine (DA). Functionally, each site of the probe could be selected for neurophysiological signal or DA detection.

The basic performance of the system was tested. Results showed that the system had low system noise and high accuracy of current. In the DA solution measurement experiment, the current response of DA in the range of 0.5 μmol / L to 20 μmol / L was obtained by chronoamperometry and increased linearly with a correlation coefficient of 0.996. At last, the amperometric currents of DA and neural spikes were recorded simultaneously by the system from the cortex to striatum of a cynomolgus monkey brain. In term of electrochemical current, current decreased slowly from the cortex to the whiter matter, and then increased to a stable value at the striatum. Meanwhile, we can also see that the typical spike shapes were diverse at three different brain areas. Results suggested that the detection system had the function of detecting both the neurophysiological signal and the electrochemical current in the monkey brain synchronously.

Keywords: Detection system, Neural spikes, Dual-mode, Monkey

Cross-Modal Transfer Learning for HEp-2 Cell Classification Based on Deeply Supervised Residual Network

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Abstract. Accurate Human Epithelial-2 (HEp-2) cell image classification plays an important role in the diagnosis of many autoimmune diseases and subsequent measurement. Inhomogeneous illumination variation lead to huge intra-class variation is a key challenge in HEp-2 cell classification. In order to meet this challenge, we propose a very deeply supervised residual network (DSRN) based framework to automatically recognize HEp-2 cell via cross-modal transfer learning strategy. Compared with existing methods utilizing either low-level hand-crafted features or DCNNs with shallow learning networks, we utilize a residual network of 50 layers (ResNet-50) that are substantially deeper can acquire richer and more discriminative feature for more accurate recognition. To further boost the recognition performance, we devise a novel ResNet based network with deep supervision. The DSRN can address the optimization problem of gradients vanishing/exploding and accelerate the convergence speed. DSRN can directly guide the training of the lower and upper levels of the network. The unstable gradient variations caused by the training process can be addressed. Different from most of the deep learning models learnt from scratch, we adopted cross-modal transfer learning pre-trained from natural image dataset and a very similar dataset (from ICPR2012 to ICPR2016-Task1) to fine-tune our own DSRN model. In contrast to the traditional deep convolutional neural network (DCNN), we have achieved state-of-the-art performance. We evaluate our proposed method on the two publicly available datasets, International Conference on Pattern Recognition (ICPR2012) and (ICPR2016-Task1) cell classification contest datasets. Our proposed framework achieves an average class accuracy of 97.14% on ICPR2012 HEp-2 dataset and a mean class accuracy of 98.42% on ICPR2016-Task1 HEp-2 dataset, which outperforms the traditional methods.

Keywords: HEp-2 cell classification, Residual network (ResNet), Deeply Supervised ResNet (DSRN), cross-modal transfer learning

Dynamic Functional Connectivity in Electroencephalographic Data: Microstate Segmentation Approach

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Abstract. The neuronal dynamic functional connectivity (dFC), defined as the fast spatio-temporal transient interactions among electroencephalographic (EEG) signals, has been often interpreted as the mechanism underlying the information transfer among different spatially-distributed cerebral cortices. Tracking the brain dFC is a burgeoning field but critical issue about analyzing methods and interpretation of results uncertainty is due to its intrinsic complexity. Reported methods for investigating dFC utilize segmentations of macrostate functional connectivity (FC) matrix with two dividing strategies: time sliding window and K-mean clustering, aiming at segregating a global FC matrix into a set of distinguished FC microstates, where each microstate represents a distinct functional interaction pattern. In this work, we analyze the dFC performance comparison between two mentioned methods in a visual cognition process using a high spatio-temporal resolution EEG system. Here, we use a well-established phase locking value (PLV) method, as a metric to investigate task-induced changes in long-range synchronization of neural activity from EEG data, obtaining a macrostate whole-brain PLV FC matrix. Prior to PLV computing, we extract instantaneous phases of EEG oscillations by using Hilbert transform in gamma-band frequencies. Furthermore, we introduce Kullback-Leibler divergence (KL-divergence) to quantify statistical dis-similarities between inferred FC microstates resulted from each approach and then to determine comparative dFC performances between the two. Our results demonstrate that the two methods are able to dissolve the macrostate FC matrix into distinct FC microstates, where each microstate shows a distinguished interaction pattern. The results also show that the sliding window method outperforms than K-mean clustering as proved in a higher KL-divergence, meaning that inferred microstates in sliding window are more distinct than that of K-mean clustering. Finally, we provide statistically comparative results of graph-based network properties; including degree, clustering coefficient, modularity and small-world network; of the two methods.

Keywords: dynamic functional connectivity, microstate, high spatio-temporal resolution EEG, K-mean clustering, time sliding window

Silent Speech Electroencephalogram Classification and Frequency Band Analysis Using Covariance Based Feature Extraction

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Abstract. Objective: The purpose of this study is to propose a method for extracting optimal features which classify silent speech electroencephalogram (EEG) and to analyze each frequency band activity in silent speech EEG. Approach: Four healthy participants participated in this study. Experimental paradigm was designed using e-Prime 2.0 software (Psychology Software Tools, Inc., Sharpsburg, PA, USA). A HydroCel Geodesic Sensor Net with 64 channels and Net Amps 300 amplifiers (Electrical Geodesics, Inc., Eugene, OR, USA) were used for silent speech EEG recording with 1000 Hz sampling rate. The sensors were located according to the international 10-20 system. We measured EEG when imagining five vowels /a/, /e/, /i/, /o/, and /u/ for three seconds from four healthy subjects. For preprocessing, we re-referenced data using common average reference. Then, we applied an IIR 4th order Butterworth band-pass filter with several bandwidths to analyze each frequency band activity of silent speech EEG. To remove the power noise, an IIR 4th order Butterworth band-stop filter was used. After preprocessing, we extracted statistical features including mean, variance, and standard deviation for each channel. Then, we applied covariance based feature extraction method for those statistical features. As the number of extracted features increases, we used eigenvector centrality feature selection method to select optimal features. We performed various classifiers including support vector machine, linear discrimination analysis, and random forest to classify silent speech EEG. Results: We found that the higher the frequency band, the better the classification accuracy of the silent speech EEG. Therefore, the higher frequency band of EEG has more information related to the silent speech. Using the proposed method in the gamma band of the EEG, the average classification accuracy for all pairwise binary classification problems was around 75% and the maximum was over 85%. Conclusion: The gamma band activity of EEG is most related to silent speech. Moreover, we confirmed that covariance based feature extraction method extracts features for classifying silent speech EEG with high accuracy.

Keywords: silent speech, electroencephalogram, gamma band activity, covariance based feature extraction

Epidural EEG Discrimination in a Single-trial Basis for Speech Perception of Rat Using Machine Learning Techniques

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Abstract. Objective: The purpose of this study is to find components that might be associated with speech representation in the rat brain and to discriminate EEG responses for each speech sound on a single-trial basis using machine learning techniques. Approach: We chose four types of sound as stimuli, /bat/, /tat/, /sat/ and /dat/ because each speech is different in manner of articulation and place or articulation. All sound stimuli we used had been generated from a text-to-speech program provided by Google. We increased the pitch of sound stimuli by one octave to accommodate the rat hearing range, and applied root mean square normalization. We placed two epidural EEG electrodes on the left and right primary auditory cortex for recording the neural responses according to speech representation in the rat brain. In order to avoid motion artifact and record the reliable epidural EEG, we anesthetized the rats with 2% isoflurane during recording time. Epidural EEG recordings were performed for 1500 seconds per each subject, during which time four types of sound stimuli were randomly presented to the rats though the experimental speaker. We obtained epidural EEG signals of 130 to 150 trials per stimulus. In order to remove the noise of obtained epidural EEG, we applied a band-pass filter (bandwidth: 2-50Hz, Butterworth). After the preprocessing procedure, we used amplitudes from 0 to 0.5 s after stimulus onset as inputs to the machine learning classifiers. We performed both conventional machine learning techniques such as support vector machine (SVM) and deep neural network technique such as stacked auto-encoder (SAE) for discriminating epidural EEG responses. Main results: The responses of the rat brain to the four speech sounds could be classified as one of the learned speech on a single-trial basis with our experimental framework. Both conventional machine learning classifier and deep learning based classifier showed excellent classification accuracy above 80% for all pairwise binary classification problems. In general, the classification performance of the deep learning based classifiers are known to outperform the conventional classifiers such as SVM and LDA. However, there was no significant difference on the classification performance between two types of classifiers in this experiment. Significance: The results of our study show that responses of the rat brain to speech can be classified for single trials with high performance above 80%. As far as I know, this is the first study to discriminate the epidural EEG responses of the rat brain to the speech sound. In light of the fact that most of the studies related to speech responses of the rat brain uses a depth electrode which is very invasive, we strongly believe that this paper, which classifies speech representations in a single trial basis with high accuracy using less invasive epidural EEG electrodes, has a very high novelty.

Keywords: Epidural EEG, Machine learning, Support vector machine, Stacked auto-encoder, EEG Speech response

Constructing an Algorithm for Cognitive and Affective Tasks Based on EEG Microstate Time-courses

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Abstract. The interplay between brain networks is crucial for understanding human cognitive-affective processing. In this project, it is suggested to focus on a recently developed model regarding the so-called "triple network" comprising the default mode network (DMN), central executive network (CEN) and the salience network (SN) in the context of performing various cognitive and emotional tasks. The "triple network" is important for the processing of salient stimuli and for guiding the selection of appropriate behavioral responses. Previous research has mainly studied the interplay between these networks using resting-state fMRI data in the context of neuropsychological disorders. Here, it is suggested instead to recruit a large eeg data set, recorded across diverse paradigms and populations, through collaboration between labs. EEG is preferred because of its high temporal resolution which enables the examination of the early stages of cognitive processes. The data set will consist of data gathered from a wide variety of cognitive and affective tasks in order to create an algorithm that will be able to differentiate between different populations of participants. Specifically, it is suggested to utilize microstate analysis in order to extract scalp potential maps from the eeg, also known as "microstates". Microstates are quai-stable potential maps, each consisting of the electrical activity recorded from large parts of the cortex. Hence, this method of microstate analysis is suitable for examining the functional organization of large-scale networks. The time-courses of specific microstate maps could serve as input features for the proposed algorithm, thus, enabling to include the dynamic aspect of functional organization as an inherent part of the Algorithm's features.

Keywords: EEG, Triple network model, Salience network, Microstate analysis

Adaptive Sparse Learning for Multi-Class Neurodegenerative Disease Classification

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Abstract. Alzheimer's disease (AD) and Parkinson's disease (PD) are the most common neurodegenerative diseases occurred in the elderly. The chronic progression nature and imperceptible neuro diminishment of these disease make the treatment progress comparatively difficult. Therefore, early diagnosis of these disease offers timely prevention treatment for the patients. With the development of neuroimaging techniques like magnetic resonance imaging (MRI), positron emission tomography (PET) and diffusion-weighted tensor imaging (DTI), the elaborate structure of the brain is revealed and further studied for understanding the anatomical and functional neuro variations. Recently, unaccountable machine learning methods have been applied to utilize the neuroimages in computer-aided diagnosis (CAD). Faced with the challenge of high dimensionality and small sample size which could induce overfitting in the process of data analysis, most existing methods design a feature selection process to reduce the dimension or a sample selection process to discard the redundant samples. This paper proposes an adaptive sparse feature learning framework to learn the most discriminative and relevant features of MRI and DTI brain images to solve the multi-classification problem for neurodegenerative disease. In order to better lighten the influence of overfitting, we integrate the idea of feature selection and subspace learning to construct a least square regression model. Specially, we apply the feature selection to the preprocessed data with an adaptively-chosen sparse degree and abandon those relatively irrelevant features. In this process, we follow the principle of Fisher's linear discriminant analysis (LDA) and locality preserving projection (LPP) to discover the underlying global and local relationships in the original data space. Together with the intrinsic relationships, this sparse feature learning framework can select the most relative and distinguishable features to enhance classification performance. Unlike most previous methods for binary classification, we perform a multi-class classification to improve the efficiency of computer-aided diagnosis. Our proposed method is validated on the baseline MRI images of 814 subjects including 192 AD patients, 402 mild cognitive impairment (MCI) and 220 normal controls (NC) from Alzheimer's disease neuroimaging initiative (ADNI) database, and another MRI and DTI images of 208 subjects including 123 PD patients, 56 NC and 29 scans without evidence of dopaminergic deficit (SWEDD) subjects from Parkinson's progression markers initiative (PPMI) database. Abundant experimental results show that our proposed method can identify subjects more accurately compared to other state-of-the-art methods. Accurate feature learning leads to the identification of the highly relevant brain regions, demonstrating the practical value for further medical analysis and diagnosis.

Keywords: Neurodegenerative disease, Sparse learning, Feature selection, Multi-classification

Informatics Paradigms for Brain and Mental Health

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High-order Functional Connectivity Based on Independent Component Analysis for Classification of Depression

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Abstract. Major depressive disorder is a common mental illness with functional abnormalities in certain brain regions and in resting-state functional connectivity networks (RSNs). More and more researches show that RSNs change dynamically in the resting state, but few existing resting-state fMRI study on major depression assumes the dynamics, especially for identifying depressive individuals from healthy controls. We propose a dynamic identification method called high-order functional network connectivity (HFNC), which is based on independent component analysis (ICA) and high-order functional connectivity. HFNC consists of the following four steps. Firstly, independent component analysis is carried out to extract time series on the nodes of RSNs. Secondly, sliding window technique is employed to generate correlation matrix for each stationary short time window. Thirdly, hierarchical clustering is performed to characterize common patterns of concatenated correlation matrices, and high-order correlation is calculated based on the mean of correlation time series of different clusters. Finally, graph theory-based features on the high-order functional connectivity networks are obtained for linear discriminative classifiers. HFNC has the following advantages: by using ICA it is a data driven method and is independent on any brain atlas, through sliding window it can capture the dynamic properties of RSNs, and via high-order correlation it utilizes higher level spatiotemporal interaction relation among RSNs. For subjects of 21 healthy controls and 20 patients with major depression, HFNC achieves 97.56% classification accuracy, much higher than results based on stationary networks. Moreover, the most discriminative components mainly locate in frontal network, sensorimotor network and visual network, which is consistent with existing stationary-based results on major depressive. Therefore, the proposed method might have potential in extracting biomarkers for depression.
Keywords: fMRI, Depression, Independent component analysis, High-order functional connectivity

Self，Mother and Other Referenced Processing in Major Depressive Disorder: A Preliminary Study

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Abstract. Major depressive disorder (MDD) is a common mental illness, its main manifestations are low mood, less interest, and slow thinking in behavior. From the view of cognition, MDD shows a negative-self bias during processing. The hypothesis of self-schema has proposed that patients of MDD has a negative self-schema, which causes information processing in a negative, distorted way(Springer US,2012). Self-schema is a hypothetical cognitive structure that is used to guide the processing of self-related information. Many studies have shown that MDD patients negative bias during cognition limited to self-related information, and rarely extended to others who are independent of themselves(Tamara Vanderwal，2008). For examples, negative-self bias are found in attention, remember with word or picture materials. However, the concept of self usually includes the representation of important others, especially in the culture of East Asians with dependent-self. It is not clear whether MDD patients has the same negative bias for important others as self-processing or not.

In this study, a classical self-referential task was used to investigate this issue. MDD patients were asked to judge the personality trait word could describe self, mother and others (such as Mao Zedong) or not. 120 positive and 120 negative personality trait words were selected from the Chinese Affective Words System (Wang, Zhou, & Luo, 2008) as materials, and there were 40 positive and 40 negative words in each referenced condition. MDD patients were instructed to press the response key with the index finger when the words could describe self, mother and other, and response key with the middle finger when the words could not. The number of time for the Yes and No responses and the reaction time (RT) were recorded during the experiment.

