An EM Approach to MAP Solution of Segmenting Tissue Mixtures: A Numerical Analysis
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Abstract—This work presents an iterative expectation-maximization (EM) approach to the maximum a posteriori (MAP) solution of segmenting tissue mixtures inside each image voxel. Each tissue type is assumed to follow a normal distribution across the field-of-view (FOV). Furthermore, all tissue types are assumed to be independent from each other. Under these assumptions, the summation of all tissue mixtures inside each voxel leads to the image density mean value at that voxel. The summation of all the tissue mixtures’ unobservable random processes leads to the observed image density at that voxel, and the observed image density value also follows a normal distribution (image data are observed to follow a normal distribution in many applications). By modeling the underlying tissue distributions as a Markov random field across the FOV, the conditional expectation of the posteriori distribution of the tissue mixtures inside each voxel is determined, given the observed image data and the current-iteration estimation of the tissue mixtures. Estimation of the tissue mixtures at next iteration is computed by maximizing the conditional expectation. The iterative EM approach to a MAP solution is achieved by a finite number of iterations and reasonable initial estimate. This MAP-EM framework provides a theoretical solution to the partial volume effect, which has been a major cause of quantitative imprecision in medical image processing. Numerical analysis demonstrated its potential to estimate tissue mixtures accurately and efficiently.

Index Terms—Expectation-maximization (EM) algorithm, maximum a posteriori (MAP) image segmentation, parameter estimation, partial volume effect, tissue mixture fraction.

I. INTRODUCTION

MAGE segmentation plays an important role in quantitative analysis of medical imaging data for various clinical applications. Traditional image segmentation algorithms cluster all image voxels into several groups and assign a unique label to each group. Each label indicates a specific tissue type for those voxels inside the corresponding group. This label-based hard segmentation is only applicable to the extreme case where only a single tissue type is present in a voxel and the observed image density at that voxel reflects the characteristics of the particular tissue type. Due to the limited spatial resolution of imaging device and the complex shape of tissue interfaces, not all voxels in each labeled group contain the same tissue type, especially for those voxels near tissue interfaces which are most likely to contain more than one tissue type. The presence of a mixture of different tissue types in a voxel is referred to as partial volume effect (PVE). Assigning one single tissue label to each voxel with the presence of PVE causes a noticeable error in the traditional hard image segmentation and compromises volumetric analysis in clinical applications, e.g., in evaluation of multiple sclerosis with cognitive impairment [1]. Improvement has been observed by soft image segmentation, which models for example the probability or likelihood of an observed datum belonging to a tissue label as a classic finite-mixture density distribution [1]–[4]. These soft segmentation algorithms [1]–[4] can reduce the PVE to some degree. However, since they still assign a discrete tissue label to each voxel (where the PVE is modeled indirectly via the classic finite-mixture likelihood cost function of the image data), their improvement was shown to be limited [1]–[4]. This is expected by their indirect modeling of the PVE. Another class of soft image segmentation utilizes the fuzzy C-mean cost function to indicate the membership of voxels in each group, where the likelihood of a voxel belonging to its group is measured by the Euclidean distance [5], [6]. This class of soft segmentation algorithms faces the same limitation due to the same reason of indirect modeling of the PVE. Directly modeling different tissue types inside each voxel for PV image segmentation is desired and has been a challenging task due to insufficient measurements to determine the percentages or fractions of different tissue types in each voxel [7]–[11]. Because of the challenge, most previous work focused on the mixture of two tissue types in a voxel [7]–[11]. Recently, Leemput et al. [12] presented a PV image segmentation algorithm which determines different tissue components in each voxel by firstly down-sampling that voxel and then labeling the down-sampled subvoxels using hard segmentation. Finally, the different tissue components in the voxel are estimated via the relative amount of each label or class in the subdivided image array of that voxel. Theoretically, this discrete PV image segmentation would approach to an accurate solution for any number of tissue types in a voxel when the down-sampling is repeated infinite times, resulting in an infinite number of down-sampled subvoxels to be labeled. However, a high down-sampling rate is time-consuming and impracticable. In this paper, we present an alternative approach, which determines the percentages of different tissue types inside each voxel in a continuous space as those previous work [7]–[11] but without the limitation of only two tissue types in a voxel.
and also avoiding the discrete labels of hard segmentation [12], and investigate its performance by numerical simulations.

II. METHODS

A. Statistical Model of Image Data

Let the acquired image $Y$ be represented by a column vector in the form of $\{Y_i; i = 1, \ldots, I\}$, where $I$ denotes the total number of voxels in the image. Each $Y_i$ is an observation of an individual random variable with mean $\bar{Y}_i$ and variance $\sigma^2_i$ at voxel $i$, i.e.,

$$Y_i = \bar{Y}_i + n_i$$  \hspace{1cm} (1)

where $n_i$ represents the noise associated with observation $Y_i$. If noise $n_i$ is assumed as statistically mutually independent among the $I$ voxels, then given the mean and variance distributions $\{\bar{Y}_i\}$ and $\{\sigma^2_i\}$ respectively, the conditional probability distribution of the acquired image $Y$ can be described by

$$p(\mathbf{Y}|\{\bar{Y}_i\}, \{\sigma^2_i\}) = \prod_{i=1}^{I} p(Y_i|\bar{Y}_i, \sigma^2_i).$$  \hspace{1cm} (2)

In medical imaging applications, $Y$ reflects the spatial distribution of $K$ tissue types inside the body. Near the interface of different tissue types, there are more than one and probably $K$ tissue types inside each voxel $i$. Ignorance of the substructures within each voxel will result in the well-known PVE. Modeling the PVE is given below.

B. Statistical Model of Tissue Mixtures

Let the contribution of tissue type $k$ in voxel $i$ to the observation of $Y_i$ at that voxel be denoted by $\{X_{ik}; i = 1, \ldots, I; k = 1, \ldots, K\}$. It is obvious that $X_{ik}$ is also an individual random variable with mean $\bar{X}_{ik}$ and variance $\sigma^2_{ik}$, i.e.,

$$X_{ik} = \bar{X}_{ik} + n_{ik}$$  \hspace{1cm} (3)

where $n_{ik}$ represents the noise associated with the generally unobservable variable $X_{ik}$. If noise $n_{ik}$ is assumed as statistically mutually independent among the $I$ voxels and the $K$ tissue types, then given the distributions $\{\bar{X}_{ik}\}$ and $\{\sigma^2_{ik}\}$ respectively, we have

$$p(\mathbf{X}|\{\bar{X}_{ik}\}, \{\sigma^2_{ik}\}) = \prod_{i=1}^{I} \prod_{k=1}^{K} p(X_{ik}|\bar{X}_{ik}, \sigma^2_{ik})$$  \hspace{1cm} (4)

where $\mathbf{X} = \{X_{ik}; i = 1, \ldots, I; k = 1, \ldots, K\}$ represents a random vector of size $I \times K$.

