Hybrid Segmentation of the Hippocampus in MR Images

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ABSTRACT

Segmentation and visualisation of the hippocampus can assist with early detection and intervention for a number of brain diseases. This paper describes a semi-automatic segmentation approach that produces accurate results with a significant reduction in operator effort compared with manual segmentation. A Geometric Deformable Model incorporates global constraints to solve many of the problems associated with previous methods. The results of our hybrid segmentation model show a good correspondence with manual segmentation by an expert operator.

1. Introduction

Magnetic Resonance Imaging (MRI) is a non-invasive medical imaging technology which allows physicians to examine human brain structures. With the rapidly increasing power and sophistication of computer processing, segmentation of brain structures from MR images has become more feasible.

The practical difficulties encountered in segmenting these datasets can be partitioned into "internal" and "external" categories. Internal difficulties arise from the natural complexity of brain topology. Although each MR brain image has a similar and recognizable shape, individual brains vary in size, features and other characteristics. External difficulties include image sampling artifacts, noise, and problems emanating from head movement during brain scanning. All of these make the design of an ideal segmentation method difficult to achieve, when that method should be automatic, simple, accurate, efficient, robust, repeatable, non-invasive and well- tolerated by patients.

The application of segmentation methods to specific brain anatomical structures offers the opportunity to discover abnormalities by non-invasive means. For example, various diseases may be evidenced by changes to the shape of a particular structure. Consequently, segmentation methods have potential as an aid to the diagnosis and monitoring of such diseases as multiple sclerosis, epilepsy and dementia, and may also be a tool in the development of drugs to cure such diseases.

For patients with Alzheimer's disease, it is believed that the hippocampus is one of the first regions of the brain to suffer attack. Each brain has two hippocampi. They are part of the brain's grey matter, located inside the temporal lobe and forming part of the limbic system, and they play an important part in memory.

A characteristic of the hippocampus structure is that it is surrounded by different kinds of tissue and so, in some places, it has an ill-defined border with neighbouring regions. In addition it is recognized as having a high surface to volume ratio. As a consequence of the challenges posed by these features, to date, in clinical practice, hippocampus volume analysis is still performed manually by a radiologist on a slice by slice basis. Such an approach has many drawbacks, for example, the process is labour-intensive and time consuming and the results lack consistency due to intra and inter-observer errors.

1.2 Paper overview

This paper starts with a review of current segmentation approaches and of the background to the Deformable Model method (since this is the main model in our hybrid segmentation approach). Then there is a review of previous approaches that had been proposed for hippocampus segmentation. There follows a description of the Geometric Deformable Model (GDM) that we have developed, together with a short explanation of how volume is measured from the GDM. Some initial results are presented and finally the results are discussed and future work is described.

2. Previous and Related work

Current proposed segmentation methods can be divided into 3 categories:

a) Low level segmentation - These methods are carried out by: (i) looking for similarity in brain intensity in order to detect brain regions (ii) looking for differences in brain intensity in order to detect structural boundaries.This type of segmentation includes techniques such as thresholding, region growing, edge detection, etc.

b) High level segmentation - The high level technique is an integration of geometry, physics and approximation theory and is capable of incorporating prior knowledge about the shape, location and orientation of target structures. Examples of this approach are deformable contour/curve(2D) [1] or surface/solid (3D) [2] models.

c) Hybrid segmentation - This segmentation method uses a combination of the above methods in a sequential pipeline. Previous research using this approach includes [4, 5].

2.1 Deformable Surface Model

Applications of Deformable Surface Models to segment a target object fall into two categories: a) "contour stiching" of the results of 2D deformable contours [3] and b) direct application to segment a target structure [2]. The former category suffers from branching problems due to adjacent contours having the potential for different control points on the contour. The latter category does not have these problems since it treats the dataset as a complete volume as opposed to a series of slices. The advantages of these methods include: i) the ability to incorporate *a priori* structural knowledge (such as the continuous nature of the brain and constraints on brain geometry), ii) accuracy to sub-voxel levels and iii) robustness in the presence of image intensity changes. The disadvantages of these methods include: i) the possibility of the model being trapped by local minima and ii) gap and model convergence problems.

