Texture Features that Correlate with the Mini Mental State Examination (MMSE) Score

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Abstract— **We present some 2D and 3D texture features computed from the grey values of MRI-T1 data. The features show strong correlation with the score in the Mini Mental State Examination (MMSE) used routinely to help diagnose Alzheimer's disease.**

I. Introduction

In this paper we use the method of graylevel dependence histograms (GLDH) as defined by Chetverikov for 2D [2] and generalized to 3D by Kovalev and Petrou [9] and derive texture anisotropy features from MRI data, that correlate well with the result of Mini Mental State Examination (MMSE) which is routinely used to help diagnose Alzheimer's disease (AD) [3].

Freeborough and Fox [5] used the 2D-GLDH method applied to MRI data, but the features they extracted did not measure anisotropy. Their MRI scans were acquired from 40 normal controls and 24 AD patients and a classification rate of 91 % was obtained. Mathias et al. [11] also used the 2D-GLDH method applied to spinal cord MR images. They found significant differences in texture between normal controls and multiple sclerosis patients, and also a significant correlation between texture and disability.

For this study we used 25 scans MRI-T1 weighted, with coronal orientation. Each data cube is $180 \times 180 \times 124$ pixels and the voxel size in mm is $(0.9375, 0.9375, 1.5)$. Thirteen of these scans are Alzheimer's patients identified as AD1, AD2, ..., AD13 and the other twelve are control volunteers identified as CO1, CO2,..., CO12. The control group was matched in age and gender with the AD group. The mean age of the patients with AD at the time of their scanning was 56.77 with an age range from 39 to 72. While the mean age of the control volunteers was 58.33 with an age range of 47 to 72.

The Mini Mental State Examination (MMSE) score for each of the patients is also available. The MMSE is a test used to detect dementia, although it is not specific to AD. The maximum score is 30 and controls will typically score 29 or 30/30. Scores between 10 and 24 are considered mild to moderate dementia cases, and scores below 10 show severe dementia. Table I displays the scores for each patient. Two of the scores do not match with the clinical diagnosis: AD3 and CO2. The AD3 scan is interesting as it comes from a patient who was imaged just before the onset of the first clinical symptoms, and at a time when there might have been ongoing structural brain changes - hence the high score for that subject.

TABLE I
MMSE Scores for each patient

Scan	MMSE	Scan	MMSE
AD1	25	CO1	30
AD2	8	**CO2**	**28**
AD3	**30**	CO3	30
AD4	25	CO4	29
AD5	23	CO5	30
AD6	25	CO6	30
AD7	28	CO7	29
AD8	22	CO8	30
AD9	19	CO9	30
AD10	–	CO10	30
AD11	14	CO11	30
AD12	24	CO12	30
AD13	12		

The scans were segmented to isolate the brain from external structures (eyes, ventricles, bones, etc.) [6]. The brains were further segmented to isolate the white and grey matter as well as the border between these two types of tissue [1].

The texture analysis technique we use effectively counts the number of pairs of voxels that appear in the same relative position and have certain fixed grey values. Therefore the relative grey values of the voxels are extremely important. In that respect MRI brain images may not be compatible with each other, depending on the initial conditions of the scanning process. A process of normalization is used in order to have the same relative grey-level values for different scans. The smallest grey-level value for the segmented scan is assigned 1 and the highest 255, and 0 labels the voxels which do not belong to the region of interest.

II. 3D Texture Representation

First we start by defining a coordinate system in our data cube: (x, y) axes are on the plane of each scan slice, z is along the axis perpendicular to each slice. Azimuthal angle ϕ is measured on the (x, y) plane from

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the direction of the x axis. A pair of values (ϕ, z) defines a unique orientation in the $3D$ space.

To characterize the texture in the data we compute the quantity [7]:

$$h(\phi, z; d) = \sum_{k=1}^{255} \sum_{l=1}^{255} (k-l)^2 C(k, l; \phi, z, d) \qquad (1)$$

where $C(k, l; \phi, z, d)$ is the number of pairs of voxels which are at distance d from each other, along the direction defined by (ϕ, z), with one member of the pair having a grey value k and the other l.

If the data are completely isotropic, function $h(\phi, z; d)$ must be independent of direction (ϕ, z) and when it is therefore plotted as the polar radius along direction (ϕ, z) in $3D$ space, it must represent the surface of a sphere. Any deviation from the shape of a sphere indicates anisotropy in the data. For practical purposes, function $h(\phi, z; d)$ is sampled at a discrete number of points (ϕ_i, z_j) where $i = 1, 2, ..., N$ and $j = 1, 2, ..., M$. The sample points are chosen in such a way that each represents a patch of constant area on the surface of a sphere [10]. We represent the discretized version of function $h(\phi, z; d)$ by $H(i, j)$ and we understand that it is calculated for various values of distance d. When plotted in $3D$ space (for fixed d) it represents a closed digital surface which we call indicatrix. An example of such an indicatrix is shown in figure 1.

