

A Variational Approach to Simultaneous Image Segmentation and Bias Correction

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Abstract—This paper presents a novel variational approach for simultaneous estimation of bias field and segmentation of images with intensity inhomogeneity. We model intensity of inhomogeneous objects to be Gaussian distributed with different means and variances, and then introduce a sliding window to map the original image intensity onto another domain, where the intensity distribution of each object is still Gaussian but can be better separated. The means of the Gaussian distributions in the transformed domain can be adaptively estimated by multiplying the bias field with a piecewise constant signal within the sliding window. A maximum likelihood energy functional is then defined on each local region, which combines the bias field, the membership function of the object region, and the constant approximating the true signal from its corresponding object. The energy functional is then extended to the whole image domain by the Bayesian learning approach. An efficient iterative algorithm is proposed for energy minimization, via which the image segmentation and bias field correction are simultaneously achieved. Furthermore, the smoothness of the obtained optimal bias field is ensured by the normalized convolutions without extra cost. Experiments on real images demonstrated the superiority of the proposed algorithm to other state-of-the-art representative methods.

Index Terms—Bias field, computer vision, energy minimization, image segmentation, variational approach.

I. INTRODUCTION

INTENSITY inhomogeneity caused by imperfection of imaging devices and subject-induced susceptibility effects can lead to serious misclassifications by intensity-based segmentation algorithms [1]–[4]. Statistically, misclassification is caused by the prolonged tail of the intensity distribution of each object, so that it is difficult to extract each object accurately based on their intensities. Intensity inhomogeneity often exists in images obtained by different modalities,

such as ultrasound, X-ray radiography/tomography, and magnetic resonance imaging (MRI). The inhomogeneity in MRI is mainly caused by nonuniform magnetic field produced by radio frequency coils as well as from object susceptibility. Intensity inhomogeneity is particularly severe in high field (e.g., 3T) MRI and ultra high field (e.g., 7T) MRI, which challenges quantitative image analysis algorithms, such as segmentation and registration [5]. Therefore, intensity inhomogeneity correction is usually a prerequisite before applying quantitative algorithms.

Intensity inhomogeneity is usually ascribed to a smooth and spatially varying field multiplying the true signal of the same object in the measured image. This spatially varying smooth field is named as bias field. Bias correction is a procedure to estimate the bias field from the measured image to reduce its side effect [1]. Existing bias correction approaches can be categorized into two categories, namely prospective [6]–[9] and retrospective [1], [2], [10]–[21] approaches. Prospective methods aim at calibrating and improving image acquisition processing by applying specific hardware or devising special imaging sequences. However, these methods cannot correct patient-induced inhomogeneity [5], [18]. Comparatively, retrospective methods only rely on the acquired images and sometimes some prior knowledge. Thus, they are relatively more general, and can be used to correct patient-induced inhomogeneity from different sources. The retrospective methods can be further categorized into several categories based on filtering [4], surface fitting [19], histogram [20], and segmentation [1], [2], [14]–[17], [22].

Among various retrospective methods, segmentation based ones are most attractive, since they unify segmentation and bias correction under a single framework to benefit from each other, simultaneously yielding better segmentation and bias correction results. In these methods, parameter model based on the maximum-likelihood (ML) or maximum a posteriori (MAP) probability criterion is often used, in which the corresponding parameters are often estimated by the expectation maximization (EM) algorithm [14], [15], [21], and [23]. However, an appropriate initialization of the EM algorithm is critical to such algorithms, which requires either a close estimate of the bias field or a coarse segmentation [22]. Manual selections of seed points for each class are often used [21], but it is subjective and irreproducible [5], [22]. In addition, since the intensity probability models in [14], [15], [19]–[21], and [23] do not exploit information of neighboring pixels belonging to the same class, the segmentation results are often sensitive to noise and the tissue borders may not be smooth [5]. Markov

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random fields (MRF) model can yield improved segmentation results that are less sensitive to noise [24], [25].

Recently, Li *et al.* [2] proposed a parametric method for simultaneous bias field correction and segmentation by minimizing a least square energy functional. The bias field is modeled as a linear combination of a set of orthogonal polynomial basis functions [15], [22]. Although this leads to a very smooth bias field, some bias fields cannot be well fitted by polynomials, such as the bias field in 7T MRI [1], [17]. Moreover, each pixel is assigned to one tissue class. However, intensities of the partial volume voxels are composed of multiple class intensities in images, and the proportion of the partial volume voxels in low-resolution datasets can be up to 30% [22]. Thus, the calculated bias field may be partially wrong. Li *et al.* [17] proposed a variational level set (VLS) approach [26], [27] to simultaneous segmentation and bias correction. However, this method needs to alternatively iterate two partial differential equations, which is very time-consuming. Furthermore, the energy functional in the VLS method is not convex in the set of characteristic functions, making it easy to be trapped into local minima [28].

This paper presents a novel variational approach to simultaneous bias correction and segmentation. By exploiting local image redundant information, we define a mapping from original image domain to another domain so that the intensity probability model is more robust to noise. We then define an ML energy functional based on the intensity distributions in each local region in the transformed domain, which combines the bias field, the membership function of each object region, and the constant approximating the true signal from its corresponding object. Finally, the ML energy functional is extended to the whole image domain, which we call the criterion of maximum likelihood in transformed domain (MLTD). The MLTD criterion achieves a global minimum with respect to each of its variables. Moreover, analysis of the MLTD criterion shows that it is a soft classification model, which assumes that each pixel intensity belongs to more than one class, while the hard classification assigns the intensity of each pixel to only one class. Therefore, the MLTD criterion obtains a better corrected bias field. In addition, the recently proposed CLIC criterion [1] can be viewed as a special case of the MLTD criterion, while the MLTD is more accurate to model inhomogeneous image intensity.

The rest of this paper is organized as follows. Section II introduces research background and related works. Section III presents the proposed algorithm in detail. Section IV shows extensive experimental results and Section V concludes the paper.

II. BACKGROUND AND RELATED WORKS

A. Statistical Model of Intensity Inhomogeneity

Let Ω be image domain; $I(x) : \Omega \mapsto \mathfrak{R}$ be a given image; $b(x) : \Omega \mapsto \mathfrak{R}$ be an unknown bias field; $J(x) : \Omega \mapsto \mathfrak{R}$ be a true signal to be restored; and $n(x) : \Omega \mapsto \mathfrak{R}$ be noise. We consider the following model of intensity inhomogeneity [5]:

$$I(x) = b(x)J(x) + n(x). \quad (1)$$

Suppose that there are N ($N = 2$ or 4 which is fixed in our experiments) objects in the image domain Ω , and Ω_i denotes the i th object domain which will be evolved over iterations. The true signal $J(x)$ is often assumed to be piecewise constant within each object domain, i.e., $J(x) = c_i$ for $x \in \Omega_i$, where c_i is a constant. The bias field b is often assumed to be smooth in the image domain Ω . Noise n is assumed to be Gaussian distributed with zero mean and variance σ_n^2 in the image domain [29]. Thus, the distribution of image intensity can be approximated to be Gaussian with mean bJ and variance σ_n^2 . However, using only one Gaussian distribution is not accurate enough to describe the statistical characteristic of image intensity. Often multiple Gaussian probability distributions are adopted to model the image intensity distribution, with each distribution modeling the image intensity in each object domain. The distribution corresponding with the domain Ω_i is [30], [31]

$$p(I(y)|\alpha_i) = \frac{1}{\sqrt{2\pi}\sigma_i} e^{-\frac{(I(y)-\mu_i(x))^2}{2\sigma_i^2}}, \quad x, y \in \Omega_i \quad (2)$$

where $\mu_i(x)$ is the spatially varying mean, σ_i is the standard deviation, and $\alpha_i = \{c_i, \sigma_i\}$ is the parameter set of the distribution. Since bias field b varies slowly, it can be assumed to be a constant in a small window [1], and we can assume that $\mu_i(x) \approx b(x)c_i$. Note that the standard deviation σ_i is modeled as a spatially varying function in [30] and [32]. Although [32] has demonstrated good performance for segmentation of images with intensity inhomogeneity by using a single level set method [33]–[35], we utilize a piecewise constant σ_i in each region because the spatially variation σ_i may be unstable due to its local characteristic [30].

