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Tissue classification based on relaxation environments

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Senior Research

Tissue Classification Based on Relaxation Environments

Final Report

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Tissue Classification Based on Relaxation Environments

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Abstract

Since the advent of magnetic resonance (MR) imaging as a sound medical imaging technique there has been a need to classify the tissues in the images created. Typically the radiologist has been responsible for the evaluation of the images produced by the MRI machine. In any given MRI there exists many different types of tissues each with a certain concentration of spin densities. Each one of these tissues has a unique T_1 and T_2 decay times along with a with a unique spin density. The T_2 values are indicative of the structure of the tissue, and if the T_2 time of a particular tissue has been previously determined the type of tissue can be determined. This is useful for automatic identification of disease, tumors, or any tissue for that matter. This information is characteristic for a particular tissue across MRI platforms. When the imaging sequence is specified that keeps the time of repetition (TR) constant, the image is a T_2
weighted image. The method used in this paper, the Direct Exponential Curve Resolution algorithm (DECRA), attempts to evaluate these unique T_2 times and classify the images. Antalek and Windig (4) have shown that by using DECRA it is possible to classify images based on T_2. The goal of this experiment is to determine the weaknesses and limitations of DECRA when applied to synthetically generated images and real images obtained from a MRI machine. This method was analyzed to see if there was a possibility of improvement for future application and improvement. To test DECRA it was applied to synthetic images and real images obtained from an imager. The synthetic images where given noise to try to simulate a real image and to see how high the signal to noise ratio had to be. DECRA was able to segment the noiseless synthetic images, but began to fail as the numbers of pixels were reduced. When it was applied to real image DECRA performed well only after manual separations of the test images. DECRA has shown that it can a viable method to segment data that is related by relaxation constants.

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Tissue Classification Based on Relaxation Environments

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Introduction

Medical imaging made great strides when techniques used in analytical chemistry where applied to human tissue. This method was originally called nuclear magnetic resonance imaging, but due to the fear of the word nuclear in the title, it has been known in the medical community as magnetic resonance (MR) imaging. Since the advent of MR imaging as a sound medical imaging technique there has been a need to evaluate the images created. A radiologist is responsible for the evaluation of the images produced by a MR imaging machine. A series of images will be taken around the region of interest and the radiologist will examine them and report their findings to a physician. Typically a radiologist must interpret the results of images obtained and this method has proved invaluable and reliable in determining tissue type in humans. The human visual system is excellent at the adaptive pattern recognition required to identify tissues in medical images. The radiologist is primarily looking for variations in contrast across the image. If brain tissue is being examined and an anomaly is detected, such as a lighter or darker region, then the radiologist will then examine this area closer. This area can be a tumor, cancerous tissue, or just an imaging artifact. It is important that this region be examined closer to determine if the anomalous region is a concern. This step in the prognosis has been proved to work reliably and accurately providing many correct prognosis. What is examined in this paper is an automatic method of image segmentation that is MR machine independent. The independence of the MR machine is crucial because different machines record record images with different imaging parameters.

Background

In any given MR image there exists many different types of tissues each with a certain concentrations of hydrogen. Hydrogens can be free or attached to another molecule. The concentrations of hydrogens in a given tissue give this tissue a certain identifying characteristic. Each one of these tissues also has a unique T_1 and T_2 decay times. T_1 and T_2
times are like fingerprints of biological tissues, and the ability to accurately determine the times has encountered many problems. T_1 and T_2 are discussed later on in more detail.

A radiologist is excellent at evaluation of medical images. The question arises, what if the region is at the same contrast level as the surrounding tissue but actually is anomalous. This may not be detected in the early stages by a radiologist, but still can exist. If a human examines an image for a pattern, then why can't a computer evaluate the same images based on pattern recognition. A method for correctly automatically evaluating MR images has not proven itself to be more accurate than a radiologist.

Many obstacles stand in the way of automatic pattern matching of MR images. It is not a simple as evaluating the density of an image and stating a tissue of a certain density is always that tissue. Different MR machines produce images of different densities that are easily overlooked by a human eye but can cause false positive results in a computer. Artifacts such as chemical shift motion artifacts, magnetic field inhomgeneity, and flow (1), all lead to erroneous results when a simple density algorithm is used. The largest factor that determines the difference is the operational parameters of the MR imaging machine. A corollary would be like taking a photograph of the same scene with two cameras, with different lenses, and different film. The resultant outputs would be different images from the same scene. Without knowing all of the acquisition factors involved an accurate evaluation of the scene could not be performed. What could be accurately determined are the objects present and maybe their color.

The amount of data available from a MR image is more than just density of an image, but by the spatial nature of the data; the image is a summation of T_1 and T_2
exponential decay times. When an organic object is placed in the strong magnetic field of the MR imager machine the spin orientation changes. A smaller electrical charge causes the spins to displace from equilibrium. The times to return back to equilibrium are the T_1 and T_2 times. The T_1 is the longitudinal spin displacement due to magnetization and T_2 is the transverse displacement. In MR images there exist unique T_1 and T_2 times for every physical structure in the human body (2). The abundance of free hydrogen to bound hydrogen differs with every biological tissue. The difference in hydrogen concentrations give rise to the T_2 times and allow MR imaging to

exist (2) Table 1 shows some example times reported by Fletcher (3).

