Research Contributions to MICCAI 2018:

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"The requisites of knowledge: a quick mind, zeal for learning, humility, foreign land, a professor's inspiration, and a life of long span." Juwaini of Nishapur (d.1085)

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Joint Correlational and Discriminative Ensemble Classifier Learning for Dementia Stratification Using Shallow Brain Multiplexes

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Abstract. The demented brain wiring undergoes several changes with dementia progression. However, in early dementia stages, particularly early mild cognitive impairment (eMCI), these remain challenging to spot. Hence, developing accurate diagnostic techniques for eMCI identification is critical for early intervention to prevent the onset of Alzheimer's Disease (AD). There is a large body of machine-learning based research developed for classifying different brain states (e.g., AD vs MCI). These works can be fundamentally grouped into two categories. The first uses *correlational* methods, such as canonical correlation analysis (CCA) and its variants, with the aim to identify most correlated features for diagnosis. The second includes *discriminative* methods, such as feature selection methods and linear discriminative analysis (LDA) and its variants to identify brain features that distinguish between two brain states. However, existing methods examine these correlational and discriminative brain data *independently*, which overlooks the complementary information provided by both techniques, which could prove to be useful in the classification of patients with dementia. On the other hand, how early dementia affects cortical brain *connections in morphology* remains largely unexplored. To address these limitations, we propose a joint correlational and discriminative ensemble learning framework for eMCI diagnosis that leverages a novel brain network representation, derived from the cortex. Specifically, we devise 'the shallow convolutional brain multiplex' (SCBM), which not only measures the similarity in morphology between pairs of brain regions, but also encodes the relationship between two morphological brain networks. Then, we represent each individual brain using a set of SCBMs, which are used to train joint ensemble CCA-SVM and LDA-based classifier. Our framework outperformed several state-of-the-art methods by 3-7% including independent correlational and discriminative methods.

Joint Prediction and Classification of Brain Image Evolution Trajectories from Baseline Brain Image with Application to Early Dementia

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Abstract. Despite the large body of existing neuroimaging-based studies on brain dementia, in particular mild cognitive impairment (MCI), *modeling and predicting* the early dynamics of dementia onset and development in healthy brains is somewhat overlooked in the literature. The majority of computer-aided diagnosis tools developed for classifying healthy and demented brains mainly rely on either using single timepoint or longitudinal neuroimaging data. Longitudinal brain imaging data offer a larger time window to better capture subtle brain changes in early MCI development, and its utilization has been shown to improve classification and prediction results. However, typical longitudinal studies are challenged by a limited number of acquisition timepoints and the absence of inter-subject matching between timepoints. To address this limitation, we propose a novel framework that learns how to *predict* the developmental trajectory of a brain image from a single acquisition timepoint (i.e., baseline), while *classifying* the predicted trajectory as 'healthy' or 'demented'. To do so, we first rigidly align all training images, then extract 'landmark patches' from training images. Next, to predict the patch-wise trajectory evolution from baseline patch, we propose two novel strategies. The first strategy learns in *a supervised manner* to select a few training atlas patches that best boost the classification accuracy of the target testing patch. The second strategy learns in *an unsupervised manner* to select the set of most similar training atlas patches to the target testing patch using multi-kernel patch manifold learning. Finally, we train a linear classifier for each predicted patch trajectory. To identify the final label of the target subject, we use majority voting to aggregate the labels assigned by our model to all landmark patches' trajectories. Our image prediction model boosted the classification performance by 14% without further leveraging any enhancing methods such as feature selection.

Do Baby Brain Cortices that Look Alike at Birth Grow Alike During The First Year of Postnatal Development?

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Abstract. The neonatal brain cortex is marked with complex and high-convoluted morphology, that undergoes dramatic changes over the first year of postnatal development. A large body of existing research works investigating 'the developing brain' have focused on looking at changes in cortical morphology and charting the developmental trajectories of the cortex. However, the *relationship* between neonatal *cortical morphology* and its *postnatal growth trajectory* was poorly investigated. Notably, understanding the *multi-scale shape-growth relationship* may help identify early neurodevelopmental disorders that affect it. Here, we unprecedentedly explore the question: "Do cortices that look alike in shape at birth have similar kinetic growth patterns?". To this aim, we propose to analyze shape-growth relationship at three different scales. On a *global scale*, we found that neonatal cortices similar in geometric closeness are significantly correlated with their postnatal overall growth dynamics from birth till 1-year-old ($r = 0.27$). This finding was replicated when using shape similarity in morphology ($r = 0.20$). On a *local scale*, for both hemispheres, 20% of cortical regions displayed a significant high correlation ($r > 0.4$) between their similarities in morphology and dynamics. On a *connectional scale*, we identified hubs of cortical regions that were consistently similar in morphology and developed similarly across subjects including the cingulate cortex using a *novel integral shape-growth brain graph representation.*

Revealing Regional Associations of Cortical Folding Alterations with In Utero Ventricular Dilation Using Joint Spectral Embedding