B. Related Works

In [1], a coherent local intensity clustering (CLIC) model is proposed for simultaneous segmentation and bias correction. For each point $x \in \Omega$, we define a local region $O_x = \{y : |y - x| \leq \rho\}$ with radius ρ . The true signal $J(x)$ in each region Ω_i is approximated to be a constant c_i . Since the bias function b varies slowly, it can also be approximated as a constant in a local region $O_x \cap \Omega_i$. Therefore, we have

$$b(y)J(y) \approx b(x)c_i, \quad y \in O_x \cap \Omega_i. \quad (3)$$

Hence, $b(x)c_i$ is the cluster center for the intensities in the neighborhood $O_x \cap \Omega_i$. A clustering criterion functional is proposed in which a weight function $w(y - x)$ is introduced to measure the similarity of each pixel intensity $I(y)$ to its cluster center $b(x)c_i$: the weight at position y far from its cluster center x is smaller than the nearby ones, meaning its intensity has less similarity than those near the center. The clustering criterion function is defined as

$$E_x^{\text{local}}(u, c, b(x)) = \sum_{i=1}^N \int_{O_x} u_i^q(y) w(x - y) |I(y) - b(x)c_i|^2 dy \quad (4)$$

where q is a positive integer, N is the assumed number of regions, u_i is the indicator function for region Ω_i ,

$u = \{u_i, i = 1, \dots, N\}$, and $c = \{c_i, i = 1, \dots, N\}$. $w(\cdot)$ in (4) is a weight function defined as

$$w(x) = \begin{cases} \frac{1}{a} e^{-\frac{|x|^2}{2\sigma^2}}, & |x| \leq \rho \\ 0, & \text{else} \end{cases} \quad (5)$$

where a is a normalization constant. Then, (4) is extended to the whole domain Ω that defines the following CLIC energy functional:

$$E_{u,c,b}^{\text{CLIC}}(u, c, b) = \int_{\Omega} \sum_{i=1}^N \int_{O_x} u_i^q(y) w(x-y) |I(y) - b(x) c_i|^2 dy dx. \quad (6)$$

Then, the objective is to minimize $E_{u,c,b}^{\text{CLIC}}$ with respect to the membership function set u (for any set X , a membership function on X is any function from X to the real unit interval $[0, 1]$), true signal set c and bias field b subject to the constraints $u_i \geq 0$ and $\sum_{i=1}^N u_i = 1$.

Recently, Li *et al.* [17] proposed a VLS method for simultaneous segmentation and bias correction with application to MRI. They defined an energy functional similar to (6) but the argument of the indicator function is level set function as follows:

$$E_{\Phi,c,b}^{\text{VLS}} = \int_{\Omega} \sum_{i=1}^N \int_{\Omega} M_i(\Phi(y)) w(x-y) |I(y) - b(x) c_i|^2 dy dx \quad (7)$$

where Φ is the level set function set, and $\Phi = \{\phi\}$ when $N = 2$ for binary-phase segmentation and $\Phi = \{\phi_1, \phi_2\}$ when $N = 4$ for four-phase segmentation. $M_i(\cdot)$ is the indicator function for the region Ω_i , whose argument is the level set function. Then, the signed distance penalized energy functional and zero level set length energy functional are added into (7) to regularize the level set function, and the final level set evolution equation with respect to the i th level set function ϕ_i is as follows:

$$\frac{\partial \phi_i}{\partial t} = - \sum_{j=1}^N \frac{\partial M_j(\Phi)}{\partial \phi_i} e_j + \nu \delta(\phi_i) \text{div} \left(\frac{\nabla \phi_i}{|\nabla \phi_i|} \right) + \lambda \text{div} \left(\left(1 - \frac{1}{|\nabla \phi_i|} \right) \nabla \phi_i \right) \quad (8)$$

where $e_i(x) = \int_{\Omega} w(y-x) |I(x) - b(y) c_i|^2 dy$, “div” is the divergence operator, $\delta(\cdot)$ is a Dirac function and λ, ν are fixed positive constants.

III. OUR METHODOLOGY

A. Principle of the Proposed Method

Let us revisit the probability density function (PDF) of the intensity $I(y)$ represented by (2). For the clustering center point x , we define a mapping $T : I(x|\alpha_i) \mapsto \bar{I}(x|\alpha_i)$ from original image intensity domain $D(T)$ to another domain $R(T)$ as follows:

$$\bar{I}(x|\alpha_i) = \frac{1}{m_i(x)} \sum_{y \in \Omega_i \cap O_x} I(y|\alpha_i) \quad (9)$$

where $m_i(x) = \|\Omega_i \cap O_x\|$ is area size of the intersection region. The intensity of pixel x is assumed to be independently

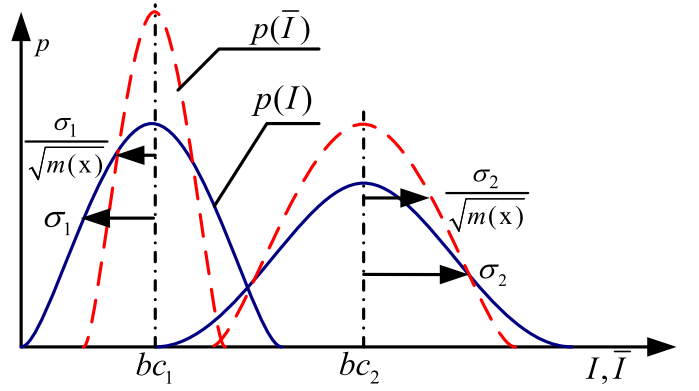


Fig. 1. Distributions of adjacent regions in the original image intensity domain (blue solid curves) and the transformed domain (red dashed curves).

distributed [36]. Thus, for all $\bar{I}(x|\alpha_i) \in R(T)$, the corresponding PDF is still a normal distribution, i.e., $\bar{I}(x|\alpha_i) \sim \mathcal{N}(\mu_i, \sigma_i^2/m_i(x))$. Refer to the red dashed curves in Fig. 1, the overlapping tails of the distributions are suppressed to some extent. Therefore, the misclassification caused by the overlapping intensity can be alleviated to some extent in the transformed domain $R(T)$. In the following, we will design our energy functional on the domain $R(T)$ by means of the well-defined relationship between domain $D(T)$ and $R(T)$.

Since intensity inhomogeneity manifests itself as a smooth intensity variation across the image [5], we can assume $I(y|\alpha_i) \approx I(x|\alpha_i)$, for all $y \in \Omega_i \cap O_x$. Furthermore, since the product of several Gaussian PDFs is still Gaussian, we have

$$\prod_{y \in \Omega_i \cap O_x} p(I(y|\alpha_i)) \approx p(I(x|\alpha_i))^{m_i(x)} \propto \mathcal{N} \left(\mu_i, \frac{\sigma_i^2}{m_i(x)} \right). \quad (10)$$

Let $X = \{\bar{I}_i, i = 1, \dots, N\}$ (we denote $\bar{I}(x|\alpha_i)$ as \bar{I}_i for convenience) where the elements $\bar{I}_1, \bar{I}_2, \dots, \bar{I}_N$ are mutually independent. Since $\bar{I}(x|\alpha_i) \sim \mathcal{N}(\mu_i, \sigma_i^2/m_i(x))$, we have the following likelihood function:

$$p(X|\alpha) = \prod_{i=1}^N p(\bar{I}_i|\alpha_i) \propto \prod_{i=1}^N \prod_{y \in \Omega_i \cap O_x} p(I(y|\alpha_i)) \quad (11)$$

where $\alpha = \{\alpha_i, i = 1, \dots, N\}$.