As a result from (1)–(4), we have the following relationship between the acquired image data $\{Y_i\}$ and the unobservable tissue variables $\{X_{ik}\}$

$$Y_i = \sum_{k=1}^{K} X_{ik}$$  \hspace{1cm} (5)

and their related items

$$\bar{Y}_i = \sum_{k=1}^{K} \bar{X}_{ik}, \quad n_i = \sum_{k=1}^{K} n_{ik}, \quad \sigma^2_i = \sum_{k=1}^{K} \sigma^2_{ik}.$$  \hspace{1cm} (6)

More specifically, let $Z_{ik}$ be the contribution percentage or fraction from tissue type $k$ in voxel $i$ to observation $Y_i$ with conditions of

$$\sum_{k=1}^{K} Z_{ik} = 1 \quad \text{and} \quad 0 \leq Z_{ik} \leq 1.$$  \hspace{1cm} (7)

Furthermore, let $\mu_k$ and $\nu_k$ be the mean and variance respectively of tissue type $k$ fully filling in voxel $i$ and define [12]

$$\bar{X}_{ik} = Z_{ik}\mu_k \quad \text{and} \quad \sigma^2_{ik} = Z_{ik}\nu_k$$  \hspace{1cm} (8)

then we have the following relationships:

$$Y_i = \sum_{k=1}^{K} Z_{ik}\mu_k \quad \text{and} \quad \sigma^2_i = \sum_{k=1}^{K} Z_{ik}\nu_k.$$  \hspace{1cm} (9)

The goal of image segmentation with consideration of the PVE is to estimate the $K$ tissue mixtures, specifically the percentages of different tissue types $\{Z_{ik}; k = 1, \ldots, K\}$ in each voxel $i$, under the condition that each tissue type $k$ can be statistically characterized by the conditional probability distribution $p(\cdot|\cdot)$ of (4) via the tissue model parameters $\{\mu_k, \sigma_k\}$. A specific conditional probability distribution is, as an example, described below.

C. Normal Statistics Model

Without loss of generality, we assume that the unobservable random variable $X_{ik}$ for each tissue type $k$ follows a normal distribution. By the relationship of (5), the acquired datum $Y_i$ also follows a normal distribution. This normal statistics model for $Y_i$ is valid in most applications of computed tomography (CT) and magnetic resonance imaging (MRI) [13]–[15]. Under this statistics model, (2) becomes

$$p(\mathbf{Y}|\{\mu_k\}, \{\nu_k\}, \{Z_{ik}\}) = \prod_{i=1}^{I} \frac{1}{\sqrt{2\pi} \sum_{k=1}^{K} Z_{ik}\nu_k} \exp \left\{ - \frac{(Y_i - \sum_{k=1}^{K} Z_{ik}\mu_k)^2}{2 \sum_{k=1}^{K} Z_{ik}\nu_k} \right\}$$  \hspace{1cm} (10)

and (4) becomes

$$p(\mathbf{X}|\{\mu_k\}, \{\nu_k\}, \{Z_{ik}\}) = \prod_{i,k=1}^{IK} \frac{1}{\sqrt{2\pi} Z_{ik}\nu_k} \exp \left\{ - \frac{(X_{ik} - Z_{ik}\mu_k)^2}{2Z_{ik}\nu_k} \right\}.$$  \hspace{1cm} (11)
Estimating the tissue percentage parameters \( \{Z_{ik}\} \) and the tissue model parameters \( \{\mu_k, \nu_k\} \) could be performed by maximizing the conditional probability distribution (10) with respect to each corresponding parameter of \( \{Z_{ik}, \mu_k, \nu_k\} \). This would result in a set of nonlinear equations. Solving these nonlinear equations can be very challenging even if it is numerically tractable [16]. Given the many-to-one mapping of (5) and the description of the unobservable variables of (11), the expectation maximization (EM) algorithm [17] would be an alternative and effective solution for this parameter estimation problem.

### D. EM Approach to Parameter Estimation Problem

In the EM framework [17], the observation at each voxel \( i \) or \( Y_i \) is considered as an incomplete random variable, while the underlying contributions of each tissue type \( k \), \( \{X_{ik}, k = 1, \ldots, K\} \), are considered as complete random variables which reflect the complete tissue mixture information in each voxel. The probability distribution relationship between the incomplete data \( \{Y_i\} \) and the complete data \( \{X_{ik}\} \) is depicted by the following integral equation under the condition of (5)

\[
P(Y_i \mid \{Z_{ik}\}; \{\mu_k\}, \{\nu_k\}) = \int_{\{Y_i = \sum_{k=1}^K X_{ik}\}} P(X_{ik} \mid \{Z_{ik}\}, \{\mu_k\}, \{\nu_k\}) dX \tag{12}
\]

where the integral is understood as the summation over all possible configurations of \( \{X_{ik}, k = 1, \ldots, K\} \), given \( Y_i \). The EM algorithm [17] then seeks the solution of maximizing the expectation of conditional probability distribution (11) of the complete data. Alternatively, the M-step of the EM algorithm tries to maximize the expectation of the complete-data log likelihood utilizing the posterior distribution of the latent variables computed in the E-step, given the observations \( \{Y_i\} \).

The conditional probability distribution (11) is basically a likelihood function given the tissue parameters. A maximum likelihood (ML) solution is usually not acceptable due to the presence of image noise. To overcome this drawback of ML approach, an a priori constraint is routinely imposed to ensure the continuity of the underlying tissue distribution and possible rapid change at the interface of different tissue structures within the body for a penalized ML (pML) or maximum a posteriori (MAP) solution.

