HIPPOCAMPUS SEGMENTATION BY OPTIMIZING THE LOCAL CONTRIBUTION OF IMAGE AND PRIOR TERMS, THROUGH GRAPH CUTS AND MULTI-ATLAS

Dimitrios Zarpalas[1,2], *Polyxeni Gkontra*[1], *Petros Daras*[1], *and Nicos Maglaveras*[2], *Senior Member, IEEE*

1: Informatics and Telematics Institute, 1st Km Thermi-Panorama Road, P.O. Box 60361, 57001 Thessaloniki, Greece. Email: {zarpalas, gkontra, daras}@iti.gr

2: Laboratory of Medical Informatics, Medical School, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece. Email: nicmag@med.auth.gr

ABSTRACT

This paper presents a new method for segmentation of ambiguously defined structures, such as the hippocampus, by exploiting prior knowledge from another perspective. An expert's experience of where to use prior knowledge and where image information, is captured as a local weighting map. This map can be used to locally guide the evolution in a level set evolution framework. Such a map is produced for every training image using Graph-cuts to calculate the most suited balance of current and prior information. Training maps are optimally adapted on the test image, through non-rigid registration, producing the Optimum Local Weighting map, which is anatomically the most suitable to this test image. Experimental results demonstrate the efficacy and accuracy of the proposed method.

Index Terms— Brain, MRI, medical image, segmentation, hippocampus, amygdala, multi-atlas, prior knowledge, level sets, boundary gradient.

1. INTRODUCTION

Segmentation of deep brain structures from MR images, such as the hippocampus, is of major importance in the study of various mental disorders, since morphological differences among healthy and diseased could be valuable disease markers. The hippocampus is located in the medial temporal lobe and is a site of structural and functional pathology in mental illnesses [7]. Manual segmentation of the hippocampus from MR images is tedious, time-consuming, susceptible to human errors, non-reproducible and expensive. These reasons constitute the motivation for developing an automatic segmentation tool.

Electronic noise, the bias field and the partial-volume effect in MR imaging cause neighboring structures of similar intensities to lack separating borders. The hippocampus-amygdala complex demonstrate this in Fig.1, since the missing and diffused boundaries between them cause erroneous segmentation.

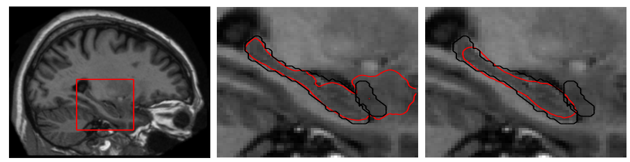


Fig. 1. (a) Brain MRI, highlighting the hippocampus and amygdala region, (b) Hippocampus segmentation with the Chan-Vese approach in red (black contour depicts the boundaries of hippocampus and amygdala), (b) Hippocampus segmentation with the Chan-Vese and variational shape prior.

Many studies have been conducted offering various techniques on hippocampus segmentation. The two major classes of methods are the multi-atlas based [12, 1, 8] and the Active Contour Models based [6, 9]. ACMs, offer a handy mathematical formulation, since implicit representation of structures and evolution through the use of level sets, can solve the correspondence problem during alignment [15]. Methods based on ACMs are broadly divided into two categories, the edge and the region-based methods. The Geometric Active Contour model (GAC) [4], one of the most popular edge-based methods, utilizes an edge-stop function. However, this method has proved inefficient for noisy images, depicting structures with weak boundaries. On the contrary, region-based ACMs use intensities' statistical information. The Chan-Vese model [5], which is based on the Mumford segmentation framework [13], is the most widely used region-based method, able to detect objects with weak boundaries. Nonetheless, for the purpose of anatomical image segmentation, both ACMs share a serious drawback: they lack anatomical information about structures undergoing segmentation. Contour evolution depends solely on current information, i.e. extracted from the test image. Addressing this, Leventon et al. presented one of the most influential works [11], by modeling anatomical information, through the use of a statistical shape-prior model, and incorporating it into the segmentation framework. The same approach was later adopted by Yang et al. in [18], and extended to include a statistical neighbor-prior model.