When $p(\alpha)$ is uniform or flat, (11) can be rewritten as $p(X|\alpha) = p(\alpha|X)$. So we can define the conditional cost energy functional with the MLTD as $E^{\text{MLTD}}(\alpha|X) = -\log(p(\alpha|X)) = -\log(p(X|\alpha))$. Putting (11) into $E^{\text{MLTD}}(\alpha|X)$, we obtain the following formula:

$$E^{\text{MLTD}}(\alpha|X) = \text{constant} - \sum_{i=1}^N \sum_{y \in \Omega_i \cap O_x} \log(p(I(y|\alpha_i))). \quad (12)$$

The constant term can be eliminated, and by taking into account all $x \in \Omega$, the total cost energy functional is formulated as follows:

$$E^{\text{MLTD}}(\alpha) = \int_{\Omega} E^{\text{MLTD}}(\alpha|X) p(x) dx \triangleq - \sum_{i=1}^N \int_{\Omega} \int_{\Omega_i \cap O_x} \log(p(I(y|\alpha_i))) dy p(x) dx. \quad (13)$$

By setting $p(\Omega_i) = 1/N$ [37], we have $p(x) = 1/N$. Then $E^{\text{MLTD}}(\alpha)$ can be rewritten as

$$E^{\text{MLTD}}(\alpha) = -\frac{1}{N} \sum_{i=1}^N \int_{\Omega} \int_{\Omega_i \cap O_x} \log(p(I(y|\alpha_i))) dy dx. \quad (14)$$

Let $\chi_{\rho}(y,x)$ and $u_i(y)$ be the membership functions of regions O_x and Ω_i , respectively, such that

$$\chi_{\rho}(y,x) = \begin{cases} 1, & |y-x| \leq \rho \\ 0, & |y-x| > \rho \end{cases} \quad (15)$$

$$\sum_{i=1}^N u_i(y) = 1, \text{ for all } y \in \Omega \quad (16)$$

where $0 \leq u_i(y) \leq 1$. With (2), (15) and (16), (14) can be rewritten as

$$E_{c,u,\sigma,b}^{\text{MLTD}} = \frac{1}{N} \sum_{i=1}^N \int_{\Omega} \int_{\Omega} \chi_{\rho}(y,x) u_i(y) \left(\frac{\log(\sqrt{2\pi}\sigma_i)}{+\frac{(I(y)-b(x)c_i)^2}{2\sigma_i^2}} \right) dy dx \quad (17)$$

where $c = \{c_1, \dots, c_N\}$, $u = \{u_1, \dots, u_N\}$, and $\sigma = \{\sigma_1, \dots, \sigma_N\}$. $E_{c,u,\sigma,b}^{\text{MLTD}}$ is convex with respect to each of its variables while fixing other ones and thereby we can efficiently obtain the closed form of solution for each variable. However, $E_{c,u,\sigma,b}^{\text{MLTD}}$ is a nonconvex function with respect to all of its variables. Thus, the final results may depend on the initial variables. In Section IV-A, we will show that the above objective function has less dependence on the different initializations of the variables (see Fig. 2).

Furthermore, we adopt the total variation (TV) of the membership function to regularize the membership function

$$E_{c,u,\sigma,b}^{\text{RMLTD}} = E_{c,u,\sigma,b}^{\text{MLTD}} + \gamma \sum_{i=1}^N \int_{\Omega} |\nabla u_i(x)| dx. \quad (18)$$

The above model is termed as regularized MLTD (RMLTD) model.

Remark 1: Our approach is essentially different from the methods proposed by Brox and Cremers [38], Paragios and Deriche [39], Wang *et al.* [32], and Zhan *et al.* [40]. In Brox *et al.* [32]'s method, their energy functional has a single integral which simply uses spatially varying means and variances instead of constant means and variances in the energy functional defined by [36]. However, our energy functional has a double integral with varying means and piecewise constant variances. Brox *et al.* introduced a Gaussian kernel to compute the spatially varying means and constant variances in their implementation. However, this may be inconsistent with theory as pointed out by Wang *et al.* [32]. Differently, the varying means and piecewise constant variances in our method are directly obtained by energy minimization [see (17) and (18)]. Paragios *et al.* [39]'s method integrates boundary information into an energy functional defined by [36]. Therefore, its means and variances are constant. Our method is different from Wang *et al.*'s method. First, we use spatially varying means and piecewise constant variances in each local region which are more stable than spatially varying variances in [32]. Second, our method can obtain the closed form of optimal

membership functions for each segmented region, which is much more efficient than Wang *et al.* [32]'s method that needs to iterate solving a level set formulation. In [40], an improved VLS method is proposed for simultaneous bias correction and segmentation based on Wang *et al.*'s method in which the local mean of Gaussian distribution is replaced by multiplication of the smooth bias field function and piecewise constant true signal. Therefore, the proposed method in [40] has similar disadvantages as Wang *et al.*'s method.

B. Energy Minimization

1) *Minimization With Respect to c:* By fixing the other variables in (18), we obtain the solution of c , denoted by $\tilde{c} = \{\tilde{c}_i, i = 1, \dots, N\}$, as follows:

$$\tilde{c}_i = \frac{\int_{\Omega} (\chi_{\rho} \otimes b) I u_i dy}{\int_{\Omega} (\chi_{\rho} \otimes b^2) u_i dy} \quad (19)$$

where \otimes denotes the convolution operator.

2) *Minimization With Respect to b:* By fixing the other variables in (18), we obtain the solution of b , denoted by \tilde{b} , as follows:

$$\tilde{b} = \frac{\sum_{i=1}^N \chi_{\rho} \otimes (I u_i)}{\sum_{i=1}^N \chi_{\rho} \otimes u_i \cdot c_i}. \quad (20)$$

Note that \tilde{b} is actually normalized convolution [28], which naturally leads to a smooth approximation of the bias field b .

3) *Minimization With Respect to σ :* By fixing the other variables in (18), we obtain the solution of σ , denoted by $\tilde{\sigma} = \{\tilde{\sigma}_i, i = 1, \dots, N\}$, as follows:

$$\tilde{\sigma}_i = \sqrt{\frac{\int_{\Omega} \int_{\Omega} \chi_{\rho}(y,x) u_i(y) (I(y) - b(x)c_i)^2 dy dx}{\int_{\Omega} \int_{\Omega} \chi_{\rho}(y,x) u_i(y) dy dx}}. \quad (21)$$

4) *Minimization With Respect to u:* By fixing the other variables in (17), the solution of u , denoted by $\tilde{u} = \{\tilde{u}_i, i = 1, \dots, N\}$, is as follows:

$$\tilde{u}_i(y) = \begin{cases} 1, & i = \arg \min_i (\psi_i) \\ 0, & i \neq \arg \min_i (\psi_i) \end{cases} \quad (22)$$

where $\psi_i(I(y)) = \int_{\Omega} \chi_{\rho}(y,x) (\log(\sigma_i) + ((I(y) - b(x)c_i)^2 / 2\sigma_i^2)) dx$. For an explanation of how to derive the above solutions, please refer to Appendixes A, B, C, and D.

5) *Minimization With Respect to u With TV Regularization:* For the objective function $E_{c,u,\sigma,b}^{\text{RMLTD}}$ with TV regularization, we obtain the solution of u by using the fast optimization algorithm proposed by [41] and [42] with procedures as follows.