### E. Prior Model for Tissue Mixture Regularization

The underlying tissue distribution is reflected by the tissue percentage distribution, or distribution of \( \{Z_{ik}\} \), across the field-of-view (FOV). Previous studies in hard segmentation of brain MR images [4], [18] have evidenced the usefulness of Markov random field (MRF) in modeling the distribution of the label images, where each label image reflects a tissue type distribution across the FOV. It is assumed that a voxel surrounded by nonbrain tissues has a very small probability to contain brain tissues. This assumption can be implemented by imposing both spatial and anatomical constraints. In this study, the concept of discrete tissue label has been evolved to \( \{Z_{ik}\} \) in continuous space and, therefore, it would be straightforward to extend the MRF model to the distribution of the tissue percentage \( \{Z_{ik}\} \). By a Gibbs functional in the well-established MRF framework [19], an a priori penalty on the tissue mixture parameter distribution \( \{Z_{ik}\} \) for each tissue type \( k \) has the following general form of:

\[
P(Z_{ik} \mid \{Z_{ik}\}) = C^{-1} \times \exp \left[ -\frac{1}{2} \beta U(Z_{ik} - Z_{ik0}) \right] \tag{13}
\]

where \( \{Z_{ik0}\} \) indicate the surrounding voxels of \( Z_{ik} \) in the neighboring system \( \varepsilon_i \). \( C \) is a normalization constant, and \( \beta \) is an adjustable parameter controlling the degree of the penalty. The energy function \( U(\cdot) \) can be written as a quadratic form of

\[
U(Z_{ik}) = \sum_{r \in \varepsilon_i} w_{ir} \cdot (Z_{ik} - Z_{ir0})^2 \tag{14}
\]

to ensure the continuity of the \( \{Z_{ik}\} \) distribution across the FOV, where index \( r \) indicates the neighbors \( \varepsilon_i \) and \( w_{ir} \) is a weighing factor for different orders of the neighbors. A sophisticated choice of \( w_{ir} \) could allow a rapid change of \( \{Z_{ik}\} \) across the FOV [19].

### F. MAP-EM Algorithm for Tissue Mixture Segmentation

Given (11)–(14), an EM approach to the MAP solution of estimating the tissue mixture percentages \( \{Z_{ik}\} \) and the tissue model parameters \( \{\mu_k, \nu_k\} \) is presented below.

1) **Initialization:** As the very first step of the EM algorithm, several parameters including \( \{Z_{ik}\} \) and \( \{\mu_k, \nu_k\} \) need to be initialized, denoted by \( \{Z_{ik}^{(0)}\} \) and \( \{\mu_k^{(0)}, \nu_k^{(0)}\} \). This step is somewhat specific to applications and may need some a priori knowledge about the concerned application [20]. For example, the number of tissue types \( K \) in the body may be known as a priori information or estimated from the image data using information criteria [2]. Given \( K \), the initialization of model parameters \( \{\mu_k^{(0)}, \nu_k^{(0)}\} \) may be as follows as an example. Each voxel is firstly assigned to one of \( K \) class labels by comparing its density to empirically-determined \( K \) thresholds, and then those voxels belonging to the same class label are grouped together to determine the corresponding mean and variance \( \{\mu_k^{(0)}, \nu_k^{(0)}\} \) respectively.

Initialization of \( \{Z_{ik}^{(0)}\} \) can be much more complicated and may need more a priori information about the concerned application [20]. Assume a second-order neighborhood would be sufficient to catch the image density transition from one tissue to another one, the initialization of mixture percentages \( \{z_{ik}^{(0)}\} \) may be as follows as an example. Given the \( K \) labeled groups, the value of \( Z_{ik}^{(0)} \) for class \( k \) in voxel \( i \) is determined as the relative amount of class \( k \) occurring in the second-order neighborhood of voxel \( i \).

2) **E-step:** This step computes the conditional expectation of the complete-data likelihood \( p(X \mid \theta) \) of (11), penalized by the MRF-modeled tissue component distribution \( p(Z) \) of (13), given the acquired data \( \{Y_i\} \) and the current parameter estimation \( \hat{\theta}^{(n)} = \{\hat{\mu}_k^{(n)}, \hat{\nu}_k^{(n)}, \hat{Z}_{ik}^{(n)}\} \).

The conditional expectation is expressed as (15), shown
at the bottom of the page. To complete the E-step of the EM algorithm, we must find the preceding conditional expectations. Following the deduction of conditional expectation, we have

$$X_{ik}^{(n)} = E_Y \sum_{ik} X_{ik} \left[ X_{ik} | Y_i, \Theta^{(n)} \right] = Z_{ik}^{(n)} \mu_k^{(n)}$$

$$+ \sum_{j=1}^K \frac{r_j^{(n)} \nu_j^{(n)}}{Z_{ij}^{(n)} \nu_j^{(n)}} \left( Y_i - \sum_{j=1}^K Z_{ij}^{(n)} \mu_j^{(n)} \right)$$

$$X_{ik}^{(n)}$$

$$= E_Y \sum_{ik} X_{ik} \left[ X_{ik}^2 | Y_i, \Theta^{(n)} \right] = \left( X_{ik}^{(n)} \right)^2$$

$$+ \sum_{j=1}^K \frac{r_j^{(n)} \nu_j^{(n)}}{Z_{ij}^{(n)} \nu_j^{(n)}} \left( Y_i - \sum_{j=1}^K Z_{ij}^{(n)} \mu_j^{(n)} \right)$$

$$\left( X_{ik}^{(n)} \right)^2$$

$$\frac{\partial Q}{\partial \mu_k} \bigg|_{\mu=(n+1)} = 0 \Rightarrow \mu_k^{(n+1)} = \frac{1}{I} \sum_{i} X_{ik}^{(n)}$$

$$\nu_k^{(n+1)} = \frac{1}{I} \sum_{i} X_{ik}^2 \nu_k^{(n)}$$

$$- 2X_{ik} \nu_k^{(n)} + \left( \nu_k^{(n)} \right)^2$$

$$\left( \nu_k^{(n)} \right)^2$$
quadratic approximation, the solution for \( K = 2 \) is given by the following closed-form formula \([22]\):

\[
Z_{2i}^{(n+1)} = A \frac{B}{\mu_2^{(n)}} \\
A = (\mu_1^{(n)} - \mu_2^{(n)})^2 (\sigma_1^{2(n)})^2 + (\mu_2^{(n)} - \mu_1^{(n)})^2 (\sigma_1^{2(n)})^2 \\
- X_i^{(n)} (\sigma_1^{2(n)})^2 + 2\beta (\sigma_1^{2(n)})^2 (\sigma_2^{2(n)})^2 \\
\times \sum_r w_r Z_{r1}^{(n)} \\
B = (\mu_1^{(n)})^2 (\sigma_2^{2(n)})^2 + (\mu_2^{(n)})^2 (\sigma_2^{2(n)})^2 \\
+ 2\beta (\sigma_1^{2(n)})^2 (\sigma_2^{2(n)})^2 \sum_r w_r 
\tag{21}
\]

and \( Z_{2i}^{(n+1)} = 1 - Z_{i2}^{(n+1)} \), where \( X_{ik}^{(n)} \), \( \mu_k^{(n)} \) and \( \sigma_k^{2(n)} \) have been given above. The solution for \( K = 3 \) is determined by two linear equations, instead of two fifth-order equations (see Appendix for more details). The number of linear equations increases to three for \( K = 4 \), four for \( K = 5 \), and up to \( K - 1 \) for \( K \) tissue types. Solving the linear equations is much less complex than solving the fifth-order equations.