First the results suggest a negative-self bias in MDD, while no such bias for abstract other, which is consistent with previous findings. MDD patients was more likely to judge the other with more positive words, and the RT showed that there is no difference for the positive or negative judging. As to the self-reference, MDD patients was more likely to judge with negative words and the RT was increased for Yes response in the positive condition. More importantly, for the mother-referenced condition, MDD patients were less likely to judge mother with negative words, and the RT showed the judgement of negative words to describe mother (Yes response) is the longest. The results indicated that there was no negative bias for mother as other. However, the increased RT in the Yes response to the mother-referential

negative condition suggested that MDD had a strong tendency to reject the negative judgement for mother.

Keywords: Major depressive disorder, negative-self bias, mother-reference, self-referential task

Neural Mechanisms Underlying Semantic Inhibition in Obsessive-compulsive Tendencies

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Abstract. Obsessive-compulsive disorder patients experience recurrent and persistent thoughts and attempt to suppress these thoughts. A previous psychological study with the negative priming effect, which refers to the increase in response time to a previous ignored stimulus, suggested reduced semantic inhibition in obsessive-compulsive disorder. Although there are neurological studies that the distributed brain areas such as left frontal and posterior temporal areas are involved in the semantic control, no study approach the dynamic relationships among these and other task-relevant brain areas with the deficit of the semantic inhibition in obsessive-compulsive tendencies. To address the issues, we aimed to investigate the phase synchronizations among these areas with the time-frequency analysis of electroencephalograph (EEG) data recorded during a word classification task. One colored Japanese word (either red or green) was presented on the display. In case of red colored word presentation, the participants were required to classify the word into semantic categories either plants or animals and respond with a keypress (i.e., the classification condition). In case of green colored word presentation, the participants were required to read the word without classification (i.e., the inhibition condition). Obsessive-compulsive tendencies were evaluated by a subjective questionnaire. Behavioral results showed the individual negative priming effect was negatively correlated with obsessive-compulsive tendencies. The EEG results showed that the alpha (8-12 Hz) phase synchronization between left frontal and motor areas was significantly higher under the classification condition than the inhibition condition. In contrast, these tendencies were not observed in the frontal-temporal and temporal-motor alpha phase synchronizations. Moreover, the alpha phase synchronization between left frontal and motor areas under the inhibition condition was positively correlated with obsessive-compulsive tendencies. The frontal and motor areas are thought to be related to the semantic and motor control, respectively. Therefore, our results suggest that dynamic linking between left frontal and motor areas might reflect reduced semantic inhibition in higher obsessive-compulsive tendencies.

Keywords: EEG, OCD, negative priming, semantic control, phase synchronization

Joint and Deep Ensemble Regression of Clinical Scores for Alzheimer's Disease Using Longitudinal and Incomplete Data

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Abstract. Alzheimer's disease (AD) is a neurodegenerative disease with an irreversible and progressive process, and thus close monitoring is essential for making adjustments in the treatment plan. Since clinical scores can indicate the disease status effectively, the prediction of the scores based on the magnetic resonance imaging (MRI) data is highly desirable. Different from previous studies at a single time point, we propose to build a model to explore the relationship between MRI data and scores, thereby predicting longitudinal scores at future time points from the corresponding MRI data. The model incorporates three parts, correntropy regularized joint learning based feature selection, deep polynomial network based feature encoding and finally, support vector regression. A temporally constrained group LASSO model is employed to find the most relevant features across different time points by feature selection. Also, the correntropy is incorporated to remove outliers. To further boost the performance, feature encoding via DPN is adopted in the renaissance of deep learning. The regression process is carried out for two scenarios. One is desirable in practice, which is to use baseline data for predictions at future time points, and the other is to further improve the prediction accuracy, which is to combine all the previous data for the prediction at the next time point. Meanwhile, the missing scores are filled in the second scenario to address the incompleteness presented in the data. The simulation results validate that the proposed model describes accurately the relationship between MRI data and scores, and thus is effective in predicting longitudinal scores.

Keywords: Alzheimer's disease, longitudinal score prediction, correntropy, joint learning, deep polynomial network.

Subtypes of ADHD Distinguished by Quantitative EEG and ERPs

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Abstract. Abnormalities in quantitative Electroencephlogram (QEEG) and Event Related potentials (ERPs) in Attention Deficit Hyperactivity Disorder (ADHD) patients have been reported for decades. This talk will focus on the typologies of ADHD (and symptoms that can mimic ADHD) that can be distinguished using a quantitative EEG and ERP analysis. Some subtypes indicate a pathology, while others suggest a maturation delay and each will respond differently to treatments.

The major pattern associated with the classic DSM criteria of ADHD (around 60% of the ADHD population) is an excessive amplitude of low frequency (4-8 Hz) above norms in frontal cortex. In some this can be in combination with a deficit of high frequency (18-21 Hz) EEG activity, known as the Theta/Beta ratio.

A smaller proportion (around 5 to 7 %) of patients are 'hyperaroused', with a raised amplitude of high frequency activity (above 21 Hz). This underlies the irritability and aggressiveness of some clients and for which stimulant medication would be contraindicated. A qEEG/ERP test-retest is able to predict the efficacy of stimulant medication.

The opposite pattern, the "inattentive only" subtype is characterised by excessive Alpha frequencies (8-12 Hertz).

Other unbalanced rhythms can predict unstable emotional, cognitive and physical states that leave individuals unable to draw on normal inhibitory and excitatory mechanisms. This affects impulsivity, alertness and attention, and will be described, with their relevant treatment options or medications. One of these is undiagnosed Epilepsy.

ERPs represent the neuronal responses associated with specific sensory, cognitive and motor events. Comparison studies between ADHD and control groups have revealed a wide range of altered ERP components. Such clinical ERP studies mainly lie in four aspects: error detection, attentional processing, memory and emotion. Firstly, error detection is most extensively investigated by the typical Go/NoGo task and the ADHD group shows reduced error related negativity (ERN), a sharp negative wave that is present selectively on error trials. Secondly, the contingent negative variation (CNV) is indicative of attentional expectancy and anticipation and used to test attentional processing. The ADHD group shows larger early CNV decrements over time. Additionally, many memory tasks indicate altered ERP components in ADHD. For example, the visual short-term memory task shows that the contralateral delay activity (CDA) amplitude emerges in an early time window for ADHD patients compared to control participants. As well, CDA amplitude was negatively correlated with severity of ADHD

symptom and, anomalies are also found in several late EPR components involved in emotional processing, e.g. P1 and P3.
Simulant drugs have been the normal treatment for most ADHD sufferers. However the efficacy has been equivocal in terms of reduction of symptoms over time and occurrence of side-effects thus therapists have been looking for effective non-drug therapies. One that has some evidence of efficacy is Neurofeedback training. By reflecting their aberrant brainwaves to the patient in real-time, it is possible by operant conditioning to normalise brain activity. Neurofeedback training has been shown to; increase the CNV, reduce the theta/beta ratio, lower the excess high frequency amplitude and thereby improve attentional status.

Keywords: ADHD Subtypes, Electroencephlogram, qEEG, ERP, Neurofeedback

Altered Brain Signatures Underlying the Affective and Cognitive Impairment in Depression

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Abstract. Background: Major depressive disorder (MDD) has been shown to be closely related to the abnormalities in brain functions and structures that cause affective and cognitive impairments. As an important aspect of cognition, it remains unclear how the interplay between emotions and mental arithmetic. And there are still few studies on the pathological mechanism of depression in combination with functional connectivity (FC) and structural connectivity (SC). Therefore, we designed an experimental task to assess the ability of mental arithmetic under emotional effect and identified the aberrant FC and SC in MDD patients.
Methods: The resting state fMRI (rs-fMRI) and diffusion tensor imaging (DTI) data were collected from 21 MDD patients and 21 healthy controls matched with gender, age and educational level. The strengths of FC and SC were quantified by Pearson correlation coefficients and the number of fiber tracts based on probabilistic tractography, respectively. And the behavioral data were tested by a 2 arithmetic operations (addition, subtraction) × 3 types of emotional valences (positive, neutral, negative) within-subjects design task. The differences between the two groups was examined by the paired t-test. And the relationships were examined between abnormal behavioral data and psychological scales including HAMD-17, PHQ-9, T-AI score with abnormal FC and SC using Pearson correlation.
Results: Compared with the HC group, the accuracy of subtraction under neutral condition was decreased in MDD group ($P = 0.034$, Tukey-Kramer corrected). Nevertheless, this response bias weren't found to be associated with abnormal functional or structural connectivity in depressed patients. Further analysis showed the decreased FCs in MDD group were found between the right middle frontal gyrus (RMFG) and right pallidum (RPAL), left cuneus (LCUN) and left fusiform gyrus (LFFG), LCUN and right cerebelum 6 (RCRBL6), right cuneus (RCUN) and LFFG, RCUN and RCRBL6, left pallidum (LPAL) and right putamen (RPUT), LPAL and left thalamus (LTHA), LPAL and right thalamus (RTHA), LTHA and left Cerebelum Crus2 (LCRBLC2), RTHA and LCRBLC2, RTHA and left putamen (LPUT), RCRBL6 and left calcarine (LCAL) RCRBL6 and left lingual gyrus (LLING), RCRBL6 and LCRBL6 compared with the HC group ($P < 0.05$, FDR corrected). More importantly, we found that the SC and FC decreased simultaneously between the left pallidum and left thalamus, which may cause executive function and mood adjustment dysfunction in MDD patients. For the psychological assessment, the score of T-AI was negatively correlated with the FC of the LCUN-LFFG, RCUN-LFFG, RTHA-LPUT, LPAL-RPUT and LPAL-LTHA respectively ($P < 0.05$, two tailed). However, no significant correlation was found for the cognitive performance.

Conclusion: In summary, the abnormalities SC and FC were detected by combining with rs-fMRI and DTI. These results provide new evidences that the frontal-striatal-thalamic circuit and cerebellum are probably the underlying neural mechanism of MDD.

Keywords: resting-state fMRI, diffusion tensor imaging, major depressive disorder, probabilistic tractography, mental arithmetic

Dectection of Electrophysiological and Neurochemical Activities in Temporal Lobe Epileptic Mouse Using Microelectrode Arrays

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Abstract. Temporal Lobe Epilepsy (TLE) is a chronic brain disorder caused by multiple causes, characterized by sudden, repeated and transient central nervous system dysfunction caused by excessive discharge of brain neurons. In demand of the research of TLE, an implantable microelectrode array (MEA) of multi-channel silicon substrates is designed, which includes electrophysiological and electrochemical detection sites to achieve high quality simultaneous detection of multi-channel electrophysiological signals and electrochemical signals. The MEA was fabricated by micro-processing. As the needle width of 200μm, the site diameter of 25μm, implantation process of brain tissue damage is small, and the detection accuracy to single cell level. In addition, the detection sites were modified with platinum black nano-particles (PtNPs), the average resistance decreased by 89 times, the relative standard deviation of 14.6%, with good consistency. At the same time, glutamate oxidase was modified by cross-linking method. The sensitivity of the glutamic acid solution was 14.5nA / μM · mm2 and the high linearity was R = 0.998 by electrochemical detection. The MEA has good selectivity for glutamate. Interfering substances include dopamine (DA), ascorbic acid (AA), serotonin (5-HT), 3,4-Dihydroxyphenylacetic acid (DOPAC). Finally, in the in vivo experiments of normal and TLE rats, the MEA was subjected to dual-mode detection of the hippocampus. There are two conclusions: 1. In analysis of the spike from hippocampus in both normal and TLE rats, the discharge of TLE rats was more intense and regular than normal rats; 2. In analysis of local field potential (LFP) in hippocampus and glutamate overflow at the same time, there are great correlations between the two factors before and during TLE. Due to seizures of TLE, glutamate levels increased in the hippocampus, and discharge power concentrated in the low frequency region. The simultaneous detection and analysis of neurological signals provides a new approach to the pathogenesis of epilepsy.

Keywords: microelectrode array, electrophysiological detection, TLE, hippocampus, seizures

Risk Factors Analysis for Late-onset Depression and the Relationship with Cognition Based on the Default Mode Sub-network

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Abstract. Background: Abnormal functional connectivity (FC) in the default mode network (DMN) is an important role in the cognitive impairment in the late-onset depression (LOD) patients. However, little is known about the FC of DMN sub-networks as the risk factors for the LOD. This study is to explore the risk predictors of the LOD based on the DMN sub-networks and further investigates the correlation with the cognition.

Methods: Total 30 LOD patients and 40 health control (HC) underwent the resting-state functional magnetic resonance imaging and cognitive assessments. Firstly, FCs within the DMN sub-networks were determined by placing seeds in the ventral medial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC). Secondly, the multivariable logistic regression was used to identify the risk predictors for the LOD patients. Finally, the correlation analysis was performed to investigate the relationship between the risk factors and the cognitive value.

Results: The study showed that the FCs between the vmPFC and right middle temporal gyrus (MTG), between the vmPFC and left precuneus (PCu), between the PCC and left PCu were the risk factors of the LOD. Furthermore, the FCs between the vmPFC and right MTG and between the PCC and left PCu significantly positively correlated with the processing speed and semantic memory($R = 0.34$, $P < 0.05$； $R = 0.46$, $P < 0.001$), while the FCs between the vmPFC and PCu significantly negatively correlated with them($R = -0.28$, $P < 0.05$; $R = -0.28$, $P < 0.05$).

Conclusions: This study confirms that the LOD patients mainly present the cognitive deficits in the processing speed and semantic memory. Moreover, the results further suggest that the FCs within the DMN sub-networks associated with cognitions can be considered as the risk factors, which may be used to predict the appearance of LOD.

Keywords: Late Onset Depression, Default Mode Sub-networks, Risk predictor, Cognition

Human Information Processing Systems

Granger Causal Analysis from Multi Spike Trains on Prefrontal Cortex of Rats during Working Memory Task and Neuronal Network Simulation

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Abstract. Functional connectivity networks of 16-channel spike trains on prefrontal cortex of rats during working memory task in vivo are explored. Experimental data were in accordance with the Guide for the Care and Use of Laboratory Animals. Micro-wire electrodes with 16 channels were planted in rats prefrontal cortex and neural activities were recorded while the rats performed a working memory task in Y-maze. Effective period of 6 seconds were selected, which is deemed to be enough to represent the entire working memory process. Action potentials spatio-temporal sequences of 4 rats, each rat 8 trails, in prefrontal cortex neuronal populations in the working memory process are used as experimental data. Spike trains of multi-channel collected in rats working memory responsibilities brain areas (prefrontal cortex) are applied instantaneous firing rate technology to continuous. Granger causality networks are calculated to study rats in the Y-maze working memory events causal network and its characteristic exponent. Rats working memory processes in prefrontal cortex Granger causality network measurements statistical results (global network efficiency, causal density, and betweenness centrality). The global network efficiency is value the higher the greater the time the network propagation effects. The causal density is value the higher the overall coordination of activities of the time, easy to predict activities of each other. The betweenness centrality of high numerical average center channel coefficient describes the centralized hub. These parameters are achieved maximum values in the 2 seconds interval before the reference point, and then declined in 1 second interval after the after reference point. In the 2 seconds interval before the reference point, networks propagations are effects, overall activities are coordinative, and cluster hubs are embodies. And spike trains in resting state and working memory state are simulated. Simulation results indicate that neurons are form a cluster in working memory state simulation, neurons are not form a cluster in resting state simulation.

Keywords: rat, working memory, spike trains, Granger causality, instantaneous firing rate

Neural Correlates of Improved Inductive Reasoning Ability in Abacus-trained Children: A Resting State Study

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Abstract. Training can induce adaptive changes in the brain and yield transfer from a trained to a non-trained cognitive skill. Spontaneous brain oscillation is important for supporting information integration and consolidation during training. Abacus-based mental calculation (AMC) training could improve math-related abilities and transfer to intelligence. Situated in a dynamically varied world, human beings have the ability of inductive reasoning to identify sequential patterns in diverse and complex environments, and then extrapolate the future instances. However, it remains unknown whether the AMC training can improve inductive reasoning ability and the underlying neurobiological underpinnings of this adaption by resting-state fMRI.