Generally, Deformable Surface Models can be sub-divided according to two kinds of surface, namely Parametric and Discrete. Parametric deformable models can be either implicit or explicit, both examples includes: superquadratics[6], finite element[7], gradient vector flow[8], level set, wavelet[9] and spherical harmonic[10] instances. Parametric surface models can facilitate image data integration and initial model creation is generally straightforward due to the technique's basis as a mathematical formulation. However, this type of approach can only handle topologically simple objects, whereas medical image structures are typically hard to describe mathematically. This approach lacks flexibility and the necessary computational is very demanding. Discrete surface deformable models are formed by triangular mesh foam[2, 11-13] where deformation is performed by constraining the model locally at its vertices, and offers the advantage of high flexibility (many degrees of freedom).

The surface of the model is deformed according to a given function, either an energy minimization and constraint modeling function or a dynamic force system. In general, the function comprises two terms: *Internal Force* and *External Force*. The internal term aims to keep the deformable model surface smooth, holds the model surface together and prevents surface points from bending too much, while the external term aims to attract the surface to desired features in the dataset. The Deformable Surface Model approach has been shown to be effective at segmenting structures such as teeth [2] , cardiac ventricles [14] and vertebrae [13].

2.2 Previous Research in Hippocampus Estimation

A review of previous attempts to segment hippocampal structures follows.

A) Automatic segmentation

i) Based on atlas/ template wrapping[15]: A digital atlas is used as the template and the method involves "wrapping" the atlas to the MR dataset. Before the wrapping stage, the atlas images need to be registered with the MR images. Imperfect registration often contributes to errors during the volume analysis process. High-accuracy results may obtained by using high-dimensional fluid registration, incorporating several user-defined landmarks lying on the hippocampus boundary. Unfortunately, this method is limited by high costs and high computational demands.

ii) Statistical shape modelling segmentation[16-18]:This is a variant of the parametric deformable model approach. An initial model surface is created parametrically, based on a mathematical function (e.g. Spherical harmonic, Fourier surface). The model is then grown. The expansion is transformed to a set of shape descriptors that are comparable across different individuals. This approach tends not to be effective since the hippocampus structure is small and its shape is highly variable across subjects. Further, "good" statistical shape deformable models are highly reliant on a large number of training set images.

B) Semi-automated method

i) Geometric deformable model based on an expert system[19]: an initial model (triangulated surface) is created by stitching up 2D contours slice-by-slice, using landmarks found by an expert system. Segmentation is based on the energy minimization of a set of constraints (internal energy: local curvature, deformation, external energy: edge detector). The use of 2D contours to generate an initial model is highly dependent on how well the model handles branching problems due to adjacent contours having the potential for different control points on the contour. High accuracy may need an expert system based on a large group of patients.

ii) Statistical shape modelling based on affine-invariant attribute vector[20]: the initial model surface is created based on a manually labelled image. Segmentation is based on energy minimization of a set of constraints (a combination of a set of affine-invariant attribute vectors) and (in the approach described) requires approximately 200 manually-defined landmarks.

iii) Methods based on purely low level segmentation are likely to be ineffective and incapable of segmenting the hippocampus structure.

3. Hybrid Segmentation Method

3.1 Method

Our proposed method is a semi-automated hybrid segmentation method, combining both low-level image processing techniques - thresholding, hole filling (based on adjacent voxel connectivity) and distance transformation, and high level image processing techniques – application of Geometric Deformable Model (discrete surface model) in a sequential pipeline. We have developed a GDM for MRI volumetric analysis, derived from the formulation of [1, 2], but incorporating a number of modifications. This method is designed to accomodate a segmentation object surface which is homeomorphic to the sphere. In our method, the model is initialised as a structure in Euclidean 3-D space isomorphic to a sphere, made up of uniformly tessellated icosahedrons.

3.2 Our Contribution

Our hybrid segmentation method incorporating a GDM approach can overcome several problems associated with previously proposed GDM methods. Contributions of our work may be listed thus:

i) Avoidance of False Local Minima

During the energy minimization of the deformable model, the model surface will typically have several local minima. If the model vertices are trapped by local minima it will prevent its convergence to the correct final shape. A solution to this problem involves the creation of an initial model that is close to the final shape of the target structure. In medical image segmentation, because of the natural variability or the action of disease, a common initial shape is hard to define. Our proposed solution is to solve local mesh deformation problems globally. In our approach, a global shape descriptor (distance map) is incorporated to identify "fake" local minima.