The presented MAP-EM framework above is based on the relationship (5) between the observed datum \( Y_i \) and the unobservable tissue contributions \( \{X_{ik}\} \) inside each voxel \( i \). This relationship is different from the model of \( Y_i = \sum_{k=1}^K Z_{ik} X_k \) used in the previous work, e.g., \([7]\). In the model of \( Y_i = \sum_{k=1}^K Z_{ik} X_k \), \( X_k \) reflects the random variable of tissue type \( k \) fully occupying a voxel, and \( Z_{ik} \) represents the fractioned random variable in voxel \( i \) and may not reflect the random variable from a fraction of tissue type \( k \). \( Z_{ik} \) is defined for more general cases of signal-dependent noise, the random variable from the mean or signal \( Z_{ik} \) shall be \( X_{ik} \), and the relationship between the unobservable mixture contributions and the observable datum \( Y_i \) shall be (5). If two tissue types occupy one half of a voxel, respectively, then the total variance shall go to \( \sigma_1^2 \), if the two tissue types are the same tissue type \( k \). This is the case by the relationship (5). Because of the difference between (5) and \( Y_i = \sum_{k=1}^K Z_{ik} X_k \), we adapt the definitions of (8) \([12]\) and the resulted expressions for the data mean and variance of \( k \) are then different from those in \([7]\). The derived MAP-EM algorithm (18)–(21) computes the tissue mixture percentages and the tissue model parameters in a continuous space and does not assume any voxel size—a noticeable difference from the down-sampling based segmentation algorithm in \([12]\).

In the following, we report numerical performance of solving the fifth-order equations, e.g., (20), and the linear equations, e.g., (21), for the tissue mixture percentages \( \{Z_{ik}\} \) in terms of accuracy and computing time.

III. NUMERICAL PHANTOM SIMULATION

A. Simulation Results for \( K = 2 \)

1) Data Simulations: For \( K = 2 \) case in which each voxel contains no more than two tissue types, a two-tissue phantom image of 256 \( \times \) 256 array size was generated as follows (the simulation is limited to two dimensions for simplicity). Tissue type 1 had a mean value of \( \mu_1 = 100 \) units and variance of \( \nu_1 = 100 \) units. Its percentage distribution \( \{Z_{1i}\} \) across the FOV is shown in Fig. 1(a). Each pixel in the upper (white) region was fully filled with tissue type 1 (\( Z_{1i} = 1 \)). The percentage decreased vertically down to zero across the (grey) strip of ten-pixel width in the middle. Each pixel had zero percentage of tissue type 1 (\( Z_{1i} = 0 \)) below the strip (i.e., the black region).

A noise image \( \{X_{i1}\} \) of tissue type 1 was simulated with Gaussian noise, where the image density \( X_{i1} \) at pixel \( i \) was given by a Gaussian noise generator \([23]\) with mean of \( X_{i1} = Z_{i1} \mu_1 \) and variance of \( \sigma_1^2 = Z_{i1} \nu_1 \). Tissue type 2 had a mean value of \( \mu_2 = 500 \) units and variance of \( \nu_2 = 300 \) units. Its percentage distribution \( \{Z_{2i}\} \) across the FOV is shown in Fig. 1(b). A noise image \( \{X_{i2}\} \) of tissue type 2 was simulated with Gaussian noise by the same procedure as simulating the noise image of tissue type 1 above. Adding these two noise images together results in the observable noise image \( \{Y_i\} \), which is shown in Fig. 1(c).

2) Implementation of (20) and (21): The MAP-EM algorithm of (18) and (19) with quadratic approximation of (21) was implemented by directly programming these three equations using C++ language. When implementing the algorithm with the mathematically exact formula of (20), we employed the QR program (C++ code) in \([23]\) to solve the fifth-order equation while (18) and (19) were directly programmed using C++ language as described above. These source codes were compiled in a Visual C++ environment on a HP XW8000 PC platform (2.4 GHz CPU and 2.0 GB RAM). The compiled programs with (20) (or theoretically exact implementation) and (21) (or quadratic approximated implementation) each ran up to 60 iterations to ensure that a stable solution is achieved. In our experiments below, a stable solution was observed after ten iterations.

3) Convergence Comparison Between (20) and (21): The convergence performance of the MAP-EM algorithm using (20) and (21), respectively, was studied by the measure of the relative error

\[
\epsilon(Z_{ik}) = \frac{\sum_{i,k} |Z_{ik}^{(n)} - Z_{ik}^{(truth)}|}{I_R}
\tag{22}
\]
TABLE I

<table>
<thead>
<tr>
<th></th>
<th>$\mu_1$</th>
<th>$\mu_2$</th>
<th>$v_1$</th>
<th>$v_2$</th>
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<tr>
<td>Result from the phantom image</td>
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<td>500.04</td>
<td>99.60</td>
<td>296.62</td>
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<tr>
<td>Iterated result with fixed $Z_{ik}$</td>
<td>100.07</td>
<td>500.02</td>
<td>99.47</td>
<td>297.35</td>
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</tbody>
</table>

TABLE II

<table>
<thead>
<tr>
<th></th>
<th>$\text{error}(\mu_1)$</th>
<th>$\text{error}(\mu_2)$</th>
<th>$\text{error}(v_1)$</th>
<th>$\text{error}(v_2)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theoretical update (20)</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.41%</td>
<td>2.18%</td>
</tr>
<tr>
<td>Approximated update (21)</td>
<td>0.05%</td>
<td>0.00%</td>
<td>0.89%</td>
<td>2.24%</td>
</tr>
</tbody>
</table>

where $I_R$ indicates the number of those pixels inside the PV horizontal strip in Fig. 1. Fig. 2 shows, as an example, the result when the initial $\{Z_{ik}^{(0)}\}$ had 50% deviation from the ground truth. Similar results were observed for other initial errors from 10% up to 90% on $\{Z_{ik}^{(0)}\}$. A stable solution after ten iterations was observed. The computing time for the iterative process was documented and plotted in Fig. 3. The QR program for the solution of (20) costs approximately 25% more computing time than the computation of (21) after 30 iterations.

4) Estimation of Tissue Model Parameters $\{\mu_k, v_k\}$: We first studied the accuracy of estimators (18) and (19) with known $\{Z_{ik}\}$. By setting the initial model parameters $\{\mu_k^{(0)}, v_k^{(0)}\}$ with 99.9% error from the ground truth of $\{\mu_1 = 100, \nu_1 = 100, \mu_2 = 500, \nu_2 = 300\}$ and fixing the mixture percentages $\{Z_{ik}^{(n)}\}$ as the ground truth of Fig. 1(a) and (b) at all iterations, we obtained the iterated results after thirty iterations $\{\mu_k^{(30)}, v_k^{(30)}\}$ as shown in Table I, where the model parameters of the phantom image were computed over those pixels inside the white and black regions in Fig. 1(c) excluding the PVE (i.e., ignoring the grey strip in the middle). These results indicate that the phantom image with Gaussian noise is accurately simulated, and the estimation of the model parameters is robust regardless of 99.9% initial error.