Twenty-seven abacus-trained children and 27 sex- and age matched non-trained children were randomly assigned to either AMC or control groups. The AMC group was performed abacus operation for approximately 1 year and for 2 to 3 hours per week. In contrast, the nontrained group received no abacus training either at school or after school. Resting-state MRI data were collected before and after training period and regional homogeneity (Reho) analysis was performed. Their intelligence quotients (IQs) and inductive reasoning ability (i.e., number- and letter-series completion task) were evaluated.

No significant differences were detected between abacus-trained children and control group in IQs. Significant higher reasoning performances were detected in abacus-trained children when compared to control group. Enhanced Reho in the rostrolateral prefrontal cortex (RLPFC) and occipital cortex were detected in abacus-trained children compared to control. Furthermore, the increased Reho in the RLPFC was positively correlated with the improved inductive reasoning skill.

Our findings suggest that resting-state fMRI could serve to reflect the modulation of training in task-related network.

Keywords: Inductive reasoning, Abacus-based mental calculation, Regional homogeneity

The Effect of Transcranial Direct Current Stimulation (tDCS) in a Rodent Model of Postoperative Delirium

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Abstract. Background: Delirium is a common manifestation of post-operative patients, especially in ICU patients. It is an acute disorder of attention and cognition with a tendency to fluctuate over time. It is associated with a high mortality and extended length of hospital stay, therefore, a new treatment is needed to recover from delirium rapidly. Meanwhile, tDCS has been investigated to apply to the various kinds of brain disorders such as stroke, dementia and depression. It is a kind of noninvasive brain stimulation technique that can induce a change of cortical excitability by applying direct electric current. It is well known that anodal tDCS can increase cortical excitability while cathodal tDCS can decrease that. Furthermore, it has been reported that those change of cortical excitability can affect neuroplasticity. In this study, we hypothesized that anodal tDCS can prevent or recover the symptoms of postoperative delirium.

Method: In order to induce postoperative delirium in a rodent, we performed a stereotactic surgery under isoflurane anesthesia. 6 adult male SD rats (17.3±3.41 weeks, 395.17±48.05g) were used. During surgery, 2.5%-3% isoflurane anesthesia was maintained via an anesthesia mask. Each side of the frontal cortex (AP: +2.0mm, ML: ±1.5mm) and the parietal cortex (AP: -4.36mm, ML: ±4.0mm) was drilled, and screw electrodes were implanted to record local field potential. In order to treat with tDCS, an epicranial tubular plastic jacket was additionally fixed with a dental cement over the right frontal cortex (AP: +2mm, ML: +1.5mm). Those operated rats were randomly assigned into two groups: anodal tDCS treatment and sham treatment groups. Each groups were treated immediately after surgery for 20min using a constant-current stimulator. For the anodal tDCS groups, a constant-current of 200μA was applied, while a constant-current which is close to zero was applied for sham groups. To assess the level of attention and consciousness, we performed buried food test as well. The buried food test was conducted before surgery, 9h and 48h after surgery. EEG was acquired 9h and 48h after surgery and analyzed using continuous wavelet transform (CWT) in alpha, theta, and delta frequency band.

Results: At 9h after surgery, the anodal tDCS group showed significantly increased time to find food, in comparison with before surgery. However, it was recovered at 48h after surgery indicating that the subjects of this group had fully recovered at this time point. On the other hand, in sham group, the time to find food was still longer at 48h after surgery. In other words, sham group had not get better until 48h after surgery. In EEG analysis, the average of relative normalized power of the CWT coefficients in delta frequency from the right frontal cortex was significantly increased, only at 9h after surgery.

Conclusion: In summary, recovery from the postoperative delirium by tDCS was found in EEG results first, and followed by recovery of behavioral symptoms afterwards. However, we could not find any sign of improvement in sham group. Our results suggest that the possibility of a rapid recovery from the postoperative delirium by tDCS.

Keywords: postoperative delirium, transcranial direct current stimulation (tDCS), EEG, stereotactic surgery

Streaming Videos, Augmented Reality and Virtual Reality as Experiential Learning: What Does the Brain Think?

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Abstract. For millennia, human beings have been learning to adapt to their environment from the earliest caveman days to today's age of computer telecommunications. Pedagogies for teaching have continuously evolved from the oral transmission of stories, culture and survival skills to written knowledge passed down from generation to generation in pictographic or text format. Education has moved from face to face instruction in neighborhood schools and state universities to the distance education of the 70's to today's on-demand, anywhere online delivery of instructional content. Our teaching and transmission of knowledge became more cerebral and less physical over time, with frequent returns to hands-on learning. We developed technologies to provide vicarious learning experiences through live action and animated films, which lead to videos, now a ubiquitous production phenomena from everyone's cell phones. The new frontiers in teaching and learning involve augmented reality (AR) with and without the live interface with a person, as in the TeachLive program to develop skills for teachers and principals in simulated environments and real time interaction with an expert role player. Labster allows pre-nursing students to have simulated, low cost experience in hospital labs, or chemistry students can safely examine procedures for handling toxic substances. Using supportive wearable technology like handsets, architects can have you design your new kitchen. Virtual reality (VR) has promising potential to train law enforcement personnel with simulated engagement in high tension, scripted scenarios. A police cadet can experience a crisis encounter imbued with underlying social or racial conflict from the perspective of the accuser, the victim/perpetrator, and the officer. Such training in cultural sensitivity could create a better police force or nurse or teacher. Immersed in a virtual 3D environment, people can experience diverse landscapes, histories, and social stories with clearly defined educational objectives. Learning experiences are generally more efficacious when they engage a student's mind, body, and emotions, when the learner has vested interest in mastering content, and when information is presented in a comprehensible manner. By engaging emotions, we can make learning more meaningful and permanent. Streaming videos, Augmented Reality and Virtual Reality can make a positive and lasting difference in teaching and learning.

Keywords: e-learning, augmented reality, virtual reality

No. B269

Examining the Connection between Social Value Orientation and the Ability to Succeed in Tacit Coordination Games

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Abstract. It is well known in the Social and Behavioral Sciences that people differ in the way they approach interdependent other. Some people are pro-self, others can be said to be pro-social and there are those who are more individualistic by nature. This social tendency is often denoted as Social Value Orientation (SVO) and it can be quantified using various behavioral tests.

Tactic coordination games are one-shot coordination games in which the players need to coordinate on a single choice out of many possibilities. however, they must do so without any sort of communication between themselves. For example, given the following set of numbers {4, 6, 7, 10, 13, 17}, each of the players need to select one number and hope that his unknown partner (which they cannot communicate with) would select the same one. Success is agreeing on a single number, regardless of the number itself.

This coordination games can be modeled in game theory as a simultaneous game where the players need to select among multiple Nash equilibria. This problem is one of the hardest problem at hand, and currently game theory does not provide a good way to select between multiple equilibria, nor a way to predict human selection to those problems. However, in contrast to game theory, experiments with human participants in tacit coordination games showed that people are very good at agreeing on a single equilibrium. These solutions that people manage to converge to are referred to as "Focal Points", and in many games, it appears that there are players who are better than others at predicting what their unknown partner would select.

The aim of the presented research was to discover whether there is a correlation between the social orientation of human participants and their ability to successfully play tacit coordination games. The intuitive hypothesis was that people with pro-social orientation would be better at estimating their partners' choice in tacit coordination tests, as pro-social behavior should require an ability to put yourself in the shoes of the other partner and infer its actions is relate (ToM reasoning).

To this aim we composed a tacit coordination questioner with questions from different domains and let participants play it after filling a SVO test. In each domain, the participants were presented with questions of varying difficulty levels: easy, medium and hard. Our preliminary results on 21 participants show the following. First, with respect to their SVO classifications, 11 subjects were classified as individualistic, 10 subjects as pro-social, and 4 as having a pro-self orientation. Second, and counter to our initial hypothesis, the results show that the joint group of participants with individualistic and pro-self orientations performed

significantly better than the pro-social group (average of 14.033 vs 12.05 correct answers, $P<0.04$ in t-test) in the coordination questioner.
The results might help to facilitate the construction of cognitive models that mimic humans' ability to coordinate. Currently, we are using EEG to elucidate the neural substrates of tacit coordination in terms of the degree of involvement of the relevant brain networks.

Keywords: coordination, cognitive model, focal points, social orientation

Influence of the Frequency Parameter on Dopamine and Firing Rate in Striatum during Electrical Stimulation of Globus Pallidus Internus in Rats

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Abstract. Deep brain stimulation (DBS) is regarded as an effective approach for treating the motor symptoms of movement disorders. However, the precise treatment mechanism was still unknow. As we know, many animal behaviour effects during DBS were studied. The precise neurons activities were unclear because of lacking specific area measurements. In this paper, a 16-channel implantable microelectrode arrays (MEAs) was fabricated using Micro-Electronic-Mechanical-System methods. The recording sites (25μm in diameter) on the tip of MEAs share a similar size with the nerve cell. Therefore, it is possible to record single or several neurons' signals. The MEAs were able to record dual-mode signals including dopamine (DA) and firing rate simultaneously. The MEA was modified with platinum nanoparticles (PtNPs), reduced graphene oxide nanocomposites (rGO) and Nafion film which is special to DA detection, in order to detect DA and firing rate more effective. The nanocomposites modification would increase specific surface area of recording sites and accelerate the transfer of electrons. The sensitivity was about 0.017 pA/μM/μm2 that was enough perfect to detect DA. Nafion, a cation exchange membrane, was modified to exclude interference such as ascorbic acid and other anions. The modified MEAs were applied into the striatum of the rats. Various frequencies (10, 60, 100, 210 and 350 Hz) of electrical GPi stimulation were trained in the anesthetized rats. The extracellular DA concentration and firing rate variation were recorded simultaneously before, during and after stimulation. The results shows that the increased DA content was maximal (7.95±0.75 μM) and the firing rate of excited neurons maximally increased from 9.96±2.30 spi/sec to 38.2±2.71 spi/sec at 100 Hz. We can observe no obvious variation of dual signals when the stimulation frequency is too low such as 10 Hz. When the frequency was too high, the DA increased less than 100 Hz, and the firing rate of excitatory cell increased less too. We can get more improvement if this result would combined with the animal behaviour effects, the DBS treatment mechanism would be more clear based on the relationship of DA response, spike rate, LFP between behaviour effects.

Keywords: Dopamine; firing rate; GPi; striatum; DBS; frequency

Brain Big Data Analytics, Curation and Management

Joint Regression and Classification via Relational Regularization for Neurodegenerative Disease Diagnosis

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Abstract. Neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD) are characterized as an irreversible neurodegenerative disorder in the elderly people. Due to the symptoms of the diseases occurring progressively, middle or late patients sustain unending mental and physical suffering, and even life threat. AD is the most common form of dementia. PD mainly has four symptoms: tremor, rigidity, bradykinesia, and postural instability. Besides these external symptoms, attendant symptoms like anxiety and sleep disorders also appear. However, there is no valid treatment for neurodegenerative disease at present. Therefore, Early and accurate diagnosis of the diseases is of great importance, which slows the disease deterioration further and alleviates mental and physical suffering for patients. In this paper, we propose a joint regression and classification framework for neurodegenerative disease diagnosis. Specifically, we devise a new feature selection method in a unified multi-task feature selection model via relational learning. Three relationships (e.g., relationships among responses, samples, and features) are consolidated to represent the similarities among responses, samples, and features. Our proposed method exploits regression variables (clinical scores and label) to jointly select the most discriminative features for clinical scores prediction and class label identification. Extensive experiments are conducted to validate the proposed method on the public available Parkinson's progression markers initiative (PPMI) and Alzheimer's disease neuroimaging initiative (ADNI) datasets. In AD diagnosis, we estimate one clinical score (minimum mental state examination (MMSE)) and one clinical label (with the value of light mild cognitive impairment (lMCI), stable MCI, AD, or normal control (NC)), from the baseline MRI data. In PD diagnosis, we predict four clinical scores (depression, sleep, olfaction, cognition scores) and one clinical label (with the value of PD, scan without evidence of dopaminergic deficit (SWEDD), or NC), from the baseline MRI and DTI data. Our proposed method can greatly improve the performance in clinical scores prediction and in class label identification compared to other state-of-the-art methods.

Keywords: neurodegenerative disease, feature selection, classification, scores prediction

Finding Open Concept Relations for Brain Diseases

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Abstract. While traditional Information Extraction (IE) focused on identifying specified relations of interest, Open Information Extraction (OIE) systems extract relational tuples from free text without requiring predefined relation types. This paper presents the study of finding open concept relations related to brain diseases from Chinese BioMedical literature (CBM) database.

A semi-supervised learning framework is constructed for open concept relation extraction, taking the CMeSH thesaurus as domain knowledge. First, we select brain disease-related literature published in recent 5 years from the CBM database as our corpus, totally 178,960 documents. After the text preprocessing with NLP tools, such as sentence segmentation, word segmentation, POS tagging, etc, we use rule-based bidirectional maximal matching algorithm to identify biomedical concepts in each sentence. Sentences that contain two or more concepts are retained as candidate sentences. It is observed that the expression of relational phrases various between different kinds of concept pairs. So we divide candidate sentences into different macro relation classes (such as disease-drugs, drugs-drugs, etc.) according to the concept ID and the tree number in CMeSH. We construct bootstrapping training sets based on manually annotated seed tuples. Then CRF-based open relation learning models are trained for each macro class, since the specific type of concept relation is relatively limited under the same relational class. Accordingly, we learn different open pattern templates, mappings from a dependency path to an open extraction that express concept relations, for each macro class. These general open relation patterns are used to extract relation tuples consisting of biomedical concepts and a relation phrase from a new arbitrary sentence, in the format (c1; rel; c2). Finally, we construct a Chinese open concept relation database for establishing a biomedical knowledge graph including brain diseases in the future.

Keywords: Open Relation Extraction, Semi-Supervised Learning, Knowledge Graph

Integrating Cognition and Emotion in Cognitive Architectures of Intelligent Agents

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Abstract. Research on the brain information processing has provided compelling explanations about human cognitive and emotional processes. However, cognition and emotion have usually been investigated separately, disregarding the implications of their interrelationships.
From a computational perspective, emotional and cognitive processes have been modeled as two separated systems, forcing cognitive architectures (CAs) of intelligent agents play the role of integrative frameworks. However, most CAs have been designed to model only cognitive functions; their design hardly allows the inclusion of mechanisms for emotional processing. Although researchers have recognized the importance of this issue and some attempts to include emotion processing in CAs have been reported, CAs still face the challenge of providing suitable environments for modeling the integration and interaction of Computational Models of Emotion (CME) and Computational Models of Cognition (CMCs).
We propose an Integrative Framework designed to serve as the underlying architecture of CAs for intelligent agents. This Integrative Framework addresses the challenge described above by providing a suitable environment for the consistent integration and subsequent interactions of CMEs and CMCs in CAs. Its design is based on findings from psychology and neuroscience. This framework adopts a multiprocess and multilevel perspective and advocates the theory that all brain processes are highly interdependent. It also presents a natural design as it takes into account evidence suggesting that there is no a single structure in the brain that is in charge of processing cognition or emotion. Instead, it is designed under the assumption that emotional and cognitive processing stems from the joint operation of several components.
The integrative framework consists of three layers that explain at a particular level of abstraction a CA: Level-1 is an abstract layer that conceptually represents the CA being developed and all its functionality, there are no computational implementations of the mechanisms in the model. Level-2 consists of abstract components that represent brain functions (e.g., perception) and psychological constructs (e.g., personality). The interrelationships between these components form a functional model that provides a high-level description of the CA. Level-3 provides a low-level description of the CA in terms of components that synthesize the operations and architectures of human brain structures such as the thalamus and amygdala. In this level takes place the computational implementation of the behaviors defined in the previous level.
We also propose a methodology to develop biologically inspired CAs whose architecture implements the Integrative Framework described above. The methodology comprises three

sequential phases (that have a correspondence to the three levels of the Integrative Framework) to translate the requirements for a CA into a computational implementation. First, these phases allow researchers to analyze and validate the requirements for a CA based on evidence from fields studying the brain information processing at a functional level, such as psychology. Then, in order to determine the synthetic brain structures to be included in the CA and their interrelationships, the methodology promotes the use of theories and models that explain the neural substrates of human emotional and cognitive functions, thus providing theoretically plausible data useful to explain the CA in biological terms.

