# Deep learning + Alzheimer's Disease

## EEG - Deep learning of resting-state electroencephalogram signals for three-class classification of Alzheimer's disease, mild cognitive impairment and healthy ageing

- Typical novel biomarkers for dementia are expensive invasive, specific, only available in specialized centres e.g. MRI >> EEG
- Data: Resting-awake, eyes-closed methods, 10 mins, 21 electrodes
- Preprocess: EEG signals are combined into tiled topographical maps governed by
   10-20 system orientation
- Model: AlexNet
- Accuracy (AD, MCI, control): 98.90%

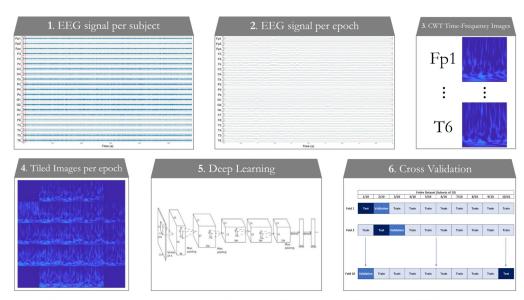
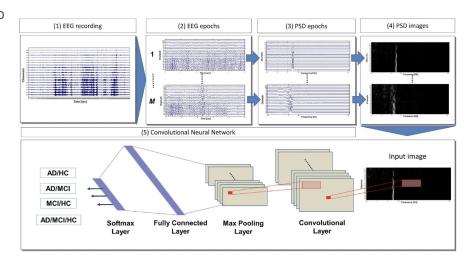


Figure 1. Experimental flow diagram showing a simplified version of the proposed model. The training folds/test folds describe a proportion of the data assigned to train or test the model respectively. Reproduced with permission from Krizhevsky et al (2012).

## EEG - A Convolutional Neural Network approach for classification of dementia stages based on 2D-spectral representation of EEG recordings

- The EEG of AD and MCI patients shows slowing effects in the brain EEG rhythms, as the AD progression is related to the relative prevalence of low frequencies (delta and theta bands) with respect to high frequencies (alpha and beta)
- Data: Resting-awake, eyes-closed methods, 10 mins, 19 electrodes
- **Preprocess**: PSD images
- Model: CNN
- **Accuracy** (AD, MCI, control): 83.3%



## MRI - Ensemble of 3D densely connected convolutional network for diagnosis of mild cognitive impairment and Alzheimer's disease

- Ensemble method (probability based fusion, not majority voting): reintegrated softmax layers of classifiers on 3D-DenseNet
- Data: Alzheimer's Disease Neuroimaging Initiative
   (ADNI) database
- Preprocess: PSD images
- Model: 3D-DenseNet
- **Accuracy**: AD/control: 98.83%, AD/MCI: 93.61%, MCI/control: 98.42%, AD/MCI/control: 97.52%

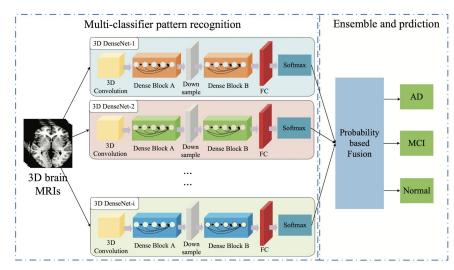


Fig. 4. Architectures of proposed ensemble 3D-DenseNet framework for AD and MCI diagnosis.

## MRI - Computer aided Alzheimer's disease diagnosis by an unsupervised deep learning technology

- Implement fully-unsupervised CNNs (PCANet) for feature
   extraction and then utilize the unsupervised predictor (kmeans)
- Data: 1 slice and 3 orthogonal panels from Alzheimer's Disease
   Neuroimaging Initiative (ADNI) database
- **Preprocess**: normalized into SPM12
- Model: PCANet: CNN + PCA, Hashing (non linear) and histogram (pooling) generating, Kmeans
- Accuracy:

slice data: AD/MCI 95.52%, MCI/control 90.63%
 slice and 3 otho: AD/MCI 97.01%, AD/control 89.15%
 MCI/control 92.6% AD/MCI/NC 91.25%

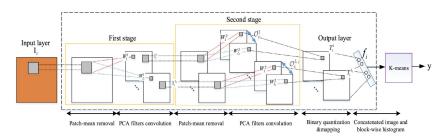


Fig. 1. Flow chart of the proposed PCANet+k-means clustering with one view of MRI image.