1) Fix u_i , solve v_i by the following formulation:

$$v_i = u_i - \theta \gamma \text{div}(q_i), i = 1, \dots, N \quad (23)$$

where θ is a fixed parameter and q_i is solved by fixed point method that iterates

$$q_i^{n+1} = \frac{q_i^n + \tau \nabla (\text{div}(q_i^n) - u_i / \theta \gamma)}{1 + \tau |\nabla (\text{div}(q_i^n) - u_i / \theta \gamma)|} \quad (24)$$

with $q_i^0 = 0$ and $\tau \leq (1/8)$ to ensure convergence.

2) Fix v_i , solve u_i by the following formulation:

$$u_i = \min \left(\max \left(\frac{v_i - \theta \gamma d_i - \theta \gamma \zeta (\sum_{j \neq i} u_j - 1)}{1 + \theta \gamma \zeta}, 0 \right), 1 \right) \quad (25)$$

where ζ is a fixed parameter.

The whole minimization procedure consists of the following three steps, which are implemented iteratively.

- 1) Keep u fixed, optimize and update the variable sets c , b , and σ .
- 2) Keep c , b , and σ fixed, optimize and update u .
- 3) Check whether the convergence has been reached. If not, return to 1).

The convergence condition is $|u_i^{n+1} - u_i^n| \leq \varepsilon$, $i = 1, \dots, N$, where $\varepsilon = 0.1$ in our experiments.

Remark 2: The solution of $\{b(x), c_i\}$ is not unique because $\{kb(x), (1/k)c_i\}$ with any positive factor k also minimizes the proposed energy functionals $E_{c,u,\sigma,b}^{\text{MLTD}}$ and $E_{c,u,\sigma,b}^{\text{RMLTD}}$. However, these scale factors do not affect quality of the correction because MR intensity is relative [43]. Furthermore, these factors have no impact on the solutions of $\tilde{\sigma}_i$ and \tilde{u}_i in (21) and (22), respectively, because their solutions are based on the multiplication of $b(x)$ and c_i where $b(x)c_i = kb(x) \cdot (1/k)c_i$. Therefore, the final segmentation and estimated bias field are robust to the initial variables.

C. Advantages of the MLTD Model

The CLIC energy functional [1] has two desirable advantages over the well-known methods proposed by Wells *et al.* [21] and Leemput *et al.* [15]. First, it is convex with respect to each of its variables and we can obtain the closed form of its solutions; second, the smoothness of the bias field is ensured by the nature of the CLIC energy functional. Therefore, we use CLIC as a reference to discuss the advantages of the proposed model.

If we set σ_i in (17) to be $1/\sqrt{2\pi}$, the membership function of region O_x to be a truncated Gaussian window, (17) will be the same as the CLIC energy functional with $q = 1$ [refer to (6)] except for some trivial constant factors. Thus, the CLIC model can be viewed as a special case of our MLTD model, and the MLTD will be more accurate to model the image with intensity inhomogeneity than the CLIC model. In [1], it is claimed that the CLIC model will yield a hard classification (the image intensity in a fixed position only belongs to one tissue) when $q = 1$ in (6). Differently, we will discuss that the proposed MLTD model leads to a soft classification (image intensity in a fixed position belongs to all tissues with a corresponding probability).

In medical imaging, partial volume voxels often have an intensity composed of multiple class intensities. For example, there is as much as 30% of partial volume voxels in low resolution datasets [22]. The partial volume effect severely influences the accuracy of estimated bias field if a hard classification method is adopted because the hard classification method assumes the image intensity in a fixed position only belongs to one tissue. Our proposed methods are soft classification methods which assume that intensity of each tissue

is composed of multiple class intensities, thereby alleviating partial volume effect to some extent.

Equation (11) can be rewritten as multivariate Gaussian distribution as follows:

$$p(X|\alpha) = \prod_{i=1}^N p(\bar{l}(x|\alpha_i)) \sim \mathcal{N}(\bar{\mu}, \bar{\Sigma}) \quad (26)$$

where

$$\bar{\mu} = \bar{\Sigma} \sum_{i=1}^N \frac{m_i(x)b(x)c_i}{\sigma_i^2}, \quad \bar{\Sigma}^{-1} = \sum_{i=1}^N \left(\frac{\sigma_i^2}{m_i(x)} \right)^{-1}. \quad (27)$$

Intuitively, every pixel (voxel) is composed of multiple classes of intensities depending on the position x , thus, the MLTD model can yield a soft classification result, and the partial volume effect [22] can be significantly eliminated. Moreover, the intensity in the transformed domain exploits information of the neighboring pixels belonging to the same class [refer to (9)], so the classification result of MLTD is less sensitive to noise, yielding smoother tissue border [5].

IV. EXPERIMENTAL RESULTS

In this section, we first demonstrate robustness of our method to different parameter initializations and then compare our method with the CLIC method [1], VLS method [17], improved variational level set (IVLS) method [40], information minimization (IM) method [18]¹ and the N4ITK method [44]²; then we apply our method to 7T MRI to further verify its performance. Note that our method can not only be applied to 2-D slices but also to 3-D images. Except for Fig. 7 that uses a 3-D MR brain image, all other experiments are tested on 2-D slices. The MATLAB source code can be downloaded from https://drive.google.com/file/d/0B_gmXtdIPtrbRTNKYmlfQTc4UXM/edit?usp=sharing.

A. Parameter Setting

It is easy to choose the parameters in our model. We first randomly initialize b with a normal distribution whose mean and standard deviation are zero and one, respectively, and then we set b to be $|b|$ that ensures its values nonnegative. The initial u_i , $i = 1, \dots, N$ are generated with a uniform distribution on the interval $[0, 1]$. Then, we normalize each u_i to be $u_i / \sum_{i=1}^N u_i$. Then, the initial c_i can be calculated by (19). After having the initial $\{b, c_i, u_i, i = 1, \dots, N\}$, we can estimate the initial σ_i via (21). Our method is stable for a large range of different ρ (e.g., $5 < \rho < 25$). In all the following experiments, we set $\rho = 10$. A small ρ makes the computation in each iteration more efficient, but the convergence is slower. On the other hand, a large ρ increases computational burden for each iteration while increasing the convergence rate because information from a large region is used.

For the RMLTD model [refer to (18)], we set $\theta = 0.001$, $\gamma = 0.01$, $\tau = 0.1$, and $\zeta = 0.1$.

Fig. 2 shows the sensitivity of our method to different parameter initializations. We use the Jaccard similarity (JS) [1]

¹<http://lit.fe.uni-lj.si/contents/tools/InhomogeneityCorrection/>

²<http://www.insight-journal.org/browse/publication/640>

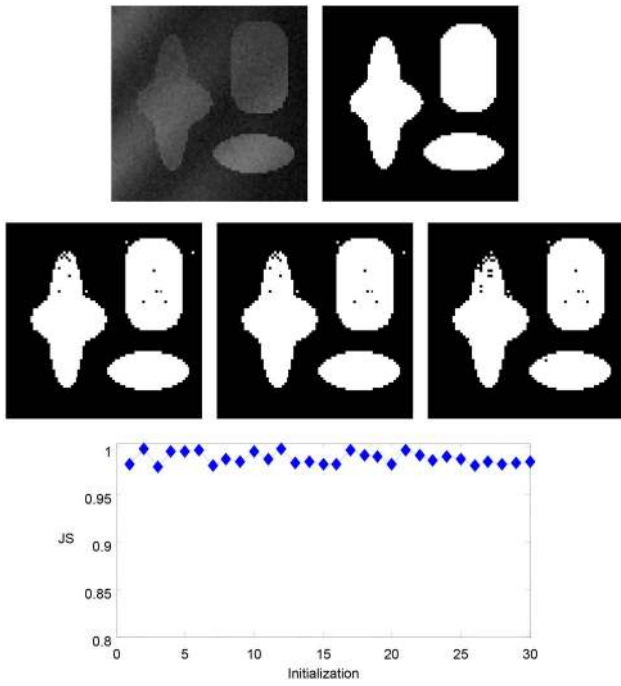


Fig. 2. Test of sensitivity of our method to different parameter initializations. Top row: left, original image; right, ground truth image. Middle row: sample segmentation results. Bottom: JS values for 30 different initializations. The mean of JS values is 0.9886 and the standard deviation of JS values is 0.0061.

as an index to measure the segmentation accuracy to quantitatively evaluate the performance of our method. The JS between two regions S_1 and S_2 is calculated by $JS(S_1, S_2) = |S_1 \cap S_2| / |S_1 \cup S_2|$, which is the ratio between the intersectional area of S_1 and S_2 and their united area. Obviously, the closer the JS value is to 1, the more similar S_1 is to S_2 . In our experiments, S_1 is the segmented region by our method, and S_2 is the ground truth. We use 30 random setting of parameter values, and compute the JS value for each parameter initialization. It can be observed that segmentation results of different initializations have no obviously visual effect (see the middle row in Fig. 2). Moreover, the JS values for 30 different initializations fluctuate narrowly with standard deviation 0.0061. This demonstrates the robustness of our method to different parameter initializations. For the following experiments, we used the similar initializations as those used in Fig. 2, and found the results are very stable for different initializations.