Table 1: Example times of various tissues

Tissue	T_1 (s)	T_2 (s)	ρ
CSF	0.80-20.	110-2000	70-230
White Matter	0.76-1.08	61-100	70-90
Gray Matter	1.09-2.15	61-109	85-125
Meninges	0.50-2.20	50-165	5-44
Muscle	0.95-1.82	20-67	45-80
Adipose	0.20-0.75	53-94	50-100

The longitudinal displacement is the change along the z-axis where the B_0 field is applied. The transverse displacement is the reorientation of the vector spinning around the z-axis See (1) for more information about the origin of the signal. The mathematical expression for a standard single-slice, single-echo, spin-echo sequence is as follows in equation 1.

$$s_i \alpha \sum \rho_i e^{-TE/(T_2)_i} \left(1 - e^{-TR/(T_1)_i}\right)$$

Equation 1

There TE is the echo time of the sequence, TR repetition time of the sequence ρ is the density of spins, T_1 is the spin-lattice relaxation time, and T_2 is the spin-spin relaxation time. (2,1) T_2 always less than T_1. What is being examined here are the T_1 and T_2
exponential decay constants. By keeping TR constant and varying TE the image will depend only on T_2 and not T_1 and *vice versa*. For this research images with constant TR times will be taken due to the reported noise in T_1 images reported by Windig (4)

Attempts to evaluate these unique T_1 and T_2
times have run into problems of many types of tissues having very similar decay times. Fletcher(3) has shown that it is possible to classify tissues based on a multispectral analysis using T_1, T_2, and ρ images using three dimensional histogram techniques (3). This is called multivariate image analysis (MIA) and is similar to a remote sensor using visible, ultraviolet, and infrared images to determine what is present in the scene. Fletcher (3) determined that by using three-dimensional histograms it was possible to segment tissues present in brain images.

But overlap in similar tissues also resulted in similar results in the histograms. The major difficulty is distilling the T_1 and T_2 times from equation One. The time for T_2 is encoded into equation one and a simple exponential curve-fitting algorithm will usually not work. Iterative multi-exponential methods can also be tried, but can be processor intensive and lack accuracy.

One method shown by Antalek and Windig (4) is DECRA. DECRA will resolve individual components of an image by using principle component analysis (PCA). A derivation of general case of PCA is in Appendix A. DECRA exploits the exponential nature of the data recording. When the images are recorded the TR time is held constant thereby holding T_1 constant. The following image in figure 1 shows a T_2 imaging sequence. As the TE time is increased the images become denser because of increased spin relaxation time.

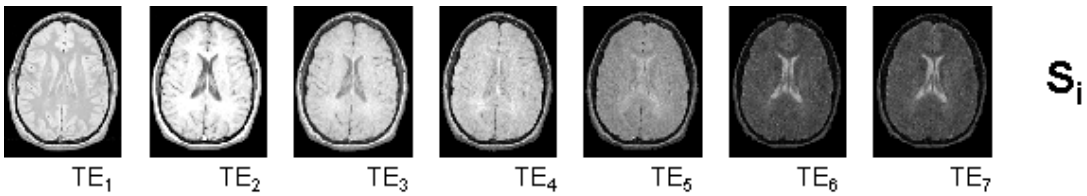

Figure 1: T_2 imaging sequence-showing variation in densities.

For this research TE was varied from times 10ms to 150ms for a total of 15 iterated images. Each image is then encoded with individual TE/T_2 times. This is accomplished by setting the imaging parameters to keep TR constant, the TE is known, leaving only T_2 to be solved. This will enable each component in each image to have a density and an exponential constant of TE incorporated into the image.

The DECRA method has shown to accurately classify and isolate T_2 times with a phantom and brain MR images. (4,3) The research done has only evaluated the algorithm with a phantom and brain images. For this research careful analysis of phantoms with known properties and biological tissues was done to further evaluate the algorithm. Another purpose of this research is to evaluate the T_2 sensitivity. DECRA was evaluated on phantoms with very similar water structures, so the sensitivity can be determined.

Theory

Operation of the DECRA algorithm

The DECRA algorithm has the name direct exponential curve resolution algorithm because it finds the exponential constants present in a series of images. A series of images each following equation 1 will be taken. The echo time, TE will be varied and the TR will be fixed. This will create a series of images where T_2 is the unknown variable. What results is a series of images similar to figure 1. This will allow for a multivariate analysis of the series, to find the principle components present. For PCA to it is required that there be data sets that are proportional. To create proportional data sets the data is split, but still remains correlated. The following Table will help to demonstrate. This table can be correlated with table 1b and the exponential assoiation can be seen.