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Abstract. Fetal ventriculomegaly (VM) is a condition with dilation of one or both lateral ventricles, and is diagnosed as an atrial diameter larger than 10 mm. Evidence of altered cortical folding associated with VM has been shown in the literature. However, existing studies use a holistic approach (i.e., ventricle as a whole) based on diagnosis or ventricular volume, thus failing to reveal the spatially-heterogeneous association patterns between cortex and ventricle. To address this issue, we develop a novel method to identify spatially fine-scaled association maps between cortical development and VM by leveraging vertex-wise correlations between the growth patterns of both ventricular and cortical surfaces in terms of area expansion and curvature information. Our approach comprises multiple steps. In the first step, we define a joint graph Laplacian matrix using cortex-to-ventricle correlations. Next, we propose a spectral embedding of the cortex-to-ventricle graph into a common underlying space where their joint growth patterns are projected. More importantly, in the joint ventricle-cortex space, the vertices of associated regions from both cortical and ventricular surfaces would lie close to each other. In the final step, we perform clustering in the joint embedded space to identify associated sub-regions between cortex and ventricle. Using a dataset of 25 healthy fetuses and 23 fetuses with isolated non-severe VM within the age range of 26-29 gestational weeks, our results show that the proposed approach is able to reveal clinically relevant and meaningful regional associations.

Figure 1: MICCAI 2018 papers.

Data-Specific Feature Selection Method Identification for Most Reproducible Connectomic Feature Discovery Fingerprinting Brain States

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Abstract. Machine learning methods present unprecedented opportunities to advance our understanding of the connectomics of brain disorders. With the proliferation of extremely high-dimensional connectomic data drawn from multiple neuroimaging sources (e.g., functional and structural MRIs), effective feature selection (FS) methods have become indispensable components for (i) disentangling brain states (e.g., early vs late mild cognitive impairment) and (ii) identifying connectional features that might serve as biomarkers for treatment. Strangely, despite the extensive work on identifying stable discriminative features using a particular FS method, the challenge of choosing the best FS method from a large pool of existing FS techniques for optimally achieving (i) and (ii) using a dataset of interest remains unexplored. In essence, the question that we aim to address in this work is: "Given a set of feature selection methods $\{FS_1, \ldots, FS_K\}$, and a dataset of interest, which FS method might produce the *most reproducible and 'trustworthy'* connectomic features that accurately differentiate between two brain states (e.g., demented vs healthy)?" This paper is an attempt to address this question by evaluating the performance of a particular feature selection for a specific data type in fulfilling criteria (i) and (ii). To this aim, we propose to model the relationships between a set of FS methods using a multi-graph architecture, where each graph quantifies the feature reproducibility power between graph nodes at a fixed number of top ranked features. Next, we integrate the reproducibility graphs with an discrepancy graph which captures the difference in performance between FS methods. This allows to identify, for a particular dataset, the 'central' node with the highest degree, which reveals the most reliable and reproducible FS method for the target brain state classification task along with the most discriminative features fingerprinting these brain states. We evaluated our method on multi-view brain connectomic data for late mild cognitive impairment vs Alzheimer's disease classification. Our experiments give insights into connectional features fingerprinting late dementia brain states.

Dynamic Multi-Scale CNN Forest Learning for Automatic Cervical Cancer Segmentation

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Abstract. Deep-learning based labeling methods have gained unprecedented popularity in different computer vision and medical image segmentation tasks. However, to the best of our knowledge, these have not been used for cervical tumor segmentation. More importantly, while the majority of innovative deep-learning works using convolutional neural networks (CNNs) focus on developing more sophisticated and robust architectures (e.g., ResNet, U-Net, GANs), there is very limited work[A1] on how to *aggregate* different CNN architectures to improve their *relational learning* at multiple levels of CNN-to-CNN interactions. To address this gap, we introduce a Dynamic Multi-Scale CNN Forest (C^{K+1}DMF), which aims to address three major issues in medical image labeling and ensemble CNN learning: (1) *heterogeneous* distribution of MRI training patches, (2) a *bi-directional* flow of information between two consecutive CNNs as opposed to cascading CNNs —where information passes in a directional way from current to the next CNN in the cascade, and (3) *multiscale* anatomical variability across patients. To solve the first issue, we group training samples into K clusters, then design a forest with $(K+1)$ trees: a *principal tree* of CNNs trained using all data samples and *subordinate trees*, each trained using a cluster of samples. As for the second and third issues, we design each dynamic multiscale tree (DMT) in the forest such that each node in the tree nests a CNN architecture. Two successive CNN nodes in the tree pass bidirectional contextual maps to progressively improve the learning of their relational non-linear mapping. Besides, as we traverse a path from the root node to a leaf node in the tree, the architecture of each CNN node becomes shallower to take in smaller training patches. Our C^{K+1}DMF significantly ($p<0.05$) outperformed several conventional and ensemble CNN architectures, including conventional CNN (improvement by 10.3%) and CNN-based DMT (improvement by 5%).