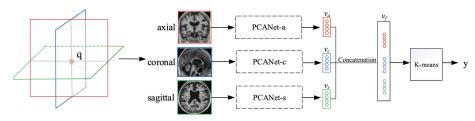


Fig. 2. Flow chart of proposed PCANet+k-means clustering with TOP data.

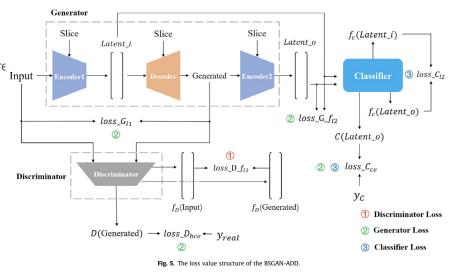
## MRI - A novel Alzheimer's disease detection approach using GAN-based brain slice image enhancement

- Difficult to extract representative high-level brain features for example in AE since disease category information is not incorporated in back propagation
   > GANs
- Data: ANDI, Open Access Series of Imaging Studies (OASIS)
- Preprocess: ANTsR (high dimensional brain mapping), FSL-VBM (compare
  grey matters of different samples in the research group on a voxel wise
  basis and transform them into a standard space and in a nii format), mirror
  flip, zero mean Gaussian noise, brightness
- Model: BSGAN-ADD: GAN-based brain slice image enhancement and CNN-based AD detection.
- Accuracy:

ADNI: AD/control: 100%, AD/MCI: 97.9%, MCI/control: 99.4%, AD/MCI/control: 98.6%

OASIS: AD/control: 99.8%, AD/MCI: 98.1%, MCI/control: 99.1%,

AD/MCI/control: 98.3%



## MRI - Alzheimer's disease detection from structural MRI using conditional deep triplet network (few-shot)

- Lack of image samples > few shot learning using deep triplet network
- Data: control/ very mild dementia/ mild dementia/ moderate AD from OASIS
- Preprocess: -
- Model: Siamese deep neural network based on VGG1 using contrastive loss
- **Accuracy**: 99.41%

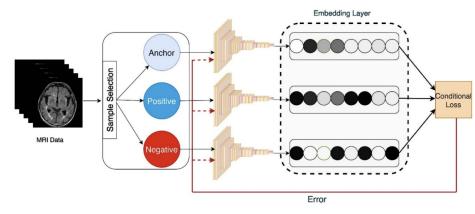


Fig. 3. The Architecture of the Proposed Model.

#### fMRI - Deep learning for brain disorder diagnosis based on fMRI images

- Demonstrates **regional**, **time-varying** changes in brain metabolism and measures **blood oxygenation** level dependent signals to human-brain
- Lower spatial resolution than structural MRI, but comes with temporal information.
- Superior when changes of the brain are minor and there is no significant structural change
- 2D/3D images, time series, a combination of both images and time series (4D images) and functional connectivity network etc.
- Functional connectivity (direct use): ADHD, austism, AD, Schiezphrenia via CN, AE, MLP, SVM
- Functional connectivity (2D matrices): amnestic mild cognitive impairment, autism via CNN
- 2/3/4D images: 3D neural network, 3D AE, 3D CNN
- Joint spatial and temporal feature exploration: CNN-LSTM, 4D spatio-temporal,
- **Graph CNN:** Derive functional connectivity matrix from task-fMRI > RO, phenotype information
- **Feature extraction:** AE but has risks of extracting features of no interest

#### fMRI - Detecting Alzheimer's disease Based on 4D fMRI: An exploration under deep learning framework

 Normally 4D data is transformed into functional connectivity or slicing them into 2D/3D images (causes apparent information loss), propose c3d lstm for AD discrimination to deal with 4D data directly