Table 1a: Exponential constant correlation Table 1

Iteration	Exponential 1	Exponential 2
1	27	8
2	9	4
3	3	2

Table 1b: Exponential constant correlation Table 2

Iteration	Exponential 1	Exponential 2
2	9	4
3	3	2
4	1	1

The exponential constant for exponential 1 is 3 and for exponential 2 is 2. The data is separated into 2 sets but they will be correlated by their exponential constant. For this research we will be dealing with images that are correlated by the exponential decay TE/T_2. To get a correlated data set first the images are unfolded. Unfolding the data, for example, is if the image is a 256 X 256 pixel image then it is unfolded to a 1 X 65536 pixel long data set. For 15 unfolded images, it would create a large data matrix of 15 X 65536 points, which requires good computing power. The ability of DECRA to distill this large quantity of data to a few exponential curves is it's greatest attribute. Images 1-14 are data sets A and 2-15 are data sets B. These images will have related known TE times and related, but unknown T_2 times. These data sets are data sets A and B in Appendix A. The problem then becomes a generalized eigen-vector/eigen-value problem. There are more steps to deal with the non-square matrixes; these are discussed in (4). Resultant are the eigenvectors that are the T_2 exponential times given directly. Each eigenvector is a T_2
exponential constant time present in the images. This method is ideal because it does not depend on densities, but rather the actual exponentials present. The exponential values will stay the same from machine to machine making this method a potential candidate for many MR machine types.

By using principle component analysis it is possible to determine the prominent number of decaying exponential curves and the T_1 and T_2
time constants present in an image without iterative exponential curve fitting. These values are indicative of the

structure of the tissue, and if the T_2
time of a particular tissue has been previously determined the type of tissue can be determined. This research will focus on evaluating the DECRA algorithm and building upon work done previously in (4) and (5).

Methods

The Computing Path

The code that operates DECRA is written in MATLAB. MATLAB is a powerful computing environment ideal for matrix algebra operations. The code used is listed in Appendix B Attempts were made to adapt the main part of the code to run on IDL (Interactive Data Language). The finding was that IDL did not have the ability to handle multiple images as large 256 X 256 data point matrixes, but the image input and output functions of IDL are superior to MATLAB. For image manipulation such as rearranging the matrixes and cutting out unwanted portions IDL was used, for all of the computing MATLAB was used. This program is a scripting high level programming language. Many of the statistical and math functions are built in. This simplifies the use but also makes it expensive. The software version that was originally used was not the same as DECRA was created in, and a student version for the PC did not support matrixes large enough to be used. The software was originally run on a UNIX system, but because having to deal with two systems with long endian and short endian byte differences, a Macintosh G3 with 64 MB of RAM was used. The virtual drive was set to 100 MB because the computer would frequently run out of memory with 15 X 65536 large data sets. The DECRA algorithm requires ample memory and processing speed, and for future versions there will be increased need for processing power due to the possible future complexities that could be developed.

Creation and Segmentation of Synthetic Images

For this research a variety of experiments where conducted. The DECRA algorithm was tested on synthetically generated images, the synthetic images where varied in size to determine the point of failure of DECRA, and then DECRA was tested on real images.

The creation of the synthetic images will add a further understanding to DECRA. To create images that would be the same as images obtained from equation 1 above, each image needs to have a characteristic exponential encoded into it. Please see figure 2 for a schematic of this explanation. Three different exponential curves where generated for three different simulated "tissues". Each one of these curves has different relaxation constants or TE/T_2
values. The same "tissues" were then multiplied by each point in the exponential curve resulting in 15 images, one for each point in the curve. This was then repeated for the other "tissues" using different exponential relaxation constants. All of the images for each point in the curve were then summed to give 15 images composed of three components with 3 different exponential curves encoded into them. This results in a series of images that all have different densities, but are all related to the original multiplier point in curve. When the synthetic images where created then a set of the same images with randomly distributed noise added was also created. This was to test the resolving ability of DECRA when noise was added. Noise is a considerable factor when images are being obtained. The signal to noise ratio can vary significantly, and this has a large effect on DECRA