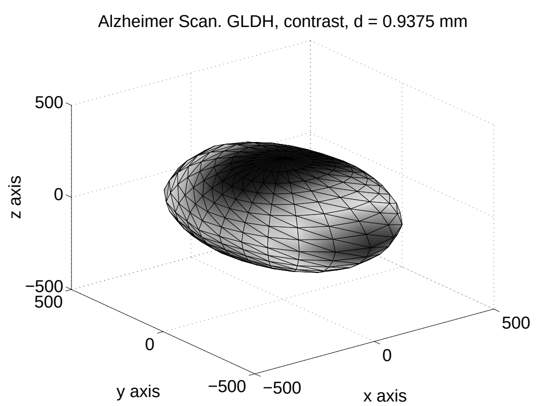


Fig. 1. Example of a 3D indicatrix

Our purpose is to measure how much the shape of this indicatrix deviates from the shape of a sphere. This will be a measure of anisotropy in the data. In the next section we define some features which are designed to measure exactly that.

III. Feature Extraction

Three features proposed by Kovalev and Petrou [9] are used to analyse the shape of the $3D$ indicatrix.

F1 is the Anisotropy Coefficient

$$F_1 = \frac{H_{max}}{H_{min}} \qquad (2)$$

F2 is the Integral Anisotropy Measure or standard deviation:

$$F_2 = \sqrt{\frac{\sum_{i=1}^{N} \sum_{j=1}^{M} \left(H(i,j) - H_m\right)^2}{NM}} \qquad (3)$$

F3 is the Local Mean Curvature or the average value of the Laplacian:

$$F_3 = \sqrt{\frac{\sum_{i=1}^{N} \sum_{j=2}^{M-1} \left(\begin{array}{c} H(i,j) - \frac{1}{4}\left(H(i-1,j)\right) - \\ \frac{1}{4}\left(H(i+1,j) + H(j,j-1)\right) - \\ \frac{1}{4}\left(H(i,j+1)\right) \end{array} \right)^2}{N(M-2)}} \qquad (4)$$

where H_{min} and H_{max} are the minimum and maximum value of the indicatrix respectively, and H_m is the mean value of all points of the indicatrix.

Another set of features can be extracted by expanding the indicatrix in terms of spherical harmonics [8]. The coefficients of such an expansion can characterise any 3D closed surface.

The equation that describes the spherical harmonic expansion of a surface $R(\theta, \phi)$ is as follows:

$$R(\theta, \phi) = \sum_{l=0}^{L} \sum_{m=0}^{l} A_{l,m} U_{l,m}(\theta, \phi) + B_{l,m} V_{l,m}(\theta, \phi) \quad (5)$$

$$U_{l,m}(\theta, \phi) = \cos(m\phi) P_l^m(\cos\theta), \qquad (6)$$

$$V_{l,m}(\theta, \phi) = \sin(m\phi) P_l^m(\cos\theta) \qquad (7)$$

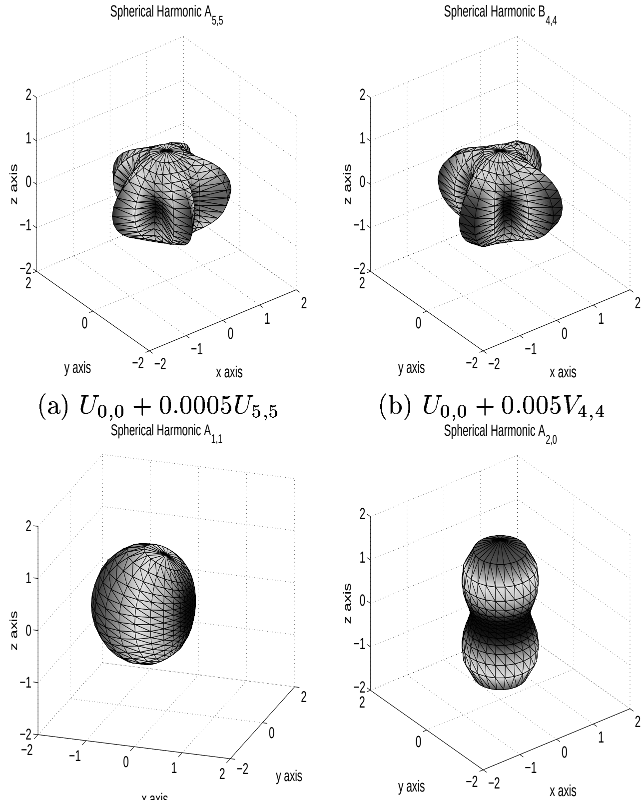
where θ is the latitude angle, ϕ is the longitude angle, and $P_l^m(\cos\theta)$ is the associated Legendre polynomial [12].

