



# MR Image texture analysis applied to the diagnosis of Alzheimer's Disease

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12th June 2016

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**Abstract**

This report will examine MRI scans of brains, using image texture analysis and machine learning

# Chapter 1

## Introduction

Alzheimer's Disease (AD) is the most common cause of dementia among people and is a growing problem in the aging populations. It has a big impact on health services and society as life expectancy increases. In 2010 the total global costs of dementia was estimated to be about 1% of the worldwide gross domestic product<sup>1</sup>. AD is the cause in about 60%-70% of all cases of dementia[1] and about 70% of the risk is believed to be genetic [6]. Currently there are no way to cure dementia or to alter the progressive course. But however, much can be done to support and improve the lives if AD is diagnosed in the early stage of progression [1]

In this report we will examine MRI data of the hippocampus using image texture analysis and apply machine learning in order to diagnose AD in patients. Our dataset contain 100 patients 50 control and 50 with AD.

We will be using two different image texture analysis method, one which will me in 2D[8][5] and the other one will be in 3D[10], from which we calculate the data to the gray level co-occurrence matrix (GLCM).

### 1.1 Problem Definition

Is it possible to classify MRI data of the hippocampus into groups of healthy controls vs Alzheimer's patient, using a predefined set of image texture metrices, with an accuracy greater than 80%?

Is there a difference in diagnosing AD successfully by calculating the co-occurence matrix in 3D compared to 2D.

---

<sup>1</sup>With the terms as of direct medical costs, direct social costs and costs of informal care

# **Chapter 2**

# **Data**

## **2.1 ADNI data**

The data in this study was provided already downloaded and preprocessed. It had been previously obtained from the ADNI database ([adni.loni.usc.edu](http://adni.loni.usc.edu)). The ADNI was launched in 2003 by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, the Food and Drug Administration, private pharmaceutical companies, and nonprofit organizations, as a \$60 million, 5-year, public–private partnership. The primary goal of ADNI has been to test whether serial MRI, positron emission tomography (PET), biological markers, and clinical and neuro-psychological assessments can be combined to measure the progression of MCI and early AD. Determination of sensitive and specific markers of very early AD progression is intended to aid researchers and clinicians to develop new treatments and monitor their effectiveness, as well as to lessen the time and cost of clinical trials. ADNI is the result of efforts of many co-investigators from a broad range of academic institutions and private corporations, and subjects have been recruited from over 50 sites across the U.S. and Canada. For up-to-date information, see <http://www.adni-info.org/>. We were provided with a random subset (50 controls, 50 AD) of the “complete annual year 2 visits” 1.5T dataset from the collection of standardized datasets released by ADNI <http://www.adni.loni.usc.edu/methods/mri-analysis/adni-standardized-data/> [12]. The complete dataset (504 subjects) comprised one associated 1.5T T1-weighted MRI image out of the two possible from the back-to-back scanning protocol in ADNI [9] at baseline, 12-month follow-up, and 24-month follow-up.

## **2.2 Preprocessing**

The data were provided for use already preprocessed. This preprocessing, and subsequent hippocampal segmentation was performed with the freely available FreeSurfer software package (version 5.1.0) [7] using the cross-sectional pipeline with default parameters. The original MRI image resolution of [0.94, 1.35] x [0.94, 1.35] x 1.2mm was conformed to a 1.0 x 1.0 x 1.0 mm resolution, and all MRIs were bias field corrected. The bias field correction in FreeSurfer utilizes the nonparametric nonuniform intensity normalization algorithm [11], often

referred to as N3. The input data for this study was therefore the corrected T1-weighted MRI image volume, and corresponding separate binary masks of left and right hippocampi.

# Chapter 3

## Method

### 3.1 Image texture analysis methods

Image texture is a feature that can help to segment images into regions of interest and to classify those regions. Textures gives us some information about the arrangement of the intensities in an image. Texture analysis is a technique for evaluating the position and intensity of signal features[5]. Statistical texture analysis methods evaluate the interrelationship of voxels, based on mathematical parameters computed from the distribution and intensities of voxels in the image.

#### 3.1.1 Co-occurrence matrix

The co-occurrence matrix (COM) is second-order statistics methods, which is based on information about colours in pair of pixels. The matrix is defined over the image with distribution values at a given offset. Mathematically we have a COM matrix  $\mathbf{C}$  which is defined over an  $n \times m$  image  $\mathbf{I}$ , with  $\Delta x, \Delta y$  being the parameterized offset, is calculated by [4]

$$C_{\Delta x, \Delta y}(i, j) = \sum_{p=1}^n \sum_{q=1}^m \begin{cases} 1, & \text{if } I(p, q) = i \text{ and } I(p + \Delta x, q + \Delta y) = j \\ 0, & \text{otherwise} \end{cases}$$

The element (5,4) in the COM can be translated to meaning how many times there exist an element in the image with GI **Fixme Note: level or intensity?** 5 and another element offset  $\Delta x, \Delta y$  from the original with greyscale intensity<sup>1</sup> (GI) 4, i.e. if the offset is (0,1)**Fixme Note: rigtigt offset?** and the first element is (x,y)(4,3) with GI 5 it would mean that element (x,y)(5,3) would have GI 4. If COM(4,4) is ten, it translates into there being ten instances with element (x,y) = 5 and (x+ $\Delta x$ ,y+ $\Delta y$ ) = 4. COMs calculated on GIs are often called gray-level co-occurrence matrices (GLCM). **Fixme Note: Skal passe til figure 3.2**

Fixme Note:  
level or  
intensity?  
Fixme Note:  
rigtigt offset?

Fixme Note:  
Skal passe til  
figure 3.2

A single image have multiple GLCMs as different offsets creates different relations. Consider a  $3 \times 3$  matrix looking at element (2,2) we can then create eight different offsets,  $\text{GLCM}_{(1,0)}$ ,

<sup>1</sup>The pixel value is a single number that represents the brightness of the pixel. Typically one is taken to be black and 256 is taken to be white and values in between make up the different shades of grey

$\text{GLCM}_{(1,1)}$ ,  $\text{GLCM}_{(0,1)}$ ,  $\text{GLCM}_{(-1,1)}$ ,  $\text{GLCM}_{(-1,0)}$ ,  $\text{GLCM}_{(-1,-1)}$ ,  $\text{GLCM}_{(0,-1)}$ , and  $\text{GLCM}_{(1,-1)}$  however they are not unique. **FiXme Note: Vise for transpose GLCM**

Focusing on the two offsets  $(0,1)$ ,  $(0,-1)$  in element  $(2,2)$  and  $(1,2)$  with GI 1 and 2 respectively increases the entry  $\text{GLCM}_{(1,0)}(1,2)$  and  $\text{GLCM}_{(-1,0)}(1,1)$  with one, showing that **FiXme Note: Er dette rigtigt?**

$$\text{GLCM}_{(0,1)} = \text{GLCM}_{(0,-1)}^T$$

FiXme Note:  
Vise for  
transpose  
GLCM  
FiXme Note:  
Er dette  
rigtigt?

There exist the same relation between

$$\text{GLCM}_{(1,1)} = \text{GLCM}_{(-1,-1)}^T$$

$$\text{GLCM}_{(0,1)} = \text{GLCM}_{(0,-1)}^T$$

$$\text{GLCM}_{(-1,1)} = \text{GLCM}_{(1,-1)}^T$$

FiXme Note:  
Vise for  
transpose  
GLCM

### FiXme Note: Vise for transpose GLCM

This leaves four different offsets for analysis  $(0,1), (-1,1), (-1,0), (-1,-1)$  in general  $(0,d), (-d,d), (-d,0), (-d,-d)$  where  $d$  is the distance which are commonly named angles  $0^\circ, 45^\circ, 90^\circ$  and  $135^\circ$  as seen in figure 3.1.

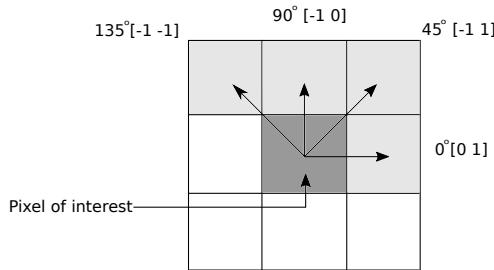


Figure 3.1: Example of the offsets for the 2D

and let figure 3.2 illustrate this concept with a  $4 \times 4$  image  $I$  with four different COM's for  $I : C_{(0,1)}, C_{(-1,1)}, C_{(-1,0)}$  and  $C_{(-1,-1)}$

I

1	1	4	4
1	1	4	4
3	4	2	2
3	4	2	2

Figure 3.2: Image I that is 4-by-4

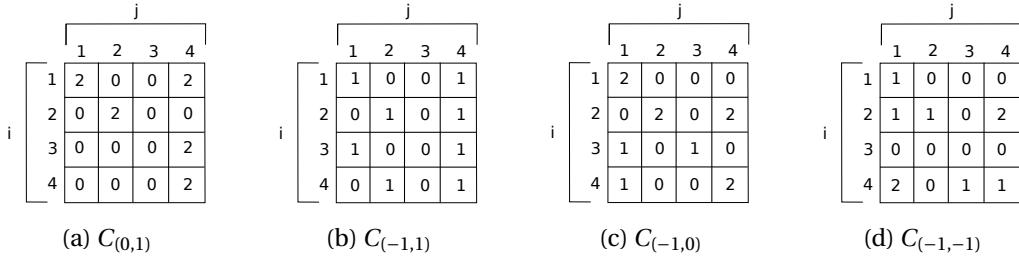


Figure 3.3: Four different COM's for a gray-tone image. Shows how the GLCM are calculated of the 4-by-4 image I 3.2.