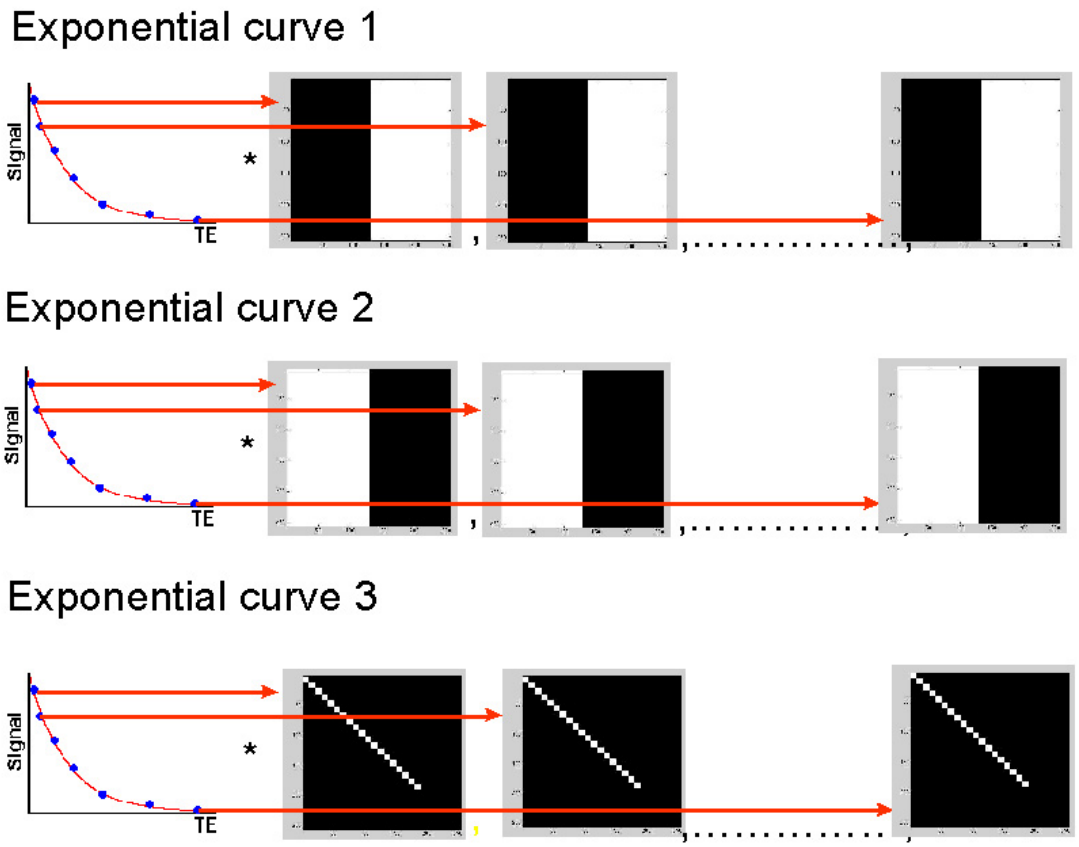

Figure 2: Schematic of encoding exponentials into synthetic images

Acquisition and segmentation of real images

It was important to test DECRA on real images. Windig et al. (5) acquired images of a human brain and determined that DECRA did have the ability to resolve T_2 values of tissues in the brain. It was thought that DECRA would have the ability to find spin densities, ρ , of hydrogen concentrations in physical structure. The objects chosen for imaging where as follows:

Water: For a base comparison

Ice: to compare to water to see if DECRA could notice a difference

Gelatin: For the free hydrogens and bonded hydrogens

Milk: for a different type of free and bonded hydrogens

Egg (uncooked): Contains a large variety of waters free and bonded

Egg (hard-boiled): to compare to the uncooked egg to see if DECRA could notice a difference

The objects where imaged on a 1.5 Mtorr GE imager at Strong Memorial hospital at a 5.0mm thickness, 12 cm field of view, TR = 1000ms, TE ranging from 10ms to 150ms in 10ms increments. The sequence used was a spin-echo sequence. 15 images where obtained each with different TE values. This is synonymous with multiplying each one of the synthetic images with a point on the exponential curve, but here the points are the different TE values. The points are like the different TE times used in this experiment. The objects where arranged according to the following diagram.

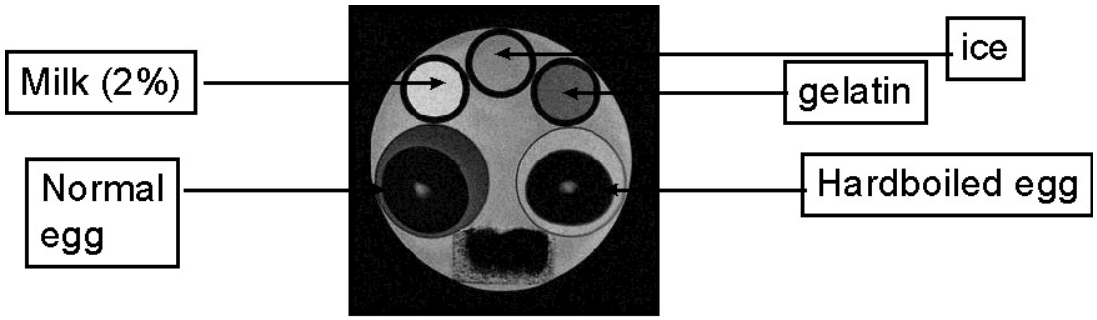

Figure 3: Arrangement of objects for imaging

Results

Segmentation of Components: Synthetic images
The synthetic images where unfolded and converted into a large 15 X 65536 point data set. This was then run through DECRA. The following is the result, which is an identical copy of the original.

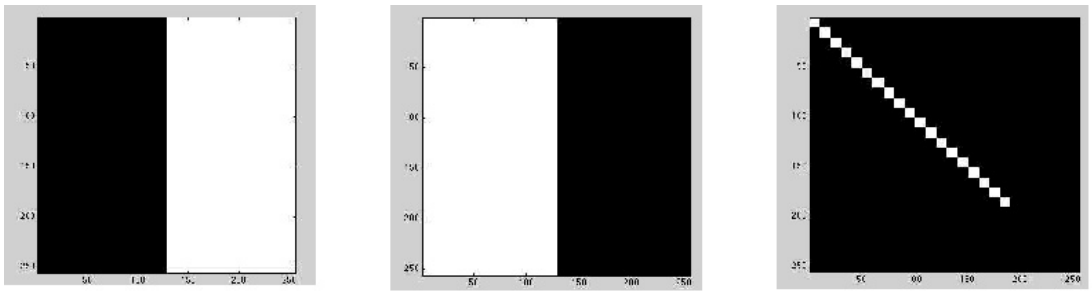

Figure 4: Results of DECRA with noiseless synthetic images.