B. Comparisons With Other Representative Methods

Fig. 3 compares our MLTD and RMLTD methods with the CLIC and VLS methods for a synthetic image with noise. The intensity of this synthetic image is severely inhomogeneous and the noise is strong. From the third image of Fig. 3(d), we can see that the segmentation result by CLIC method is not visually satisfying because some background intensities are misclassified as the object intensities. The segmentation result by VLS method [see the third image of Fig. 3(e)] is better than the CLIC method but there still exist some obvious misclassifications. In general, MLTD yields the best segmentation results among the three methods. However, there still exist some small dot regions that are misclassified due to the

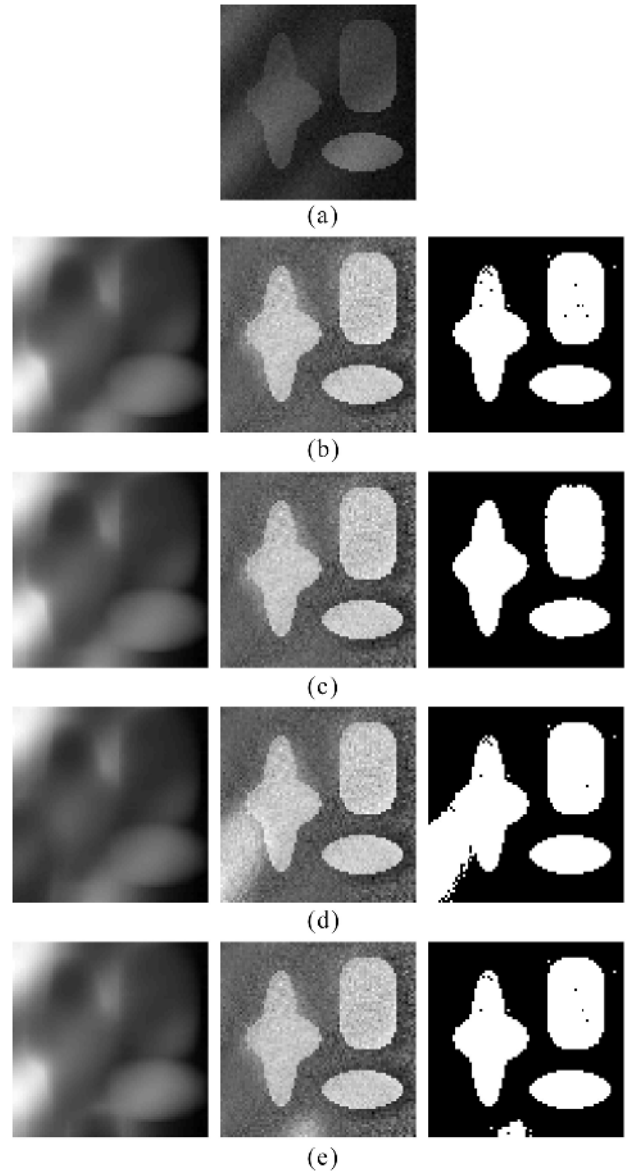


Fig. 3. Application to a synthetic image with noise. (a) Original image. Results of (b) MLTD, (c) RMLTD, (d) CLIC, and (e) VLS. (b)–(e) From left to right: estimated bias fields, bias corrected images, and binary segmentation results.

strong noise. Fig. 3(c) shows results by RMLTD method. We can see that adding the TV regularization term can effectively remove the noise in the final segmentation result.

We test the seven competing methods on 30 Brainweb normal subjects (1 mm isotropic spacing, no added noise, discrete anatomical labeling) with stimulated bias fields with 0%, 20%, and 40% intensity inhomogeneity, respectively, from McGill Brain Web.³ The 5%, 10%, and 20% levels of Gaussian noises are then added to these images.

In Fig. 4, we use box plots to illustrate the distribution of JS values of white matter (WM) and gray matter (GM) generated by five methods without the IM and N4ITK methods because they are only designed for bias correction. The top limit is calculated from the 25th percentile of the data