Keywords: Computational Modeling, Cognition and Emotion, Cognitive Architecture, Intelligent Systems, Integrative Models

Synchronous Detection of Neuronal Firing under a Nerve Stimulation System Control

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Abstract. Deep brain stimulation (DBS) provides a recognized research intervention for neurological disease currently. However, there is a lack of traditional electrical stimulator to observe neuronal firing activity synchronously. The aim of the present study was to realize concurrent detection of neuronal signals better under a nerve stimulation system control. The whole experimental platform consists of neuro-stimulator, neural signal detector (DMNSRS), integrated signal processing and stimulating software, stimulating microelectrode and microelectrode array (MEA) recordings. Herein, we designed an integrated software, which could control not only neuro-stimulator but also detection instrument at the same time to meet the demand of editing nerve stimulation waveform and of concurrent detection. As to achieve synchronization better and simplify data analyze, the actual stimulation signals applied to the experiment object could be collected back to data acquisition card. Practicably, combined with homemade MEA detecting device, which was modified with platinum black through electrochemical deposition and covered by 10 μL 0.5 %wt Nafion ethanol solution, medial forebrain bundle (MFB) DBS effects were observed significantly through the changes of electrophysiological signals in caudate putamen (CPu) of Sprague-Dawley (SD) rat, and the signal-to-noise ratio (SNR) was 5:1 after stimulation. Experimental results showed that the frequencies of neurons firing were increased significantly after fourth stimulation, there were three channels responded quickly and firing amount rose from 0 to 25 per second in CH2, but a delay time was displayed in CH3. Interestingly, the similar characteristics of spike was expressed in CH1 and CH2, whereas CH3 show a different shape, whose repolarization duration and total spike duration were shorter than former two. According to the above features, the possible reason maybe that neurons from CH1 and CH2 responded with an excitatory response, while response belong to CH3 exhibited the action of inhibitory neurons in some extent. The comprehensive nerve stimulation system provides a good human-computer interaction window, high reliability of the output waveform and fast signal acquisition, which can be used as an effective tool for DBS in the field of neuroscience research.

Keywords: DBS; Synchronous Detection; Neuronal Firing.

Construction of Stroke Management System Based on Django Framework

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Abstract. Stroke or cerebrovascular accident is a group of diseases of the nervous system injury of brain function because the blood supply to the brain is blocked. Its sudden onset, disturbance of consciousness and focal neurological dysfunction are the main clinical features of stroke[1]. According to the World Stroke Organization (WSO) report, around the world each year nearly 6 million people died from stroke. In our country, every 21 seconds a person died of stroke. Cerebral vascular disease is one of the three major causes of death in human diseases at present[2]. Because of the features of stroke: disease etiology, risk factors, uncertainty and complexity of clinical prognosis, the clinical research is carried out difficultly. And the establishment of stroke network data management platform can be with personal information, stroke information, clinical information which were collected and analyzed[3]. It can realize the use of data information scientifically, instantaneous search, the function of data mining. That can provide service for the research, clinic and preventive. With the advent of information age, computer data processing technology has penetrated into all fields of medicine. The establishment of information management system of stroke is the inevitable trend of modern scientific management. In this situation, this paper developed a set of stroke database management system[4]. The website system developed by B/S (Browser/Server) architecture, the architecture is divided into three layers which is the front end, back-end and database, using Python and Mysql to the development of the whole system[5]. Using Django as a development framework, which greatly improves the efficiency of system development and increases the maintainability of the system. The back-end database is based on Mysql[6]. It can store the pathological information of patients with stroke. The front end is based on the Bootstrap framework, combined with JavaScript and CSS, realizing the design of information inquiry system for stroke patients. Stroke database management system designed in this paper realized the input, storage, retrieval, modification, maintenance and sharing of pathological data of patients with stroke[7]. It realizes electronic management of pathological data, greatly improves the efficiency of pathological work. With the development of society, the modern means of application with data management, is the inevitable trend of the development of the discipline. The clinical pathological system in this paper can be applied to the information of patients with stroke in hospital management. And it provides a good platform for clinical and basic research of stroke, also made useful exploration for the management work of other clinical departments.

Keywords: Stroke; Management System; Django; B/C Schema

BI’17 Abstracts

(Workshop /Special Session)

Workshop on Semantic Technology for eHealth (STeH 2017)

Developing a Clinical Pharmacology Knowledge Graph

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Abstract. Given the diversity in genetics, environment, behaviors and social factors, drug therapy often fails to provide the most efficient way to treat patients and even cause substantial harm. While our growing ability to gather immense information on an individual's health status and other profiles gives us more opportunities to explore the optimal solutions and also compels a shift of health care from one-drug-treats-all towards more personalized medicine. Precision medicine, a rapidly expanding field fostering fundamental changes in personalized health care, provides us unprecedented insights in biomedical sciences. In this context, novel tools need to be developed to help clinicians or clinical pharmacists to integrate and analyze large amounts of available data with the goal to identify the entry points for the optimal treatment of a certain patient. Ontologies provide a novel means for organizing, integrating, and standardizing the knowledge domains specific to an area in a compact, formalized and computer-readable form and can also serve as a reference for knowledge exchange. So this study suggests a clinical pharmacology knowledge graph to facilitate the integration and aggregation of genes, drugs and diseases and demonstrate its application to classify and analyze a large subset of the open access databases in bioinformatics and pharmacogenomics fields. Based on previously reported biomedical ontologies, such as Gene Ontology, Disease Ontology, and UMLS etc. this knowledge graph depicts available pharmacological, pharmacogenetics and drug safety profiles of drugs. As a whole three main relationships are included and they are Gene-Disease (Phenotype) relationships mainly coming from ClinVar, Disease (Phenotype)-Drug relationships mainly from SIDER and Gene-Drug relationships from Drugbank. The novelty of this knowledge graph lies in the integration of diverse datasets linked by a model to formally define these concepts and mapping some of the related entities to this validate its practicability.

Keywords: Clinical pharmacology, Knowledge graph, Ontology

Cell-Lines Centered Semantic Model for Connecting Genes, Mutations and Cancers

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Abstract. Cancers nearly always arise as a consequence of genetic alterations such like mutations. And in the multiple-step development of caner, these mutations contribute to the loss of control of cell proliferation, differentiation and the acquisition of capabilities, such as tissue invasion, metastasize and angiogenesis. Finding the function roles that gene mutations play in cancer cellular process is important for the research of cancer. And extracting semantic relationships of genes-mutations, genes-cancers and mutations-cancers from biomedical literature is a significant challenge in the advancement of precision medicine of cancer. So, we construct a cell-lines centered semantic model for connecting resources about genes, mutations and cancers. Which integrates existing data resources about cancer genetics and semantic relationships extracted from biomedical literature. We propose a selection and linkage of data resources relevant to cancer genetics, including such as ClinVar, OMIM, COSMIC and HGMD, and define the mappings among these databases. We integrate the relationships extracted from biomedical literature and the relationships from data resources for example the annotations of gene and the function of regulation of cellular process in GO. And we normalize these relationships and map them to a standardized ontology. We turn selected data and relationships into a standardized RDF graph. The semantic network we construct contributes to find new genes and mutations related with cancer by machine learning for RDF statements. Most significantly, Such findings will lead to a better understanding of cancer mechanisms and sematic relationships between entity pairs related with cancer genomics, which can then be translated to clinical practice.

Keywords: Ontology, Semantic web, Data integration, Cancer cell biology

No. S05206

Making Semantic Annotation on Patient Data of Depression

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Abstract. Patient data, more exactly, electronic medical records (EMR), usually contain a lot of free texts. Those unstructured medical data cannot be easily understood by computers. In addition, the standard system of EMR is not unified, which is not conducive to the sharing and exchange of data. Moreover, EMR data have a strong privacy, which hinders the sharing and use of medical data and makes it impossible to provide a wider range of medical services and conduct more in-depth medical researches .Thus, the data integration of EMR has become one of the most important and essential issues in the field of e-health. This paper presents a method of the realization of semantic EMR by making semantic annotations on free texts in medical records. We will show how to use NLP tools to create semantic annotation with well-known biomedical terminologies/ontologies such as SNOMED CT. In particular, we will describe how to make the semantic annotations on a set of virtual patient data for depression, which are generated by using the Advanced Patient Data Generator (APDG), a knowledge-based patient data generator. We will discuss how those patient data of depression can be used in the system of Smart Ward of Depression for the semantic integration. The Smart Ward project, which is funded by National Natural Science Foundation of China for a major international cooperation project, aims to develop a knowledge-based platform that provides knowledge integration and clinical support. In short, our goal is to use semantic technology to improve the sharing and utilization of medical data and the interoperability among systems.

Keywords: Semantic Technology, Electronic Medical Record, Semantic Annotation, Data Integration, Depression

Feature Extraction for Science Concepts from fMRI Data of Naturalistic Reading: A Deep Learning Model

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Abstract. Neural networks based on deep learning algorithms have gained popularity in the last few years in computer vision and natural language processing. However, it is not until recently that researchers have begun to apply Deep Neural Networks (DNN) on large-scale neuroimaging data, and the DNN applications in the neurobiology of language remain scarce. In the current study, we applied a multi-layer deep neural network (Hinton & Salakhutdinov, 2006) to an fMRI dataset collected from 50 native English speakers who performed a naturalistic reading task in which five short science texts were presented sentence by sentence. Our fMRI volumes were collected based on a novel technique that allows the collection of both BOLD signals and eye-movement data and the analysis of fMRI data using the onset of first fixation on a word as time window for modeling the hemodynamic response for specific words during naturalistic reading (Schuster et al., 2016; Desai et al., 2016). The fMRI image data were preprocessed, segmented into anatomical regions of interests based on the AAL brain atlas (Tzourio-Mazoyer et al., 2002), and used as input in a Deep Belief Network (DBN). DBN is an unsupervised deep learning architecture based on Restricted Boltzmann Machines, through which the hierarchical feature representations emerge on each hidden layer of the DBN, and these "internal" representations of the inputs can be further probed via visualization tools such as t-SNE and SOM. We constructed our model by using 3 hidden-unit layers in the network, with the size of 500, 300 and 100 respectively. The representation in the final level of the DBN is further fed into different types of classifiers (i.e. SVM, Supervised SOM, and another DNN) to complete different classification tasks including different topics of the text (math, engineering, space, environment, or technology), different words (concrete vs abstract), and different type of participants (expert vs. novice readers, or readers with high vs. low working memory). In addition to the precision of such classifications based on fMRI images, a main focus of the current study is to extract feature representations through the hierarchical structure of the DBN, which will serve as the key signatures of the target science concepts acquired by the brains of the readers. In particular, we are interested in how the DBN model can reveal stages of the acquisition of science concepts from spontaneous, naturalistic, reading of texts in normal adults and child readers. The low-level to high-level feature gradient that emerges across the layers of the DBN may be particularly useful for understanding (1) how different brain regions might process different types of features, (2)

how individual differences in reading comprehension, verbal working memory, or executive function might be related to differences in the level of representation in the same brain region across individuals, and (3) how concepts may develop over time within and across brain regions.

Keywords: Deep Belief Network (DBN), fMRI, Naturalistic reading

Special Session on BigNeuron Project (BP 2017)

S09201 Hatu: A Scalable Software System for Collaborative Neuron Reconstruction

S09202 Automatic Tracing of Ultra-Volume of Neuronal Images

S09203 Local Neuron Radius Estimation in Volumetric Microscopy Images

S09204 Neuron Stalker: Automatic Neuron Reconstruction Based on Spherical Gradient Sampling

S09205 Retrieving Similar Substructures on 3D Neuron Reconstructions

S09206 Searching Specified Structures in Virtual Neuron

S09207 Creating a Functional Probabilistic Atlas of hMT/V5+ in a Large Population

S09208 Semantic Cell Segmentation Using Deformable U-Net

S09210 Neural Mechanisms Underlying Behaviors Revealed by Trajectory Data Mining and Visualization

S09211 Exploring the Brain Networks Under Free Listening to Audio Excerpts via Supervised Dictionary Learning

S09212 Efficient Visualization of Reconstructed Neuronal Network with Modern OpenGL

Hatu: A Scalable Software System for Collaborative Neuron Reconstruction

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Abstract. Rapid progress in light microscopy has enabled large-scale imaging of brain samples, posing a big data challenges to the step of digital neuron reconstruction. Encouraged by impressive tools developed recently (e.g. Vaa3D-TeraFly and UltraTracer) for tracing neurons from big images, here we present a new system based on the server-client architecture to fill in the gap between individual tracing and collaborative proof-editing. The system consists of three parts: 1) a database server for managing image and reconstruction data, 2) a web-based client for user interaction and 3) a computing service for driving automatic tracing. The database server manages and serves image data by adopting the distributed, versioned, image-oriented dataservice (DVID) originally developed for reconstructing EM connectome. Reconstruction data are stored in the same database in the standard SWC format. The client can be launched in any modern browser, showing image data and neuron structures to a user, who can then perform tracing through mouse operations. Designed for reducing manual work, the computing service provides a RESTful interface for any client to invoke automatic tracing at a given image location. To ensure a smooth workflow of multi-user editing, we implemented a novel versioning framework based on tree matching for the SWC model, through which multiple proofreaders can merge their results easily and correctly. Our testing results showed that further development of our system based on the current architecture would lead to a powerful platform for collobrative tracing. A large group of users should be able to reconstruct neurons in terabytes of image data together with minimal duplication and conflicts, as long as the servers are powerful enough to handle heavy loads.

Keywords: neuron tracing, SOA, BigNeuron

No. S09202

Automatic Tracing of Ultra-Volume of Neuronal Images

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Abstract. Despite substantial advancement in the automatic tracing of neurons' morphology in recent years, it is challenging to apply the existing algorithms to very large image datasets containing billions or more voxels. We introduce UltraTracer, a solution designed to extend any base neuron-tracing algorithm to be able to trace virtually unlimited data volumes. We applied this approach to neuron-tracing algorithms with completely different design principles and tested on challenging human and mouse neuron datasets that have hundreds of billions of voxels. Results indicate that UltraTracer is scalable, accurate, and about 3 to 6 times more efficient compared to other state-of-the-art approaches.

The three-dimensional (3-D) morphology of a neuron is crucial for establishing its connections and function in the context of brain circuits (Ascoli, 2015). Reconstruction of such neuron morphology from optical images is an important challenge in neuroscience (Acciai, et al, 2016). Substantial international efforts, e.g. the DIADEM competition (Liu, 2011) and the collaborative BigNeuron initiative (Peng, et al, 2015), have led to sizeable advances in this field. Yet, it remains an open and critical question how to effectively reconstruct, or trace, extremely large 3-D image volumes of long projection neurons having potentially complex arborization patterns.

Typically, due to the limited field of view of optical microscopy, the 3-D image volume of a large mammalian neuron, e.g. a pyramidal neuron, is produced using tiled scanning over the brain area where the neuron resides. When the voxels have sub-micron size in 3-D, the overall volume of such a neuron often amounts to tens of billions or even trillions of voxels. Most published neuron tracing methods to date were not designed to handle such a massive amount of data.

Here we introduce an intuitive, explorative method called UltraTracer to effectively trace virtually infinite 3-D image volumes. We extend UltraTracer to be a container of a variety of different base tracing algorithms that bear different design principles, enabling UltraTracer to aggregate the merits of previous methods. We have found UltraTracer suitable for reconstructing very large neuron morphology from a number of tests.