Noise addition was then explored. The addition of uniform noise to the 15 images was to simulate noise present in a real image. When the same images where run through DECRA with noise addition the following results where obtained.

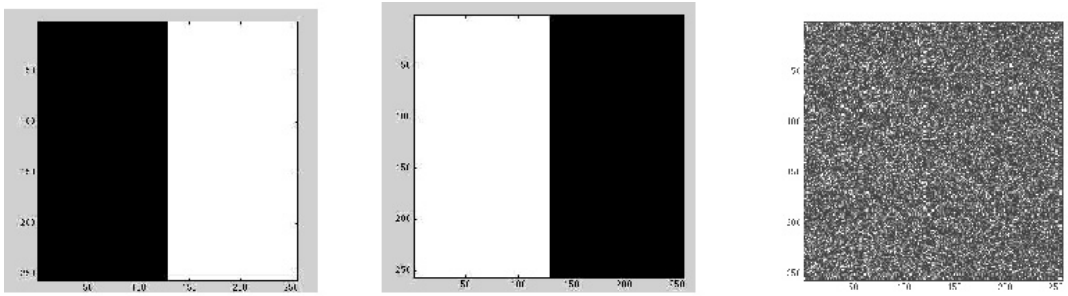

Figure 5: Results of DECRA after addition of noise to the images.

Segmentation of components: Real Images

Initially the images obtained where run through DECRA without any modification. This was to test the effect of DECRA without pre-processing of the images. The initial results showed that no useful information was derived from this action. The following is the result of having DECRA try to locate 2 components in the image sequence.

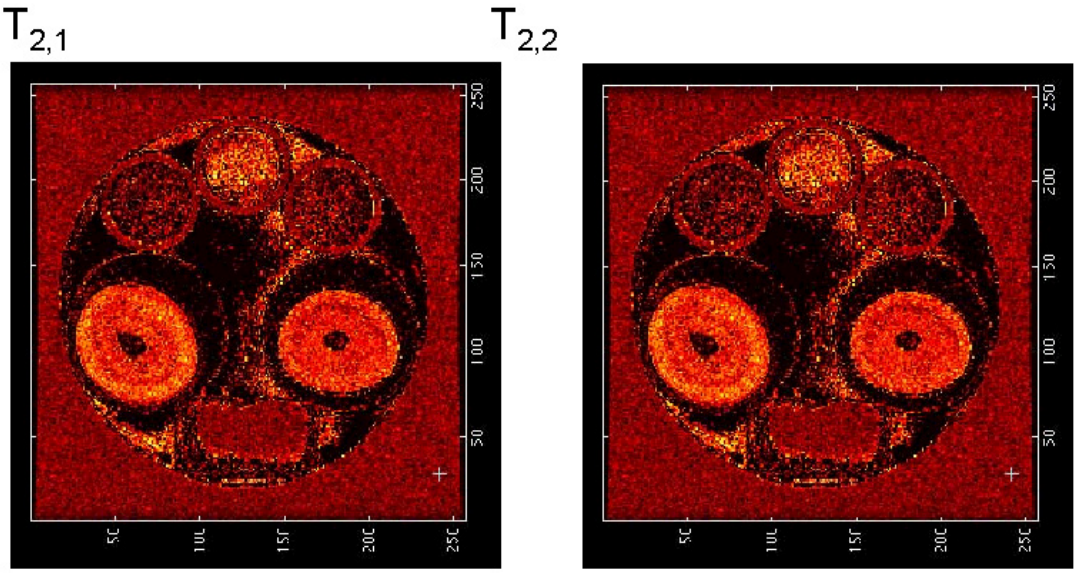

Figure 6: Initial Results of DECRA without any pre-processing

These results did not appear promising so some manual segmentation was done. Everything but the hard-boiled egg was manually removed from the image. A method to zero the background was also used. The background zero function looks in the top corner of the image and finds the maximum value there. It then makes all pixels in the image with a value less than that zero. This is to reduce the amount of noise in the image. This method assumes that there is no relevant information in the top left of the image. The following is the image that was then run through DECRA. One hardboiled egg was separated from the other objects to reduce the amount of other information in the image.