We then repeated the above experiment by updating the mixture percentages $\{Z_{ik}^{(n+1)}\}$ with (20) and (21), respectively, from the initial of $\{Z_{ik}^{(0)}\}$ being the ground truth. The iterated results after thirty iterations are shown in Table II. The percent error reflects the difference of the iterated result from the corresponding ground truth. The updates by (20) and (21) generated similar results. There is some difference in the estimate of $\nu_1$ due to a smaller mean and larger variance for tissue type 1 in the phantom image, as compared to that of tissue type 2. This difference was observed in all the experiments performed in this study.

5) Performance Comparison Between (20) and (21): To show the robustness of the MAP-EM segmentation algorithm for different initial estimates on the mixture percentages, we repeated the above experiment by allowing the initial $\{Z_{ik}^{(0)}\}$ with various % deviations from 10% up to 99.9%. The percent deviations were generated by sampling each $Z_{ik}^{(0)}$ using the Gaussian noise generator [23] with a given percent standard deviation from its ground truth $Z_{ik}$ in Fig. 1. The iterated results after 30 iterations are shown in Table III. The value in the upper right corner of each cell was from the theoretically exact solution (20), while the value in the lower left corner of each cell was from the quadratic approximated solution (21). The percentage error of estimating the tissue mixture percentages $\{Z_{ik}\}$ in the table was computed from those pixels in the PV horizontal strip in Fig. 1. Because of the penalty, the percentages $\{Z_{ik}\}$ in the white and black regions of Fig. 1 were accurately estimated. Both implementations with exact solution (20) and approximated solution (21) generated similar
results. Some difference in estimating the variance of tissue type 1 \( \{ \nu_1 \} \) was observed and explained before.

6) Further Simulation Studies for \( K = 3 \): A three-tissue phantom image of 256 × 256 array size was generated following the same procedure as described in Section III-A-1 above for Fig. 1. Tissue type 1 had a mean value of \( \mu_1 = 230 \) units and variance of \( \nu_1 = 180 \) units. Its percentage distribution \( \{ Z_{11} \} \) across the FOV is shown in Fig. 4(a). A PV strip of 10 pixel unit width is present vertically and horizontally, respectively, between the white \( (Z_{11} = 1) \) and black \( (Z_{11} = 0) \) regions. A noise image \( \{ X_{1i} \} \) of tissue type 1 was simulated with Gaussian noise, where the image density \( X_{1i} \) at pixel \( i \) was given by a Gaussian noise generator [23] with mean of \( \nu_1 = Z_{1i} \mu_1 \) and variance of \( \sigma^2_{1i} = Z_{1i} \nu_1 \). Tissue type 2 had a mean value of \( \mu_2 = 500 \) units and variance of \( \nu_2 = 300 \) units. Its percentage distribution \( \{ Z_{2i} \} \) across the FOV is shown in Fig. 4(b). A noise image \( \{ X_{2i} \} \) of tissue type 2 was simulated with Gaussian noise by the same procedure as simulating the noise image of tissue type 1 above. Tissue type 3 had a mean value of \( \mu_3 = 800 \) units and variance of \( \nu_3 = 500 \) units. Its percentage distribution \( \{ Z_{3i} \} \) across the FOV is shown in Fig. 4(c). A vertical PV strip of 10 pixel unit width is present between the black \( (Z_{3i} = 0) \) region on the left and the white \( (Z_{3i} = 1) \) region on the right. A noise image \( \{ X_{3i} \} \) of tissue type 3 was simulated with Gaussian noise by the same procedure as simulating the noise image of tissue type 1 above. Adding these three noise images together results in the observable noise image \( \{ Y_{i} \} \), which is shown in Fig. 4(d).

The update of the tissue model parameters \( \{ \mu_k, \nu_k \} \) was performed by (18) and (19) with 99.9% initial error, i.e., the same as the initial estimation in \( K = 2 \). Various initial errors from

### Table III

Comparison of Iterated Tissue Model Parameters and Tissue Mixture Percentages Using the Theoretical Solution (20) (Upper Corner in Each Cell) and the Approximated Solution (21) (Lower Corner in Each Cell), Where \( \beta = 0.5 \) Was Used

<table>
<thead>
<tr>
<th></th>
<th>( \text{err}(Z_{11}) )</th>
<th>( \text{err}(Z_{12}) )</th>
<th>( \text{err}(\mu_1) )</th>
<th>( \text{err}(\mu_2) )</th>
<th>( \text{err}(\nu_1) )</th>
<th>( \text{err}(\nu_2) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% deviation</td>
<td>2.66%</td>
<td>2.66%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.42%</td>
<td>2.19%</td>
</tr>
<tr>
<td>20% deviation</td>
<td>2.64%</td>
<td>2.64%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.41%</td>
<td>2.19%</td>
</tr>
<tr>
<td>30% deviation</td>
<td>2.66%</td>
<td>2.66%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.41%</td>
<td>2.19%</td>
</tr>
<tr>
<td>40% deviation</td>
<td>2.64%</td>
<td>2.64%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.41%</td>
<td>2.19%</td>
</tr>
<tr>
<td>50% deviation</td>
<td>2.66%</td>
<td>2.66%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.42%</td>
<td>2.19%</td>
</tr>
<tr>
<td>60% deviation</td>
<td>2.67%</td>
<td>2.67%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.42%</td>
<td>2.19%</td>
</tr>
<tr>
<td>70% deviation</td>
<td>2.66%</td>
<td>2.66%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.42%</td>
<td>2.19%</td>
</tr>
<tr>
<td>80% deviation</td>
<td>2.67%</td>
<td>2.67%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.42%</td>
<td>2.19%</td>
</tr>
<tr>
<td>90% deviation</td>
<td>2.69%</td>
<td>2.69%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>1.40%</td>
<td>2.19%</td>
</tr>
<tr>
<td>99.9% deviation</td>
<td>2.64%</td>
<td>2.64%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>0.88%</td>
<td>2.25%</td>
</tr>
</tbody>
</table>

### Table IV

Comparison of Iterated Tissue Model Parameters and Tissue Mixture Percentages Using the Theoretical Solution (A7) and (A8) and the Approximated Solution (A9) and (A10).