Keywords: neuron reconstruction, UltraTracer, large scale, BigNeuron

Local Neuron Radius Estimation in Volumetric Microscopy Images

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Abstract. Accurate estimation of local neuron size of complex 3D neuron structures imaged by microscopy is very important for quantification of neuronal morphology. If the local neuron radius of a neuron structure can be automatically and accurately estimated, this could be extremely useful for a series of neuron tracing algorithms such as Vaa3D-Neuron. Previously, the Rayburst sampling algorithm and Multistencils Fast Marching method are developed to estimate the neuron size in 2D images or 3D volumetric microscopy images. However, local neuron diameter obtained by the Multistencils Fast Marching method and Rayburst sampling is not accurate enough, because the Rayburst sampling algorithm requires an accurate detection of the neuron centerline, which is not easy and time-consuming practically. And the intensity threshold of the neuron surfaces in this model is a fixed empirical number, so it cannot handle challenging dataset where the diameter of the neuron varies much. In this paper, we propose to estimate the neuron local radius of any interest point in a given neuron, by first detecting its corresponding neuron centerline point using Multistencils Fast Marching method and then estimating the local neuron radius by the Rayburst sampling algorithm. Besides, an adaptive intensity threshold algorithm by analyzing the intensity distribution of the neighborhood around the in interest point has been proposed to handle challenging dataset where the intensity value of the neuron varies much. Compared with the previous work, the experimental results show that the proposed method could improve the local neuron radius detection accuracy a lot in challenging datasets.

Keywords: Local neuron radius, Neuron tracing, Rayburst sampling, Multistencils Fast Marching Method

Neuron Stalker: Automatic Neuron Reconstruction Based on Spherical Gradient Sampling

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Abstract. The study of neuron morphology is important in computational neuroscience, because it reveals the detailed connectivity information of neuronal networks. Nowadays, the majority of neuron morphology reconstruction results are still generated by manual labelling, which are labour-intensive and not practical to apply on the large-scale neuronal population reconstruction of the whole brain. Due to the significance of neuron morphology stated above, we proposed a neuron tracing framework named Neuron Stalker. Neuron Stalker framework consists of the neuron image enhancement, seed detection and spherical gradient based tracing. The neuron image is enhanced with the Frangi Vesselness filter and then the filtered image is segmented with the graph-cut algorithm. The resultant segmentation image is the input for the seed detection. Seed detection consists of ridge detection and redundant seeds removal. The seeds are initially detected by searching the locations with high vesselness scores. When two seeds are close to each other, one seed is removed to avoid the possibility of redundant tracing results. After the seeds are detected, multiple Neuron Stalkers traverses from the initial seed locations following the spherical gradient sampling strategy. To begin with, the spherical gradient sampling obtains 3D discrete gradient vector of the whole original neuron image. At the location of each step of Neuron Stalker, a sphere centering at this location is sampled by multiple disks. A disk can be defined by two angles and the radius represented using the polar system. Each sampled point on the disk has its own gradient vector flow as the force and vector path from the current Neuron Stalker location to its own 3D location, therefore each sampled point has a corresponding torque by cross multiplication of the vector path and the force. The number of sampled points on each disk to generate the summation of torque can be adjusted to speed up the calculation. Finally, each Neuron Stalker moves along the direction orthogonal to disk with the minimum gradient vector flow torque summation. After all Neuron Stalkers moved several steps, all nodes are then connected by using the minimum spanning tree. The proposed neuron reconstruction framework named Neuron Stalker is implemented as the Vaa3D plugin.

Keywords: 3D Neuron Reconstruction, BigNeuron, Neuron Morphology

Retrieving Similar Substructures on 3D Neuron Reconstructions

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Abstract. Automatic neuron tracing methods might do weak at some substructures of neurons. In this case, users need to pay more attention to these substructures and their similar substructures. Vaa3D (vaa3d.org) is a popular open source platform with many plugins or neuron utilities to visualize digital neuron, tracing its morphology, analysis or process neuron structures. Under the Vaa3D platform, these unsatisfactory substructures can be marked as template substructures. In this work, we propose a method to retrieve all similar substructures from single or multiple neuron reconstruction(s). The method consists of four steps: (1) calculating the mean length of all nodes to all terminal nodes in the marked substructure; (2) constructing subsections at each candidate node on whole reconstruction trees by fast marching method, which consists of nodes with length to the candidate node smaller than the mean length of the marked substructures; (3) computing 19 morphology features based distances between the marked substructures and all subsections; (4) sorting the distance for each marked substructure and selected ones with smaller values. The proposed method has two advantages: (1) by using the mean length of the marked substructure, rotating transformation can be avoided while constructing subsections on the whole reconstruction tree; (2) by using fast marching method, nodes belonging to a subsection can be found easily and quickly. The retrieving procedure can be implemented as a plugin of Vaa3D. Experiments on some small reconstruction trees and large reconstruction trees demonstrate that the proposed method can successfully retrieve all similar substructures in the whole trees.

Keywords: 3D neuron reconstruction, substructure retrieving, fast marching

No. S09206

Searching Specified Structures in Virtual Neuron

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Abstract. Finding specific neuron structures is helpful to improve the efficiency of neuron tracing and further structure-functional analysis. Virtual Reality (VR) technology provides us a visually visible way to observe and specify the neuron structures intuitively. In this work, we present 3D neuron structures with virtual reality technology and implement an interactive system for searching the neuron structure specified by users in virtual reality space. The workflow of the interactive neuron structure searching system mainly consists of the following stages. (1) Modeling and rendering the reconstructed 3D neuron structures in virtual reality space. (2) Marking the regions of interests (ROIs) in the virtual neuron through interactive user operations. (3) Extracting the neuron substructures from the ROIs marked by users and generating the features of the extracted neuron substructures. (4) Traversing the entire neuron and searching for the neuron substructures which are similar to the specified ones, the similarity measure is constructed based on the distances between the feature vectors of the specified neuron substructure and the local neuron trees located in the searching window. (5) Highlighting the searching results, i.e. the found similar substructures, in the virtual neuron. The VR-based neuron structure searching system is implemented based on Vaa3D platform. Experiments indicate that the proposed VR-based interactive system achieves a user-friendly interface for neuron structure presentation and analysis. The system is convenient to be used to find multiple candidate neuron structures of user interests. Moreover, utilizing both the statistical and morphological features, the proposed searching system is robust to the neuron structure deformation.

Keywords: Neuron structure searching, Virtual reality, Vaa3D platform

Creating a Functional Probabilistic Atlas of hMT/V5+ in a Large Population

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Abstract. Visual motion perception is an essential ability for us to survive. It is widely acknowledged that the human MT/V5+ (hMT/V5+), which shows larger activation for motion information than static information, is the core neural machinery for motion perception. As a result, accurate delineation of hMT/V5+ in human brain is crucial to study the neural mechanism of motion perception. Until now, several hMT/V5+ atlases have been published based on different criteria such as microstructural architecture, connectivity and topology. However, no hMT/V5+ atlas were constructed according to its functional selectivity which is the original criterion used to discover the hMT/V5+. Here, based on a large cohort of subjects (N = 509), we created a probabilistic atlas of hMT/V5+ using functional MRI on functional selectivity criterion. Specifically, we firstly delineated the hMT/V5+ in subject-specific surface space using a semi-automated procedure. Then, each subject-specific map was transformed into fsaverage space through cortex-based alignment, and averaged to create a probabilistic map of hMT/V5+. We then quantified how the hMT/V5+ atlases constructed based on other criteria (e.g., cytoarchitecture, connection and topology), correspond to the selectivity hMT/V5+ atlas. We found these atlases showed different correspondences to our hMT/V5+. The topology atlas had the highest correspondence to our selectivity based hMT/V5+ atlas, and the connection based atlas showed the lowest correspondence. Further, a two-fold cross validation procedure was used to estimate the accuracy of the different atlas in predicting the individual hMT/V5+. As expected, we found selectivity hMT/V5+ atlas showed better individual prediction than other atlases. Taken together, relative to other non-selectivity based atlases, the selectivity-based hMT/V5+ atlas could better represent the functional hMT/V5+ in individuals, and was more suitable to functional selectivity analysis. We hope such an atlas can be a more accurate atlas for further hMT/V5+ activation analysis.

Keywords: motion perception, hMT/V5+, functional MRI, probablistic map, cross validation

No. S09208

Semantic Cell Segmentation Using Deformable U-Net

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Abstract. Reliable cell nuclei segmentation from the background on 3D images is a crucial step for the further neuron tracing and morphological analysis. A major challenge for more robust segmentation methods is the large variations in the size, shape and viewpoint of the cells, combining with the low image quality caused by noise and artifacts. To address this issue and inspired by the latest success in applying deep learning on natural image analysis, in this work we propose a deep learning-based cell nuclei segmentation method based on a 3D U-Net structure with deformable convolution layers. The U-Net architecture for deep learning has been shown to offer a precise localization for image semantic segmentation. As reported in previous literatures, comparing with traditional unsupervised image segmentation methods, the proposed deep learning-based method can achieve much higher accuracy and/or in much shorter amount of time. Moreover, the deformable convolution layer enables the free form deformation of the feature learning process by adding offsets to the regular grid sampling locations in the standard convolution, which are learned from the feature maps. Thus, the deformable layers can make the whole network more robust to the variations in cell shapes, locations and transformations, as well as different image settings.

The proposed network is consisted of 4 layers of deformable convolution and the corresponding deconvolution operations, thus achieving a semantic end-to-end learning architecture between the image and annotations. The model is implemented in Python Tensorflow (https://github.com/XiangLi-Shaun/deformableConvolution) and tested on neuron cell images with annotation ("gold166") provided by the BigNeuron Project and obtained accurate results.

Keywords: cell segmentation and classification, deep learning, UNet, deformable convolution

Neural Mechanisms Underlying Behaviors Revealed by Trajectory Data Mining and Visualization

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Abstract. To study how brain controls behaviors, it is usually required to manipulate the activity of neurons and to observe the change of certain phenotype. Since 1960s, pioneers like Seymour Benzer have started to use Drosophila as a model organism to investigate mechanisms underlying behaviors. With the recognition by 2017 Nobel Prize on works of circadian rhythm, neuroethological researches in fruit flies have no doubt made a great contribution to neuroscience during these decades. It was once a challenge to record every response generated by the subjects during the entire behavioral experiment. Thanks to the development of computer vision techniques, such situation is resolved by obtaining the moving trajectories of multiple individuals with powerful tools already published. However, we still need a standardized system to extract biological information out of trajectory data. Here we present "DigTrack" to accomplish this process, especially for large-scale studies. It utilize up to 33 basic behavioral parameters to describe per-fly per-frame status. By combining such parameters, numerous behaviors with different biological meanings could be objectively quantified. Furthermore, statistical data can be intuitively visualized to facilitate an unbiased interpretation of the results. Finally, by applying this system, we have successfully revealed the functions of different populations of neurons regulating social interactions in Drosophila. Taken together, "DigTrack" enables a much more detailed and systematic analysis on trajectory data to decipher the neural mechanisms underlying complex behaviors. With minor modifications, this system would also extend our abilities to analyze trajectories of other moving agents, ranging from cellular organelles, migrating cells, to insects and mammals.

Keywords: Behavior, Neuroscience, Drosophila, Data-mining, Visualization

Exploring the Brain Networks under Free Listening to Audio Excerpts via Supervised Dictionary Learning

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Abstract. In recent years, natural stimuli such as audio excerpts have received increasing attention in neuroimaging studies. Compared with conventional simple, idealized and repeated artificial stimuli, natural stimuli contain more unrepeated, dynamic and complex information that are more close to real-life. However, there are still two limitations in current fMRI analysis methods. Firstly, there is no direct correspondence between the stimuli and any sensory or cognitive functions of the brain, which makes it difficult to apply traditional hypothesis-driven analysis methods (e.g., the general linear model (GLM)). Secondly, traditional data-driven methods (e.g., independent component analysis (ICA)) are purely data-driven and ignores the quantitative modeling of stimuli, which may limit the power of analysis models. In order to alleviate these problems, in this paper, we propose a supervised dictionary learning based framework to explore the brain activities under free listening to audio excerpts conditions. The basic idea of our framework is that there are meaningful neural correlates between computational audio features and functional brain activities and these audio features could be used as constraints in identifying corresponding brain activities. To be specific, we first adopt a few biologically-plausible auditory features to quantitatively model the audio excerpts. Then we modify the dictionary learning procedure and constrain these features in dictionary learning procedure to learn the involved brain activity patterns and brain networks. After that, we jointly analyze the corresponding brain activities across all the subjects and identify the meaningful brain networks. Experiments proved that meaningful auditory feature related brain networks could be identified and the proposed method demonstrate great superiority compared with traditional methods.

Keywords: Nautural Stimulus, fMRI, Dictionary learning

No. S09212

Efficient Visualization of Reconstructed Neuronal Network with Modern OpenGL

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Abstract. Digital reconstruction of neuronal morphologies is an essential step for brain circuit mapping. While many software systems have been developed to solve the reconstruction problem, relatively little effort has been devoted to the visualization system. Efficient rendering of reconstructed neuronal morphology in 3D, along with its image context, offers a smooth user experience and allows for faster reconstruction. However, rendering large neuronal structure is still a bottleneck in many popular software systems. For example, a reconstructed digital neuron represented in the standardized SWC file format, when rendered conventionally, can contain over 5 million triangles. Such high number of triangles will cause a lot of stress on normal desktop GPU and thus reduce rendering throughput. To reduce the GPU stress, we have developed a new 3D rendering engine based on modern OpenGL in our open source neuronal reconstruction software neuTube. Our new engine is built upon GLSL (OpenGL shading language) and is specially designed for the efficient rendering of neuronal structures. We decompose neuronal structures into geometric primitives, such as line, sphere, conical frustum, etc. And then render different types of primitives in their corresponding shaders. The vertex shader finds bounding boxes of the geometric primitives on the screen, which usually contains only two triangles for each geometric primitive, and then the fragment shader solves ray-quadric interactions for each pixel inside the rasterized bounding box. Our new 3D engine reduces the number of triangles by over 100-folder compared with the conventional rendering, thus greatly extending the number and complexity of neurons that can be handled during reconstruction or visualization. Furthermore, we have built a new visualization software based on the same 3D engine, with which users can easily visualize, explore, and create animations of a large-scale neuronal network.

Keywords: visualization, neuronal morphology, SWC, 3D engine, software

Workshop on Mesoscopic Brainformatics (MBAI 2017)

Neuroscience Information Toolbox: An Easy-to-Use Toolbox for Mesoscopic EEG-fMRI Multimodal Fusion Analysis

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Abstract. Recently, multimodal fusion has been pursued in an effort to obtain important information to investigate brain function and dysfunction in mesoscopic scale, and integrating electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) may noninvasively obtain more comprehensive mesoscopic information on brain activity with both satisfied spatial and temporal resolutions. However, a more flexible and easy-to-use toolbox for EEG-fMRI multimodal fusion is required. Here, we have therefore developed a freely available and open-source MATLAB toolbox, named Neuroscience Information Toolbox (NIT), for EEG-fMRI multimodal fusion analysis as well as batch processing of fMRI data. The NIT consists of three modules: 1) fMRI module, in which fMRI batch preprocessing, nuisance signal (e.g. headmotion, linear trend, white, CSF and global signals) removing, band-pass filtering and calculation of resting-state measures (e.g. functional connectivity density) are contained; 2) EEG modules, in which EEG re-referencing (e.g. average and REST reference), extracting EEG features (including event onset, power and amplitude), marking and adding interested events (e.g. epileptic discharges) and plotting EEG figures are contained; and 3) fusion modules, in which fMRI-informed EEG analysis (Network-based Source Imaging, NESOI) and EEG-informed fMRI analysis (including general linear modal (GLM) and local multimodal serial analysis (LMSA)) are included. The NIT was designed to provide a convenient and easy-to-use for researchers, especially for novice users. It can be downloaded for free at http://www.neuro.uestc.edu.cn/NIT.html, and detailed information including introduction of NIT, user manual and example data are also available at this website. We hope the NIT is a promising toolbox for exploring mesoscopic brain information in various EEG-fMRI studies.