ii) Treatment of Problems Associated with Gaps

The use of edge points extracted from the dataset as external forces is proposed by several researchers[14, 21]. The identification of those voxels possessing high intensity gradient functions as border voxels is often not correct, since strong edges are sometimes created by the action of noise. In addition, extracted edge points will tend to have a number of spurious and undesirable edge fragments and gaps, and this will cause the problem of mesh point leakage. In order to solve these problems, we propose a new external energy component that combines with the target object global shape information (distance map) and directional derivatives to localize the model vertices at the correct edge.

iii) Convergence Problems

If only a fine mesh is used to segment the target structure, the model may not converge, or it may require many iterations to converge to the correct target shape. Our approach of integrating a distance map with the external "force" effectively prevents the surface from stopping at the wrong edges, due to its ability to provide global shape information about the target structure. Thus, it can both guide the process of adaptive adjustment of the time step as well as enabling fine segmentation.

3.3 Processing Stages

Brain MR Images are assumed to be composed of a number of constant intensity objects in a well-separated background. It is known that the hippocampus is constructed from grey matter. From histogram data, the intensity range of grey matter can be found, which allows the use of a very simple double threshold method to remove the white matter and Cerebrospinal Fluid (CFS) detail surrounding the hippocampus. In this process, it is often the case that the selected thresholds are unable to cover some local minima or maxima, and so "holes" are created as a result. To address this problem it is necessary to use 2D, 8-neighbourhood-connectivity information to fill in the holes left from the double-thresholding process. 2D 8-neighbourhood connectivity information is used rather than 3D, 6/18/26-neighbourhood connectivity information, as the hippocampus is a very thin, small structure which is not appropriate to bigger neighbourhood connectivity. After the hole-filling process, a distance transformation technique is used to construct a distance map for each voxel to the nearest non-object voxel. Values on the distance map show that neighbouring voxels are highly corelated, internal voxels will have larger distance values. This aims to provide global information about the hippocampus at the surface deformation stage.

The operation of the GDM is based on constraint modelling and cost function minimization. Our GDM incorporates *5 constraints* which are integrated together to form a local cost function (potential function) associated with each vertex in a 3D model. The geometric model is iteratively deformed to a position that minimizes its local cost function (Equation 1) with a coarse (large time step) to fine (small time step) approach.

The local cost function $C(x,y,z)$ at the current location is given as:

$$C(x,y,z) = a0 * D(x,y,z) + a1 * F(x,y,z) + a2 * M(x,y,z) + a3 * A(x,y,z) + a4 * NN(x,y,z). \quad \text{-----} \ (1)$$

Where ao, a1, a2, a3, a4 are individual weights for the following constraints:

1) Deformation Potential: $D(x,y,z)$ This constraint generates a "force" that tends to expand the model, analogous to an inflation force acting on a balloon.

$$D(x, y, z) = (x, y, z) \quad (xo, yo, zo)$$

Where: (x,y,z) is the position of current model point. (xo, yo, zo) is the position of focal point.

2) Feature Event: $F(x,y,z)$ This constraint counteracts the deformation force. The feature event integrates the distance map with gradient information to form a robust and reliable indication of the boundary of an anatomical structure.

3) Maintaining topology: $M(x,y,z)$ This constraint tends to preserve the model surface smoothness by minimizing the local curvature between each model point and its neighbours.

$$M(x,y,z) = \frac{\left\| (x,y,z) \ \frac{1}{n} \sum_{1}^{n} x_j, y_j, z_j \right\|}{Max_{j,k} \left\| x_j, y_j, z_j \quad (x_k, y_k, z_k) \right\|}$$

Where n is the number of neighbours ofthe current model point and (x_j, y_j, z_j) & (x_k, y_k, j_k) are neighbours of current model point.

4)Angular: $A(x,y,z)$ This constraint is based on the sum of the angles that comprise the local surface and tends to keep the local mesh surface as smooth and as regular as possible, avoiding the generation of long, thin mesh triangles.

5) Non-Neighbouring Vertices Distance: $NN(x,y,z)$ In some circumstances the surface of a 3D GDM can self-intersect and this constraint is designed to counteract this effect. Non-neighbouring vertices (i.e. vertices unconnected to the current vertex) that are close to the current vertex will lead to a large constraint, preventing mesh surfaces from intersecting.

Manual stopping landmark: The hippocampus is connected with other grey matter structures (with the amagala at the "head" and caudate nucleus at the "tail"). As a result, sometimes there is no obvious boundary to characterize the small structure. Two manually defined coronal slice markers are required to limit the hippocampus from growing into other small grey matter areas at the head and the tail of the hippocampus.