**FiXme Note:**  
Tjek om det  
passe

**FiXme Note: Tjek om det passe** The co-occurrence matrix is quadratic with the number of rows and columns equal to the amount of GI, for example if we have 256 GI we get a  $256 \times 256$  GLCM.

Extending this method to three-dimensions it is necessary to look on how the offsets are defined because the size of the GLCM is defined by the amount of GIs and not by the images it is derived from. Considering a  $3 \times 3 \times 3$  matrix we have a possible of 26 offsets. In two-dimensions it is possible to eliminate half of the offsets because of the relation  $\text{GLCM}_{d,d}^T = \text{GLCM}_{-d,-d}$ , and it is the same case in three-dimensions with the relation being  $\text{GLCM}_{d,d,d}^T = \text{GLCM}_{-d,-d,-d}$ . This leaves 13 offsets which are illustrated below.

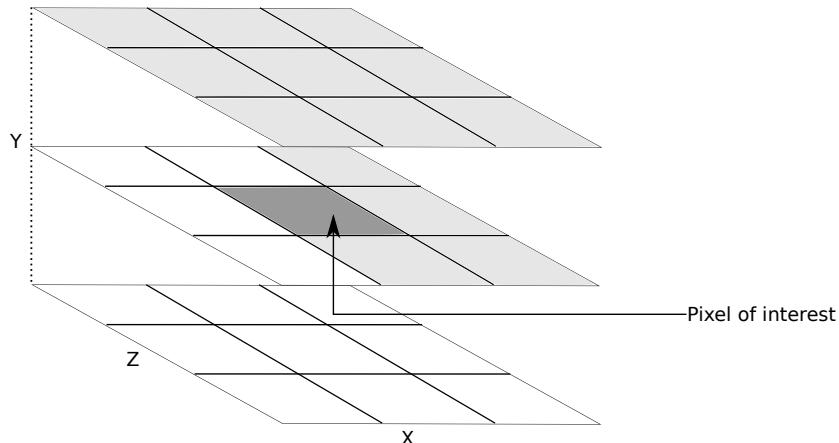


Figure 3.4: Example of the offsets for the 3D

To create a two-dimensional GLCM on three-dimensional image we create slices through the

image. Given a  $n \times m \times l$ ,  $n = 20$ ,  $m = 20$   $l = 20$ , image we can create a slice for each  $n$ .  $\text{Slice}_1$  is equal to the matrix  $M( n = 1 \times m \times l)$ ,  $\text{Slice}_2 = M( n = 2 \times m \times l)$ , and so on, giving a total of 20  $m \times l$  images instead. It is possible for each slice to calculate the  $\text{GLCM}_{d,d}$  for each slice, and we define  $\text{GLCM}_{d,d} = \sum_{n=1}^2 \text{GLCM}_{d,d}(\text{Slice}_n)$

These slices are done in all three directions of the image for the four difference offsets resulting in 12 GLCMs. There is an overlap between six of the GLCMs. Slicing through  $n$  axis with offset  $(0,d)$  is equal to slicing through the  $m$  axis with the same offset. Slicing through the  $m$  axis with offset  $(-d,d)$  is equal to slicing through the  $l$  axis with offset  $(-d,0)$ . Slicing through the  $l$  axis with offset  $(-d,d)$  is equal to slicing through the  $n$  axis with offset  $(d,0)$ , which is the transposed offset of  $(-d,0)$ . Removing the duplicates leaves nine GLCMs which we calculate at distances  $d = (1,2,\dots,10)$ , giving a total of 90 GLCMs for each mri scan.

The three-dimensional versions is also calculated for distances  $d = (1,2,\dots,10)$  resulting in 130 GLCMs for each mri scan.

### 3.1.2 Texture features from co-occurrence matrix

To compare the differences between the GLCMs 13 different features are computed. They are the same as used in [8] except for one difference. The difference is how the correlation is calculated as  $\sum_{i,j} \frac{(i-\mu_i)(j-\mu_j)g\text{lcm}(i,j)}{(\sigma_i \cdot \sigma_j)}$ , where  $\mu_i$ ,  $\mu_j$ ,  $\sigma_i$ ,  $\sigma_j$  are the means and standard deviations of  $C_i$  and  $C_j$  respectively. This correlation is called the Pearson product moment correlation coefficient and it determines how correlated a pixel is to its neighbour, over the whole image[2][3]. We calculate two versions of these features, one where we normalized the COMs and one where we do not.

## 3.2 Machine learning

Machine learning is a method used to create complex models and algorithms that lend themselves to prediction, when the models are exposed to new data that should be able to teach themselves to grow and change. There are several different categories of machine learning, one of them being supervised learning. In supervised learning given a large sample of input and output pairings, the goal is to find the complex function that maps that relation between input and output. With a sufficient large dataset it would be possible to train a supervised algorithm to predict output values for some new input values that it have not seen before.

### 3.2.1 10-fold cross-validation

Given a model with unknown parameters and a training set to which the model can be fit then the fitting process optimizes the models parameters to fit the training data. Validating this model against independent data (test data) from the same data pool as the training, it will generally turn out that the model does not fit the test data as well as the training data. It is known as overfitting and is a problem when the size of the training data set is small. Cross-validation is used to counteract overfitting.

Dividing the entire data set into 10 groups at random, one subsample is saved for testing and the reamining nine is used to fit the model. The procedures is done so all subsamples get to be used to validate exactly one time and the validation result can then be averaged to produce a single estimation. This solves the problem of overfitting, as the validation data set is never used in to fit the model. **Fixme Note: how does this remove overfitting?**

Fixme Note:  
how does  
this remove  
overfitting?

### 3.2.2 Feature selection

Feature selection is the process of selection af subset of relevant features for use in model contruction. The main goal of feature selection is to choose a subset of the entire set of input features so the subset can predict the output with an accuracy comparable to using the entire set to predict the output, but with a large reduction in the computational cost. When a dataset contains many feautres that are either redundant og irrelevant it is possible to remove them without incurring much loss of information. Features may be redundant due to the prescence of another feature with which it is strongly correlated, while they may be very informative for the model their information have already been provided by a different feature. Only choosing a subset of the possible features have the added advantage of decreasing the complexity of the model.

Sequential forward feature selection(SFS) is a greedy algorithm to choose features. It starts off with finding the best possible single feature to describe the model. Given the feature set of that single feature, the next step is to find which other feature would improve the predictiveness of the model and then add that to the set of selected featuers. It continues to grow the set of selected features, until the goal have been reached. The goal can either be a specific amount of features, a specific accuracy for the model or it can stop if all choices of a new feature would decrease the accuracy. A problem with SFS is due to its greedy nature, there is no guarantee that the first feature selected is part of the optimal solution. Given three features  $X_1$ ,  $X_2$  and  $X_3$  where  $X_1$  is the best single feature,  $X_2$  is second best and  $X_3$  the worst, it does not necessitate that pairing  $X_1$ ,  $X_2$  is better than  $X_2$ ,  $X_3$ , nor does it secure any other relation, meaning that the SFS does not guarantee the optimal solution. Which leads to one of the drawbacks of this feature selection, if a feature is selected it is not possible to exclude it later even if it would increase the evaluation score to do so.

```
1 The algorithm for SFS with 10-fold cross validation
2 Step 1:
3 Set selected features Y = \emptyset
4 X = entire featurerset
5 Seperate dataset into 10 folds of equal size with 5 of each class , {K1,K2 ,...,K10}.
6
7 Step 2:
8 For feature i= 1 to No. of features
9   for fold j=1 to No. of folds
10    Train a k-nn model on {Y,Xi} using fold K1,2,...,10\ Kj as training
11    Calcualte missclassification error of model on Kj
12 Average the error for all 10 folds.
13
14 Step 3:
15 F = feature with lowest error
16 X = X \ F
```

```
17 Y = Y ∪ F
18
19 Step 4:
20 Continue step 2-3 until the missclassification error worsen or 15 features have been
   ↵ selected.
```

The algorithm is run on 10 different  $k$  values for the k-nn model,  $k = 1, 2, \dots, 10$ .