Keywords: EEG-fMRI, multimodal fusion;, mesoscopic brain information;, MATLAB toolbox;, open source

No. S12204

The China-Canada-Cuba (CCC) Axis

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Abstract. The CCC-Axis brings together research teams from multiple cities in China, Canada and Cuba to: (i) investigate the basic mechanisms of dementia, movement disorders and epilepsy, (ii) identify early disease biomarkers, (iii) foster clinical translation of the basic findings, and (iv) assess the impact of different lifestyle experiences (sleep, physical exercise, nutrition) on these disorders. The proposal builds upon a long history of scientific interaction among the applicants, a mature IT infrastructure (CBRAIN/LORIS) that already supports a global data-sharing and analytics network and shared prior work on establishing standardized neuroimaging protocols. It takes advantage of unique opportunities presented by the rise of global data-sharing initiatives and national brain projects in China, Canada and Cuba. This initiative will allow us to acquire harmonized data and share them across national boundaries such that we can remove methodological hurdles and focus on exploring questions that transcend the restrictions imposed by studying local cohorts. Why is Alzheimer's disease the dominant form of dementia in the West, while vascular dementia is more prevalent in China? Why is prevalence of Parkinson's disease much higher in China than other industrialized countries? Examining study cohorts from different countries will afford us a unique insight into the influence of genetic, lifestyle and nutritional differences upon the evolution of disease pathology. While we do not propose to collect new data with this proposal, the establishment of a common IT framework, standardized neuroimaging protocols, and dissemination of existing data/software through this platform sets the scene for more ambitious (and expensive) multi-national initiatives. We will utilize two IT platforms currently being deployed in each country. CBRAIN is a web portal that provides researchers with access to high-performance computing resources (both terrestrial and cloud-based). LORIS is a web-based databasing system that supports multi-centre, multi-domain data collection and and curation. The home institution for these platforms is McGill U. in Montreal and they are used on 22 countries. Technical teams from Chengdu, Bejing and Havana have all visited McGill in recent months to work with the McGill group on the local deployment of this IT ecosystem, e.g. on the Baidu web services platform in China. This project will foster a wider data-sharing network across China. It will leverage existing partnerships borne of previous FRQS-Cuba funding for harmonization of MRI data acquisition. The Québec team includes international leaders in neuroimaging and neuroinformatics (Evans, Poline, Glatard, Duchesne, Descoteaux), electrophysiology and optical imaging (Benali, Grova, Gallagher) and clinical/cognitive neuroscience (Doyon, Chertkow). Working closely with partners in Havana (Valdes-Sosa, Galan-Garcia), Chengdu (Yao, Biswal), Shanghai (Poo, Wang) and Bejing (He, Gong), we will

build a analytic environment able to acquire, process and integrate data from EEG, MEG, NIRS, fMRI, DTI and MRI within a common framework across countries.

Keywords: CBRAIN/LORIS, EEG toolbox

Reinstating Electrophysiology into Global Brain Projects via CBRAIN and LORIS

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Abstract. Electrophysiology provides functional data with time a resolution data that is crucial to study brain functions and disorders. It is also THE translational bridge to population health in all economic settings. In spite of this it is an imaging modality sadly neglected in current Global Brain Projects.

We intend to remedy this situation as part of the C-C-C collaboration by integrating electrophysiology (EEG and MEG) into the CBRAIN portal. Towards this end we are:

• incorporating the tomographic quantitative EEG (qEEGt) toolbox developed by the CNEURO into CBRAIN. qEEGt is Statistical Parametric Mapping for EEG source spectra.

• Adopting the BIDS-EEG format for storing data into the LORIS framework

• Releasing, as part of the data repositories, the data from the Cuban Human Brain Project. This is the only large national effort to integrate EEG with other imaging modalities

• Creating conditions for linking to other datasets and other data repositories

We will illustrate the usefulness of multimodal imaging studies to discover EEG biomarkers with examples from the Barbados Nutrition Study and population based study of hypertension in Havana in which an EEG version of source mutivoxel pattern analysis allows accurate classification of subjects.

Keywords: EEG and MEG, BIDS-EEG

Workshop on Novel Methods of the Brain Imaging in the Clinical and Preclinical Neuroscience (NMBICPN 2017)

S07201 Rapid Volumetric Three-Photon Fluorescence Microscopy

S07202 In Vivo Optical Imaging and Application in Brain Research

S07203 Implantable Imaging Devices for Observation of Neural Activities

S07204 The Promise of Large-Scale Brain Recording with Optoacoustics

No. S07201

Rapid Volumetric Three-Photon Fluorescence Microscopy

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Abstract. Three-photon fluorescence microscopy is known for its ability for extending imaging depth in scattering tissues in vivo. In a standard 3PE microscopy, a scanned Gaussian beam is focused inside the tissue. Limited by the low-repetition-rate laser sources used for the three-photon excitation wavelength, the microscopy system suffers from a slow scanning speed. For volumetric imaging, the imaging speed is even slower due to the on serial focal scanning in axial dimension.

Here we present a rapid volumetric three-photon fluorescence microscopy based on the axially elongated Bessel focus. We used a refractive axicon to generate a Bessel beam, and by scanning the needle-like laser beam, a 300-μm × 300-μm × 300-μm volume with a single scan at 5 Hz could be obtained.

Using axially elongated Bessel focus to extend the depth of field has also confirmed to be an effective solution for two-photon fluorescence microscopy. Nonetheless, the intensity distribution of zero-order Bessel function in the transverse plane shows strong side lobes, which results in hazy backgrounds, especially when a high NA is used. We conducted the comparison of the same sample imaged with either two-photon or three-photon fluorescence microscope. Because the 3PE fluorescence obeyed the power-cubed dependence, the axial point spread functions measured from 0.2-μm-diameter beads shows that the three-photon excited Bessel beam has much less side lobes than that excited by the two-photon excitation. Therefore, the volumetric three-photon fluorescence imaging shows better signal to background ratio, as shown by the imaging results in fruit flies and zebrafish larvae in vivo.

Keywords: Three-photon microscopy

In Vivo Optical Imaging and Application in Brain Research

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Abstract. Within the last years, brain optical imaging methods have yielded revolutionary results when applied to the clinical and preclinical neuroscience research.

Physically, optical imaging methods are based on the idea that photon reflections and fluorescence are highly responsive to the physiological changes in the brain. The neural activity of the living neural tissue can be visualized directly - by the use of voltage- and calcium sensitive dye imaging, or indirectly, through the use of metabolic-related optical imaging: optical imaging of intrinsic signal (IOS), photoacoustic tomography (PT), voltage-sensitive dye imaging (VSDi) and the near-infrared Spectroscopy (NIRS). The most common of these methods is IOS, which is based on the optical changes in the features of neural tissue associated with local oxygenation and deoxygenation. It can be realized without any extrinsic chemical probes, in exposed brain or transcranially in human patients or in experimental animals. PT is a hybrid imaging technique based on the direct conversion of light's energy into ultrasonic waves. Being exclusively sensitive to the local oxygen consumption, PA is applicable for the functional imaging based on the local oxygenation and the cerebral blood circulation. Very powerful optical imaging methods, VSDi offers an excellent opportunity to study the neural activity in vivo with high spatial and temporal resolution - up to a few microns and milliseconds, respectively.

Angled fluorescence laminar optic tomography (aFLOT), in contrast to VSDi alone, is based on direct visualization of the neural activity and allows visualization of neural network activity. Our team recently combined VSDi with aFLOT. This approach allows visualization of neural activities in vivo in three dimensions (3D) with a 5 ms temporal resolution. All of the above mentioned methods are mainly applicable for experimental neuroscience but some of them also suitable for the clinical studies.

Keywords: angled fluorescence laminar optic tomography, brain optical imaging, functional brain mapping, voltage-sensitive dye

Implantable Imaging Devices for Observation of Neural Activities

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Abstract. Optical imaging is one of the important methods for brain functional imaging. Especially, fluorescent imaging, using fluorescent proteins, is necessary for observation of specific neurons. Microscopes are widely used for imaging neural activities. However, the size of microscopes is very large in comparison to mice or rats, which are the observation targets in most cases. Thus, the animals are fixed under the microscope for in-vivo imaging. Although an imaging fiber can be used for imaging under freely moving condition, it is a little stiff and limits the motion of the observation target. In addition, in order to observe the deep brain of a mouse, a rod-shaped GRIN lens is used. However, it has a relatively high invasiveness because its cross-section for sufficient observation area is large.

To solve these issues, we propose the use of ultra-small implantable complementary metal-oxide-semiconductor (CMOS) image sensors. By starting from image sensor design, we fabricate imaging devices in the shape of needles or plates with minimum dimensions. They can be placed in the vicinity of observation targets and, thus, a high spatial resolution is achieved without any lens. This simple structure makes the devices small and light-weight in comparison to mice.

As a light source, μLEDs can be used. By removing substrate from the active layer of an LED, the thickness is reduced to less than 10 μm. This feature allows a reduction in the total thickness of the device, thereby achieving low invasiveness.

In our experiment, our imaging device was placed on the brain of a mouse. We verified that our sensor has a sufficient signal-to-noise ratio to detect blood concentration changes as a result of stimulation. We also tried fluorescent imaging using the device with emission filters. The result shows that fluorescence intensity distribution from green fluorescent protein can be observed.

Keywords: Implantable image sensor, CMOS image sensor, In-vivo imaging, Fluorescence imaging

No. S07204

The Promise of Large-Scale Brain Recording with Optoacoustics

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Abstract. Non-invasive observation of fast spatiotemporal activity patterns of large neural populations is a longstanding goal of neuroscience. Not only would such abilities significantly promote our knowledge on brain function and its pathophysiology but they are also expected to accelerate development of novel therapies targeting neurological and neuropsychiatric disorders. The progress is hampered by the limited capacity of state-of-the-art functional neuroimaging tools, which do not permit simultaneous monitoring of whole-brain activity with an adequate spatio-temporal resolution. In contrast to other imaging techniques, optoacoustics combines the benefits of both optics and ultrasound by probing rich and versatile optical contrast across a wide domain of penetration scales into optically dense tissues while maintaining excellent spatio-temporal resolution representative of ultrasound imaging. Our recent efforts in the field of optoacoustic functional and molecular imaging have established new technological platform employing spherical matrix arrays, parallel acquisition hardware, GPU-based data processing, and fast laser tuning systems in order to enable acquisition and visualization of entire tissue volumes at video rates. This has offered unparalleled imaging capacities among the current bio-imaging modalities to monitor, fully non-invasively, the volumetric changes in multiple hemodynamic parameters in the mouse brain, track fast kinetics and bio-distribution of contrast agents, and achieve volumetric deep tissue handheld functional angiography in humans. Here we demonstrate the ability to optoacoustically track neural dynamics using calcium indicators in highly scattering brains of adult zebrafish and mice in vivo, thus offering unprecedented capabilities for functional whole-brain observations of fast calcium dynamics. In combination with optoacoustics' well-established capacity for resolving vascular hemodynamics, the newly developed platform opens new vistas in the study of large-scale neural activity and neurovascular coupling in health and disease.

Keywords: Large-scale neuroimaging, optoacoustic tomography, photoacoustics, neurophotonics

Workshop on Big Data and Visualization for Brainsmatics (BDVB 2017)

S03202 DiffusionKit: A Light One-Stop Solution for Diffusion MRI Data Analysis

S03203 Whole-Brain Level Reconstruction of Pyramidal Cells in the Neocortex of Mice

S03204 Morphological Analysis of Chandelier Cell Based on 3D High-Resolution Brain Imageset

S03205 A Nonlinear Three-Dimensional Image Registration Method for Optical Microscopic Whole Brain Dataset

S03206 A Platform for the Analysis of the Distribution of Brain-Wide Neurons

S03207 An Automatic Method for Classification of Three-Dimensional Neuronal Cell Body

S03208 Whole-brain 3D Affine Registration for High-Resolution Whole Brain Dataset

S03209 Identifying Weak Signals in Inhomogeneous Neuronal Images for Large-Scale Tracing of Neuritis

S03210 Accurately Identifying Closely Packed Neurites at Crossover Points to Enhance the Reconstruction of Neuronal Population

S03211 Convolutional Neural Network-Based Automated Segmentation of Brain Contour

S03212 The 3D Reconstruction of Brain Vascular Network of Whole Mouse Brain

S03213 Fast Reconstruction of Neural Projection Pattern in Whole Mouse Brain

S03214 The 3D Compression of TB-Scale Brain Image Stack Based on Video Coding

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S03216 A Scalable Image Processing Pipeline for Reproducible Terascale Brain Atlasing

DiffusionKit: A Light One-Stop Solution for Diffusion MRI Data Analysis

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Abstract. Background: Diffusion magnetic resonance imaging (dMRI) techniques are receiving increasing attention due to their ability to characterize the arrangement map of white matter in vivo. However, the existing toolkits for dMRI analysis that have accompanied this surge possess noticeable limitations, such as large installation size, an incomplete pipeline, and a lack of cross-platform support. Thus, a comprehensive and cross-platform support toolkit with a full pipeline for analyzing and visualizing diffusion MRI data is expected to substantially facilitate studies using diffusion MRI data.

New Method: In this work, we developed a light, one-stop, cross-platform solution for dMRI data analysis, called DiffusionKit. It delivers a complete pipeline, including data format conversion, dMRI preprocessing, local reconstruction, white matter fiber tracking, fiber statistical analyses and various visualization schemes. Furthermore, DiffusionKit is a self-contained executable toolkit, without the need to install any other software.

Results: The DiffusionKit package is implemented in C/C++ and Qt/VTK, is freely available at http://diffusion.brainnetome.org. The website of DiffusionKit includes test data, a complete tutorial and a series of tutorial examples. A mailing list has also been established for update notification and questions and answers.

Comparison with Existing Methods: DiffusionKit provides a full-function pipeline for dMRI data analysis, including data processing, modeling and visualization. Additionally, it provides both a graphical user interface (GUI) and command-line functions, which are helpful for batch processing. The standalone installation package has a small size and cross-platform support. A considerable comparison is listed in Table 3.

Conclusions: DiffusionKit provides a complete pipeline with cutting-edge methods for dMRI data analysis, including both a GUI interface and command-line functions. The rich functions for both data analysis and visualization will facilitate and benefit dMRI research.

Keywords: Diffusion MRI, DTI, HARDI, Brain network, DiffusionKit

Whole-Brain Level Reconstruction of Pyramidal Cells in the Neocortex of Mice

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Abstract. The mammalian brain is highly wired not only between neurons in a local microcircuitry but also between brain regions in the global brain net work. Although connections between different brain regions have been largely revealed using various labeling and imaging techniques such as retrograde labeling and functional MRI, it is still unclear how a specific neuron type contributes to the global net work at the whole brain wide. Combining with sparse labeling of neurons in the brain using transgenic and virus infection techniques, a new imaging system – fluorescence Micro-optical Sectioning Tomography (fMOST) made it possible to obtain high resolution images of neurons in a mouse brain (X: 0.3 μm, Y: 0.3 μm, Z: 1 μm). Using whole-mouse-brain image stacks, we have started to reconstruct single pyramidal cells (PCs) in the neocortex at a whole brain level with Neurolucida 360 system. It was found that different PC types have featured projection patterns in the neocortex mainly including somatosensory cortex (SSC) and visual cortex (VC). L2/3 PCs in the SSC have contralateral projections forming symmetrical axonal clusters in two hemispheres (n = 4). But L2/3 PCs in the VC seem to have only ipsilateral projections (n = 5). L5UTPCs have both ipsilateral and contralateral projections in the SSC while only contralateral projections in the VC . L5TTPCs project to multiple subcortical regions in both SSC and VC of the ipsilateral hemisphere . L5STPCs with different apical dendrites (possible subtypes) seem to project to different subcortical regions in the VC . These preliminary results suggest that different PC types classified based on its featured dendritic structures may have the same or different axonal projections depending upon the different functional cortical regions of neocortex.