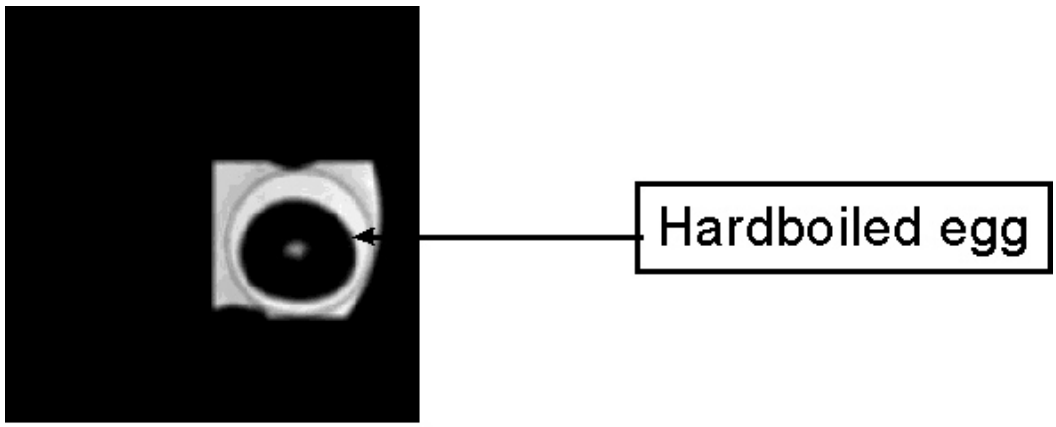

Figure 7: Manually separated image of hard-boiled egg

After running it through DECRA three components where resolved. The following images are the three resolved components.

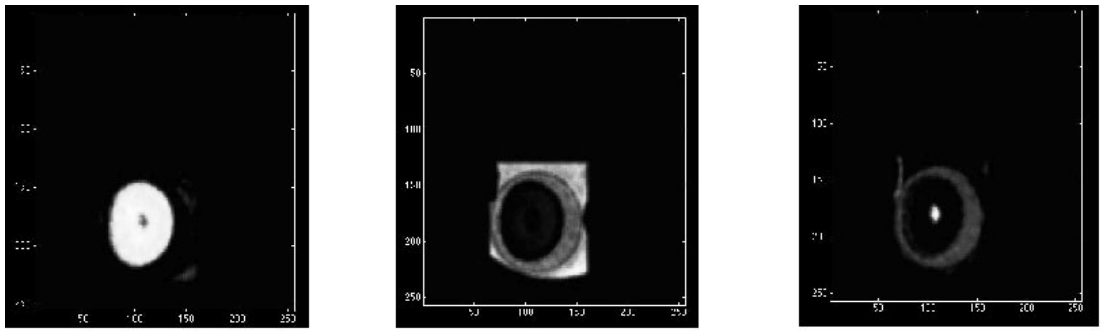

Figure 8: Three components resolved after DECRA

It was noticed that DECRA would resolve more components when there was larger portion of a particular signal available. It was then decided to cut out both eggs to see if more components could be resolved. The following is the image used with the uncooked egg on the left and the hard-boiled egg on the left

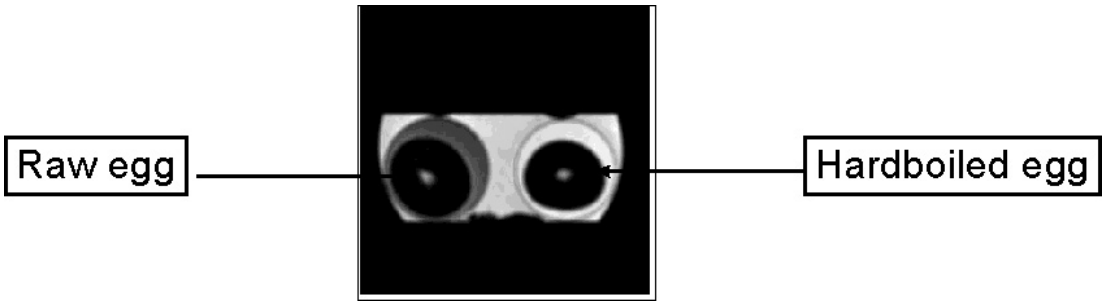

Figure 9: Manual separation of hard-boiled and uncooked eggs

The following four components where resolved using DECRA.

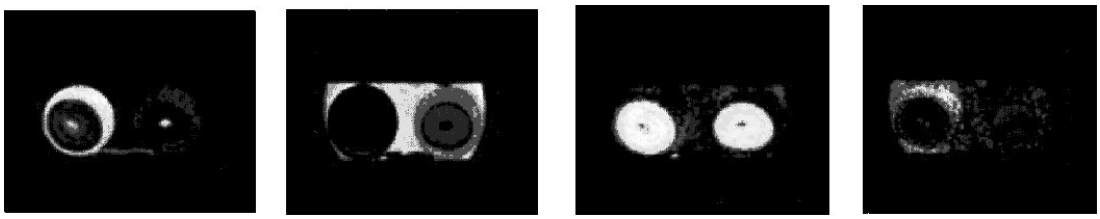

Figure 10: Four components resolved after DECRA

When DECRA was run, the number of components that are desired to be resolved is set. The limit is the number of images that are used. The components where resolved by first setting the number of components to attempt to resolve to three and then four, and then all the images that had actual exponentials where included. The resultant eigenvalues that where resolved would have an exponential decay making it possible to determine if they where actually exponentials. DECRA would also find components that where not pure components, but noise components. This information was ignored but noted.