### 3.2.2.1 Naive

## 3.2.3 K Nearest Neighbors algorithm

The K Nearest Neighbor (KNN) is a method that is used for classification and regression. It should be noted, that KNN is a non parametric lazy learning algorithm, which means that it does not make any assumptions on the underlying data distribution. In other words, it means that the training phase is fast and KNN keeps all the training data. It should be noted that KNN makes decision based on the entire training data set and in the KNN an object is classified by majority vote of its neighbors, with the object being assigned to the class most common amongst its  $KNN$ 's. 3.5

Since the training phase is minimal, then it should be noted that the testing phase is very costly for KNN in both memory and time and often it can be a worst case for time needed, since all points might take part in the decision making.

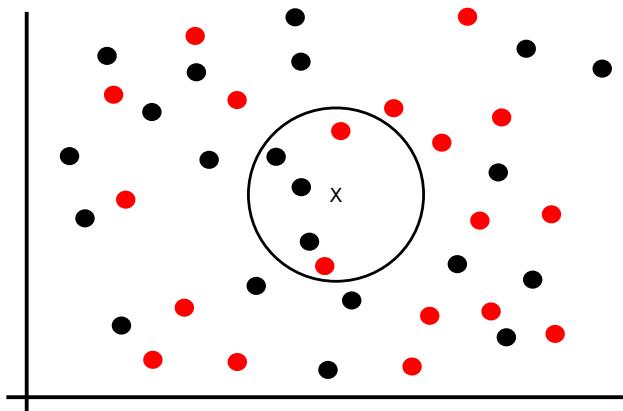


Figure 3.5: The KNN grows a spherical region until it encloses  $k$  training samples, and labels the test point by a majority vote of these samples. In this  $k = 5$  case, the test point  $x$  would be labelled the category of the black points

Because the KNN classifier predicts the class of a given test observation by identifying the observations that are nearest to it, the scale of the variables matters. Imagine that we have a large scale variables, they will have a much larger effect on the distance between observations and hence the KNN classifier, than variables on a small scale. Often a good way to handle this problem is to standardize the data.

The disadvantage of KNN is that choosing a  $k$  may be tricky, so we are left to test the algorithm on multiple  $k$ 's and often it needs a large number of samples for better accuracy.

Typically will the KNN classifier be based on a distance, commonly it is based on the Euclidean distance between a test sample and the specified training samples. Let  $x_i$  be an input sample with  $p$  features  $(x_{i1}, x_{i2}, \dots, x_{ip})$ , and  $n$  be the total number of input samples  $i = 1, 2, \dots, n$  and  $p$  the total number of features  $j = 1, 2, \dots, p$ . The Euclidean distance between sample  $x_i$  and  $x_l$ ,  $l = 1, 2, \dots, n$  is defined as  $d(x_i, x_l) = \sqrt{(x_{i1} - x_{l1})^2 + (x_{i2} - x_{l2})^2 + \dots + (x_{ip} - x_{lp})^2}$

### 3.3 Erode

Each patients hippocampus has been segmented in the MRI scan. The problems we can run into are that the background will blur with the segmentation i.e. the hippocampus. Performing a erosion can solve this problem and we can focus on the hippocampus, with the maximum number of details. As seen in figure 3.6a the erosion has not been performed yet, but we might have some problems with data surrounding the hippocampus is blurring out the edges of the hippocampus. To solve this, we create a mask to separate the hippocampus from the background data and end up with what is left in figure 3.6b

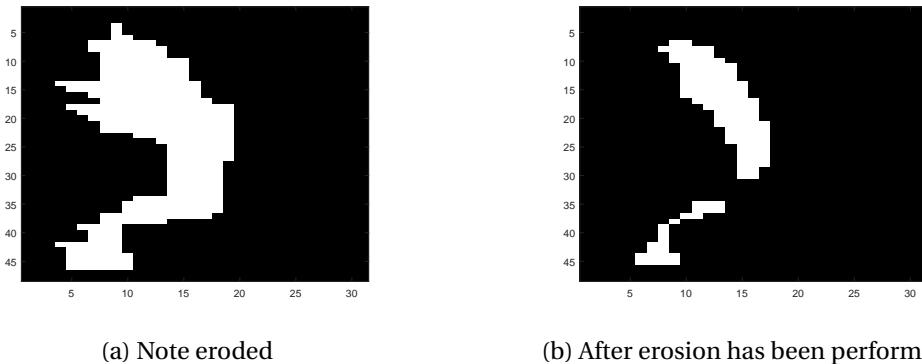


Figure 3.6: Hippocampus at slice 10 on the X-axis as bitwise

The erosion we have used is called a city-block metric and can be seen in figure 3.7.

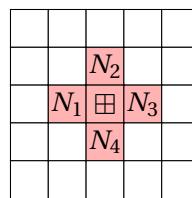


Figure 3.7: Text

To give an example of how the erosion works, it will be illustrated and we will use the city-block metric for this purpose. So we will use figure 3.7 and erode the image in figure 3.8.

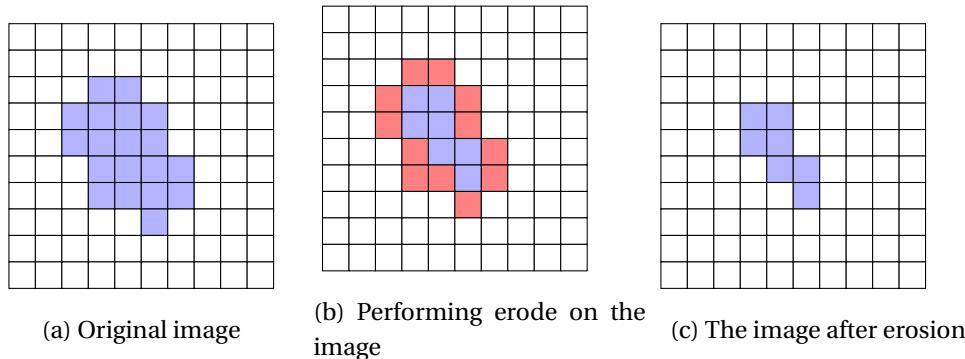


Figure 3.8: Example of a city-block erosion with before and after

As seen in figure 3.8 the noise (background) have been removed. This is an example in 2D. Now we wish to extend the erosion city-block to 3D. As seen in figure 3.7 it have 4 neighbours and when we extend this to 3D we will end up with 6 neighbours instead as seen in figure 3.9 and the concept is still the same as in 2D

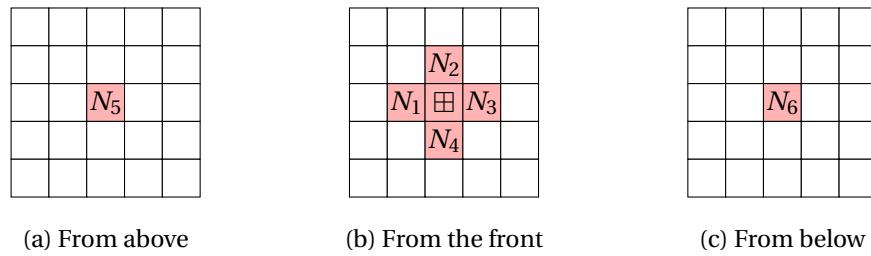


Figure 3.9: 2D example of the 3D city-block

# Chapter 4

## Implementation

### 4.1 Preparation of Data

The mri files are  $256 \times 256 \times 256$  matrices but we are only interested in the small part which overlaps with the masks from segmentation, i.e. where the elements in segmentation is either 1 (left hippocampus) or 2 (right hippocampus). We have created the function HippoMatrix, which takes three variables, which file to load, whether or not erosion should be performed, and if the left or right hippocampus is desired. First we assign a value based on if we are looking for the right hippocampus, as they are associated with 1 and 2 respectfully. If erosion is desired we create the city-block for erosion by taking advantage of distances calculations,  $\text{distance} = \sqrt{x^2 + y^2 + z^2}$ . All parts of the city-block have distance 1 from the origin point. With the city-block defined we can use matlab's built in function imerode to perform the erosion. **Fixme Fatal: insert snip of code.+ link imerode page**

Looping through the entire segmentation matrix we identify all the datapoints where segmentation is one for the left hippocampus or two if we are trying to identify the right hippocampus. For each instance in segmentation we save the coordinate  $(i,j,k)$  and the  $\text{mri}(i,j,k)$  value in an array as  $v(1) = (i_1, j_1, k_1, \text{mri}(i_1, j_1, k_1))$ . **Fixme Fatal: snip of main loop, explain left is also used incase of right**

On the basis of this we can create a three-dimensional matrix which contains all the datapoints,  $\text{hippoBox} = \max(i) - \min(i) + 1 \times \max(j) - \min(j) + 1 \times \max(k) - \min(k) + 1$ . Then we simply loop through our array with the relevant data and input them into  $\text{hippoBox}$ , all other elements inside the matrix are set to NaN. **Fixme Fatal: snip of last loop**

The return value from the function is the matrix  $\text{hippoBox}$  containing only the relevant data.