<table>
<thead>
<tr>
<th>( { Z_{1i} } )</th>
<th>( { Z_{12} } )</th>
<th>( { Z_{13} } )</th>
<th>( \mu_1 )</th>
<th>( \mu_2 )</th>
<th>( \nu_3 )</th>
<th>( \nu_1 )</th>
<th>( \nu_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theoretical</td>
<td>1.30%</td>
<td>3.16%</td>
<td>1.96%</td>
<td>0.03%</td>
<td>0.01%</td>
<td>0.01%</td>
<td>0.01%</td>
</tr>
<tr>
<td>Approximated</td>
<td>1.33%</td>
<td>3.04%</td>
<td>1.86%</td>
<td>0.03%</td>
<td>0.01%</td>
<td>0.01%</td>
<td>0.01%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>( \mu_3 )</th>
<th>( \nu_1 )</th>
<th>( \nu_2 )</th>
<th>( \nu_3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theoretical</td>
<td>0.02%</td>
<td>0.13%</td>
<td>1.53%</td>
</tr>
<tr>
<td>Approximated</td>
<td>0.02%</td>
<td>0.16%</td>
<td>1.52%</td>
</tr>
</tbody>
</table>
Fig. 5. Comparison of iterated tissue mixture percentages against iteration number using the theoretical solution (solid line) and the approximated solution (crosses). Top left reflects the error rate of $Z_{i1}$, top right reflects the error rate of $Z_{i2}$, and bottom shows the error rate of $Z_{i3}$.

10% to 99.9% were selected for the tissue mixture percentages relative to the ground truth in the pictures of Fig. 4. The initial tissue percentages were updated by both the theoretical solution of (A7) and (A8) and the quadratic approximation (A9) and (A10). Since the $QR$ program in [23] is valid only for a single equation of (20), not a set of more than one equation of high orders, we adapted the Newton’s gradient program [23] to solve the set of two fifth-order equations (A7) and (A8). The linear equations (A9) and (A10) were coded directly by C++ language. Both the Newton’s program and C++ code of (A9) and (A10) were complied and executed by the same computer, as described in Section III-A-II. The results after 30 iterations are shown in Table IV for 50% initial error. The percentage error of estimating the tissue mixture percentages $\{Z_{ik}\}$ in the table was computed from those pixels, which contain three tissue types, in the PV square area in the center of Fig. 4(d). Both the theoretical solution and the quadratic approximation generated similar estimates of the tissue model parameters and the tissue mixture percentages, the same observation as seen in the study for $K = 2$.

The convergence performance of the MAP-EM algorithm using the theoretical solution (A7)–(A8) and the quadratic approximation (A9)–(A10) respectively is compared in Fig. 5. Equation (22) was used, here $I_R$ now indicates the number of those pixels inside the PV square region of three tissue types in the center of Fig. 4(d). A stable solution after 40 iterations was observed. A faster convergence for a tissue type of smaller mean and variance was noted. A larger number of iteration is needed for pixels containing more tissue types. The computing time for the iterative process was documented and plotted in Fig. 6. The Newton’s gradient program for solving the fifth-order equations (A7)–(A8) has the same efficiency in computation compared to directly solving the linear equations (A9)–(A10).
IV. DIGITAL BRAIN MRI PHANTOM STUDY

A. Brain MRI Phantom Simulation

A more realistic MRI brain digital phantom was simulated via the anatomical model available online\(^1\), which consists of a set of 3-D “fuzzy” tissue membership volumes, one for each tissue type (e.g., cerebrospinal fluid (CSF), grey matter, white matter, etc.). Since the voxel values in these volumes reflect the proportions of the tissues present in the voxels in the range of \([0, 1]\), it is straightforward to obtain the tissue mixture distribution \(\{Z_{ik}\}\) for each tissue type \(k\) for the PV model of (5)–(9). For the purpose of this study, a noise-free 3-D image volume was firstly simulated using the T1 sequence of the MRI simulator provided at the BrainWeb, where only those voxels labeled as CSF, grey matter and white matter were extracted because of their dominating contribution to the phantom. Then the statistical mean associated with each of the three tissue types, denoted by \(\{\mu_1, \mu_2, \mu_3\}\), was computed by referring to \(\{Z_{ik}\}\). For each voxel \(i\) to be simulated, three independent Gaussian random variables of mean \(\mu_{ik}\) and variance \(\nu_{ik}\) corresponding to the three tissue types were generated individually and summed together, where \(\{\nu_1, \nu_2, \nu_3\}\) were user-defined tissue variances, reflecting different noise levels. Based on the above arguments, a digital MRI brain phantom of size \(181 \times 217 \times 181\), consisting of three tissue types, CSF, grey matter, and white matter, was simulated and its 82nd slice is shown in Fig. 7(a). The associated parameter sets of means and variances are listed in Table V.

B. Estimation of Tissue Model Parameters, Given Ground Truth as Initial

In this section, the ground truth of \(\{\mu_k, \nu_k\}\) for CSF, grey matter and white matter, as well as \(\{Z_{ik}\}\) for each voxel were given as initial values of \(\{Z_{ik}^{(0)}, \mu_k^{(0)}, \nu_k^{(0)}\}\) and the MAP-EM algorithm was run up to 100 iterations to ensure a stable estimation is achieved. For comparison purpose, both theoretical and approximated solutions as outlined by (20) and (21) were implemented and the results are tabulated Table VI. Both solutions have a similar performance in parameter estimation.

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\(^1\)http://www.bic.mni.mcgill.ca/brainweb/
C. Estimation of Tissue Model Parameters, Given Deviated Initials

Different from Section IV-B above where \( \{ Z_{ik}^{(0)} , \mu_k^{(0)} , \nu_k^{(0)} \} \) were initialized as the ground truth values, a more practical initialization strategy was taken in this section. Though the resulting \( \{ Z_{ik}^{(0)} , \mu_k^{(0)} , \nu_k^{(0)} \} \) would have certain deviations from their true values, this initialization strategy is considered to be more realistic, and can be summarized into the following steps.

1) According to the histogram of the synthetic MRI brain phantom, each voxel \( i \) was preassigned a discrete label from \( \{ 1, 2, 3 \} \), representing CSF, grey matter and white matter respectively via a thresholding operation, denoted by \( I_i \in \{ 1, 2, 3 \} \).

2) Based on \( I_i \), \( \{ \mu_k , \nu_k \} \) were calculated by grouping voxels which belong to the same labeled class. Although \( \{ \mu_k , \nu_k \} \) obtained in this way could not exactly reflect the true statistical properties, especially for \( \{ \mu_k , \nu_k \} \), they could be refined after sufficient EM iterations steered by \( Z_{ik} \) which is the most impacting factor.