Subdivision: The GDM is refined through a series of iterative steps until it converges to match the desired anatomical structure. During this process, global and local resampling is applied in order to maintain a uniform density of vertices [2, 22].

Volumetric analysis: The volume of the GDM is calculated after each stage of deformation. At each iteration, the vertices of a model face are deformed from their current positions to new positions. The projection between the current and deformed face positions can be considered as being composed of a set of tetrahedrons. The change in volume of the GDM at each iteration is calculated as the sum of the volumes of the tetrahedrons making up each face projection. This volume calculation does not depend on voxel count and is capable of sub- voxel accuracy.

4. Result

The experimental data set consists of a simulated sphere (a 64x64x64 matrix) and a well-documented set of MR T1-weighted images from an elderly patient. The MR images occupy a 182x218x182 matrix and were obtained on a Siemens 1 Tesla MRI scanner using the following scanning protocol : TR: 11.4ms; TE: 4.4ms; Flip Angle: 15 degree; Effective thickness: 1.41mm; Slab thickness: 180mm; Acquisition time: 6 minutes 7 seconds.

Figure 1 illustrates the results of segmenting a dataset containing a known spherical volume. Figure 2 demonstrates the ability of our semi-automated method of segmentation to segment the hippocampus from a real MRI dataset. A comparison between the calculated volumes obtained (a) by counting voxels and (b) as an output of our model is shown in Table 1.

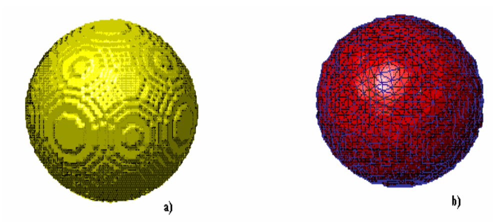

Figure 1 Segmentation of a sphere volumetric dataset: a) Rendered sphere b) extracted sphere from our model.

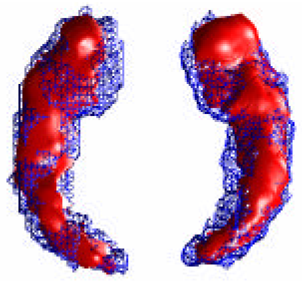

Figure 2 Overlay of coarse stage of our model (red colour) on manual segmentatuion results (blue colour)

Object	Voxel count volume	Model volume	%
Sphere	54435	54402	0.061
Hippocampus Left	1659	1786.8	7.70
Hippocampus Right	1654	1727.4	4.43

Table 1

The results in Table 1 indicate that our model produces a volume estimate that is close to that produced by voxel counting, with a particularly accurate result obtained for regular geometric shapes with clearly defined boundaries (e.g.: Sphere). For left and right hippocampi segmentation, the overlaid results shown in Figure 2 above clearly demonstrate that our coarse mesh model has a strong correspondence with the results of manual segmentation by an expert operator (blue mesh). The model volume gives a slightly larger result than the volume obtained by counting voxels in the manually segmented hippocampus. This may be due to partial mesh leakage to adjacent small grey matter regions. Incomplete coverage of some hippocampus areas is due to high surface to volume ratios in these parts. The result shows that the the difference in volume recorded by our model is within 4-8% of that recorded by manual segmentation.

5. Discussion and Future Work

We have proposed and demonstrated hybrid segmentation in a sequential pipeline, incorporating geometric deformable models and image processing techniques. Compared with semi-automated methods such as [20], our approach is significantly less user-intensive since we only need 2 manual landmarks rather than 200 manual selected control points to constraint the model. The use of a distance map has significantly improved the ability of our model to converge to a near-optimal solution (solving the energy minimization & constraint modelling problems globally), since the model tends not to be trapped in an internal region by "fake" minima. Real minima should be associated with voxels which have low values on the distance map; this is used to overcome image gap and convergence problems. Although the current model needs interactive initialization, the approach is far less user intensive than manual segmentation by radiologists in clinical practice.

Our model is currently well-suited to hippocampus segmentation for visualization purposes. Ongoing work includes applying the model to repeat MRI scans (to investigate changes in hippocampal structures over time), further refinement of volumetric accuracy and extension of the model towards fully-automatic segmentation of brain structures.

6. References

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