³<http://www.bic.mni.mcgill.ca/brainweb/>

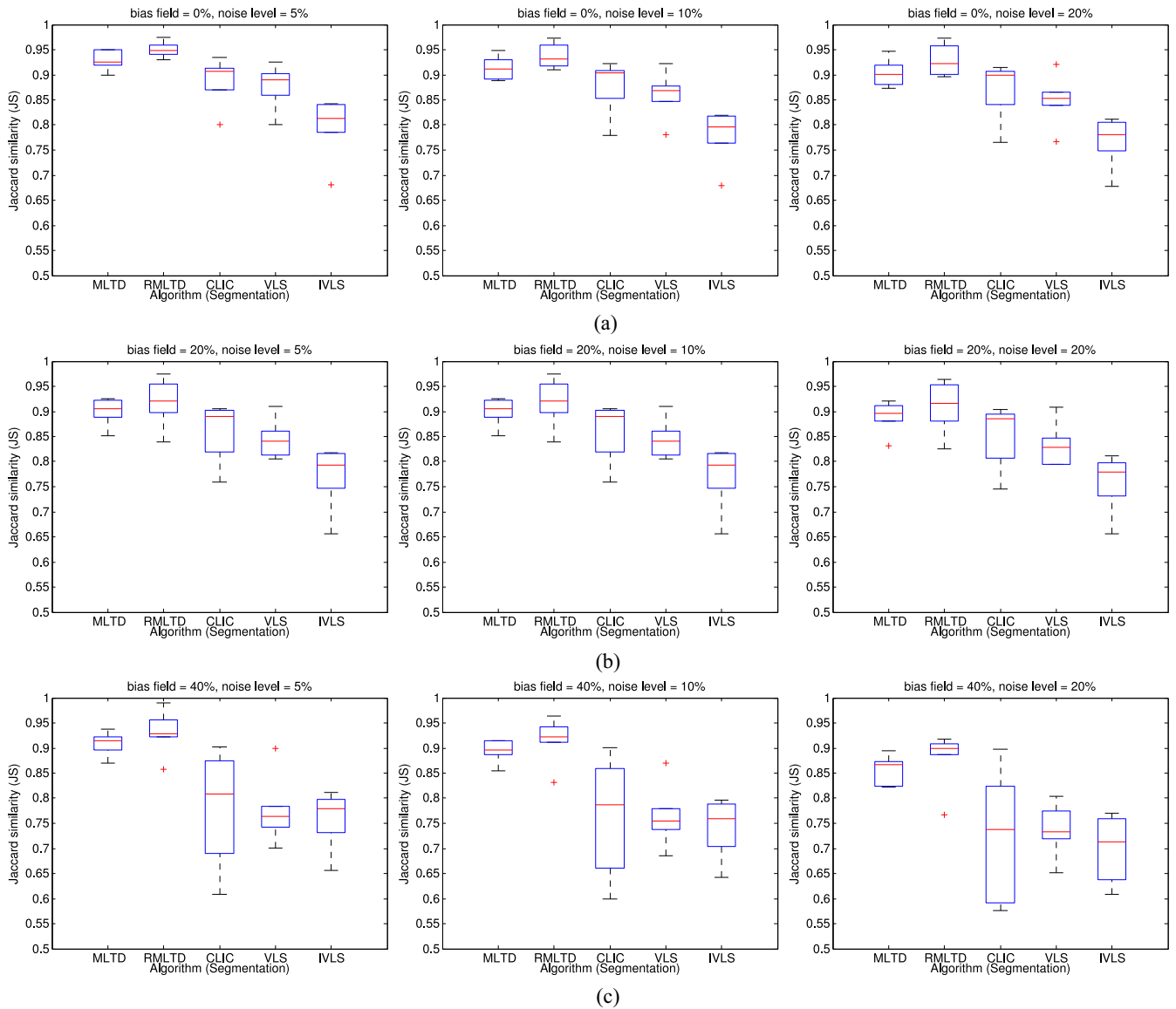


Fig. 4. Segmentation results: JS analysis for the BrainWeb data with different levels of bias fields and noises. (a) Segmentation results with 0% bias field. (b) Segmentation results with 20% bias field. (c) Segmentation results with 40% bias field.

while the bottom is from the 75th percentile ($p_{25\%}$ and $p_{75\%}$, respectively). The median value is denoted by the horizontal red line. The extent of the box plot whiskers is in the range $[p_{25\%} - 1.5(p_{75\%} - p_{25\%}), p_{75\%} + 1.5(p_{75\%} - p_{25\%})]$, and any datum outside of that range is considered as an outlier that is denoted by the “+” symbol. Obviously, our methods achieve the highest JS values among all the competing methods in most cases, which demonstrates the superiority of our methods to state-of-the-art variational methods.

We use the agreement of the estimated bias fields with the ground truth ones as another performance assessment which is evaluated by correlation coefficient between them. Other metric (e.g., the normalized ℓ_2 -norm of the difference between the estimated bias field and the true one [45]) can also be adopted for assessment. However, we have found that the experimental results based on these two metrics have no significant difference. Thus, we only report the results in terms

of correlation coefficients which are shown in the box plots of Fig. 5. Again, our method achieves much better performance than other competing methods in most cases. Furthermore, we note that the segmentation-based methods (i.e., MLTD, RMLTD, CLIC, VLS, IVLS) often perform better than those without segmentation (i.e., IM, N4ITK), which gives the fact that segmentation and bias correction can benefit each other to achieve much more accurate results.

In Fig. 6, we compare the efficiencies among our methods, the CLIC method, the VLS method, the IVLS method, and the N4ITK method in processing images in Fig. 5. We report the average processing time for 30 images with different levels of noises and inhomogeneous intensity. Since our MLTD method and the CLIC method utilize the membership function to indicate different partitions, and both of their energy functionals have only one global minimum with respect to each variable, they are much more efficient than the VLS method. The VLS

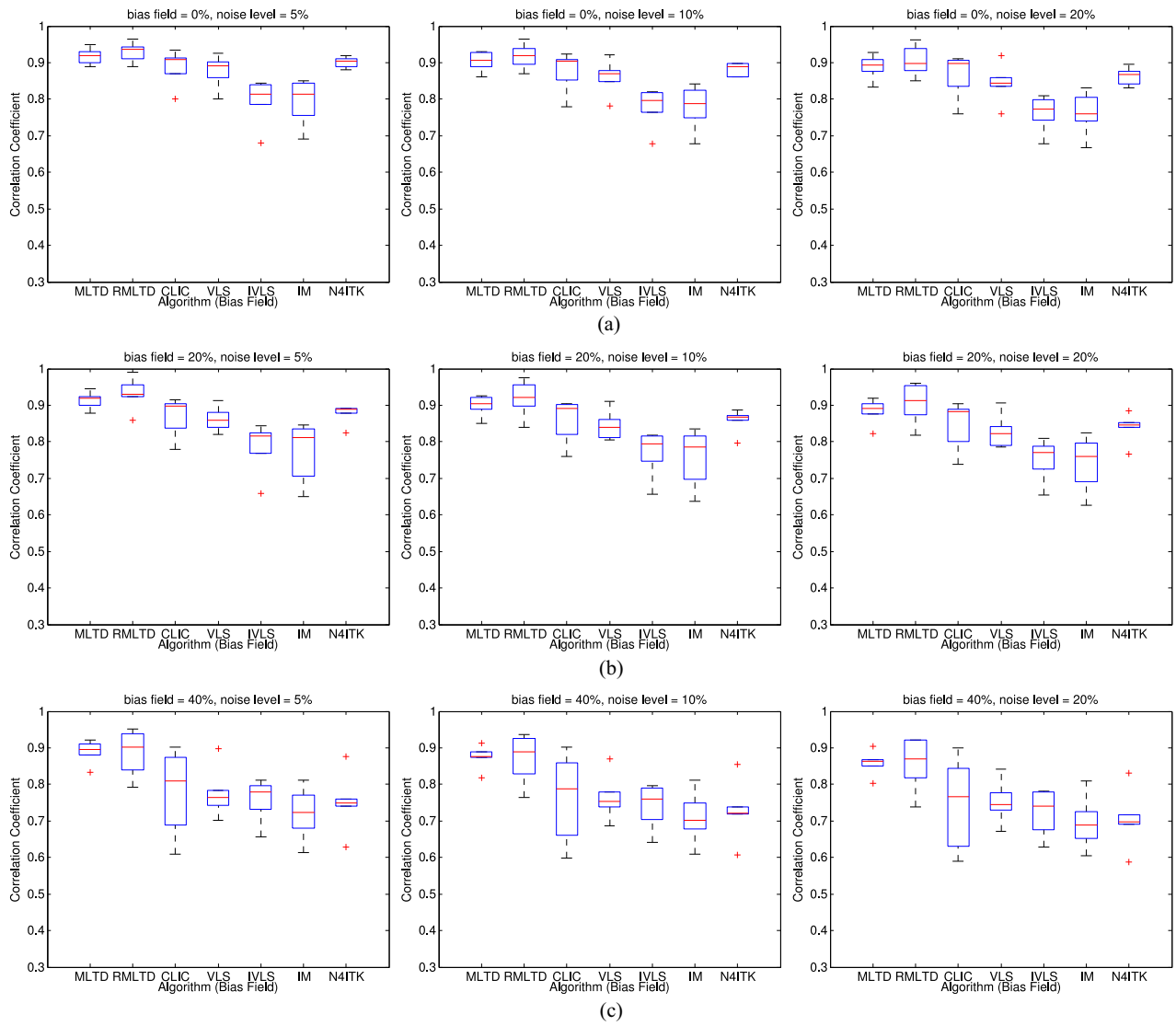


Fig. 5. Bias field results: correlation coefficient analysis for the BrainWeb data with different levels of bias fields and noises. (a) Results of estimated bias field with 0% bias field. (b) Results of estimated bias field with 20% bias field. (c) Results of estimated bias field with 40% bias field.

method has to evolve two partial differential equations, which is very time-consuming (see the green line in Fig. 6). Similar problem also exists in the model proposed by [46] and the IVLS method. For the N4ITK method, it has to estimate the parameters of the B-spline, which is very time-consuming. The iterations of MLTD is typically between 10 and 15 for these 30 images, so is the CLIC method. However, our method has to compute the standard deviation term in (21), which makes it a little less efficient than the CLIC method in some cases. For the RMLTD method, we have to iterate three formulations [i.e., (23)–(25)] many times to obtain the stable solution of membership function, leading it less efficient than MLTD and CLIC.