Data: 4D fMRI from ADNI

- **Preprocess**: SPM, DPARSF, REST

Model: C3d-LSTM

Accuracy: AD/MCI: 92.11, MCI/control: 88.12%,
 AD/control: 97.37%, AD/control/MCI: 89.47%

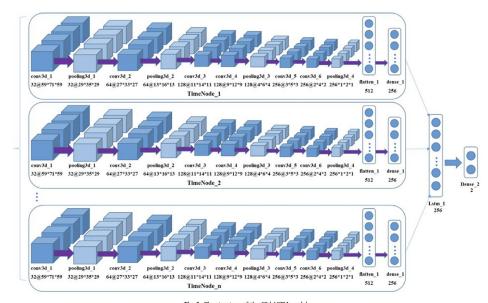
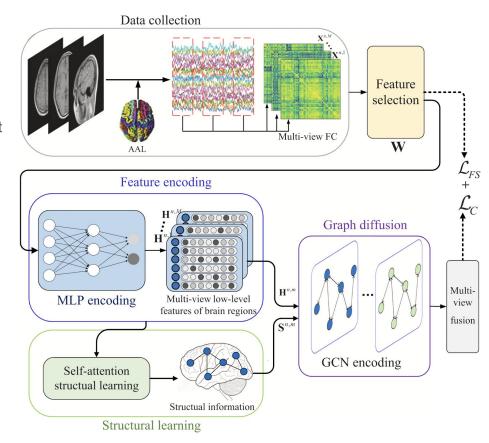


Fig. 1. The structure of the C3d-LSTM model.

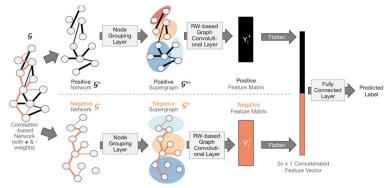
#### fMRI-XAI - Dementia analysis from functional connectivity network with graph neural networks

- High-level features in graph diffusion process via GNN
   framework for brain disease diagnosis via jointly learning
   global relationships (self attention) and selecting the most
   discriminative brain regions (feature selection)
- Data: rs-fMRI from ADNI for frontotemporal dementia,
   OCD and AD
- Preprocess: DPARSF, FCNs, parcellated into 90 ROIs according to the AAL
- Model: GNN with self attention
- **Accuracy** Acc: 89.78%



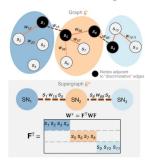
fMRI-XAI - GroupINN: Grouping-based Interpretable Neural Network for Classification of Limited, Noisy Brain Data

- Explains relationship between brai subnetworks and cognitive functions and node grouping instead of clustering
- Data: task-based fMRI from HCPt
- Preprocess: voxel-level time series were spatially averaged according to the parcellation > 264 distinct
   ROIs with a time series for each.
- Model: GNN with self attention
- Accuracy 85% fewer model parameters than baseline deep models



(a) Overview: the functional graph (correlation-based) is first split into positive and negative networks, each coarsened by node grouping layer, convoluted by random-walk-based graph convolutional layer, flattened, concatenated and finally sent to the fully connected layer.

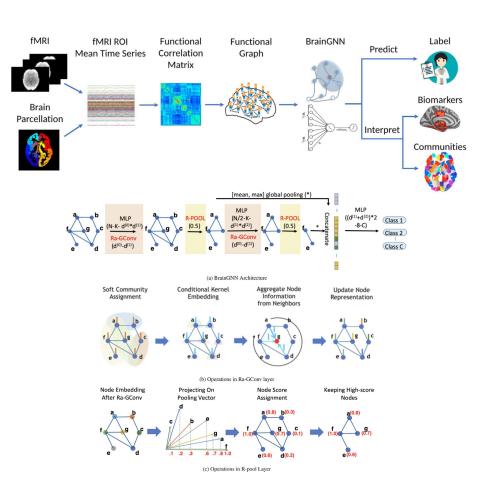
Figure 2: GroupINN Architecture



(b) Example: In the node grouping layer indicative edges are learned to be placed across groups.