Predicting Emotional Intelligence Scores From Multi-Session Functional Brain Connectomes

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Abstract. In this study, we aim to predict emotional intelligence scores from functional connectivity data acquired at different timepoints. To enhance the generalizability of the proposed predictive model to new data and accurate identification of most relevant neural correlates with different facets of the human intelligence, we propose a joint support vector machine and support vector regression (SVM + SVR) model. Specifically, we first identify most discriminative connections between subjects with high vs low emotional intelligence scores in the SVM step and then perform a multi-variate linear regression using these connections to predict the target emotional intelligence score in the SVR step. Our method outperformed existing methods including the Connectome-based Predictive Model (CPM) using functional connectivity data simultaneously acquired with the intelligence scores. The most predictive connections of intelligence included brain regions involved in processing of emotions and social behaviour.

Multi-View Brain Network Prediction From a Source View Using Sample Selection via CCA-based Multi-Kernel Connectomic Manifold Learning

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Abstract. Several challenges emerged from the dataclysm of neuroimaging datasets spanning both healthy and disordered brain spectrum. In particular, samples with missing data views (e.g., functional imaging modality) constitute a hurdle to conventional big data learning techniques which ideally would be trained using a maximum number of samples across all views. Existing works on predicting target data views from a source data view mainly used brain images such as predicting PET image from MRI image. However, to the best of our knowledge, predicting a set of target brain networks from a source network remains unexplored. To fill this gap, a multi-kernel manifold learning (MKML) framework is proposed to learn how to predict multi-view brain networks from a source network to impute missing views in a connectomic dataset. Prior to performing multiple kernel learning of multi-view data, it is typically assumed that the source and target data come from the same distribution. However, multi-view connectomic data can be drawn from different distributions. In order to build robust predictors for predicting target multi-view networks from a source network view, it is necessary to take into account the shift between the source and target domains. Hence, we first estimate a mapping function that transforms the source and the target domains into a shared space where their correlation is maximized using canonical correlation analysis (CCA). Next, we nest the projected training and testing source samples into a connectomic manifold using multiple kernel learning, where we identify the most similar training samples to the testing source network. Given a testing subject, we introduce a cross-domain trust score to assess the reliability of each selected training sample for the target prediction task. Our model outperformed both conventional MKML technique and the proposed CCA-based MKML technique without enhancement by trust scores.

Figure 2: Georges *et al.*, CNI-MICCAI 2018, Bnouni *et al.*, MLMI-MICCAI 2018, Lisowska *et al.*, PRIME-MICCAI 2018, and Zhou *et al.*, PRIME-MICCAI 2018.

XmoNet: a Fully Convolutional Network for Cross-Modality MR Image Inference

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Abstract. Magnetic resonance imaging (MRI) can generate multimodal scans with complementary contrast information, capturing various anatomical or functional properties of organs of interest. But whilst the acquisition of multiple modalities is favourable in clinical and research settings, it is hindered by a range of practical factors that include cost and imaging artefacts. We propose XmoNet, a deep-learning architecture based on fully convolutional networks (FCNs) that enables cross-modality MR image inference. This multiple branch architecture operates on various levels of image spatial resolutions, encoding rich feature hierarchies suited for this image generation task. We illustrate the utility of XmoNet in learning the mapping between heterogeneous T1- and T2-weighted MRI scans for accurate and realistic image synthesis in a preliminary analysis. Our findings support scaling the work to include larger samples and additional modalities.

Keywords: Fully convolutional networks · MRI · multimodal · image generation.

Intact Connectional Morphometricity Learning using Multi-View Morphological Brain Networks with Application to Autism Spectrum Disorder

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Abstract. The morphology of anatomical brain regions can be affected by neurological disorders, including dementia and schizophrenia, to various degrees. Hence, identifying the morphological signature of a specific brain disorder can improve diagnosis and better explain how neuroanatomical changes associate with function and cognition. To capture this signature, a landmark study introduced, brain *morphometricity*, a global metric defined as the proportion of phenotypic variation that can be explained by brain morphology derived from structural brain MRI scans. However, this metric is limited to investigating morphological changes using low-order measurements (e.g., regional volumes) and overlooks how these changes can be related to each other (i.e., how morphological changes in region A are influenced by changes in region B). Furthermore, it is derived from a *pre-defined* anatomical similarity matrix using a Gaussian function, which might not be robust to outliers and constrains the locality of data to a fixed bandwidth. To address these limitations, we propose the *intact connectional brain morphometricity* (ICBM), a metric that captures the variation of *connectional* changes in brain morphology. In particular, we use *multi-view morphological brain networks* estimated from multiple cortical attributes (e.g., cortical thickness) to learn an intact space that first integrates the morphological network views into a unified space. Next, we *learn* a multi-view morphological similarity matrix in the intact space by adaptively assigning neighbors for each data sample based on local connectivity. The learned similarity capturing the shared traits across morphological brain network views is then used to derive our ICBM via a linear mixed effect model. Our framework shows the potential of the proposed ICBM in capturing the connectional neuroanatomical signature of brain disorders such as Autism Spectrum Disorder.

Figure 3: Bano *et al.*, PRIME-MICCAI 2018, and Bessadok *et al.*, CNI-MICCAI 2018.

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