Fig. 7 shows the results by our method for a low-resolution 3T 3-D MR image. Similar to [2], we select three sagittal slices in order to better visualize the results. From left to right, the four columns show the original images, estimated bias fields, the bias corrected images, and the segmentation results, respectively. From the right column, we can see each tissue in

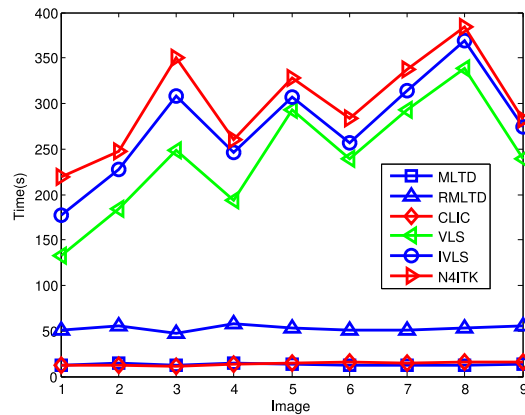


Fig. 6. Efficiency comparisons among the six methods: MLTD, RMLTD, CLIC, VLS, IVLS, and N4ITK.

the bias corrected images is very homogeneous. The segmentation results also highly agree with the brain anatomy (see the fourth column in Fig. 7). The image size is $150 \times 120 \times 150$.

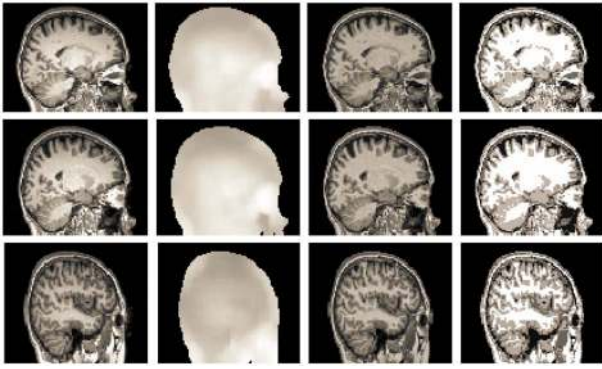


Fig. 7. Sagittal slice view of the 3-D segmentation and bias corrected results. Column 1: original images. Column 2: estimated bias fields. Column 3: bias corrected results. Column 4: segmentation results.

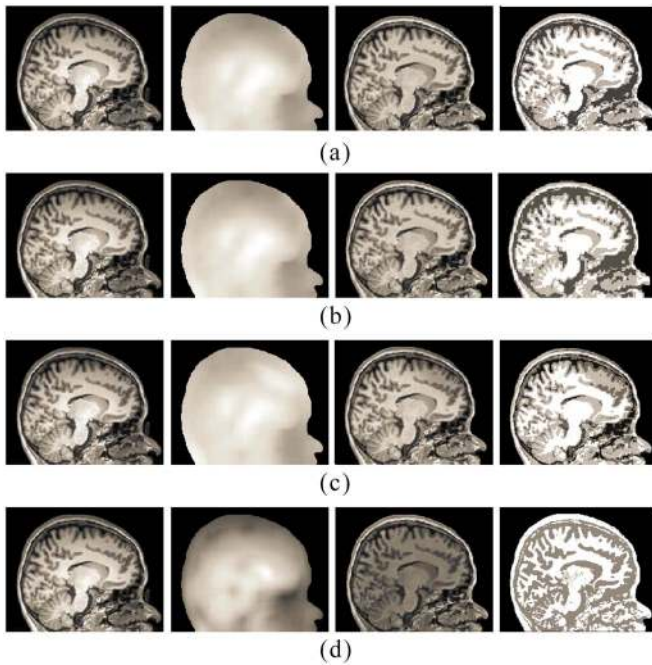


Fig. 8. Experiments on 3T MRI. From left column to right one: original image, estimated bias fields, bias corrected images, and binary segmentation results. Results of (a) MLTD, (b) RMLTD, (c) CLIC, and (d) VLS.

The computational time for preprocessing this image is 165.3 s in MATLAB on a Pentium Dual-Core 2.10 GHz CPU with 2 GB RAM.

Fig. 8 compares results by MLTD and RMLTD, CLIC and VLS on a 3-tesla MRI. The estimated bias fields, bias corrected images, and segmentation results are shown in the second, third, and fourth columns of Fig. 8(a)–(d), respectively. We can observe that the segmentation result by RMLTD model has less noise than MLTD model because the TV regularization in RMLTD has smoothing effect on the segmentation result. The histogram of the original MRI image and the histograms of the bias corrected images by our methods, CLIC and VLS are shown by Fig. 9. In the histograms, the right two significant peaks correspond to the GM and WM, respectively. The peak of the cerebrospinal fluid (CSF) is not distinct since its volume

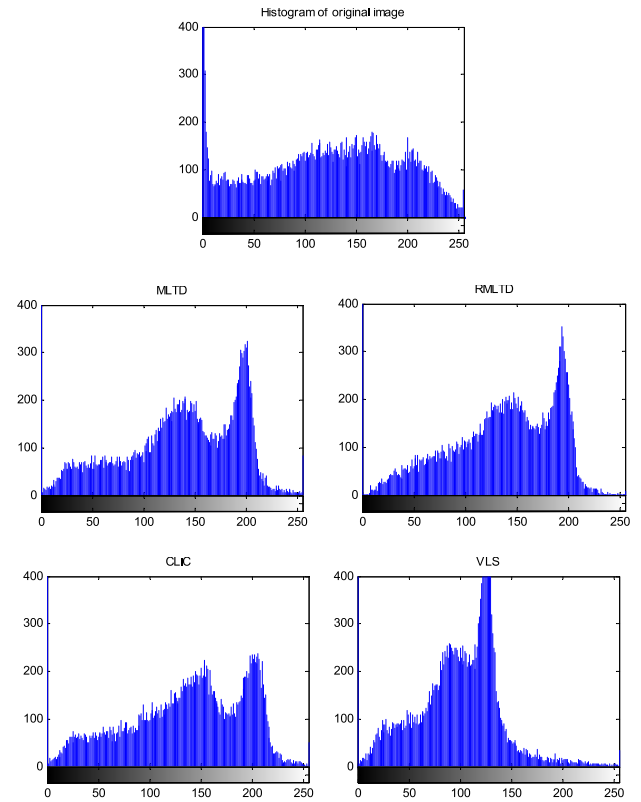


Fig. 9. Histograms of original image and bias corrected images in Fig. 8.

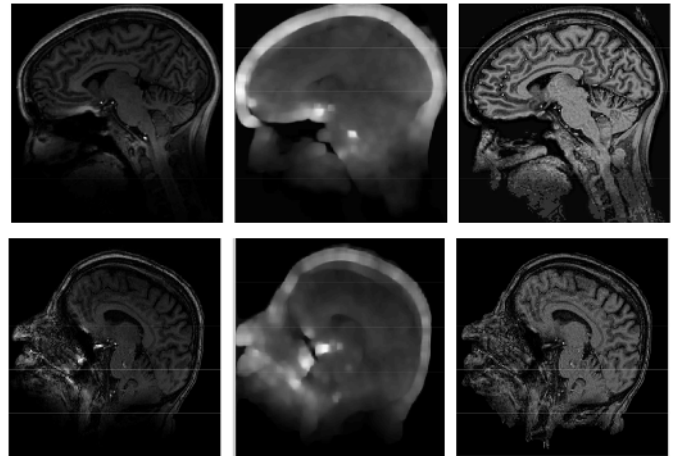


Fig. 10. Bias correction results on two 7T MRI images by the proposed method. Column 1: original images. Column 2: estimated bias fields. Column 3: bias corrected images.

is relatively small [1]. From the histograms of the bias corrected images recovered by MLTD, CLIC, and VLS, we see that the histograms of specific tissues approximately satisfy Gaussian distribution but with significantly different variances. These results validate that our model is better consistent with the intensity distribution of the image with intensity inhomogeneity than CLIC and VLS which do not consider the variance of intensities belonging to different tissues. Moreover, the segmentation results of MLTD are much closer to the brain anatomy than CLIC and VLS.