Keywords: 3D reconstruction whole-brain level Somatosensory cortex visual

Morphological Analysis of Chandelier Cell Based on 3D High-Resolution Brain Imageset

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Abstract. Identifying all neuron types is necessary for understanding brain architecture. The sufficient complete fine neuron structure is the fundamental data for the study of neuron types. However, complete fine neuron morphology is not easy to acquire, thus leading to disagreement on the determination of cell types in brain.

Here, combined genetic viral targeting with fluorescence Micro-Optical Sectioning Tomography (fMOST), we got the three-dimensional high-resolution brain-wide image data of complete fine neuron structure. Particularly, we studied the neocortical chandelier cells, the most distinctive axo-axonic interneuron.

We reconstructed several chandelier cells in neocortex from layer 2 to 6 in mPFC, MC and SSC. For those chandelier cell whose soma in layer 2, we discovered 3 types according to their axon distribution patterns along the columnar depth: intra-laminar type, across-laminar type and trans-laminar type. And the dendrite pattern of layer 2 chandelier cells mainly reflects sub-layer distribution. For those chandelier cell whose soma in layer 3, 4, 5 or 6, because of reconstructed data insufficiency, we just distinguished them by soma location according to brain regions and layers. And we found that the cells whose soma were in different layers had different axon and dendrite distribution patterns, but this phenomenon was not obvious about brain regions. Finally, we performed unsupervised clustering on layer 2, 5 and 6 chandelier, and this result conformed to manual classification.

We reconstructed and analysed three-dimensional complete chandelier cell morphology, summarized several chandelier cell types from cortex layer 2 to 6 based on their dendrite and axon arborization patterns which reflected input and output connectivity.

Keywords: chandelier cell, cell-type, neuron morphology, 3D reconstruction, axon distribution pattern

A Nonlinear Three-Dimensional Image Registration Method for Optical Microscopic Whole Brain Dataset

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Abstract. The relationship between structure and function is always the major endeavor in modern neuroscience. Therefore, mapping the structure, connectivity, type with function in individuals is essential for brain function defined. The latest developed Micro-Optical Section Tomography (MOST) and fluorescence MOST (fMOST) serial imaging technology achieved the high temporal-spatial and specific spatial location image datasets, which offered an opportunity to the brain atlas construction of neuron types, neural circuits and network, vascular network. However, the ensuing challenges are the huge, high resolution, different quality brain datasets require an accurate brain spatial location, which is the foundation brainsmatics (known as brain-spatial information science). It has always been a manual way to recognize brain regions and nucleus by anatomist which was time-consuming and error-prone. As an extension of MOST / fMOST serial imaging techniques, we proposed an interactive nonlinear three dimensional registration method to solve the spatial location of these huge and high resolution brain datasets and it could be conducted by anyone who has very few anatomical experience. The newly acquired three dimensional brain images were therefore automatically and accurately aligned into the three dimensional reference space. In addition, an assessment method for registration of batch was also proposed for adapting to the mass and high resolution brain datasets, it combined the subjective results with objective results to evaluated registration effect rapidly. In summary, our nonlinear three dimensional registration method established an effective solution for three dimensional spatial localization of whole-brain studies such as neuron types, neural circuits and network, vascular network.

Keywords: Nonliner registration, brain dataset, three dimensional, high resolution

A Platform for the Analysis of the Distribution of Brain-Wide Neurons

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Abstract. Specific type neurons play a key role in various brain functions. Identifying the brain-wide distribution of these neurons can increase the current understanding of its functions in various neural circuits and activities. However, these studies were mainly analyzed through two-dimensional cell counting. Manual sectioning and imaging is time-consuming and laborious. Therefore, the comprehensive organization of brain-wide specific neurons network has not been systematically and quantitatively analyzed. Here, we develop a platform for the analysis of given-type neurons in the whole brain using the advanced whole-brain optical imaging and stereological cell counting. Firstly, we used brain-wide positioning system (BPS), the latest model of fMOST and a dual-colour precision imaging system, enabled the acquisition of specific labeled neurons in the whole brain with co-located propidium iodide (PI, a nuclear dye) stained cytoarchitecture at the voxel resolution of 0.32 × 0.32 × 2 μm. Secondly, we used NeuroGPS (Neuronal Global Position System) that is an automated localization of neuros for brain circuits using L1 minimization model to locate the neurons across different brain areas without human intervention. It is robust to the broad diversity of shape, size and density of the neurons in a mouse brain, so the center and number of the whole brain neurons is quite reliable. Thirdly, we performed an affine transformation and a symmetric image normalization in Advanced Normalization Tools (ANTS) to achieve the three-dimensional co-registration of the PI-stained dataset with the Allen template dataset and quantified the distribution of neurons in each region. Lastly, we use this platform to analysis of the distribution of CRH neurons. The quantitative results showed that CRH neurons were widely distributed with different density in the brain regions. The demonstration illustrated that this platform could potentially become a routine tool for neuroscience study.

Keywords: Corticotropin-releasing hormone, Neuron, Three-dimensional reconstruction, Automatic segmentation, Brain-wide dataset

An Automatic Method for Classification of Three-Dimensional Neuronal Cell Body

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Abstract. Brain signals measurement involving counting and classification is very important for neurological disease and cerebral development in brain research. But the number of cells or synapses in the brain is quantitatively big, which is impossible to manually segment and count. Besides, the classification of neurons is the basis to analyze different types of neurons how to coordinate in brain activity. Meanwhile, the differences in cell number and cell morphology patterns, is also an important criterion for brain regions division. However, currently popular methods cannot automatically solving neuron segmentation and classification. Recent advances have permitted imaging at single cell resolution for an entire mouse brain using the Nissl staining method with the micro-optical sectioning tomography image system（MOST）. Based on three-dimensional images of mouse brain datasets which were captured from MOST, firstly, we have developed an automated three-dimensional cell detection and segmentation method using concave points clustering and random walker segmentation. Secondly, we calculate some morphological characteristics of every single cell such as surface area, volume, shape factor, rectangular body, average radius and eccentricity. Lastly, in order to solve the difficulties of large amount of data and various types of mouse cells, we propose an automatic neuron cell classification. This classification is a kind of combination of Nearest neighbors and Decision trees based on prior knowledge. Applying this method on the primary visual cortex, barrel cortex and cerebellar cortex to automatically identify cell types, all the results achieved a high accuracy after quantitative assessment. Thus our proposed method provides an effective implementation of the cell counting and classification for neuroscientists. Furthermore, this new fully automatic method will bring great convenience to handle big data problems in neuroscience.

Keywords: Cell counting, Cell segmentation, MOST, Cell classification, Neuronal morphology

No. S03208

Whole-Brain 3D Affine Registration for High-Resolution Whole Brain Dataset

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Abstract. Three-dimensional whole brain imaging at high resolution brings large fine images, thus helps people decipher the brain structure and function. With the development of the Micro-Optical Sectioning Tomography (MOST) serial techniques, we can obtain the single cell resolution images and the brain-wide neuronal networks with several TB image data. However, there are problems of stereotaxic deviation and deformation of samples frequently causing in sample preparation and imaging process, which seriously affect the analysis of localization of brain space at high resolution, such as cell localization, projection localization and nucleus localization. Three-dimensional affine registration can transform the moving image to align to the fixed image, so affine registration can correct the stereotaxic space and morphology to standard.while, registration is a complex computation process, which consumes a lot of time and memory, so registration for large data at high resolution is a formidable challenge.

To solve this issue, we develop a high performance three-dimensional affine registration method for large image data to correct the stereotaxic space and morphology. We firstly down sampling high resolution images to the low resolution, then affine registration at low resolution images and get the affine parameter, finally use the high performance computing technology to transform the high resolution data with the affine parameter. We chose Micro-Optical images dataset with 1×1×1 μm isotropic, which contains 516GB. Allen Mouse Common Coordinate Framework (CCFv3) as fixed image, and it consumed 32h and 68GB memory to align the image dataset. With our method, we can align several TB whole brain Micro-Optical images data from diverse samples to a standard stereotaxic space efficiently with single cell resolution, which makes the analysis of localization more standard and convenient.

Keywords: Large Micro-Optical images data, Stereotaxic deviation, 3D Affine Registration, High performance computing

No. S03209

Identifying Weak Signals in Inhomogeneous Neuronal Images for Large-Scale Tracing of Neurites

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Abstract. Reconstructing neuronal morphology across different regions or even the whole brain is important in many areas of neuroscience research. Large-scale tracing of neurites constitutes the core of this type of reconstruction and has many challenges. One key challenge is how to identify a weak signal from an inhomogeneous background. Here, we addressed this problem by constructing an identification model. In this model, empirical observations made from neuronal images are summarized into rules, which are used to design feature vectors that display the differences between the foreground and background, and a support vector machine is used to learn these feature vectors. We embedded this identification model into a tool that we previously developed, SparseTracer, and termed this integration SparseTracer-Learned Feature Vector (ST-LFV). ST-LFV can trace neurites with extremely weak signals (signal-to-background-noise ratio <1.1) against an inhomogeneous background. By testing 12 sub-blocks extracted from a whole imaging dataset, ST-LFV can achieve an average recall rate of 0.99 and precision rate of 0.97, which is superior to that of SparseTracer (which has an average recall rate of 0.93 and average precision rate of 0.86), indicating that this method is well suited to weak signal identification. We applied ST-LFV to trace neurites from large-scale images (approximately 105 GB). During the tracing process, obtaining results equivalent to the ground truth required only one round of manual editing for ST-LFV compared to 20 rounds of manual editing for SparseTracer. This improvement in the level of automatic reconstruction indicates that ST-LFV has the potential to rapidly reconstruct sparsely distributed neurons at the scale of an entire brain.

Keywords: Machine learning, Neuron reconstruction, neurites tracing, signal identification, large-scale data analysis

Accurately Identifying Closely Packed Neurites at Crossover Points to Enhance the Reconstruction of Neuronal Population

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Abstract. The reconstruction of neuronal populations, i.e., identifying individual neuron from densely packed neurons, is a key step to understanding neuronal circuit connectivity and signal neuron information processing. Compared to single neuron reconstruction, Neuronal population reconstruction can provide ways to better understand its topological organization, the spatial distribution pattern of neurites, the connecting pattern between neurons and many others. An open challenge in neuronal population reconstruction is to identify the closely apposed neurites at crossover points. Namely, a large number of neurites from different neurons cross paths, introducing difficulty in identifying individual neurites. Sparse neuronal labeling technique can specifically lighten up a few neurons whose somata can be well separated. This technique mitigates this challenge, but cannot solve it entirely. To overcome this challenge, we constructed an identifying model and applied it into the initial reconstructions, provided by NeuroGPS-Tree. In this identifying model, multi-scale morphological characteristics of the neurites at crossover points are induced and analyzed. The induced information fits with the rules that use in the manual identification. This identifying model ensures the unambiguously assignment of neurites at crossover points and largely promote the reliability of neuronal population reconstruction. We applied this identifying to analyze diverse images. The results demonstrated that the reconstruction accuracy of above 90% can be achieved. Furthermore, we applied this identifying model in the large-scale reconstruction (more than 100 GB). In the reconstruction, with this identifying model, the results equal to the gold standard required only few manual editings, vastly boosting the automatic reconstruction level of NeuroGPS-Tree platform.

Keywords: Neuronal population reconstruction, Pattern recognition, Dense reconstruction

Convolutional Neural Network-Based Automated Segmentation of Brain Contour

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Abstract. The development of imaging technologies with high resolution make it possible for researches of cells and vessels in neuroscience. The developed Micro-Optical Sectioning Tomography (MOST) serial techniques made it possible to obtain brainwide 3D data acquisition technology with micron scale resolution. But there exists a common problem in the projection of nerve fibers, the reconstruction of neurons and vessels or some other researches of brain like the registration of brain regions: owing to the limitation of imaging instrument and condition, background noise is inevitable in data, which will impede the progress of these researches. Thus, it is essential to segment the contour of the brain to eliminate the effect of these noises in the background. However, since the brainwide 3-dimensional data of mice brain with such high resolution have large size of data, it is time-consuming to label the contour of brain by hand with such huge data. Traditional image segmentation methods such as OTSU and level set-based methods, are not capable to handle data with complex characters such as the 3D dataset of whole brain. Thus, it is required to develop an algorithm with high speed and accuracy to deal with the complex characters of brainwide 3D dataset. With the development of hardware, the capability of CPU and GPU had a significant improvement, machine learning methods had been widely used in the field of image processing. Unlike traditional image processing methods, neural networks can extract abstract features directly from raw inputs. We proposed a convolutional neural network(CNN)-based method to realize the segmentation of the mice brain automatically. We built an end-to-end convolutional neural network which is capable to segment the brain tissue directly from propidium iodide-stained brain sectionals. We demonstrated that this method is applicable and effectively to the segmentation of mice brain data, and it could be extended to other image processing issues in biomedical application.

Keywords: Machine learning, Convolutional neural network, Brain contour, Tissue segmentation, image processing

The 3D Reconstruction of Brain Vascular Network of Whole Mouse Brain

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Abstract. The realization of the mammalian brain function is closely linked to the support of vessels. The blood vessels in brain provide energy for the activity of neurons and excrete the waste. However, there exists a common problem that our knowledge about brain's vessel networks is not enough for relative researches. Therefore, it requires a complete three-dimensional cerebral vascular atlas to achieve a better understanding of the complex brain function and pathology. Recently, there exists great progress in the cerebral vessels imaging technology, and many of these technologies could be used to obtain cerebral vascular datasets with high resolution. With the development of the Micro-Optical Sectioning Tomography (MOST) serial techniques, brain-wide 3D datasets could be obtained, which makes it possible to reconstruct the cerebral vascular atlas in stereotaxic coordinates. We modified the Nissl staining method and combined it with the MOST techniques to acquire vascular networks information data simultaneously. We acquired several mouse cerebral vascular datasets containing both the vessels and cytoarchitecture of the whole mouse brain with a voxel resolution of 1 μm. Pial surface vessels and connected penetrating vessels are traced by software after the 3D datasets were obtained. Fine vessels tracing were implemented with the skeletonization method and 19 main brain regions were labeled by hand after the 3D datasets were obtained. We annotated the traced vessels by their orientation, location and the vessel's type. Then, we reconstructed the complete vascular network atlas with arteries and veins of the whole mouse brain. We have calculated the density distribution of blood vessels, and the result shows that the vessel density is different among different brain regions. Our work provides an important resource and approach for quantitative study of brain function and diseases.

Keywords: Whole mouse brain, Three-dimensional reconstruction, Cerebral vascular atlas, Vascular distributing patterns

Fast Reconstruction of Neural Projection Pattern in Whole Mouse Brain

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Abstract. The neural connectivity is fundamental for understanding how the brain processes information at multiscale, and essential to studying brain functions and diseases, even beneficial for brain inspired intelligence. Despite the fundamental importance of neuronal connectivity, our knowledge of it still remains pretty vague. Precisely tracing neural projection at high resolution, which is fundamental for exploring anatomical connectivity, has led great challenges. Here, we proposed a pipeline of brain-wide neural projection reconstruction and analysis. With Micro-Optical Sectioning Tomography (MOST) serial imaging instruments and various labelling techniques, we acquired brain-wide high resolution image dataset of labelled neural structures and cytoarchitecture reference. Binarization algorithm was applied to each section image to segment signal from background, then multistencils fast marching method was used to trace neural projection based on detected signals, and the traced neural projection were integrated for visualization and analysis, the final computational projection path can exactly illustrate the connectivity of interconnected brain regions or nucleus. Tested on several datasets, our method is proved to be efficient for acquiring precise brain-wide neural projection by directly comparing projection path with original signal in the whole brain. After registration to Allen reference atlas (known as Allen Mouse Common Coordinate Framework, CCF), we performed the localization of brain-wide neural projections to get the projection pattern, and tried to establish brain connectivity model based on neural projection path along with signal density. In summary, our method is precise and efficient in brain-wide neural projection reconstruction, which is beneficial for studying neural connectivity and understanding working mechanism of the brain.