These methods and their descendants [20, 21, 17] mainly

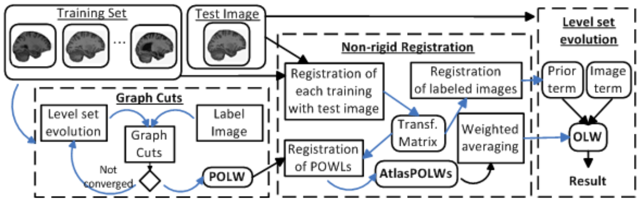


Fig. 2. The proposed method in a block diagram.

focused on ways of modeling prior knowledge, and neglected to model how a human expert would utilize his/her experience. A human expert would rather trust the image information on boundary regions with strong edges, and would use his/her experience on the regions with weak edges. Hence, a local weighting scheme seems to mimic more the human's understanding, contrary to a global one that is widely used. The first attempt to model such prior knowledge was presented in [19], where the Gradient Distribution on Hippocampus Boundary map (GDHB) was built, based on the gradient values across the boundary of the hippocampus. GDHB defines the extend one should trust the image or the prior information, at every boundary location.

In this paper, we extend the GDHB concept and present a new framework for defining a local weighting map. The empirical GDHB information is now calculated through an optimization procedure that tries to produce the most accurate segmentation on the training set, compared to the ground-truth, offering one Pseudo-Optimal Local Weighting map per training image. Each POLW is adapted on the test image, through a registration step. Merging all the adapted POLWs offers the final, actually optimal weighting map, called OLW.

2. PROPOSED METHOD

A schematic representation of the proposed method is depicted in Fig.2. For each training image, a Pseudo Optimal Local Weighting map (POLW) is defined by the use of graph-cuts, by formulating the problem of finding a POLW as a labeling problem, where labels represent the extend to which the image and prior terms contribute to the energy functional for segmentation. This map is pseudo-optimal, because the ground-truth label image is used to define the POLW. Graph-cuts minimize an energy function that imposes minimum difference between the shape resulting from the evolution of the level set for a training image at each iteration and the level set function that represents the corresponding ground-truth segmentation. Each training image is then both affine and non-rigidly registered to the test. Regarding the registration step, the demons algorithm [16] was preferred to tackle variation in a more efficient way. The resulting transformation matrix is used to further register the label images and the POLWs of the training images. Averaging the registered labeled images results to L, the spatial distribution of the hippocampus labels. A weighted average of the POLWs is computed, weighted by the similarity between the gradient of the test image and the gradient at a narrow-band around the contour of the hippocampus of the registered training image. The result is the final OLW.

The empirical spatial distribution map L, is used as prior knowledge into a level set segmentation framework, where OLW defines the optimal local balancer between the prior and the image term.

2.1. Level set framework

An evolving curve C is defined, as an implicit representation in the image domain $\Omega \in R^2$, indicating the zero level set of a signed distance function $\phi : R^2 \rightarrow \Omega$

$$C = \{(x, y) \in \Omega \mid \phi(x, y) = 0\} \tag{1}$$

where $\phi(x, y) < 0$ inside the contour C and $\phi(x, y) > 0$ outside the contour C. The evolution of curve C in the proposed method, is driven by the locally-weighted sum of the two terms; the gray-level information of the image and the prior knowledge of the spatial distribution of the hippocampus labels, which have been extracted after the registration of the labeled images.

$$E_{Im}(M) = \lambda_1 \int_{\Omega_1} M \circ |I(\mathbf{v}) - c_1^I|^2 d\mathbf{v} + \lambda_2 \int_{\Omega_2} M \circ |I(\mathbf{v}) - c_2^I|^2 d\mathbf{v} \tag{2}$$

$$E_{Pr}(M) = \mathrm{v}_1 \int_{\Omega_1} M \circ |L(\mathbf{v}) - c_1^L|^2 d\mathbf{v} + \mathrm{v}_2 \int_{\Omega_2} M \circ |L(\mathbf{v}) - c_2^L|^2 d\mathbf{v}$$

The image term is modeled as in [5] and equals E_{Im} in equations 2, where the operation $\circ$ notates the Hadamard product (in [5] M equals the identity matrix). The prior term E_{Pr} is modeled with the exact same way as the image term, but instead of working in the image domain, the map L computed by the spatial distribution of the hippocampus labels is used [19]. The total energy is then calculated through the local blending with OLW:

$$E_{Total} = E_{Im}(OLW) + E_{Pr}(1 - OLW) \tag{3}$$

Towards minimizing the total energy (equation 3), the contour's C update becomes:

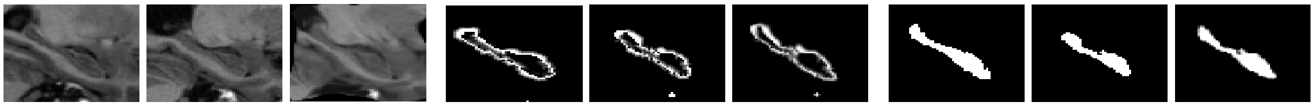
$$\begin{aligned} \frac{\vartheta\phi}{\vartheta t} &= \delta_\epsilon(\phi)\Big[\mu \operatorname{div}\left(\frac{\nabla\phi}{|\nabla\phi|}\right) - \nu \\ &-OLW \circ \left(\lambda_1(I - c_1)^2 - \lambda_2(I - c_2)^2\right) \\ &-(1 - OLW) \circ \left(\mathrm{v}_1(L - d_1)^2 + \mathrm{v}_2(L - d_2)^2\right)\Big] \end{aligned} \tag{4}$$

where I is the test image, c_1 and c_2 are the average intensities inside and outside the contour in I respectively, and similarly d_1 and d_2 for L. λ_1 and λ_2, and v_1 and v_2, balance the importance between the terms inside and outside the contour.

2.2. Calculating POLW through Graph Cuts

Graph cuts have been widely used as energy minimizers. Hereby, the Maxflow algorithm is used [3, 2, 10], to minimize an energy functional which allows the calculation of the POLW for a given training image.

In the proposed formulation, to each voxel v a label f_v corresponds. Each voxel's label f_v maps to POLW(v), i.e. the amount of contribution of the image term in the energy



(a) (b) (c) (d) (e) (f) (g) (h) (i)

Fig. 3. Non-rigid registration: (**a**) the test image, (**b**) a train image, (**c**) train image (b) registered to test image (a), (**d**) target OLW of test image (a) - unknown, (**e**) POLW of training image (b), (**f**) registered (e) to (a), (**g**) ground-truth hippocampus mask of (a) - unknown, (**h**) ground-truth of image (b), (**i**) registered (h) to (a).

model for that voxel. The range of f_v is $[0,1]$ [1], thus the amount of contribution of the prior term equals to $1 - f_v$.

Given a training image A and its corresponding label image B, which serves as the ground truth, the goal is to define an optimal labeling **f**, offering the respective POLW. That POLW, when used in the level set framework, should converge the evolution on the ground-truth. Thus, finding the optimal labeling is equivalent to minimizing an energy functional $E(\mathbf{f})$ that requires the difference between i) the resulting zero level set by the use of the calculated POLW in the segmentation framework, and ii) the zero level set extracted by the corresponding ground-truth image, to be minimum.

According to graph cut theory, the energy functional can be formulated as:

$$E(\mathbf{f}) = \sum_{v \in \mathcal{V}} D_v(f_v) + \sum_{v \in \mathcal{V}, q \in Nv} V_{v,q}(f_v, f_q) \qquad (5)$$

where $\mathcal{V}$ is the set of all voxels in A, D_v is the individual voxel cost for voxel v, and measures how well label f_v fits for voxel v given the ground-truth image. N_v denotes the set of neighboring voxels of v and $V_{v,q}(f_v, f_q)$ is the interaction potential between voxels v, q that penalizes discontinuities between neighboring voxels, thus encouraging spatial coherence.

$$D_v = \frac{\vartheta \phi}{\vartheta t}(f_v) - GT(v) \ \ , \ \ V_{p,q} = \min(K, |f_p - f_q|) \quad (6)$$

where $\frac{\vartheta \phi}{\vartheta t}$ is given by equation (4) and GT stands for the ground-truth zero level set.

2.3. Adapting POLWs through registration

Images of the hippocampus are characterized by severe variation among different subjects. It is therefore of significant importance to define an OLW that is produced by an adaptive way, instead of using a common one for all testing images. Inspired by the multi-atlas concept, we consider as atlases not only the labels of training images, but also the POLWs. These atlases-POLWs will be subsequently combined to produce a more efficient OLW for each test image based on its anatomy, as in Fig. 5(a). It should be noted that multi-atlas was preferred over one single atlas, since this choice increases the accuracy of the final result. POLWs are then registered and merged through a weighted averaging.

[1]In terms of implementation, f_v should be integer values and get $[0, 1, \ldots, 100]$, which are then divided by 100.

$$OLW = \sum_{i=1,..,n} s_i \cdot AtlasPOLW_i \qquad (7)$$

where n is the total number of training images, and s_i represents the similarity between the test image's gradient and the gradient on a narrow band around the contour of the registered training image i. The similarity measure used is the squared differences of the gradients. Fig.3 demonstrates the registration process.