**Fixme Fatal:**  
insert snip of  
code.+ link  
imerode  
page

**Fixme Fatal:**  
snip of main  
loop, explain  
left is also  
used incase  
of right

**Fixme Fatal:**  
snip of last  
loop

### 4.2 Data Calculations

In our function file, we do a lot of stuff that will be described in details. But in this file, we load our labels file, and take care of calculating every patient file to find a GLCM and from this GLCM we find the GLCM features.

First we check whether we have a patient with AD or not and name them respectively to their group.

Now we calculate the GLCM for the 2D and 3D which we have two functions doing the work. These functions, `glcm2dFast` and `GLCM3D`, take the HippoMatrix data, as mentioned in preparation data, and the desired distance that we wish to calculate to.

Now we initiate two cells for the GLCM Features which we derive using the function `GLCMDerivations` which will take the GLCM data and if we wish to normalize the GLCM or not as input.

```
1 data_glc2D = glcm2dFast(HippoMatrix(files(j).name, erode, leftright), 10);
2 data_glc3D = GLCM3D(HippoMatrix(files(j).name, erode, leftright), 10);
3
4 data_Derivations2D = cell(90, 1);
5 data_Derivations3D = cell(130, 1);
6
7 for k = 1:size(data_Derivations2D, 1)
8     data_Derivations2D{k} = GLCMDerivations(data_glc2D{k}, norm);
9 end
10 for k = 1:size(data_Derivations3D, 1)
11     data_Derivations3D{k} = GLCMDerivations(data_glc3D{k}, norm);
12 end
```

Lastly we save the data to their respective folders.

#### 4.2.1 Calculating GLCMs

To calculate the GLCMs in two-dimensions we have taken advantage of Matlab's built-in function `graycomatrix`. It calculates as described in methods. It is then a matter of giving the proper offsets, and the right number of GIs. We can then loop through the `hippoBox` slices and sum up the GLCMs. **Fixme Fatal: snip af glcm2dallangels hvor vi udregner**

We ultimately save all 90 glcms in a cell. **Fixme Fatal: Fodnote der beksriver hvad en cell er?**

To implement the three-dimensional GLCMs we have created our own function. The function `GLCM3D` takes a `hippoBox` as data and how many distances desired. I then for each distance loop through the entire matrix, and for each element it checks if it is `NaN` value and larger than zero. The check utilizes that `NaN` is not larger than zero, so `data(i,j,k) > 0` returns false incase of `data(i,j,k) = NaN`. The reason we also insist that it should also be larger than zero is because a few of the right hippocampus include GI of value zero in their `hippoBox`, but as zero is the value the MRI scans have outside the brain we choose to ignore the few instances. To include them would mean we had to increase our GLCMs by 1 in size, which would make them differ from the GLCMs derived in two-dimensions, making the comparison unfair. In addition Matlab starts their index for their matrices with one and not zero so we would also have to add every index with one creating greater complexity. **Fixme Fatal: snip af første if.** Given that the datapoint is relevant, i.e. larger than zero, we then have to look at the thirteen offsets, to see if we need to increment an element in one of the GLCMs. For each offset check if the offset is inside the `hippoBox`, and is the offset element a non `NaN` nonzero value. If so we then increment the relevant GLCM, lets say it is the offset(`d,0,0`), `d =`

Fixme Fatal:  
snip af  
glcm2dallangels  
hvor vi  
udregner  
Fixme Fatal:  
Fodnote der  
beksriver  
havd en cell  
er?

Fixme Fatal:  
snip af første  
if.

1, in element  $\text{GLCM}(d, 0, 0)(x, y)$  ( $\text{hippoBox}(i, j, k), \text{hippoBox}(i+1, j, k)$ ). **Fixme Fatal: indsæt en if statement**

Fixme Fatal:  
indsæt en if  
statement

We have defined our thirteen offsets as  $\{(d, 0, 0), (d, 0, d), (0, 0, d), (-d, 0, d), (d, -d, 0), (d, -d, d), (0, -d, d), (-d, -d, d), (-d, -d, 0), (-d, -d, -d), (0, -d, -d), (d, -d, -d)\}$ . Because of the relationship between the offsets, as in  $\text{GLCM}_{(d, 0, 0)} = \text{GLCM}_{(-d, 0, 0)}^T$ , the results do not change depending of the dimensions as long as there are no offsets where  $\text{offset}_i = \text{offset}_j^T$  holds. We calculate those thirteen offsets for distances one through ten, and save all 130 GLCMs in a cell. **Fixme Fatal: indsæt en if statement**

Fixme Fatal:  
indsæt en if  
statement

## 4.3 Naive feature

only done it 3D Left Hippo Features selected: 8 Imoc2: A7D2, A3D3, A13D3 Imoc1: A13D9, A7D6 Entro: A13D10, A7D6 SumAv: A7D6

### 4.3.1 Calculating(Computing) the GLCM Features

Fixme Note:  
Snak om  
Datacalcula-  
tion  
filen

#### Fixme Note: Snak om Datacalculation filen

In the implementation of the GLCM Feature derivation we are taking two inputs. The first input variable is the GLCM matrix and the second is wether we wish to normalize the data.

Fixme Note:  
Lav et  
eksempel  
(diagram) af  
hvordan  
cxminusy og  
cplusy ser ud  
  
Fixme Note:  
Snakke om  
optimeret  
altså filerne  
Cx+-y

What we are doing first is to make sure that all variables are implemented. Firstly we find the size of the GLCM which will be the greylevels. Hereafter we can initiate the  $C_x$ ,  $C_y$ ,  $C_{x+y}$  and  $C_{x-y}$  since we know the size of the GLCM.

For the pixel values in the GLCM we are using MATLAB's `ind2sub` function, that is a command that determines the equivalent subscript values corresponding to a single index into an array. **Fixme Note: Lav et eksempel (diagram) af hvordan cxminusy og cplusy ser ud.** We are using these variables in the GLCM Features as seen in Appendix A.

To calculate the  $C_{x+y}$  and  $C_{x-y}$  we have two for loops as seen in Appendix A.3 and A.4 where N of course is the greylevels. **Fixme Note: Snakke om optimeret altså filerne Cx+-y**

To find the mean and standard deviation for  $C_x$  and  $C_y$  we just use the functions that MATLAB have.

The GLCM features, as seen in Appendix A, utilizes MATLABs use of vectorization. This is rewarding in the vectorized code appears more like the mathematical expressions and makes the code easier to understand and is shorter. There is often a performance gain in using vectorized code than the corresponding code containing loops.

It should be obvious for the reader to tell that the code looks alot like the mathematical expression like in Appendix A.

```
1 HXY1 = -nansum(glcm(tmpsub) .* log(cX(I).*cY(J)));
2 HXY2 = -nansum(cX(I).*cY(J).*log(cX(I).*cY(J)));
3 HX = -nansum(cX.*log(cX));
4 HY = -nansum(cY.*log(cY));
5 HXY = -nansum(glcm(:).*log(glcm(:)));
```

```
6
7 stats.angularSecondMoment      = sum(glcm (:).^2);
8 stats.contrast                 = sum(abs(I-J).^2.*glcm(tmpsub));
9 stats.correlation               = (sum(I.*J.*glcm(tmpsub))-muX*muY)./(stdX
   ↪ *stdY);
10 stats.variance                = sum(((I - mean(glcm (:))).^2).*glcm(tmpsub));
11 stats.inverseDifferenceMoment = sum(glcm(tmpsub)./(1+(I-J).^2));
12 stats.sumAverage              = sum(bsxfun(@times,(2:2*nGrayLevels)',cXplusY
   ↪ ));
13 stats.sumVariance             = sum(((2:2*nGrayLevels) - stats.sumAverage)
   ↪ '.^2.*cXplusY((2:2*nGrayLevels)-1,1));
14 stats.sumEntropy              = nansum(cXplusY.*log(cXplusY));
15 stats.entropy                  = HXY;
16 stats.differenceVariance     = var(cXminusY);
17 stats.differenceEntropy       = nansum(cXminusY.*log(cXminusY));
18 stats.informationMeasuresOfCorrelation1 = (HXY - HXY1)./(max(HX,HY));
19 if (strcmp(norm, 'normalize') == 1)
20   stats.informationMeasuresOfCorrelation2 = sqrt(1-exp(-2.*(HXY2 - HXY)));
21 else
22   stats.informationMeasuresOfCorrelation2 = NaN;
23 end
```

As seen from line 19 to 23, we have an if-statement. This checks if we call our plot on the normalized data or not, since the values on informationMeasuresOfCorrelation2 end up being  $\pm\infty$  when the data are not normalized. **FiXme Note: Snakke om hvorfor normalized data. Features vi har valgt fra freebourug har gjort det og måske gjort i det mente om at de kan ende med pæne værdier – i method muligvis**

FiXme Note:  
Snakke om  
hvorfor  
normalized  
data.

