PET image classification using HHT-based features through fractal sampling

7th. International Work-Conference on the Interplay between Natural and Artificial Computation

June 20, 2017

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Presentation Outline

- Alzheimer's disease (AD) is the first most common neurodegenerative disorder in the elderly. Currently, there is no cure for AD and their causes remain unknown. A precise diagnosis plays a decisive role to start the treatment in the early stages of the disease. However, it remains a challenge $\rightarrow$ CAD systems
- A number of neuroimage modalities have been proposed for its use in the differential diagnosis of AD:
  - Magnetic Resonance Imaging (MRI)
  - Single Photon Emission Computerized Tomography (11^C-SPECT)
  - Positron Emission Tomography (18^F-FDG PET)
- Several works using statistical and machine learning techniques have been proposed to extract relevant patterns in the images:
  - Multivariate methods (PCA, ICA, etc.)
  - Image analysis techniques (texture analysis).

- In this work we used a different approach:
  - Objective: use 1D signal processing methods to extract relevant features from 3D images.
  - Challenge: Transforming a 3D images to 1D signals while preserving 3D neighbourhood (voxel spatial relationship)
- Database: 68 CN subjects + 70 AD patients

Methodology

Image preprocessing

- PET images from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database.
- Co-registration: each image is spatially normalized to the MNI space (PET Template)
- Intensity normalization was applied to be able to compare the uptake value in areas of specific activity.

Methodology

Brain Parcellation

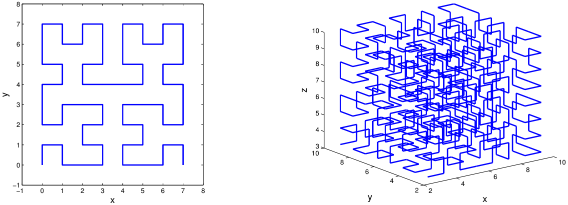
Brain is parcelled into 116 regions according to the Automated Anatomical Labelling (AAL) atlas

The best-fitting parallelepiped is computed for each region

Only the most 42 relevant regions are extracted, according to *Huang et. al, 2009*

	Frontal Lobe		Parietal Lobe		Occipital Lobe		Temporal Lobe
1	Frontal_Sup_L	13	Parietal_Sup_L	21	Occipital_Sup_L	27	Temporal_Sup_L
2	Frontal_Sup_R	14	Parietal_Sup_R	22	Occipital_Sup_R	28	Temporal_Sup_R
3	Frontal_Med_L	15	Parietal_Inf_L	23	Occipital_Mid_L	29	Temporal_Pole_Sup_L
4	Frontal_Med_R	16	Parietal_Inf_R	24	Occipital_Mid_R	30	Temporal_Pole_Sup_R
5	Frontal_Sup_Medial_L	17	Precuneus_L	25	Occipital_Inf_L	31	Temporal_Mid_L
6	Frontal_Sup_Medial_R	18	Precuneus_R	26	Occipital_Inf_R	32	Temporal_Mid_R
7	Frontal_Mid_Orb_L	19	Cingulum_Post_L			33	Temporal_Pole_Mid_L
8	Frontal_Mid_Orb_R	20	Cingulum_Post_R			34	Temporal_Pole_Mid_R
9	Rectus_L					35	Temporal_Inf_L 8301
10	Rectus_R					36	Temporal_Inf_R 8302
11	Cingulum_Ant_L					37	Fusiform_L
12	Cingulum_Ant_R					38	Fusiform_R
						39	Hippocampus_L
						40	Hippocampus_R
						41	ParaHippocampal_L
						42	ParaHippocampal_R

- Once the images have been normalized, voxels are sampled throughout the 3D volume:
  1. The 3D image is converted into a sequence of intensity values
  2. Spatial neighbourhood has to be preserved, keeping the relationship between voxels, as this is an essential source of information.
  3. Neighbour voxels in the 3D space should be also neighbours in the 1D space.
- Sampling is performed by means of Hilbert-Peano 3D homogeneous fractal curves.
  - Basically, it is a function $f : \mathbb{R} \to \mathbb{R}^n$
  - Continuity is preserved $\to$ adjacency condition
  - The curve is uniquely defined by fixing initial and final subintervals and the rotation matrix
  - It can be generated by the iterative application of affine transformations



(a) (b)

Figure: Example of 2D (a) and 3D (b) Hilbert curves

Methodology

Feature extraction. Empirical Mode Decomposition (EMD)

- EMD allows decomposing a signal into AM and FM components, namely *Intrinsic Mode Functions* (IMF) along with a trend component (residue).
- The main advantage of EMD is that can be applied to non stationary and non-linear signals.
- Unlike other decomposition methods such as Fourier decomposition or Wavelet decomposition, EMD does not use predefined basis functions. The basis is empirically computed by the so called sifting method.
- The Sifting process consists on:
  1. Identify all the local extrema in the signal.
  2. Connect all the local maxima by a cubic spline line as the upper envelope.
  3. Repeat the procedure for the local minima to produce the lower envelope.