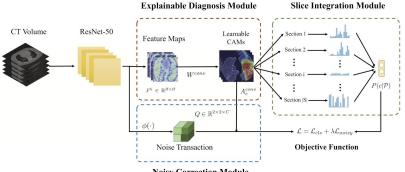
## fMRI-XAI - Braingnn: Interpretable brain graph neural network for fmri analysis

- GNN framework to analyze fMRI and discover neurological biomarkers, designed the ROI-aware graph convolutional layers
- Data: Austism from Biopoint Autism Study (Biopoint)
- Human Connectome Project (HCP)
- **Preprocess**: parcellate brain images into 84 ROIs
- Model: BrainGNN: ROI aware GNN (ROI selection pooling layers to highlight salient ROIs ) with topK poolling loss and group-level consistency loss
- **Accuracy**: AD/MCI: 92.11, MCI/control: 88.12%, AD/control: 97.37%, AD/control/MCI: 89.47%



#### Unbox the black-box for the medical XAI explainable AI via multi-modal

- 1) XAI via dimension reduction: ICA, laplacian eigenmaps (e.g. H MRS brain tumour), weights of NN > important features
- 2) **XAI via feature importance**: topK features, sensitivity analysis, DeepLIFT (interpretability via back prop), Guided backpropagation, layer wise relevance propagation, SHAP etc.
- 3) **XAI via attention mechanism**: Relation extraction, mechanistic explanation (HIV genome), visually interpretable cardiac failure and cataract risk prediction, class activation maps,
- 4) XAI bia knowledge distillation: Decision Trees, rule based, textual reasoning for interpretability
- 5) XAI via surrogate representation: LIME,



Noisy Correction Module

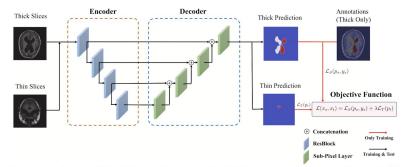


Fig. 9. Overview of our proposed XAI model for explainable segmentation. Here ResBlock represents the residual block proposed in the ResNet [165]

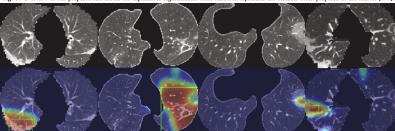
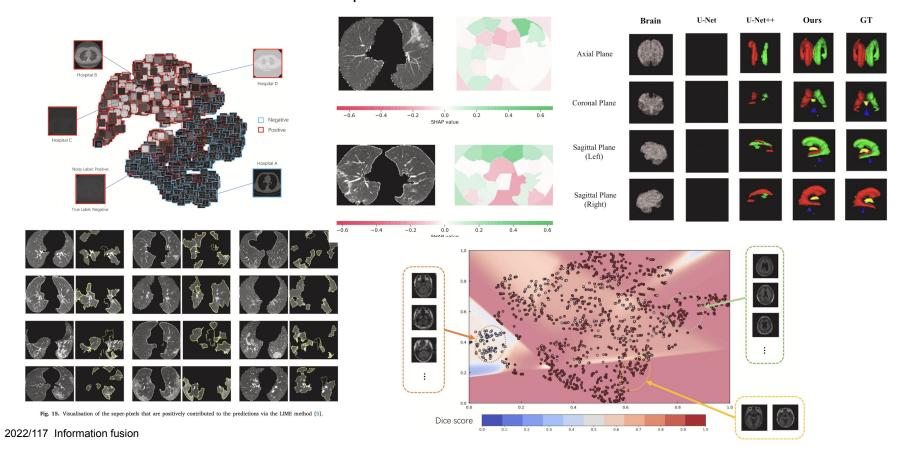


Fig. 13. Examples of the CAMs Acon generated by our proposed EDM for classifying COVID-19 positive patients. The first row contains the original CT-scan image slices, and the second row illustrates the heatmaps of CAMs Acon with bounding boxes confined to the infected areas.

#### XAI - Unbox the black-box for the medical explainable AI via multi-modal



### To do

- Domain knowledge in Alzheimer's Disease
- Domain knowledge in fMRI
- XAI in medical fields
- Features of the softwares
  - Demographic data
  - Preprocessing: denoise, segmentation, etc
  - Models
  - XAI: patient specific, group base (compare to similar cases)