C. Further Application to 7T MRI

Finally, we show the segmentation results of our method on a 7T MRI image in Fig. 10. From left to right, the original images, estimated bias fields, and the bias corrected images are shown in the three columns, respectively. Obviously, the image qualities are significantly improved, and some regions whose intensity contrast is too low to be identified are able to be distinguished easily after correction.

V. CONCLUSION

In this paper, we proposed a novel variational approach to simultaneous estimation of the bias field and segmentation of images with intensity inhomogeneity. Our method combines information of the neighboring pixels belonging to the same class, which makes it robust to noise. Moreover, the proposed method yields a soft segmentation, which can eliminate the partial volume effect [22] to some extent. Comparisons with other representative methods on synthetic and real images demonstrated the effectiveness and advantages of the proposed algorithm.

APPENDIX A

Let us revisit (17), which can be rewritten as

$$\begin{aligned} E_{c,u,\sigma,b}^{\text{MLTD}} &= \frac{1}{N} \sum_{i=1}^N \int_{\Omega} \int_{\Omega} \chi_{\rho}(y,x) u_i(y) \left(\frac{\log(\sqrt{2\pi}\sigma_i)}{+\frac{(I(y)-b(x)c_i)^2}{2\sigma_i^2}} \right) dy dx \\ &= \int_{\Omega} \sum_{i=1}^N \psi_i(y) u_i(y) dy \end{aligned} \quad (28)$$

subject to $u_i \geq 0$, $\sum_{i=1}^N u_i = 1$, where

$$\begin{aligned} \psi_i(y) &= \int_{\Omega} \chi_{\rho}(y,x) \left(\log(\sigma_i) + \frac{(I(y) - b(x)c_i)^2}{2\sigma_i^2} \right) dx \\ &= \chi_{\rho} \otimes \left(\log(\sigma_i) + \frac{(I - bc_i)^2}{2\sigma_i^2} \right). \end{aligned}$$

Assume the optimal solution of the constant true signal c_i is \tilde{c}_i , by calculus of variations, we have

$$\begin{aligned} \frac{\partial E_{c,u,\sigma,b}^{\text{MLTD}}}{\partial \tilde{c}_i} &= \int_{\Omega} \sum_{j=1}^N \frac{\partial \psi_j(y)}{\partial \tilde{c}_i} u_i(y) dy \\ &= \int_{\Omega} \frac{\partial \psi_i(y)}{\partial \tilde{c}_i} u_i(y) dy \\ &= - \int_{\Omega} \left(\chi_{\rho} \otimes \frac{(Ib - b^2 \tilde{c}_i)}{\sigma_i^2} \right) u_i(y) dy = 0 \\ &\implies \tilde{c}_i = \frac{\int_{\Omega} (\chi_{\rho} \otimes b) I u_i dy}{\int_{\Omega} (\chi_{\rho} \otimes b^2) u_i dy} \end{aligned}$$

which corresponds to (19).

APPENDIX B

In (28), we assume that the optimal b is \tilde{b} and add variation η to the variable \tilde{b} such that $b = \tilde{b} + \delta\eta$. Keeping other variables except for b fixed, differentiating with respect to b

and letting $\delta \rightarrow 0^+$, we have

$$\begin{aligned} &E_{c,u,\sigma,\tilde{b}+\delta\eta}^{\text{MLTD}} \\ &= \int_{\Omega} \sum_{i=1}^N \int_{\Omega} \chi_{\rho}(y,x) u_i(y) \left(\frac{\log(\sigma_i)}{+\frac{(I(y)-(\tilde{b}(x)+\delta\eta(x)c_i))^2}{2\sigma_i^2}} \right) dy dx \\ &\implies \frac{\partial E_{c,u,\sigma,\tilde{b}+\delta\eta}^{\text{MLTD}}}{\partial \delta} \\ &= \int_{\Omega} \sum_{i=1}^N \int_{\Omega} \chi_{\rho}(y,x) u_i(y) \left(\frac{I(y) - \tilde{b}(x)c_i}{\sigma_i^2} \right) \eta(x) c_i dy dx \\ &\implies \tilde{b}(x) = \frac{\int_{\Omega} \chi_{\rho}(y,x) I(y) \sum_{i=1}^N u_i(y) \frac{c_i}{\sigma_i^2} dy}{\int_{\Omega} \chi_{\rho}(y,x) \sum_{i=1}^N u_i(y) \frac{c_i^2}{\sigma_i^2} dy} \\ &= \frac{\sum_{i=1}^N \chi_{\rho} \otimes (I u_i)}{\sum_{i=1}^N \chi_{\rho} \otimes u_i \cdot c_i} \end{aligned}$$

which corresponds to (20).

APPENDIX C

In (28), assume the optimal solution of the constant true signal σ_i is $\tilde{\sigma}_i$, by calculus of variations, we have

$$\begin{aligned} \frac{\partial E_{c,u,\sigma,b}^{\text{MLTD}}}{\partial \tilde{\sigma}_i} &= \int_{\Omega} \sum_{j=1}^N \frac{\partial \psi_j(y)}{\partial \tilde{\sigma}_i} u_i(y) dy = \int_{\Omega} \frac{\partial \psi_i(y)}{\partial \tilde{\sigma}_i} u_i(y) dy \\ &= - \int_{\Omega} \left(\chi_{\rho} \otimes \left(\frac{1}{\tilde{\sigma}_i} - \frac{(I - bc_i)^2}{\tilde{\sigma}_i^3} \right) \right) u_i(y) dy = 0 \\ &\implies \tilde{\sigma}_i = \sqrt{\frac{\int_{\Omega} \int_{\Omega} \chi_{\rho}(y,x) u_i(y) (I(y) - b(x)c_i)^2 dy dx}{\int_{\Omega} \int_{\Omega} \chi_{\rho}(y,x) u_i(y) dy dx}} \end{aligned}$$

which corresponds to (21).

APPENDIX D

In (28), fixing other parameters except for the parameter u , minimizing $E_{c,u,\sigma,b}^{\text{MLTD}}$ with respect to the indicator function u is equivalent to the following linear programming problem:

$$\begin{aligned} \arg \min_u E_{c,u,\sigma,b}^{\text{MLTD}} &= \int_{\Omega} \sum_{i=1}^N \psi_i(y) u_i(y) dy \\ &\iff \arg \min_u \Psi^T u \end{aligned}$$

subject to $u \geq 0$, $\mathbf{1}^T u = 1$, where $\Psi = (\psi_1, \dots, \psi_N)$ and $\mathbf{1} = (1, \dots, 1_N)^T$.

First, without loss of generality, we assume the components of Ψ are sorted in increasing order with $\psi_1 = \psi_2, \dots, = \psi_k \leq \psi_{k+1} \leq \dots, \leq \psi_N$. Then, we have $\Psi^T u \leq \psi_1(\mathbf{1}^T u) = \min_i(\psi_i)$. For all feasible Ψ , the equality is satisfied if and only if $\sum_{i=1}^k u_i = 1$, $u_i \geq 0$, $i = 1, \dots, k$, $u_i = 0$, $i = k+1, \dots, N$. Therefore, we have the optimal solution \tilde{u}_i as follows:

$$\tilde{u}_i = \begin{cases} 1, & i = \arg \min_i(\psi_i) \\ 0, & i \neq \arg \min_i(\psi_i) \end{cases}$$

which corresponds to (22).

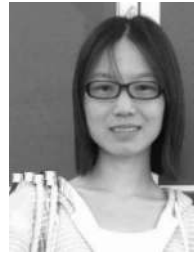
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