3) The final and crucial step is to initialize \( \{ Z_{ik}^{(0)} \} \). For each voxel \( i \), the number of contributing tissue types \( \{ N_i \} \) was alternatively determined via its six-connected neighbors in 3-D image domain. Fig. 8 illustrates such initialization process in the case of 2-D image space where “C,” “G,” and “W” represent CSF, grey matter and white matter, respectively.

Once \( \{ N_i \} \) have been determined for each voxel, \( \{ Z_{ik}^{(0)} \} \) were accordingly initialized in such a way that if \( N_i = 2 \), i.e., voxel \( i \) contains a mixture of CSF and grey matter for example, then \( Z_{i1}^{(0)} = 0.5, Z_{i2}^{(0)} = 0.5, \) and \( Z_{i3}^{(0)} = 0. \) For the case of \( N_i = 3 \), then \( Z_{i1}^{(0)} = 0.33, Z_{i2}^{(0)} = 0.33, \) and \( Z_{i3}^{(0)} = 0.34. \)

The estimated model parameters \( \{ \mu_k , \nu_k \} \) and tissue mixture components \( \{ Z_{ik} \} \) after 100 EM iterations by the MAP-EM algorithm with both theoretical and approximated solutions are summarized in Table VII, and the distribution maps of \( \{ Z_{ik} \} \) in the 82nd slice corresponding to each tissue type are shown in Fig. 7(b) and (c), respectively. For visual judgment, the profiles of CSF, grey matter and white matter along both vertical and horizontal directions by sampling a one-pixel-wide stripe on Fig. 7(b) and (c) are shown in Fig. 9(a)–(c).

Both solutions showed some different performances in parameter estimation for mixed cases of \( K = 2 \) and \( K = 3 \) across the FOV when the initials \( \{ Z_{ik}^{(0)} , \mu_k^{(0)} , \nu_k^{(0)} \} \) were estimated from the acquired image data. In light of the numerical simulation studies above where the cases of \( K = 2 \) and \( K = 3 \) are known across the FOV, the different performances of the two solutions for mixed cases of \( K = 2 \) and \( K = 3 \) across the FOV are likely due to the determination of the number of tissue types in a voxel from the current iteration for the next iteration. The theoretical solution uses the QR program for voxels containing two tissue types (\( K = 2 \)) and the Newton’s gradient program for voxels containing three tissue types (\( K = 3 \)). The approximated solution applies the same strategy for the set of linear equations (A9) and (A10) for any \( K \) value. The following investigations will provide more insights on the difference.

D. Computational Analysis

In this section, the theoretical and approximated solutions were compared from two aspects: 1) converging speed and 2) computing time.

1) Converging Speed: The model parameters \( \{ \mu_k , \nu_k \} \) are usually converging to a stable estimate in less iterations than the mixture percentages \( \{ Z_{ik} \} \) do. So we report the converging speed of \( \{ Z_{ik} \} \) as iteration number goes up. Curves describing how the error rate of \( \{ Z_{ik} \} \) varies along the EM iterations for each tissue type \( k \) are shown in Fig. 10. Since the constraint of \( Z_{i1} + Z_{i2} + Z_{i3} = 1 \) leads to two degrees-of-freedom and, therefore, only the changes of \( \{ Z_{ik} \} \) associated with CSF and grey matter were plotted. The theoretical solution converged to a stable estimate in less iteration number and had a slightly larger relative error defined by (22), compared to the approximated solution.

2) Computing Time: The computing time of the theoretical and approximated MAP-EM solutions for segmenting the 3-D MRI brain phantom image of \( 181 \times 217 \times 181 \) array size is shown in Fig. 11 in unit of seconds as the iteration goes up. The computing time of the theoretical MAP-EM solution is almost five times more than that of the approximated solution for an equivalent EM iteration. Comparing Figs. 3 and 6–11 in terms of computing time for segmenting the corresponding 2-D numerical and 3-D MRI brain phantoms, respectively, it can be seen that the number of voxels containing two tissue types is much larger than the number of voxels containing three tissue types in the 3-D MRI brain image. This is because that the theoretical solution consumes more computing time for \( K = 2 \) than the approximated solution at an equivalent iteration. In clinical applications, we expect to have more voxels containing two tissue types than voxels containing three or more tissue types and, therefore,
the approximated solution may have an advantage over the theoretical solution in computing efficiency. By the results of Table VII and Fig. 9, both the approximated solution and the theoretical solution have a similar performance in estimating model parameters and mixture percentages of the three tissue types in the 3-D MRI brain image.
Estimator (20) is mathematically exact. It is a fifth-order equation and would generate five possible values for each $Z_{ik}$ when the QR program in [23] is used. In most cases, the constraint of $0 \leq Z_{i1} \leq 1$ eliminated the other four possible values. Sometimes we encountered a choice of one from two possible values for $Z_{i1}$ in the range of $[0, 1]$. In these cases, we chose the one which was closer to the previously iterated value. In contrast, (21) determines a value for each $Z_{i1}$ in the range of $[0, 1]$. However, because the quadratic approximation is made at the $n$th iteration, then the estimator (21) for $Z_{i1}$ at the $(n + 1)$th iteration is somehow bounded to the result at the $n$th iteration, causing a slower initial convergence compared to the theoretical solution (20) (see Figs. 2 and 10). For $K > 2$, the QR program is no longer applicable. When the Newton gradient program in [23] is used, a same convergence speed was obtained as that of the quadratic approximation (see Fig. 5). This is because of the Newton gradient program searches the solution from the $n$th iterated result, a similar bound to the $n$th iteration as that in the quadratic approximation. For digital implementation of both theoretical solution and quadratic approximation, we modified the condition $0 \leq Z_{i1} \leq 1$ to be $0,01 \leq Z_{i1} \leq 0,99$ to avoid $Z_{ik}$ being zero (or avoid numerical instability when $Z_{ik}$ is in the denominator).

Both estimators of the theoretical solution and the quadratic approximation generated similar results for the tissue mixture percentages $\{Z_{ik}\}$, leading to a similar estimate of the tissue model parameters $\{\mu_k, \nu_k\}$ by (18) and (19). The computational efficiency was also similar for both estimators when the Newton’s gradient program was used to solve the set of fifth-order equations for the theoretical solution. There is no noticeable benefit to solve a set of fifth-order equations for the tissue mixture percentages (e.g., (A7) and (A8) in Appendix), as compared to solving a set of linear equations by the quadratic approximation (e.g., (A9) and (A10) in Appendix), unless a more accurate program, similar to or better than the QR program, is available to solve the fifth-order equations. Therefore, the quadratic approximation may be a choice for practical applications at present time.

