

## Longitudinal guided level-sets for consistent neonatal image segmentation

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**Introduction:** Accurate segmentation of neonatal brain MR images in longitudinal MRI studies plays an important role in revealing neurodevelopmental disorders, including autism and schizophrenia. Due to poor image quality, it still remains challenging to segment neonatal brain images. Most existing methods are voxel-based and work only on the single time-point image, and thus cannot benefit from the tissue distribution information which could be provided by the late-time-point images. For example, it is relatively easy to segment the two-year-old image (or even the one-year-old image), thus the tissue distribution in the brain can be better estimated. Due to the similarity of anatomical structures of the same subject at different developmental stages, the tissue distribution estimated in the late-time-point image can thus be used to better guide tissue segmentation of the neonatal image. In this paper, we propose a novel longitudinal guided level-sets method for consistent neonatal image segmentation by combining local intensity information, atlas spatial prior, cortical thickness constraint, and longitudinal information into a variational framework. The longitudinal information is formed as a new distance constraint term. Evaluation on a number of real neonatal brain images shows very promising segmentation results.

**Method:** Our motivation is based on the fact that the global brain structures of the same subject keep similar at different developmental stages [1]. Therefore, the distance between the tissue boundaries of neonatal image and the corresponding tissue boundaries of the late-time-point image should be in a certain small range. The proposed framework consists of three steps. First, we use the adaptive fuzzy c-means (AFCM) [2] and the coupled level sets [3] to segment late-time-point image (Year2) and neonatal image (Year0), respectively. Second, based on their segmentations, we warp the segmentation image of Year2 into Year0 space using HAMMER [4]. Third, we use the warped segmentation result of Year2 to guide Year0 image segmentation. Let  $\phi_1^L$  and  $\phi_2^L$  be interfaces of WM/GM and GM/CSF of the warped Year2 image, respectively. Using Heaviside function  $H$ , we employ three level set functions  $\phi_1$ ,  $\phi_2$  and  $\phi_3$  to define regions  $M_1 = H(\phi_1)H(\phi_2)H(\phi_3)$ ,  $M_2 = (1 - H(\phi_1))H(\phi_2)H(\phi_3)$ ,  $M_3 = (1 - H(\phi_2))H(\phi_3)$ , and  $M_4 = 1 - H(\phi_3)$ , to represent WM, GM, CSF and background, respectively. Therefore, the distance between the zero-level-surfaces of  $\phi_1$  (or  $\phi_2$ ) and  $\phi_1^L$  (or  $\phi_2^L$ ) should be in a certain small range. Let the allowed range be  $[d_1, D_1]$  with  $d_1 < 0$  and  $D_1 > 0$ . We can define the longitudinal constraint term for  $\phi_i$  as:  $E_{long}(\phi_i) = [1 - (H(\phi_i^L - d_1) - H(\phi_i^L - D_1))] \left[ (H(\phi_i^L - d_1) - H(\phi_i))^2 + (H(\phi_i^L - D_1) - H(\phi_i))^2 \right]$ . To utilize the cortical structural information which has a nearly consistent thickness  $[d, D]$  (with  $d > 0$  and  $D > 0$ ), cortical thickness constraint terms can be defined for  $\phi_1$  and  $\phi_2$ , respectively, as:  $E_{dist}(\phi_1) = [1 - (H(\phi_2 - d) - H(\phi_2 - D))] \left[ (H(\phi_2 - d) - H(\phi_1))^2 + (H(\phi_2 - D) - H(\phi_1))^2 \right]$ ,  $E_{dist}(\phi_2) = [1 - (H(\phi_1 + D) - H(\phi_1 + d))] \left[ (H(\phi_1 + d) - H(\phi_2))^2 + (H(\phi_1 + D) - H(\phi_2))^2 \right]$ . We employ the local Gaussian distribution fitting with atlas prior  $p_{prior_i}$  as a data driven term,  $E_{L\_Prior} = \int \left( \sum_{i=1}^4 \int -\omega_\sigma(x - y) \log(p_{prior_i}(y)p_{i,x}(I(y)M_i)dy) dx + \nu \sum_{i=1}^3 \int |\nabla H(\phi_i(x))| dx \right)$ . Note that  $p_{prior_i}$  is a subject-specific atlas [1], constructed from the warped brain tissue distribution of Year2. Finally, we can define the longitudinal guided level-sets energy as follows,

$$F = E_{L\_Prior} + \alpha(E_{dist}(\phi_1) + E_{dist}(\phi_2)) + \beta(E_{long}(\phi_1) + E_{long}(\phi_2))$$

where  $\alpha$  and  $\beta$  are the bending parameters. Note that in the previous methods, the distance constraint terms were typically defined explicitly and incorporated into the gradient descent flows. In contrast, the proposed energy is derived as a minimization problem in a variational framework.