- Once the first IMF c_1 is extracted, the first residue is computed as $X(t) = c_1 + r_1$
- r_1 is treated as a new signal to be decomposed, resulting in subsequent residues r_j: $r_{n-1} - c_n = r_n$
- The sifting process finally stops when the residue, r_n, becomes a monotonic function from which no more IMF can be extracted.
- The original signal $X(t)$ can be now expressed as

$$X(t) = \sum_{j=1}^{n} c_j + r_n$$

Methodology

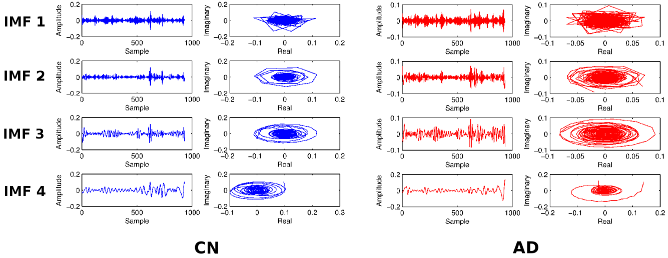
Feature extraction. Hilbert Spectral Analysis (HSA)

- Hilbert Transform allows to obtain the analytic representation of a signal: $z_i(t) = x_i(t) + j\mathcal{H}\{x_i(t)\}$
- $z_i(t)$ has no negative frequency components
- $z_i(t)$ allows computing instantaneous amplitude $a(t)$, instantaneous frequency $f(t)$ and instantaneous phase $\phi(t)$ which has sense for non-stationary signals
- $a(t) = \sqrt{re(z_i(t))^2 + im(z_i(t))^2}$
- $\phi(t) = tan^{-1}\frac{im(z_i(t))}{re(z_i(t))}$
- **Descriptive statistics can be extracted from $a(t)$ and $\phi(t)$**

Methodology

Feature extraction. Hilbert-Huang Transform

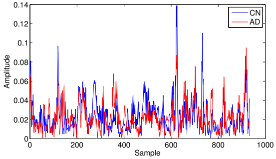
- **Now, let's put all together: EMD + HSA = Hilbert-Huang Transform (HHT)**
- Consists on applying HSA over each IMF component, obtaining their corresponding analytic representation

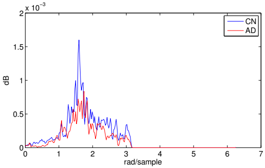


Methodology

Classification. Ensemble of Linear SVMs

- **Now, let's put all together: EMD + HSA = Hilbert-Huang Transform (HHT)**
- Consist on applying HSA over each IMF component, obtaining their corresponding analytic representation
- Example of amplitude and power spectrum of 1st IMF computed for average CN and AD images:

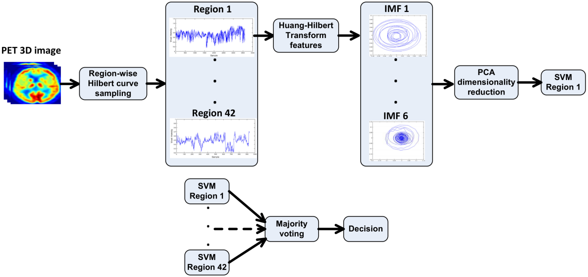




Methodology

The overall method

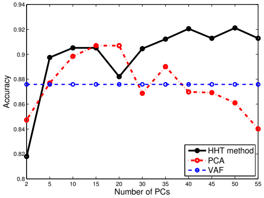
Overall feature extraction and classification method

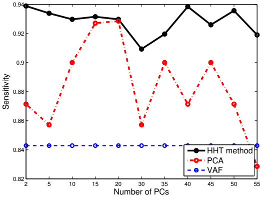


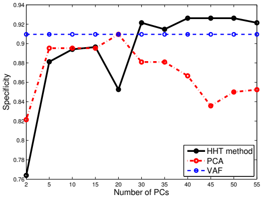
Results

Accuracy, Sensitivity, Specificity

- VAF, PCA over VAF and the HHT method are compared.
- Best results are provided by the HHT method (accuracy = 0.92).







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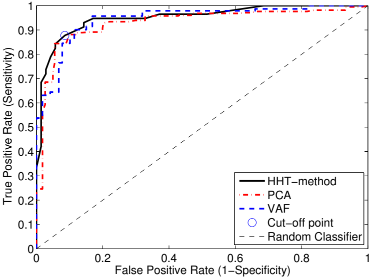
- ROC curve for the classifier reports an AUC of 0.95.



Conclusions and Future Work

Conclusions

- A 3D fractal sampling method is used over brain regions to convert 3D images into time-varying signals.
- Time series analysis techniques can be used.
- We proposed the use of Hilbert-Huang transform to extract features
- Discriminative features are computed providing a classification accuracy values up to 92% and AUC of 0.95 outperforming the VAF approach and PCA approaches.

Future work

- Use the same method to implement Functional PCA based on EMD basis
- FPCA EMD based to model the voxel intensity variations in time $\rightarrow$ longitudinal analysis

Thank you for your attention!

Questions?

Comments?

Volunteers?

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