Features vi  
har valgt fra  
freebourug  
har gjort det  
og måske  
gjort i det  
mente om at  
de kan ende  
med pæne  
værdier – i  
method  
muligvis

## 4.4 Plotting the GLCM features

Now that we have calculated the 13 GLCM features, we can plot them. Remember that one GLCM matrix have one specific distance for a specific offset, so this equals 90 GLCMs for the 2D, after some cuts and 130 GLCMs for the 3D version. To plot, you would simply have to call the function simpleAllplot that takes 4 inputs, the DATA which are the GLCM data, NumberOfPatients i.e. how many patients we wish to plot, looping which tells the function how many features it should count on, counting from feature one and Lastly in the simpleAllplot function we give us self the possibility to chose between plotting the mean values, for a specific number of patients or both.

We have discussed how our plain data is sorted when datacalculation, now we wish to sort it differently for our plots, so it is easier to handle. Since we have 13 GLCM features we create 13 cells to easier name our plots for the for loop sorting the data. The way we chose to sort our data is to have it in the following way Dataset (NumberOfPatients\*10, 9, 13). So we have 9 subplots per Feature where each subplot for every plot have distance 1 to 10

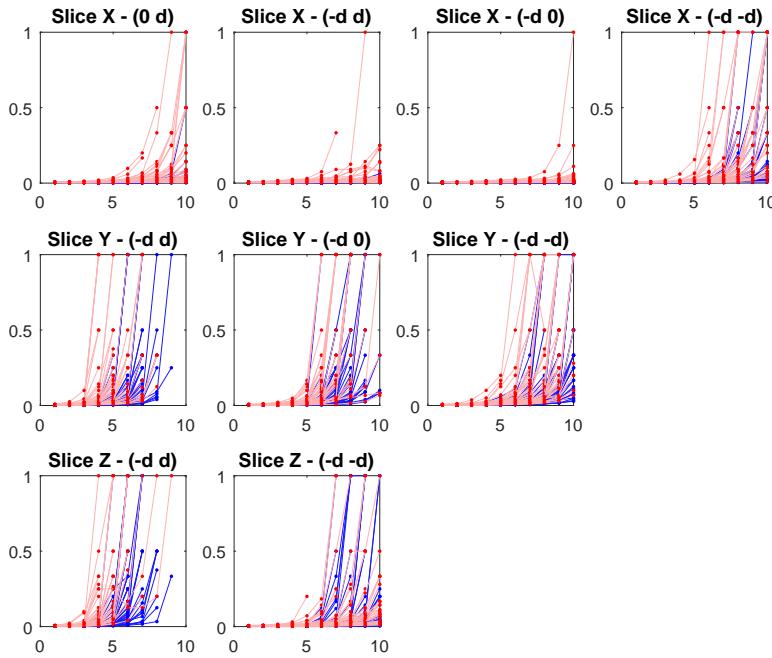


Figure 4.1: Plot of the Angular Second Moment features where the data have been normalized and eroded. This is the left Hippocampus. The red are the patients with AD and the blue are the rest

## 4.5 Forward feature selection

We want to use cross validation on our feature selection. To do achieve this we need to create 10-folds for our patients, which means we have to randomize the order of the patients. We use Matlab's build in function `datasample` to randomize the data and the pick five Control patients, followed by five AD, for each fold, which we continue until all 100 patients have been selected, leaving us with 10 folds with each five control and five AD.

To make the data easy to work with we sort it into a matrix,  $F = (\text{No. of patients} \times \text{No. of offsets} \times \text{No. of GLCM features} \times \text{No. of distances})$ . It is not necessary to split the matrix up into one for each fold, it is easier just to remember the first ten are fold one, fold two are  $F(11-20, :, :, :)$ , etc.

Firstly we wish to calculate how well each feature is at predicting on its own. So we create a matrix,  $\text{evaluate} = (\text{No. of offsets} \times \text{No. of GLCM features} \times \text{No. of distances})$ . For the two-dimensional data  $\text{evaluate}$  is a  $9 \times 13 \times 10$ , which is equal to 1170 different features for each patient, in three-dimensions we have  $13 \times 13 \times 10 = 1690$ . This huge amount of features allow us to make a preliminary cursory feature elimination, where any feature that is not complete i.e. any feature that has a NaN value for one or more of the patients we choose to ignore. In practice this is done by setting their entry in  $\text{evaluate}$  to zero. The check for NaN is done with

```
1 if (~isempty(find(isnan(dataset(:, i, j, k)) == 1, 1))) == 1
```

For the GLCM feature  $j$  calculated at offset  $i$  with distance  $k$ , it finds for all the time that value is NaN for all the patients, and checks if that set is an empty set. If the set is not empty it returns 0, which is negated and is equal to 1, so the if statement returns true and evaluate( $i, j, k$ ) = 0. We set it to zero as we evaluate each features over how well it predicts, and not how many missclassifications it makes. It is a trivial difference as  $1 - \text{succes} = \text{error}$ .

The prediction of each feature is evaluated using the function knnWithCrossval. The function splits the data up into the appropriate sets and trains a knn for each training set. We use Matlabs fitcknn function to fit the model, with euclidean distance, standardized data and for  $k = 1, 2, \dots, 10$ . However we run the entire feature selection for each  $k$  separately. The functions returns the averaged prediction score for the folds. We then find the feature with the highest accuracy and for the next iteration of evaluations the selected data is used in the creation of the knn models in knnWithCrossval.

```
1 knnmmodels{i} = fitcknn(horzcat(trainKfolds{i}, chosenTrainKfolds{i}), label90, '
  ↪ Distance', 'euclidean', ...
2   'NumNeighbors', k, 'Standardize', 1);
```

Where horzcat is a horizontal concatenation of matrices. If the best evaluation of the features is worse than if no new feature is selected the algorithm breaks, and returns a matrix of selected features and iterated accuracy, as well as the last best feature not to be selected. Incase of ties for best feature we select the first entry in the matrix.

# Chapter 5

## Result

### 5.1 Plots of 2D data

#### 5.1.1 Left Hippocampus, normalized and eroded

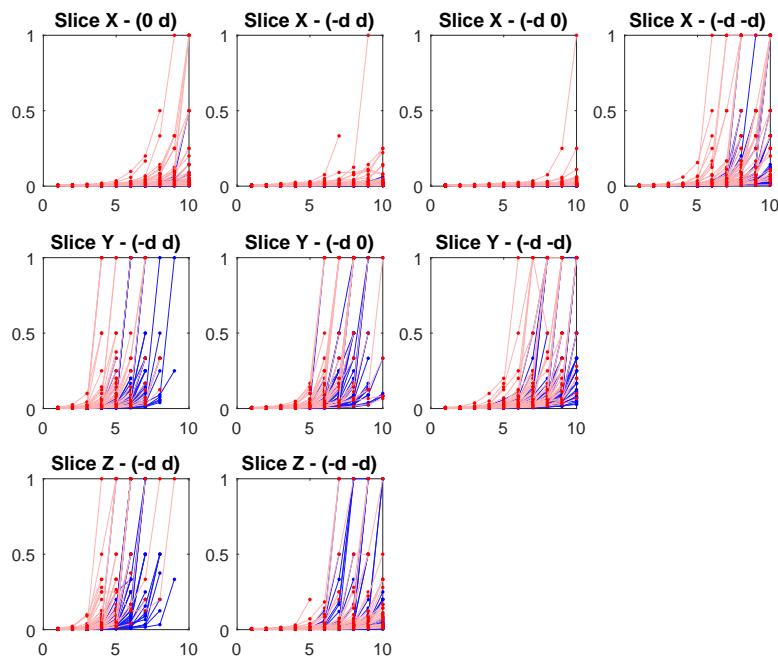


Figure 5.1: Plot of the Angular Second Moment features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

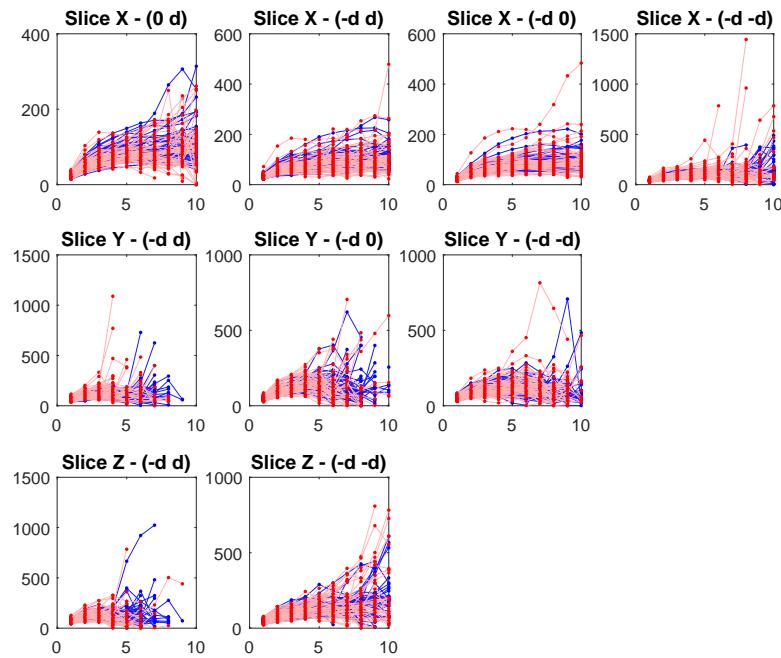


Figure 5.2: Plot of the Contrast features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