V. DISCUSSION AND CONCLUSION

In the mathematical derivation of the MAP-EM algorithm, we assumed $K$ to be the total number of different tissue types inside the body. The tissue model parameters $\{\mu_k, \nu_k\}$ of these $K$ tissue types were estimated using all the image data $\{Y_i\}$ by (18) and (19). In the implementation of (20) and (21) for estimation of the tissue mixture percentages $\{Z_{ik}\}$, only datum $Y_i$ and its neighbors were used. Then the number of tissue types in each voxel varied across the FOV. In other words, the total number of tissue types $K$ inside the body can be much greater than two, while the estimators (20) and (21) remain valid if a voxel contains no more than two tissue types. Similarly, estimators of (A7) and (A8) and (A9) and (A10) in Appendix are still valid if a voxel contains no more than three tissue types, despite the total number of tissue types in the body is far beyond three. This was demonstrated by clinical studies in segmenting patient abdominal CT images for virtual colonoscopy application [20].
Further validation of the algorithm by clinical studies is needed and is currently under investigation for CT colonoscopy application [20], where several practical issues regarding the MAP-EM implementation (e.g., initialization procedure, neighboring system optimization for increase or decrease of the number of tissue types at a concerned voxel, iteration speedup, recovery of submerged polyps inside tagged colonic materials, etc.) were studied. The whole implementation pipeline including postsegmentation strategies for removal of tagged colonic materials and extraction of mucosa layer from the MAP-EM segmentation was comprehensively evaluated by 52 patient CTC studies, which were downloaded from the website of the Virtual Colonoscopy Screening Resource Center, by two well-trained and experienced radiologists.

APPENDIX

This section provides the derivation for solution of \( \{Z_{ik}^{(n+1)}\} \) by setting the partial derivative of \( Q(\Theta|\Theta^{(n)}) \) with respect to \( Z_{ik} \) to zero under the conditions (17). Equation (15) can be rewritten as

\[
Q(\Theta|\Theta^{(n)}) = -\frac{1}{2} \sum_{i=1}^{I} \sum_{k=1}^{K} Q_{i,k}(Z_{ik}) \tag{A1}
\]

where the energy function on the neighborhood of voxel \( \tilde{i} \) in the conditional expectation term \( Q_{i,k}(Z_{ik}) \) at the \( n \)th iteration is understood as

\[
U(Z_{ik}) = \sum_{r \in Z_{i}} w_{ir} \cdot (Z_{ik} - Z_{rk}^{(n)})^2. \tag{A2}
\]

For \( K = 1, Z_{i1} \equiv 1 \) from the conditions (7), and \( Q(\Theta|\Theta^{(n)}) \) is independent from \( Z_{i1} \) and, therefore, the partial derivative of \( Q(\Theta|\Theta^{(n)}) \) with respect to \( Z_{i1} \) is zero for all voxels. This is expected. In this case, the mean and variance estimates by (18) and (19) become

\[
\mu_1 = \frac{1}{I} \sum_{i=1}^{I} Y_{i}, \quad \sigma_1 = \frac{1}{I} \sum_{i=1}^{I} (Y_{i} - \mu_1)^2. \tag{A3}
\]

These estimates are also expected for an image consisting of a single tissue type. For \( K = 2 \), we have

\[
Q(\Theta|\Theta^{(n)}) = -\frac{1}{2} \sum_{i=1}^{I} \{Q_{i,1}(Z_{i1}) + Q_{i,2}(1 - Z_{i1})\}. \tag{A4}
\]

By setting the partial derivative of \( Q(\Theta|\Theta^{(n)}) \) with respect to \( Z_{i1} \) to zero, we had obtained (21). For a special case of \( Y_{i} = \mu_1^{(n)} \) or \( Y_{i} = \mu_2^{(n)} \) and ignoring the penalty term, (21) converges to a stable solution of \( Z_{i1}^{(n+1)} = Z_{i1}^{(n)} \).

For \( K = 3 \), we have

\[
Q(\Theta|\Theta^{(n)}) = -\frac{1}{2} \sum_{i=1}^{I} \{Q_{i,1}(Z_{i1}) + Q_{i,2}(Z_{i2}) + Q_{i,3}(1 - Z_{i1} - Z_{i2})\}. \tag{A6}
\]

By setting the partial derivative of \( Q(\Theta|\Theta^{(n)}) \) with respect to \( Z_{i1} \) and \( Z_{i2} \), respectively, to zero, we can obtain two fifth-order equations for the solutions of \( Z_{i1}^{(n+1)} \) and \( Z_{i2}^{(n+1)} \)

\[
a_{11} \xi_1 + b_{11} \xi_1 + c_{11} \xi_1^2 + d_{11} \xi_1 + e_{11} = 0, \tag{A7}
\]

\[
a_{21} \xi_2 + b_{21} \xi_2 + c_{21} \xi_2^2 + d_{21} \xi_2 + e_{21} = 0, \tag{A8}
\]

where \( \xi_1 = Z_{i1}^{(n+1)} \), \( \xi_2 = Z_{i2}^{(n+1)} \), and all the coefficients have been determined by the results at the \( n \)th iteration. By the quadratic approximation (A5) and setting the partial derivative of \( Q(\Theta|\Theta^{(n)}) \) with respect to \( Z_{i1} \) and \( Z_{i2} \), respectively, to zero, we have two linear equations of

\[
A_1 Z_{i1}^{(n+1)} + B_1 Z_{i2}^{(n+1)} + C_1 = 0, \tag{A9}
\]

\[
A_2 Z_{i1}^{(n+1)} + B_2 Z_{i2}^{(n+1)} + C_2 = 0, \tag{A10}
\]

where the coefficients \( A_i, B_i, \) and \( C_i \) have been determined by the results at the \( n \)th iteration.

For \( K = 4 \), we can derive three fifth-order equations, similar to (A7) and (A8), to estimate \( Z_{i1}, Z_{i2}, \) and \( Z_{i3} \) with \( Z_{i4} = 1 - Z_{i1} - Z_{i2} - Z_{i3} \). By the quadratic approximation, we can derive three linear equations, similar to (A9) and (A10), to estimate \( Z_{i1}, Z_{i2}, \) and \( Z_{i3} \) with \( Z_{i4} = 1 - Z_{i1} - Z_{i2} - Z_{i3} \). In general cases of \( K \) tissue types, we can derive theoretically \( K - 1 \) equations under conditions (7) to estimate the \( K \) tissue mixture percentages in each voxel. In practice, there are very few cases where \( K \) goes beyond 4.

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Errata

Erratum to “An EM Approach to MAP Solution of Segmenting Tissue Mixtures: A Numerical Analysis”

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