3. RESULTS

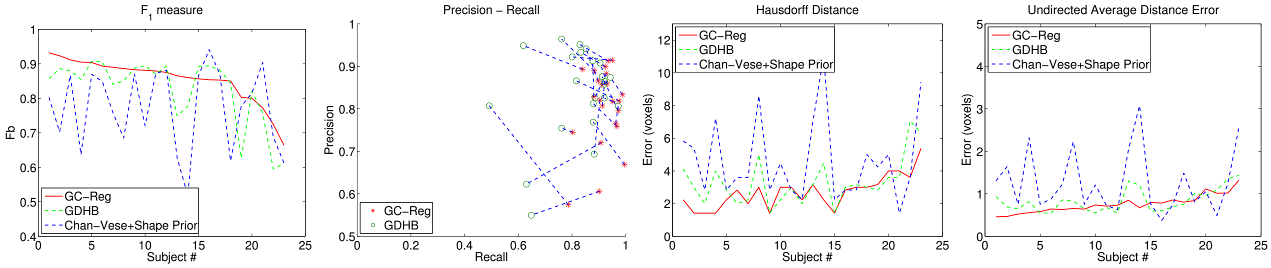
The proposed method was tested on 23 images taken from the OASIS database [14]. Ground-truth images were provided by a professional radiologist who manually segmented the 23 hippocampal volumes.

All experiments were conducted in a leave-one-out procedure at the central sagittal slice of each MRI. Our method's performance (abbreviated as GC-Reg) was evaluated by comparing with two other methods: the ancestor of this work, the GDHB method and the Chan-Vese method with variational shape prior (indexed as SP in the figures). SP indicates the performance of [18], neglecting any neighbor prior, since this work is focused purely on hippocampus segmentation. The comparison results are presented in detail in Fig.4 and overall in Table I, while the comparison metrics used are the undirected distance error, the Hausdorff distance, precision vs recall and F_1 a.k.a. Dice coefficient which measures set agreement. Visualization of the segmentation results are provided in Fig.5.

Table 1. Averaged Comparison Results

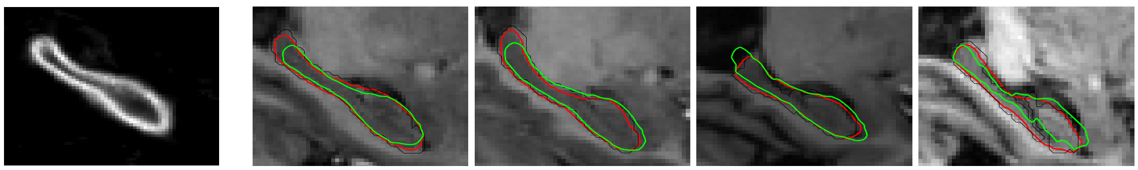
	F_1	Precision	Recall	Haussdorf	Un. Ave.
GC-Reg	**0.86**	0.81	**0.92**	**2.57**	**0.74**
GDHB	0.83	**0.84**	0.83	3.29	0.82
SP	0.77	0.82	0.76	4.65	1.26

The experimental results demonstrate the superiority of the proposed method, verified by all metrics, with the exception of precision. Even for extremely difficult cases, included in the database, the proposed method produces very good results (Fig.5(e)). Results evidently verify that local weighting alleviates the challenging task of hippocampus segmentation. In addition, the use of OLW, clearly surpasses the empirical GDHB.



(a) (b) (c) (d)

Fig. 4. In (a), (c) and (d), red line depicts the proposed method, green line the GDHB, and blue line the SP. (a) F_1/Dice Coefficient, (b) Precision-Recall (the lines connect the performance of the proposed method and the GDHB for the same subject; the more close to the upper right corner the better), (c) Hausdorff distance and (d) Undirected average distance error.



(a) (b) (c) (d) (e)

Fig. 5. (a) The OLW of (b). (b)-(e) Segmentation results: red line depicts the proposed method, green the GDHB, while black the ground-truth, for subjects 1, 4, 14, 19, respectively.

4. CONCLUSIONS

This paper proposes a novel concept for calculating Optimal Local Weighting maps by the use of graph cuts for a set of training images. The OLWs are used to achieve optimal and local balance between the region-based and prior energy terms incorporated in a serious number of segmentation frameworks presented until today, as well in ours. The OLWs of the training images are subsequently combined in an adaptive way by means of a multi-atlas approach in order to produce an OLW for the target image that fits its anatomy. The results validate the sophisticated proposed concept, while demonstrate the superiority of the proposed method.

5. ACKNOWLEDGEMENTS

The authors would like to thank the OASIS team for providing us with their dataset and give special thanks to Angelos Baltatzidis M.D., Radiologist for building the training set by performing the manual segmentations of hippocampus.