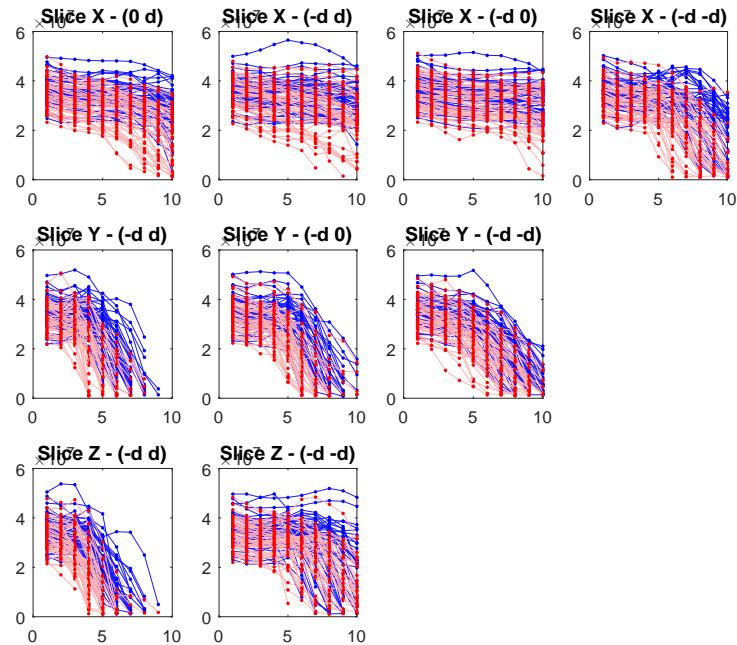


Figure 5.3: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

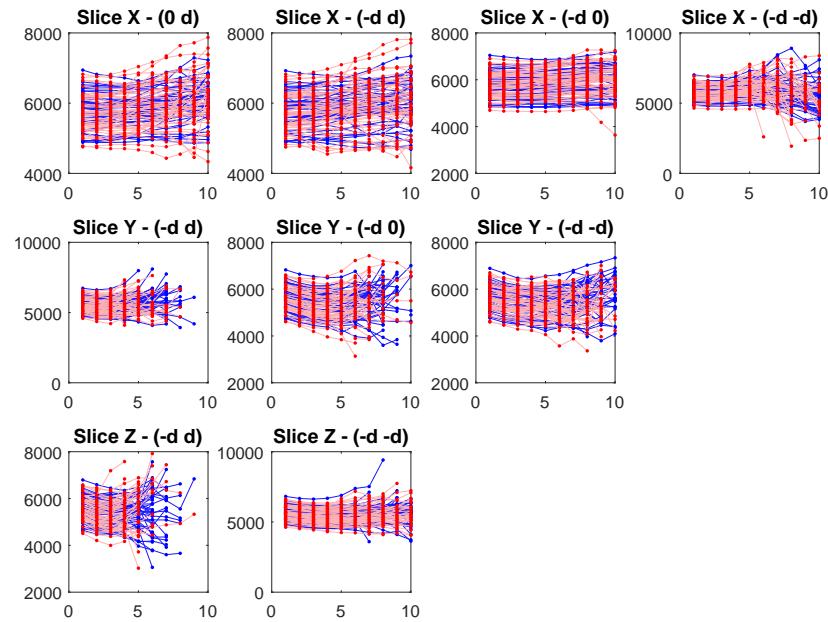


Figure 5.4: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

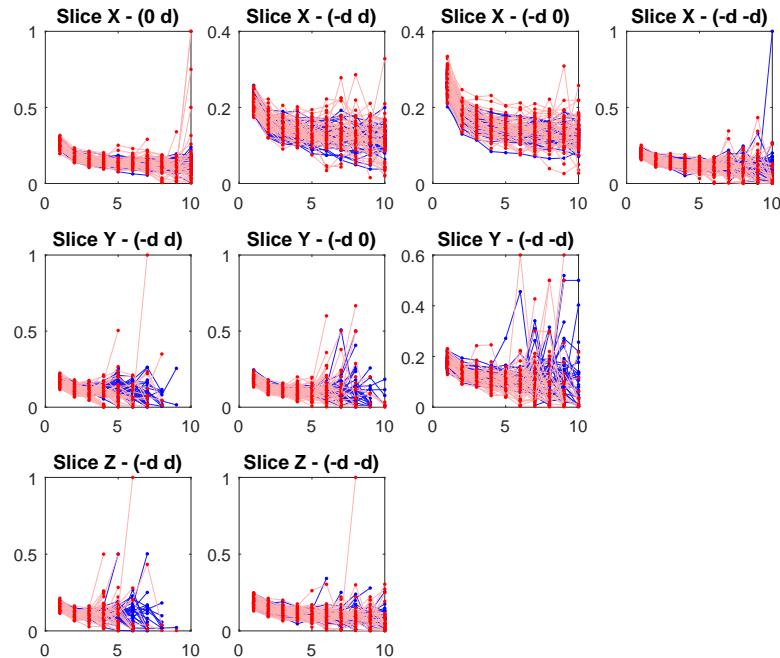


Figure 5.5: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

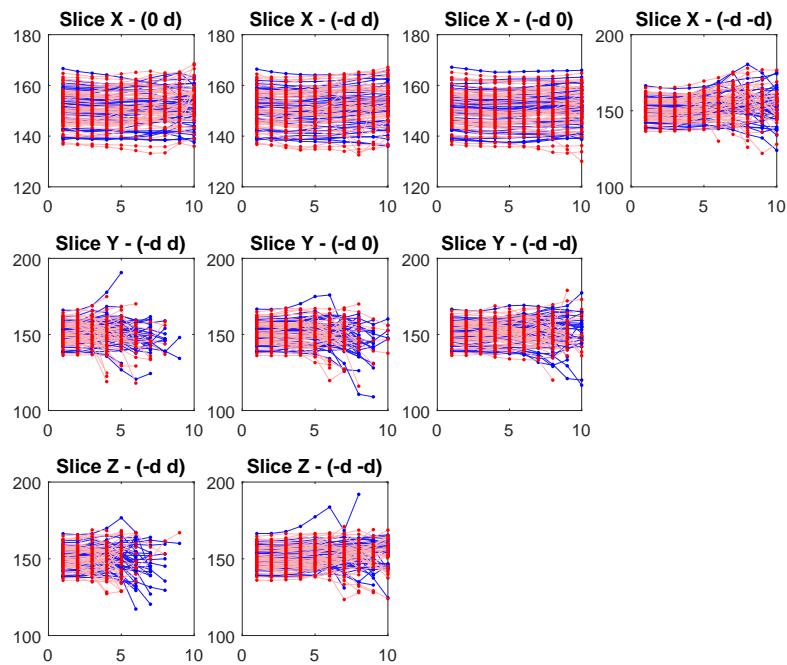


Figure 5.6: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

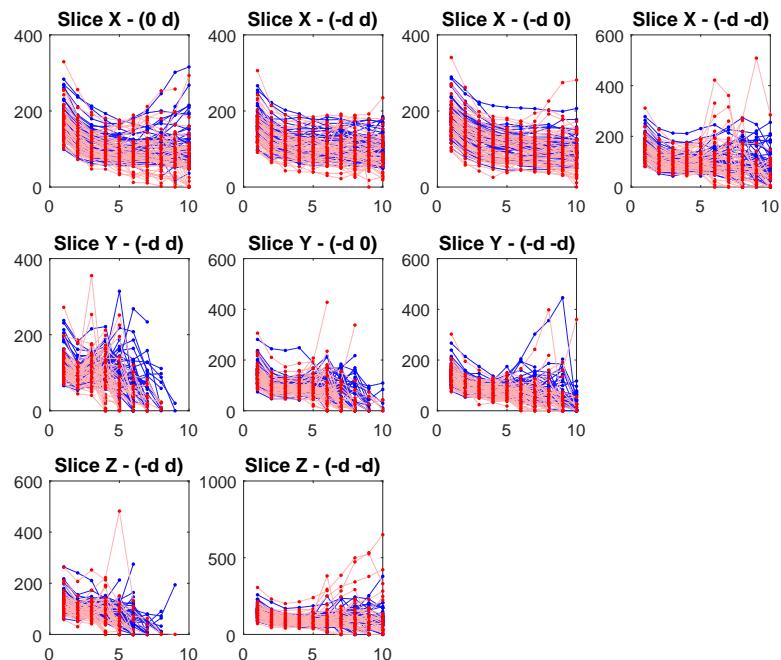


Figure 5.7: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

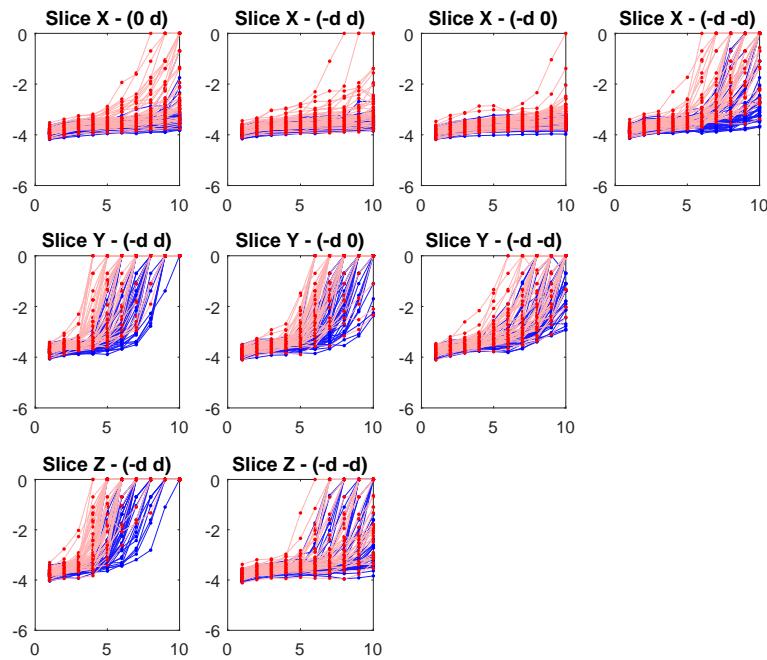


Figure 5.8: Plot of the Correlation features where the data have been normalized and eroded.  
The red are the patients with AD and the blue are the rest