Discussion

DECRA has shown that it has the ability to resolve individual components in an image based on T_2 values and spin density. The results of DECRA can be seen in figures 8 and 10 . In figure 8 it is possible to discern between the yolk of the hard-boiled egg and the uncooked egg. This shows that DECRA does have the ability to discern similar tissues within an image. What can be seen is that DECRA does not find every component that is present in the image series. An ideal segmentation algorithm would be able to look at an image series and find every type of tissue present in those images. DECRA could extract only three components from the single egg. What is limiting DECRA is the signal to noise ratio. As was seen in the synthetic images it is possible to perfectly identify the T_2 values with noiseless images. The synthetic images also had clusters of values surrounded entirely by zero. Real images will have small regions that will have a particular T_2 value with a neighboring pixel having a completely different value. It was seen that this signal averaging can cause more components to be resolved due to a larger signal in the signal to noise ratio. It was also notice that the increase in unlike components in one image would cause DECRA to fail and resolve nothing but noise. When the components are similar there is a larger signal from a particular tissue that can increase the resolving power. The human body has many tissues that are like and unlike that could cause problems. One solution to this would be abandoned going at the image blindly, but rather approach the problem knowing what you are looking for. For example, for a particular imaging sequence of the brain where white matter was being sought after, additional pixels with the same known white matter T_2 times could be added. They could be put in the background of the images or a border could be added enlarging the image size giving unlimited possibility to weighting of an image. This could then be repeated changing the weighting values until all possible combinations had been exhausted. This would require vast computational power for today's standards, but could be a possibility with faster computers. This was not successfully done for this paper but could be done for future work on DECRA

Addition of Noise to Synthetic images

It was determined that noise addition played a significant part in the ability of DECRA to resolve components within a series of images. It was also noticed that the sections with a larger number of pixels with the same exponential decay constants had a better resolving ability. The question was then explored as to what was the

minimum number of pixels that could be resolved in the presence of noise. An experiment was conducted to determine at what point DECRA would not resolve all of the components present, resolve one component, and resolve two components. Noise had to be added because DECRA had the ability to resolve a component that was only one pixel large. To perform the experiment an image was created with two regions, each with different exponential decay constants. As one region was reduced in the number of pixels the other became larger. This was repeated until DECRA only could resolve one component. The following graph shows the results.

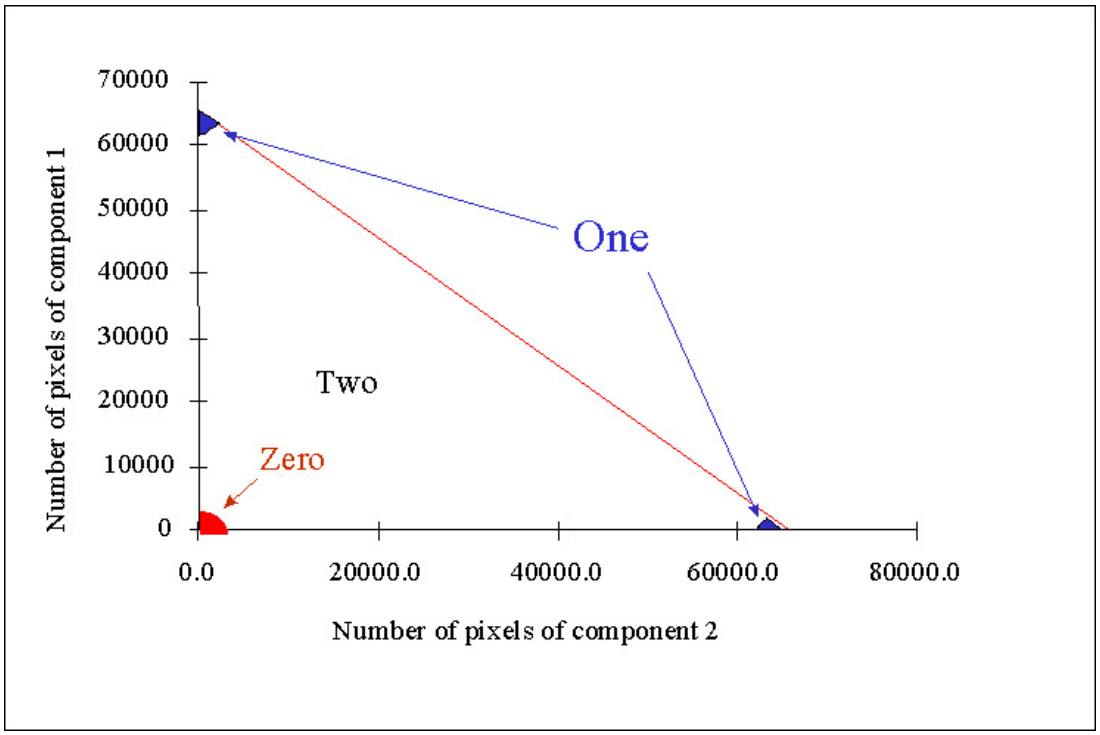

Figure 11: Results of changing number of pixels on DECRA resolving ability

The resolving ability varied greatly with the addition of noise so the noise was kept constant as in an actual MR image.