6. REFERENCES

[1] P. Aljabar, R.A. Heckemann, A. Hammers, J.V. Hajnal, and D. Rueckert, "Multi-atlas based segmentation of brain images: atlas selection and its effect on accuracy", Neuroimage, 46(3), pp. 726-38, 2009.
[2] Y. Boykov and V. Kolmogorov, "An Experimental Comparison of Min-Cut/Max-Flow Algorithms for Energy Minimization in Vision". IEEE TPAMI, 26(9), pp. 1124-1137, 2004.
[3] Y. Boykov, O. Veksler, and R.Zabih, "Efficient Approximate Energy Minimization via Graph Cuts", IEEE TPAMI, 20(12), 2001.
[4] V. Caselles, R. Kimmel, and G. Sapiro, "Geodesic active contours", International Journal of Computer Vision, 22(1), pp. 61-79, 1997.
[5] T. Chan and L. Vese, "Active contours without edges", IEEE Trans. Image Processing, vol. 10, pp. 266-277, 2001.
[6] T. F. Cootes, C. J. Taylor, D. H. Cooper, and J. Graham, "Active shape models-Their training and application", Com.Vis.Im.Und., 1995.
[7] N. DeCarolis and A. Eisch , "Hippocampal neurogenesis as a target for the treatment of mental illness: a critical evaluation", Neuropharmacology; 58(6):884-93, 2010.
[8] R.A. Heckemann, J.V. Hajnal, P. Aljabar, D. Rueckert, A. Hammers,"Automatic anatomical brain MRI segmentation combining label propagation and decision fusion", Neuroimage, 33(1), pp115-26, 2006.
[9] M. Kass, A. Witkin, and D. Terzopoulos,"Snakes: Active contour models", International Journal of Computer Vision, 1987.
[10] V. Kolmogorov and R.Zabih, "What Energy Functions can be Minimized via Graph Cuts", IEEE TPAMI, 26(2):147-159, Feb 2004.
[11] J. M. Leventon, E. Grimson, and O. Faugeras, "Statistical shape influence in geodesic active contours", Proc. IEEE Conf. Comp. Vision Pattern Recognition, 2000.
[12] F. van der Lijn, T. den Heijer , MM. Breteler, and WJ. Niessen, "Hippocampus segmentation in MR images using atlas registration, voxel classification, and graph cuts",Neuroimage, 43(4), pp.708-20, 2008.
[13] D. Mumford and J. Shah, "Optimal approximation by piecewise smooth function and associated variational problems", Communication on Pure and Applied Mathematics 42, pp. 577-685, 1989.
[14] D. Marcus, T. Wang, J. Parker, J. Csernansky, J. Morris, and R. Buckner, "Open Access Series of Imaging Studies (OASIS): Cross-Sectional MRI Data in Young, Middle Aged, Nondemented, and Demented Older Adults", Journal of Cognitive Neuroscience, 2007.
[15] S. Osher and R. Fedkiw. "Level Set Methods and Dynamic Implicit Surfaces", Springer, 2002.
[16] H. Wang, L. Dong, J. O?Daniel, R. Mohan, A. S. Garden, K.K Ang, D.A. Kuban, M. Bonnen, J.Y. Chang, and R. Cheung, "Validation of an accelerated 'demons' algorithm for deformable image registration in radiation therapy", Phys. Med. Biol. 50 (12), pp. 2887-2905, 2005.
[17] P. Yan, A.A. Kassim, W. Shen, and M. Shah, "Modeling interaction for segmentation of neighboring structures", IEEE Trans. on Information Technology in Biomedicine, vol. 13, no.2, pp. 252-262, 2009.
[18] J. Yang, L.H. Staib, and J.S. Duncan, "Neighbor Constrained Segmentation with Level Set Based 3D Deformable Models", IEEE Trans. on Medical Imaging, vol. 23(8), 2004.
[19] D. Zarpalas, A. Zafeiropoulos, P. Daras, and N. Maglaveras, "Hippocampus Segmentation using a Local Prior Model on its Boundary", International Conference on Machine Vision, Image Processing and Pattern Analysis, Venice, 2011.
[20] K. Zhang, L. Zhang, H. Song, and W. Zhou, "Active contours with selective local or global segmentation: A new formulation and level set method", Image Vision Computing, 2010.
[21] Y. Zhang, B.J. Matuszewski, L.-K. Shark, and C.J. Moore,"Medical Image Segmentation Using New Hybrid Level-Set Method", International Conference BioMedical Visualization, 2008.