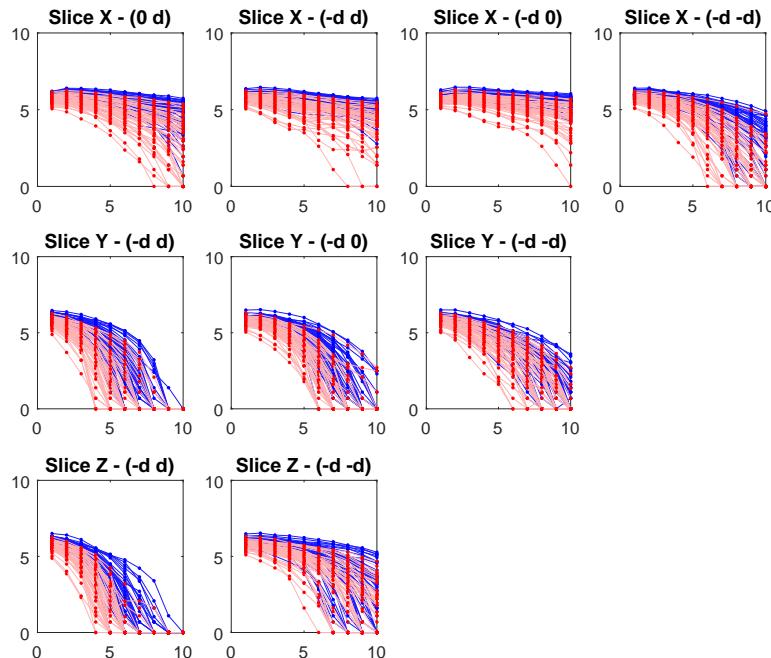


Figure 5.9: Plot of the Correlation features where the data have been normalized and eroded.  
The red are the patients with AD and the blue are the rest

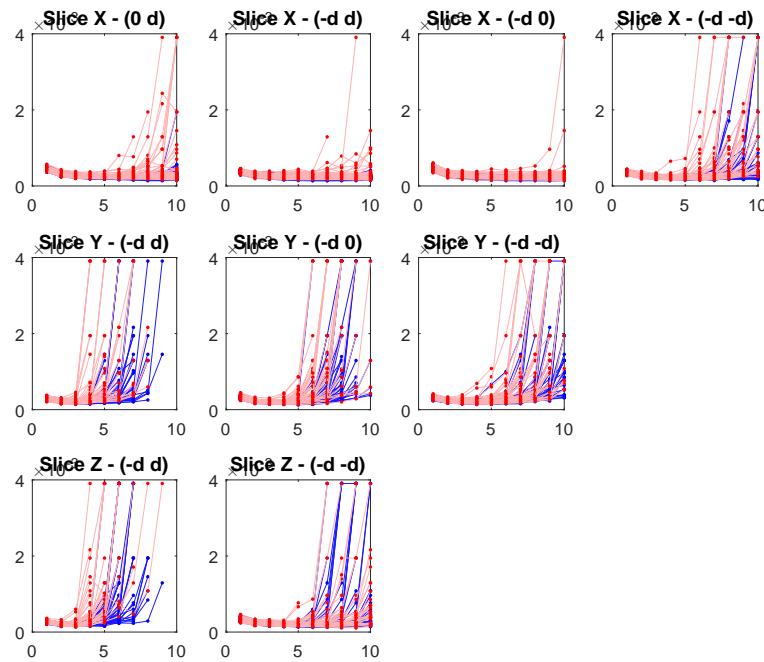


Figure 5.10: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

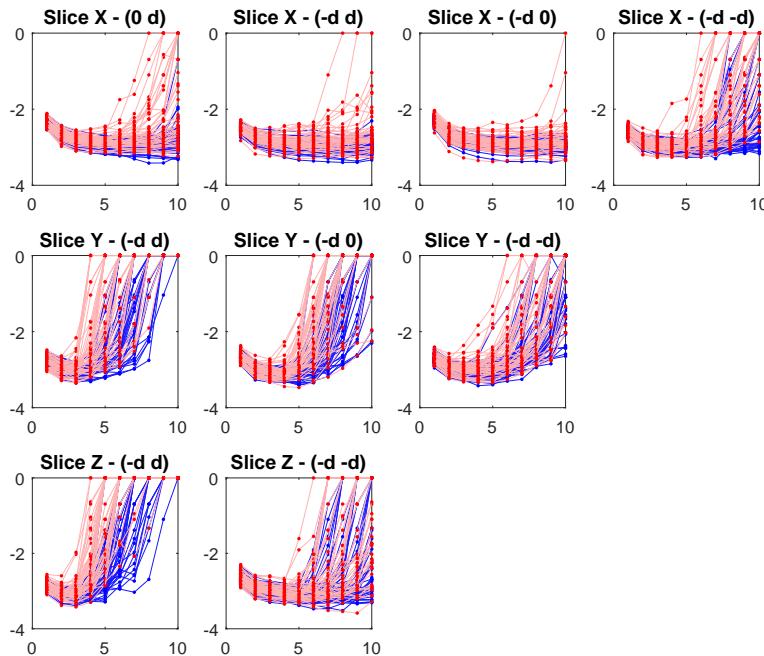


Figure 5.11: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

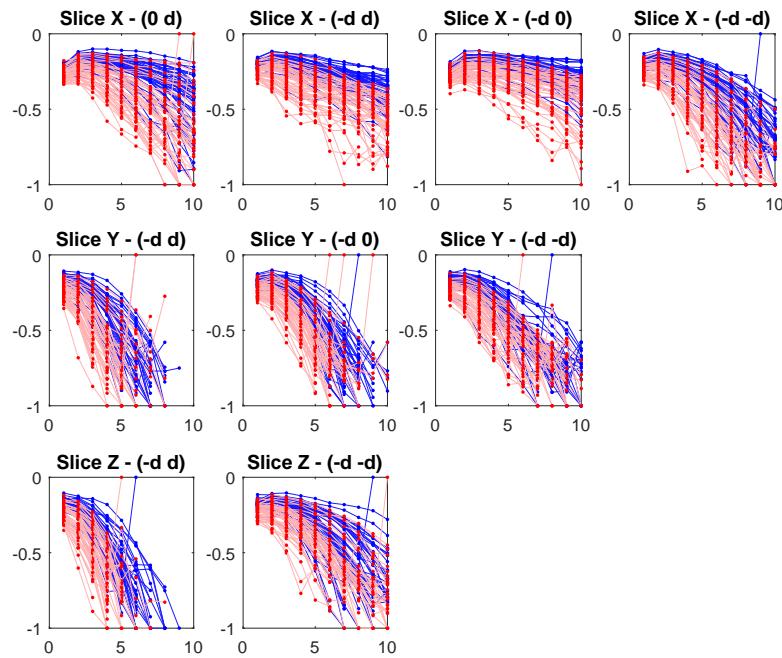


Figure 5.12: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

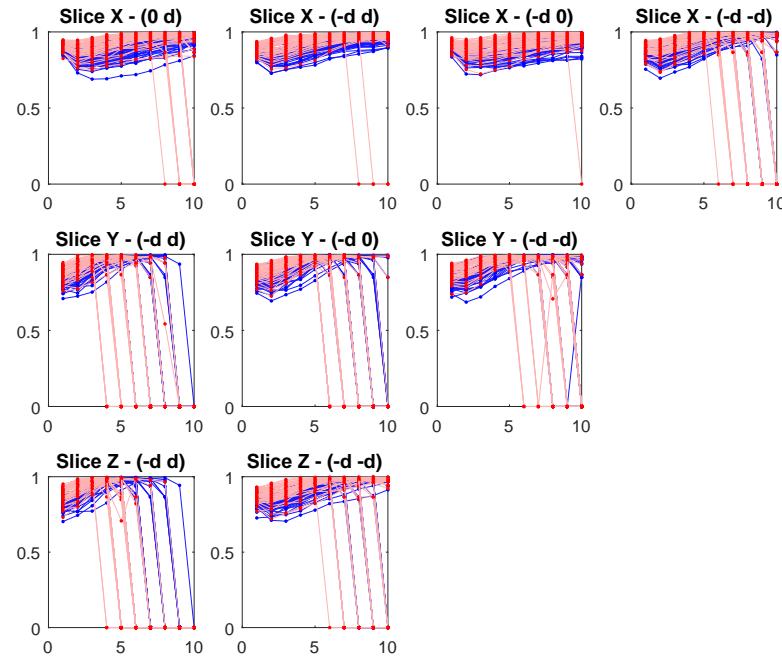


Figure 5.13: Plot of the Correlation features where the data have been normalized and eroded. The red are the patients with AD and the blue are the rest