**Result:** Our method has been tested on 8 real neonatal brain images. Two representative subjects are shown in the first column of Fig. 1, with manual segmentations shown in the last column. The results of Shi et al.'s method [1] without using surface model, Wang et al.'s method [3] without using longitudinal information, and the proposed method using both surface model and longitudinal information are shown in the columns 2, 3 and 4, respectively. Zoomed portion of the segmentation results is shown in each sub-figure for better visual inspection. Fig. 2 shows the 3D rendering of WM/GM surfaces for a randomly-selected subject, with the Year2 surface shown in the last column. From the zoomed views in the two bottom rows, it can be clearly seen that there exist holes and handles in the results of Shi et al. and Wang et al.'s methods, while the results of the proposed method are more reasonable and more consistent with the Year2 results. Taking the manual segmentation as ground truth, we conduct a quantitative comparison on all 8 subject images. We use the Dice ratio (DR), defined as  $DR = 2|A \cap B| / (|A| + |B|)$ , to measure tissue overlap rate for manual segmentation  $A$  and automatic segmentation  $B$ . The DR ranges from 0 to 1, and the larger it is, the better the segmentation. The mean and standard deviation of DR values of the WM and GM achieved by the proposed method are  $(0.94 \pm 0.01, 0.92 \pm 0.01)$ , compared to  $(0.87 \pm 0.02, 0.86 \pm 0.02)$  by Shi et al.'s method [1] and  $(0.91 \pm 0.02, 0.89 \pm 0.02)$  by Wang et al.'s method [3]. The comparison demonstrates the advantage of the proposed method in accurately segmenting neonatal brain images.

**Discussion:** We have proposed a novel longitudinal guided level-sets method for consistent neonatal image segmentation. The longitudinal information is utilized as a new distance constraint term. Compared to the previous methods with the similar distance constraint terms, the minimization of proposed energy in this paper is strictly derived from a variational principle. The proposed method has been validated on a number of real neonatal brain images with very promising results.

**References:** [1]. Shi, F., et al., NeuroImage, 49(1) (2010) 391-400. [2]. Pham, D.L. and Prince, J.L., IEEE Trans. Med. Imaging, 18(9) (1999) 737-752. [3]. Wang, L., et al., MIAR, (2010) 1-10. [4]. Shen, D. and Davatzikos, C., IEEE Trans. Med. Imaging, 21(11) (2002) 1421-1439.

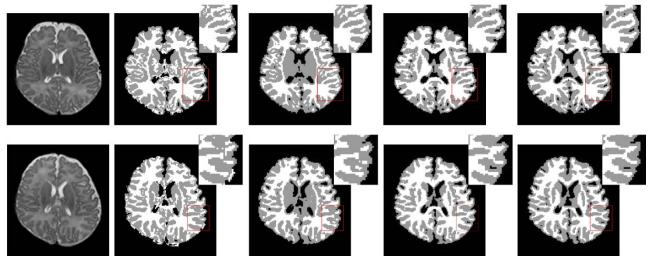


Fig. 1. Segmentation results on two representative subjects. Left to right: original T2 images, results of Shi et al. [1], Wang et al. [3], the proposed method, and the ground truth.

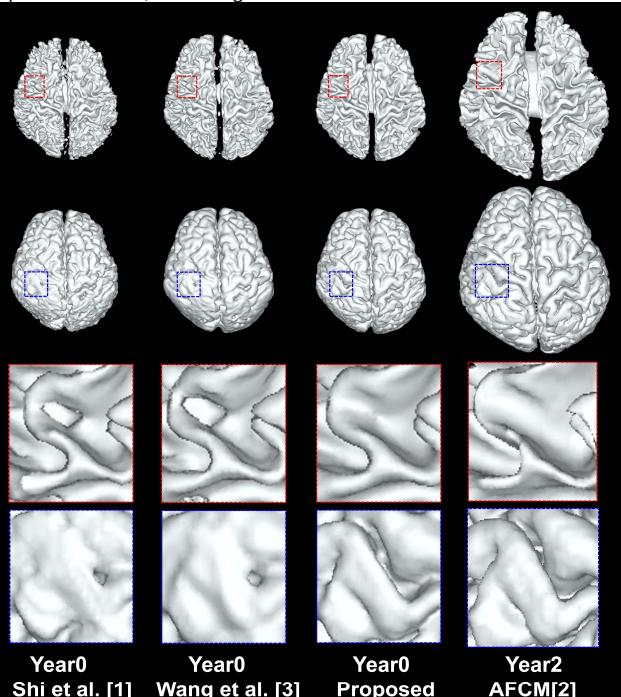


Fig. 2. 3D rendering of WM/GM surfaces on the real subject. The last two rows show the zoomed views of the first two rows.