Coefficient $A_{0,0}$ is the mean radius of the indicatrix, i.e. $A_{0,0} = H_m$. All the other non-zero coefficients represent different types of anisotropy. Figure 2 shows the type of anisotropy represented by some low order coefficients.

IV. Features correlating with the MMSE score

We extracted anisotropy features from four different brain regions: the whole brain, white matter, grey matter, and the border between white and grey matter. We define the border between grey and white matter by performing a dilation of $3 \times 3 \times 3$ in the voxels from the transition white-grey matter. In every single region five different distances d were used: $0.9375mm$[1], $1.5mm$, $2mm$, $2.5mm$ and $3mm$, ie 5 separate indicatrices were contracted from each region. Table II presents the summary of the experiments performed and the best features identified. The last column gives the correlation coefficient of the particular feature with the MMSE score.

[1]Note that due to the intraslice resolution being $0.9375\ mm$, the use of $d = 0.9375\ mm$ corresponds to 2D analysis if not grey level interpolation takes place. However, since we perform 3D trilinear interpolation to find grey values at arbitrary positions, we extract 3D information even when d is less than the interslice distance.



(a) $U_{0,0} + 0.0005U_{5,5}$ (b) $U_{0,0} + 0.005V_{4,4}$

(c) $U_{0,0} + 0.5U_{1,1}$ (d) $U_{0,0} + 0.7U_{2,0}$

Fig. 2. Spherical Harmonics superimposed on the unit sphere

The features which best correlate with the MMSE score were computed from the grey matter (shown highlated in table II). Figure 3 shows feature $A_{1,1}$ plotted versus the MMSE score, where the correlation between these two seemingly independent variables is very clear.

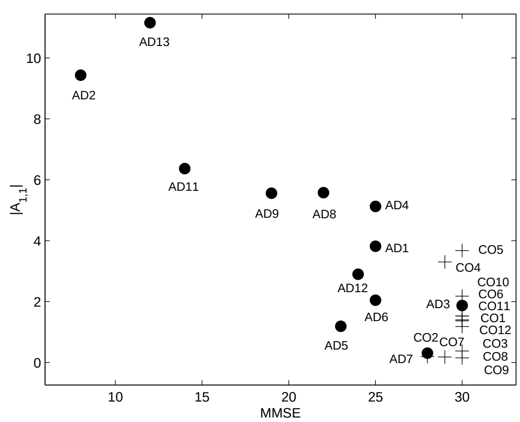


Fig. 3. Feature $|A_{1,1}|$ in grey matter for $d = 0.9375mm$ versus the result of the MMSE test (•) Alzheimer's Disease, (+) Control scans

V. Discussion

In this section we are trying to assess the validity of our approach by performing various tests. In particular, we are examing. 1. Whether 2D are adequate or 3D data are necessary for the derivation of such features. 2. Whether the correlations we found are stronger or weaker than correlations with the age of the subjects. 3. Whether the features we computed reflect more the shape of the region of interest than the texture inside it. Results of the experiments examining each one of the above points are presented below:

1. The strongest correlation is shown by features computed for $d = 0.9375mm$, which is the interpixel distance. To see therefore whether similar results could be obtained by performing 2D analysis, we constructed the 2D indicatrix for each slice separately and measured its anisotropy:

$$h(\phi; d) = \sum_{k=1}^{255} \sum_{l=1}^{255} (k-l)^2 C(k, l; \phi, d) \tag{8}$$

Figure 4 presents an example of a 2D indicatrix.