## 5.2 Plots of 3D data

### 5.2.1 Left Hippocampus, normalized and eroded

# **Chapter 6**

## **Discussion**

In this paper when calculating the GLCMs we have chosen to work with offsets similar to those used in the paper by Peter A. Freeborough and Nick C. Fox [8] in contrast to the radius method used by Rouzbeh Maani, Yee Hong Yang, Sanjay Kalra [10]. The reason we chose to work with offsets is because we wished to compare our results with [8]

lille intro :)

Start med at snakke om Normalized Erode

Sammenligne med 2D og 3D

Hvorfor er 2D bedre end 3D eller omvendt.

Overfitting

Diskutere valg af offsets og Offsets vs radius

FFS vs naive selection

På baggrund af graferne hvorfor det kan være svært at få gode res.

### **6.1 GOD SECTION TITEL**

In the previous chapter we saw the plots of our data, which are early AD patient, more specific 24-month follow-ups. As our data consists of early AD patients, it can be very difficult to differentiate one from another and thus make it challenging to get some good results.

Hvorfor, hvorfor ikke normalisere.

Diskutere Erode vs Ikke Erode

Snakke om 60/40

Plots af breaks i accuracy og ændring i k for knn

## **Chapter 7**

# **Conclusion**

# **Appendices**

## Appendix A

# Co occurrence matrix derivation features

$$C_x(i) = \sum_{j=1}^N C(i, j) \quad (\text{A.1})$$

$$C_y(i) = \sum_{i=1}^N C(i, j) \quad (\text{A.2})$$

$$C_{x+y}(k) = \sum_{i=1}^N \sum_{\substack{j=1 \\ i+j=k}}^N, \quad k = 2, 3, \dots, 2N \quad (\text{A.3})$$

$$C_{x+y}(k) = \sum_{\substack{i=1 \\ |i-j|=k}}^N \sum_{j=1}^N, \quad k=0,1,\dots,N-1 \quad (\text{A.4})$$

Where A.5 is the Angular second moment

$$f_1 = \sum_{i=1}^N \sum_{j=1}^N \{C(i, j)\}^2 \quad (\text{A.5})$$

and A.6 is the Contrast

$$f_2 = \sum_{n=0}^{N-1} n^2 \{C_{x+y}(k)\} \quad (\text{A.6})$$

and A.7 is the Correlation

$$f_3 = \frac{\sum_{i=1}^N \sum_{j=1}^n ij C(i, j) - \mu_x \mu_y}{\sigma_x \sigma_y} \quad (\text{A.7})$$

where  $\mu_x, \mu_y, \sigma_x$  and  $\sigma_y$  are the means and standard deviations of  $C_x$  and  $C_y$  respectively.

The A.8 is the Variance

$$f_4 = \sum_{i=1}^N \sum_{j=1}^N (i - \mu)^2 C(i, j) \quad (\text{A.8})$$

and A.9 is the Inverse Difference Moment

$$f_5 = \sum_{i=1}^N \sum_{j=1}^n \frac{1}{1 + (i - j)^2} C(i, j) \quad (\text{A.9})$$

and A.10 is the Sum Average

$$f_6 = \sum_{i=2}^{2N} i C_{x+y}(i) \quad (\text{A.10})$$

and A.11 is the Sum Variance

$$f_7 = \sum_{i=2}^{2N} (i - f_6)^2 C_{x+y}(i) \quad (\text{A.11})$$

and A.12 is the Sum Entropy

$$f_8 = \sum_{i=2}^{2N} C_{x+y}(i) \log(C_{x+y}(i)) \quad (\text{A.12})$$

and A.13 is the Entropy

$$f_9 = - \sum_{i=1}^N \sum_{j=1}^N C(i, j) \log(C(i, j)) \quad (\text{A.13})$$

and A.14 is the Difference Variance

$$f_{10} = \text{variance of } C_{x-y} \quad (\text{A.14})$$

and A.15 is the Difference Entropy

$$f_{11} = - \sum_{i=0}^{N-1} C_{x-y}(i) \log(C_{x-y}(i)) \quad (\text{A.15})$$

and A.16 is the Information measures of correlation

$$f_{12} = \frac{HXY - HXY1}{\max\{HX, HY\}} \quad (\text{A.16})$$

and A.17 is the Information measures of correlation

$$f_{13} = \sqrt{1 - \exp\{-2(HXY2 - HXY)\}} \quad (\text{A.17})$$

Where HX and HY are the entropies of  $C_x$  and  $C_y$  and

$$HXY = - \sum_{i=1}^N \sum_{j=1}^N C(i, j) \log\{C(i, j)\} \quad (\text{A.18})$$

$$HXY1 = - \sum_{i=1}^N \sum_{j=1}^N C(i, j) \log\{C_x(i)C_y(j)\} \quad (\text{A.19})$$

$$HXY2 = - \sum_{i=1}^N \sum_{j=1}^N C_x(i)C_y(j) \log\{C_x(i)C_y(j)\} \quad (\text{A.20})$$

# Bibliography

- [1] Dementia. <http://www.who.int/mediacentre/factsheets/fs362/en/>. Accessed: 2016 April.
- [2] Mathworks graycopros. <http://se.mathworks.com/help/images/ref/graycoprops.html>. Accessed: 2016 May.
- [3] Pearson product. [https://en.wikipedia.org/wiki/Pearson\\_product-moment\\_correlation\\_coefficient](https://en.wikipedia.org/wiki/Pearson_product-moment_correlation_coefficient). Accessed: 2016 May.
- [4] Fritz Albregtsen et al. Statistical texture measures computed from gray level cooccurrence matrices. *Image processing laboratory, department of informatics, university of oslo*, pages 1–14, 2008.
- [5] G Castellano, L Bonilha, LM Li, and F Cendes. Texture analysis of medical images. *Clinical radiology*, 59(12):1061–1069, 2004.
- [6] Anne Corbett Carol Brayne Dag Aarsland Emma Jones Clive Ballard, Serge Gauthier. Alzheimer's disease. *Lancet*, 377:1019–1031, March 2011.
- [7] Bruce Fischl, David H Salat, Evelina Busa, Marilyn Albert, Megan Dieterich, Christian Haselgrove, Andre Van Der Kouwe, Ron Killiany, David Kennedy, Shuna Klaveness, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. *Neuron*, 33(3):341–355, 2002.
- [8] Peter A Freeborough and Nick C Fox. Mr image texture analysis applied to the diagnosis and tracking of alzheimer's disease. *Medical Imaging, IEEE Transactions on*, 17(3):475–478, 1998.
- [9] Clifford R Jack, Matt A Bernstein, Nick C Fox, Paul Thompson, Gene Alexander, Danielle Harvey, Bret Borowski, Paula J Britson, Jennifer L Whitwell, Chadwick Ward, et al. The alzheimer's disease neuroimaging initiative (adni): Mri methods. *Journal of Magnetic Resonance Imaging*, 27(4):685–691, 2008.
- [10] Rouzbeh Maani, Yee Hong Yang, and Sanjay Kalra. Voxel-based texture analysis of the brain. *PloS one*, 10(3):e0117759, 2015.
- [11] John G Sled, Alex P Zijdenbos, and Alan C Evans. A nonparametric method for automatic correction of intensity nonuniformity in mri data. *Medical Imaging, IEEE Transactions on*, 17(1):87–97, 1998.

- [12] Bradley T Wyman, Danielle J Harvey, Karen Crawford, Matt A Bernstein, Owen Carmichael, Patricia E Cole, Paul K Crane, Charles DeCarli, Nick C Fox, Jeffrey L Gunter, et al. Standardization of analysis sets for reporting results from adni mri data. *Alzheimer's & Dementia*, 9(3):332–337, 2013.