Keywords: brain connectivity, neural projection, multistencils fast marching, signal detection

The 3D Compression of TB-Scale Brain Image Stack Based on Video Coding

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Abstract. With the developing of imaging technologies in neuroscience, now it is possible for researchers to acquire high-resolution microscopic images that can demonstrate fine cells and vessels well. The developed Micro-Optical Sectioning Tomography (MOST) serial techniques is one of the developed imaging technologies, and make it possible to obtain brain-wide 3D data acquisition technology with micron scale resolution. However, with the increasing of resolution, the image data it produces absolutely get increasing too. Without compression, to image a cubic centimeter volume specimen in the resolution of $0.32 \times 0.32 \times 1$ um, could produce image data at the size of 18 TB. And the data size increases linearly with the increment of the volume size of specimen. The storing of this scale of data is very expensive and hard to maintain. To extract information from this scale of data is a very challenging or even impossible task. Thus, it is essential to compress the data. Fortunately, as the image data is continuously sectioning image data, there are much redundancy in the data, which means that the data is potential to be compressed effectively. The traditional way to compress the data include JPEG, LZW and so on, most of them only eliminate the two-dimensional redundancy and didn't take the advantage of similarity between sequence images to compress the data more effectively. The video coding technologies using in video compression, can make use of this similarity perfectly. However, the commonly used video encoders such as libx264 could not handle such large image data, so we have to block the origin data to small volume to compress them. We proposed a way to compress the sequence sectioning data by blocking and video coding, and built the related utility to perform this blocking and coding effectively. The compressing radio of the data is less than 10%, with the HPC, the computing time is less than 10 hours. We demonstrated that this method can compress the data effectively and quickly.

Keywords: Compression, Video Coding, Sequence Image Data

Whole-Brain Projectome of Paraventricular Hypothalamic Nucleus Oxytocin Neurons

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Abstract. Oxytocin is a neuropeptide secreted by the hypothalamus. It is conserved across mammals and has been shown to plays important roles in the nervous systems, including the regulation of social (recognition, affiliation, aggression) and non-social (stress and memory) behaviors. Oxytocin neurons in the hypothalamus are mostly located in the paraventricular hypothalamic nucleus (PVH) and the sopraoptic neuclei (SON). We focused on PVH oxytocin neurons in this study, because they account for most of the projections within the brain, while SON oxytocin neurons mostly projects to the pituitary gland. PVH oxytocin neurons have reported projections to the medial amygdalar nucleus, the bed nuclei of the stria terminalis and other brain regions that regulate social behavior. Axonal release by oxytocin neurons is critical for local precise spatiotemporal regulation in its different target brain regions, especially its long range targets. Interestingly, the distribution of oxytocin receptors is different between virgin female, lactating female and male mice, suggesting important regulation on oxytocin signaling by sex and experience. Thus, to understand the mechanism by which oxytocin regulates various behaviors, it is critical to determine the projectome of PVH oxytocin neurons at high resolution and in the whole brain. To achieve this goal, we established viral techniques to label oxytocin neurons densely or sparsely with bright fluorescent proteins, to respectively investigate their whole brain projection patterns and the axonal arborizations of single neurons. Two months after injections, brains were fixed and imaged using the brain-wide positioning system (BPS), an three-dimensional, dual-color, automated microscopy method for localizing neural structures with cytoarchitectonic landmarks at a single-cell resolution. Oxytocin projection patterns were acquired in whole

brains, with propidium iodide counterstain to mark cytoarchitectonic landmarks, at sub-micro resolution: ~5000 images at a voxel size of 0.32 x 0.32 x 2 μm for dense labelling (3.0 T data per mouse) and ~10,000 images at a voxel size of 0.32 x 0.32 x 1 μm for sparse labelling (7.2 T data per mouse). For dense labeling, images were analyzed in 50 μm coronal sections, and absolute intensities in different target regions were quantified. To accurately quantify the intensities in different brain regions, co-registration of the propidium iodide-stained dataset with Allen Mouse Brain Atlas anatomic reference atlas was performed, with manual validation and amendments. Significant qualitative, but not quantitative differences, were observed between female virgin, female lactating and male mice. For single neuron projections, tracings were carried out using continuous data cubes of 500 x 500 x 150 μm from whole-brain datasets (1.0 T data per mouse after compression) using Amira Software and custom macros. Preliminary data shows that each oxytocin neuron projected to multiple brain regions, and that different oxytocin neurons likely have distinct sets of target groups.

Keywords: Oxytocin, Neural circuits, Projectome, fMOST

A Scalable Image Processing Pipeline for Reproducible Terascale Brain Atlasing

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Abstract. With novel imaging technologies that produces new modalities and higher resolution, neuroscientists can explore more valuable information from the brain. However, this brings challenges to efficiently processing, integrating, analyzing and visualizing such big data. We present a platform that aims to provide a high-performance data processing pipeline to integrate data into a common brain atlas space, following a semantic and provenance based scheme. This allows not only semantic and spatial query of the data but also automated provenance tracking, ensuring the reproducibility of the data processing workflow.

A data processing pipeline has been established to process whole brain mouse image stacks acquired by fMOST imaging system, in which neurons are sparsely stained and can be reconstructed to morphology. The pipeline consists of four major components: 1) Data preprocessing, which includes intensity normalization, shading artifact correction as well as isotropic resampling to ensure that the images are in a standardized format for integration. To cope with large data size and boost the computation performance, these modules are developed using distributed computing frameworks (MPI, Spark). The data is distributed into small blocks and is processed in parallel on a high-performance computing (HPC) infrastructure containing a cluster of 35 nodes. 2) Data anchoring to a brain atlas, spatial anchoring or alignment allows data from different subjects or modalities being positioned in an identical reference system. This is achieved via landmark-based image registration using thin-plate-spline transformation. 3) Data transformation, both the image stack and the reconstructed morphology are transformed to align with the atlas using the transformation obtained from the image registration step. 4) Data visualization, the image stack is converted into the Blue Brain Image Container format (BBIC), a hierarchical representation of volumetric data encapsulated in a HDF5 file allowing visualization in a web application through a dedicated RESTful image service.

To facilitate the automation of the processing pipeline on a cluster based computing

environment, the components are managed by a dedicated web service. Jobs can be asynchronously submitted to the web service using a versatile client interface (e.g. Jupyter notebook, web application, etc.) through a RESTful API. This will automatically register the involved data and processing steps into a knowledge graph platform – Blue Brain Nexus.

The Blue Brain Nexus is a domain-independent, provenance-based and semantic data management platform. Through a knowledge graph, it enables the description of a domain of application for which there is a need to create and manage entities, store and manage their provenance and relate them. A provenance template has been designed to standardize the representation of all the data entities and processing activities for brain atlasing. Schemas, which are developed using shape constrained language (SHACL) to ensure the validity and quality of the data description and provenance, captures both semantic information of the data and its spatial coordinates in a common atlas space.

Future work will focus on improving the automation of processing workflow and designing strategies for federated data ingestion.

Keywords: brain atlasing, high-performance computing, knowledge graph

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Wide Field and Fiberscopic Fluorescence Imaging of Brain in the Murine Model

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Abstract. Non-invasive monitoring of vasculature dynamics and neurological reactions in the brain are of great importance towards functionality study of the brain. Fluorescence imaging as an optical method can provide high spatial resolution and serve as a complementary technique for CT or MRT imaging. However, due to strong tissue scattering properties from scalp, cranium, dura matter and fluids, present fluorescence-based technologies require invasive sample preparations such as craniotomy, cranial windows or skull-thinning procedures. To diminish this invasion, we propose and built a near-infrared fluorescence-based imaging setup for non-invasive brain imaging on live murine model with scalp and skull intact. The vasculature features are monitored via the inherent photoluminescence of the injected non-toxic indocyanine green fluorescence dye. An optimization of excitation power level in relation with the scattering observation and signal-to-noise ratio enhancement is performed. The study promotes future development of a non-invasive 3D monitoring of vasculature dynamic and neurological reactions in the brain. Freely behaving mouse brain imaging is another hot topic where fiberscopic imaging of cells within the mouse cortex is required. Here, we applied structured illumination microscopic (SIM) technique to a fiber endoscope to suppress background noise and enhance axial resolution, allowing in vivo depth-resolved fiberscopic imaging of cells within the mouse cortex. The lateral resolution enhancement of the super-resolution fiberscope was analyzed using numerical and analytical studies. We compared the performance of linear structured illuminated and wide-field illuminated fiber microscopes in fluorescent brain samples and showed that sequentially rotated one-dimensional pattern illumination and its reconstruction algorithm significantly improve the lateral resolution and signal-to-noise ratio. Finally, we successfully demonstrated the system performance through in vivo imaging within the mouse brain.

Keywords: fluorescence imaging, non-invasive, brain imaging, fiberscopy

Robust Sparse Canonical Correlation Analysis for Brain Imaging Genetics

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Abstract. In recent years, using imaging measurements as the quantitative endophenotypes, brain imaging genetics, which studies how genetic variations influence the structures or functions of the brain, is becoming more and more popular in biology and biomedicine studies. Sparse canonical correlation analysis (SCCA) has been a powerful tool in brain imaging genetics given that it can identify bi-multivariate correlations and extract a subset of features simultaneously. Mathematically, the existing SCCA models can be recast to an alternative two-step penalized least squares regression method. Therefore, these SCCA algorithms are not robust due to the least squares risk of being sensitive to outliers. This will limit the power of the SCCA methods. To address this issue, in this study, we propose a novel robust SCCA formulation that uses the capped norm loss function which is more robust to and performs more stable than the least squares risk loss function. In the new model, the thresholding parameter is not fixed heuristically in advance, but decided during the optimizing process. Since the new objective function is difficult to solve, we employ the re-weighted strategy and propose an iterated algorithm to find the optimal solution. Using both synthetic data sets and real imaging genetics data sets, the results show that the robust SCCA method obtains more stable results than those from the existing SCCA methods. Specifically, it can not only identify desirable sparse canonical weights, but also yields higher or similar correlation coefficients than those existing SCCA methods. This demonstrates that the robust SCCA is indeed insensitive to outlying observations and assures stable modeling.

Keywords: Brain imaging genetics, Sparse canonical correlation analysis, Bi-multivariate analysis, Robust SCCA

Genome-Wide Network-Based Analysis of AV-45 PET Measures in the ADNI Cohort

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Abstract. Background: To overcome the limitation of pre-defined gene sets, we perform a network-based dense module search (DMS) method on AV-45 PET measures for identification of the underlying Alzheimer's disease (AD) moderate and weak signals that genome-wide association studies(GWAS) may ignore. Leveraging on the joint effect of multiple genes may increase our understanding of the underlying biology of AD.

Methods: 774 subjects with both baseline AV-45 PET measures and genome-wide array data downloaded from ADNI were included in our analysis. SNP-trait association test was performed using quality controlled genotype data including 563,980 single nucleotide polymorphisms (SNPs), with age, gender, and diagnosis as covariates. Gene-wise p-values using the most significant SNP's p- value were translated into prior scores for vertices in a protein-protein interaction network downloaded from Protein Interaction Network Analysis platform (PINA) [1]. After network propagation, modules discovered by DMS [2] were further evaluated whether they were significantly associated with the disease AD by permutation test. Significantly enriched modules were finally selected to do the pathway analysis using Enrichr [3].

Results: After permutation test, the network-based DMS method identified 24 significantly enriched modules(156 genes) with Bonferroni corrected p-value ≤ 0.05. A subsequent pathway analysis on this module detected 13 pathways. Two neurodegenerative diseases including alzheimer's disease and parkinson's disease were with adjusted p-value ≤ 0.001.

Conclusions: The DMS analysis method revealed a number of highly connected significant PPI pairs involving multiple confirmed disease-susceptibility genes not found(e.g.TAX1BP1) in the SNP- and gene-based association analyses. These results can be effectively used to examine a collection of predefined SNP sets based on prior biological knowledge for revealing additional disease-predisposing genes of modest effects in GWASs. Work is in progress to systematically compare all the identified modules with relevant KEGG pathways.

Keywords: network-based analysis, AV-45 PET measure

Discovering High Level Genetic Associations with Imaging Phenotypes Using Tissue-specific Functional Interaction Networks

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Abstract. Network-based genome-wide association study (GWAS) approach, which integrates biological networks with genetic associations, aims to identify network modules associated with the studied phenotype. It provides valuable information to help understand molecular mechanisms of the interested phenotypic outcome. The limitations of the existing approaches include time-consuming search strategy and lacking of phenotypic specificity.

To bridge this gap, we developed a novel two-step tissue-specific module identification framework based on an improved NetWAS (i.e., network-guided GWAS) method. In the first step, we integrated tissue-specific network with GWAS results in regression models (Ridge regression and support vector regression), in addition to support vector machine (SVM) classification which was initially employed in NetWAS, for reprioritizing genetic associations. In the second step, we constructed candidate modules using link clustering based on reprioritized associations and extracted those enriched by top GWAS findings.

We demonstrated the performance of the proposed framework on two brain tissues relevant to Alzheimer's disease (AD): hippocampus and amygdala. GWAS of the FDG-PET imaging measures in the hippocampus and amygdala regions from 989 ADNI participants were performed. Hippocampus- and amygdala-specific networks were downloaded from GIANT (http://giant.princeton.edu/). Three machine learning-based models (Ridge, SVR and SVM) were constructed using the network connectivity as features and GWAS gene-level p-values as responses. Genetic associations were reprioritized according to their predictions (in Ridge and SVR) or distances from hyperplane (in SVM). Area under the ROC curve (AUC) measures were computed to assess the reprioritization performances using documented AD risk genes as gold standard. Functional annotation was performed to evaluate the functional relevance of identified modules.

Three machine learning-based reprioritization strategies outperformed original GWAS in both hippocampus- and amygdala-specific studies, including yielding higher AUCs and denser connections among top genes. This demonstrates the promise of the NetWAS strategy. Regression models outperformed classification, suggesting that continuous measures can provide additional valuable information on top of binary status. Modules identified from both

tissue-specific studies were functionally annotated by neurodegenerative diseases, cognition, learning and memory.

Keywords: GWAS, tissue-specific network, module identification, Alzheimer's disease

An Online Visual Exploratory System for Mining Large-Scale Imaging Genomic Data

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Abstract. Background In recent years, research fields such as genomics, medical genetics and neuroinformatics have accumulated unprecedented amounts of data. These data types are complex, large in number, which contains the value is immeasurable. For this reason, we have developed a visualization system that can extract the more significant information from genetic data and combine this information with the brain image to give the researcher more intuitive visualization.

Results Taking the single gene information of the Alzheimer's Disease Neuroimaging Initiative (ADNI) as an example, including 563,980 single nucleotide polymorphisms (SNPs). Through the pre-processing to obtain the required data format, and then upload this data to the database. Researchers can set different p thresholds and call the JavaScript module to draw the Heatmap Plot. The server requires the current point position and the P-value information in the Heatmap Plot, generates the nifti image in Background, and reads the image into the nifti tool to show the user. On this basis, the CHR information for this location can also be submitted to the Manhattan Plot module, plotting the Manhattan Plot fragment corresponding to this CHR and the entire Manhattan Plot.

Conclusions This study combines Heatmap Plot, Manhattan Plot, and BrainImage, and interacts with each other. The data in the Heatmap Plot can display the Manhattan Plot for the corresponding phenotype and the phenotype information in the BrainImage to the corresponding SNP (different regions use different P values for color rendering). The visualization system uses WEB technology to achieve a cross-browser and cross-platform to provide services to users, to help researchers conduct a comprehensive analysis of genetic information.

Keywords: Big Data; Visualization; Online; Alternation