Conclusion

The DECRA algorithm has shown that it has the ability to segment synthetic images, and real images. For this research a number of experiments where tried that tried to simulate a real imaging environment. Synthetic images where generated in mind with an imaging situation that would be difficult for a human observer to detect. The synthetic images where at first made without any random noise added to see how DECRA would work in an ideal

situation. A synthetic image of only one pixel of a digital count other than 0 was tried and DECRA successfully resolved this one pixel. The method used for creation of the synthetic image is important for DECRA to function. To encode the exponential used each non-zero pixel is multiplied by a point on an exponential curve. This exponential curve is similar to the TE/T_2
exponential curve values that are encoded during the image acquisition stage. What results is a series of image arrays each one encoded with a different exponential. The data is then compiled into a very large data matrix. This matrix contains the entire series of image arrays and then it performs an eigen vector/eigen value analysis to determine the principle components of the images. The principle components resolved are the eigen values and are also the exponential relaxation constants. The exponential values are directly given eliminating curve fitting techniques andreducing the number of steps involved that may require approximations.

Noise in the images played a large part in the ability of DECRA to resolve components. It was shown that DECRA worked perfectly when no noise was present in the images. A random distribution of noise was multiplied by the image series to simulate noise in an actual MR imager. The algorithm required many more pixels to resolve components than in the noiseless images. To determine when the algorithm would not be able to resolve components a image of two components was made. The number of pixels was changed increasing the number of pixels of one component and reducing the other. This was performed until DECRA failed to find two components and only one. figure 11 reflects the effect noise can have on DECRA.

Real Images obtained proved to be a challenge. Ideally an algorithm would be able to take an image that did not have significant preprocessing done to it, and segment out all the present components. DECRA did find many components but after removing objects from the image manually until all that remained was a section that had similar components. This one egg was run through DECRA and 3 components where found. In an egg there are many more components that are where not segmented. If the egg where composed of 10 different structures and nothing other than these structures DECRA would be able to find 10 different components. The egg has many pixels that have large variations in their values, some of which is noise.

When the two eggs where run through DECRA there was a larger number of pixels that have similar values in each egg. This increases the signal/noise ratio increasing the number of components DECRA finds.

One future method could be to determine the desired T_2 values that are desired and enlarge the image weighting it with this value. This would increase the signal from this particular T_2 value, increasing the likelihood it would be found. This could be repeated for every desired tissue until a fully segmented image is made. What would first have to be determined is the pixel value or range that particular MR machine would produce for a given tissue. A calibration of a phantom with known T_2 or T_1
values could be imaged and then the pixel values would be known. These methods would all require increased processor power. For each component desired DECRA would have to be rerun, but it is one possibility for future research.

The DECRA algorithm shows great promise for a machine independent method of segmenting MR images. The possibility of being able to find cancerous tissue before the detection by a radiologist is important. DECRA has shown that it does have the ability to segment images based on their T_2 relaxation values. The segmented areas are the major areas of the image, which suggests that there can be more information in smaller pixel groupings of the image. DECRA shows great promise for the future of automated segmentation of MR images.

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Tissue Classification Based on Relaxation Environments

Jordan Guinn

List of Symbols

Symbol	Definition
PCA	principle component analysis
ρ	rho spin relaxation time
B_o	static magnetic field
DECRA	direct exponential curve resolution algorithm
MIA	Multivariate image analysis
MR	Magnetic Resonance
PCA	principle component analysis
T_1	Longitudinal magnetization relaxation time
T_2	Transverse magnetization relaxation time
TR	Time of Repetition

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Tissue Classification Based on Relaxation Environments

Jordan Guinn

Appendix A: Mathematics of the DECRA Algorithm: Derivation of a General Case of PCA

Mathematics of the DECRA Algorithm

The data set consists of 15 T_2 weighted images, each image has common T_2 values

$$A = CP^T$$

$$B = C\alpha P^T$$

A is images 1-14

B is images 2-15

$$C = A(P^T)^+$$

$$C\alpha = B(P^T)^+$$

Solve for C in each

$$C\alpha = A(P^T)^+\alpha$$

$$C\alpha = B(P^T)^+$$

$$A(P^T)^+\alpha = B(P^T)^+$$

$(P^T)^+$ = Eigenvectors
α = Eigenvalues

let $Z = (P^T)^+$

leaving:
$AZ\alpha = BZ$

This is the generalized eigenvector problem where Z contains the eigenvectors and α contains the eigen values

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Appendix B: Files Used for this Research

Files that were created for this project. All files ending with a pro extension are IDL programs, and if they end with a .m extension, then it is a MATLAB file. Very little information will be given here because most of these functions are application specific and there is nothing general about them.

cut.pro	takes an input array and cuts out hard-wired sections. It also uses the following zero function, and smoothes the image.
zero.pro	zeros out the background , or makes all values less than the greatest value in a region 10,10:10,10 equal to zero
pinv.pro	finds the pseudo-inverse of a matrix
diag.pro	takes a single column matrix and makes it a diagonal matrix
readmri.pro	reads in MR images, or any image in a raw format with no header. (automatically swaps bytes)
writemri.pro	writes out binary data, only writes integer values
autocut.pro	an example of mass production on the image set. This was done to avoid typing things over and cuts out a portion of an image
demodeim.m	DECRA algorithm in MATLAB
readimag.m	read im .skw images in MATLAB
auto2.m	Automatically reads in 15 .sk files with fixed names

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