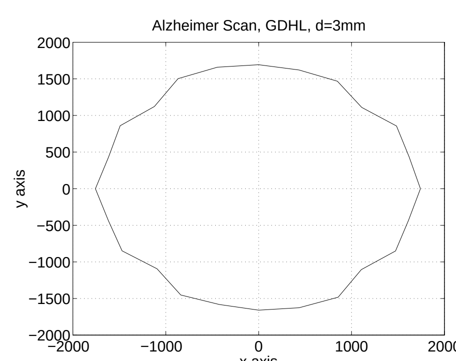


Fig. 4. Example of a 2D indicatrix

TABLE II

THE BEST FEATURES IDENTIFIED BY ALL EXPERIMENTS

Component	Best Features		Correlation with MMSE
Whole brain	$\|A_{5,4}\|$	$d = 0.9375$	-0.749
	$\|B_{3,2}\|$	$d = 2.5$	-0.747
	$\|A_{5,1}\|$	$d = 2.5$	-0.739
White matter	$\|A_{5,3}\|$	$d = 2$	-0.750
	$\|A_{5,5}\|$	$d = 0.9375$	-0.647
Grey matter	$\|A_{1,1}\|$	$d = 0.9375$	**-0.876**
	$\|A_{5,5}\|$	$d = 0.9375$	**-0.845**
	F_3	$d = 0.9375$	**-0.830**
	F_3	$d = 1.5$	**-0.822**
	$\|A_{1,1}\|$	$d = 1.5$	**-0.818**
	$\|A_{1,1}\|$	$d = 3$	**-0.818**
	$\|A_{5,3}\|$	$d = 0.9375$	**-0.817**
	$\|A_{4,0}\|$	$d = 2$	**-0.813**
	F_3	$d = 2$	**-0.810**
Grey/white border	$B_{1,1}$	$d = 2.5$	-0.734
	$B_{1,1}$	$d = 3$	-0.729
	$B_{1,1}$	$d = 2$	-0.701

TABLE III
THE BEST FEATURES IDENTIFIED BY 2D ANALYSIS ON GREY MATTER

Best Features		Correlation with MMSE
$\|a_4\|$	$d = 2$	-0.875
$\|a_1\|$	$d = 2$	-0.862
a_4	$d = 2$	-0.859
a_8	$d = 3$	-0.855
$\|a_1\|$	$d = 1.5$	-0.853
$\|a_{12}\|$	$d = 2.5$	-0.828
a_5	$d = 0.9375$	-0.824
a_6	$d = 0.9375$	-0.821
a_9	$d = 0.9375$	-0.821
a_1	$d = 0.9375$	-0.817

Features F_1, and F_2 can be computed using equations 2 and 3, and F_3 is now defined by

$$F_3 = \sqrt{\frac{\sum_{i=1}^{N} \left(\frac{1}{2}H(i-1) + \frac{1}{2}H(i+1) - H(i)\right)^2}{N}} \quad (9)$$

Further anisotropy features may be computed from the Fourier descriptors of this 2D shape:

$$R(\phi_i) = a_0 + \sum_{k=1}^{N/2} (a_k \cos(\phi_i) + b_k \sin(\phi_i)) \quad (10)$$

Table III presents the results for the best features computed from the grey matter region when only 2D analysis is performed. As 2D analysis is performed on each slice separately, the value of each feature was averaged over all slices of the same subject before attempting the correlation analysis.

2. The correlation between the texture features and the age of the subjects (indepently of the clinical diagnosis) is smaller than 0.6 (except for $B_{2,2}$ with correlation of 0.674 at $d = 0.9375mm$ and 0.694 at $d = 1.5mm$). Furthermore this correlation considering only the control subjects is also smaller than 0.6 (except for $A_{5,2}$ with correlation 0.626 at $d = 0.9375mm$ and $B_{5,1}$ with correlation of 0.613 at $d = 3mm$). It is clear that for these particular scans the process of aging was not strongly reflected in the texture of grey matter.

3. We chose the distance d to be small to avoid any interference with the main characteristics of the brain (eg. size, shape or border between tissues). In order to test if the features truly measure the micro-textural characteristics of the brain rather than its large scale structure, another set of experiments was performed. The values of the voxels of the grey matter were substituted by random values, and both texture methods (3D-GLDH and 2D-GLDH) were applied. In all cases the correlation obtained between the features and the MMSE scores was not greater than 0.6.

VI. CONCLUSIONS

The method of graylevel dependence histograms (GLDH) can be used to produce many features strongly correlated with the MMSE scores when applied to the grey matter component of MRI-T1 scans.

Our experiments showed that the features computed reflected the microtextural[2] properties of the brain rather than the shape of each region of interest, and they correlate with the condition of the patient rather than his/her age.

In general the AD brains presented greater anisotropy in their grey matter texture at the tested scales than control brains. 2D features correlated with the MMSE scores as well as 3D features, pointing that most of the texture information is already available in the individual layers.

An advantage of our approach is that only one scan is required to compute the features. This is a different approach from the method of quantifying volume change between registered repeated scans as a diagnostic marker [4].

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[2]Texture anisotropy at scales of the order of $1mm$