

NORMALIZATION OF JOINT IMAGE-INTENSITY STATISTICS IN MRI USING THE KULLBACK-LEIBLER DIVERGENCE

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ABSTRACT

We describe a novel algorithm for altering global intensity statistics of magnetic resonance images (MRI) to fit a model distribution while preserving local feature contrast. Our algorithm estimates a multiplicative correction field that alters the intensity statistics of an image or set of images to best match those of a model. This is achieved by minimizing the Kullback-Leibler divergence between the observed and desired intensity distributions. This procedure is effective for the discovery and removal of undesirable intra-individual and inter-individual signal intensity changes caused by developmental processes, disease processes or MR scanner intensity artifacts. Ultimately our goal is to improve the quality of segmentations obtained by classification of tissues on the basis of signal intensities by removing undesirable signal differences both within a subject, where tissue of the same composition may appear differently in different parts of the acquisition volume, and between subjects in cases where both inter-subject and inter-acquisition variability are confounds. Validation experiments with synthetic data indicate the algorithm can successfully remove typical signal intensity inhomogeneities, and illustrative results demonstrate successful intensity normalization applied to a segmentation problem.

1. INTRODUCTION

MR signal intensity properties depend strongly upon the underlying tissue type, but also upon developmental processes, disease progression and scanner-related intensity artifacts. These effects, combined with subject-related variations, serve to confound segmentation procedures by blurring the boundaries between tissue classes.

We have developed a novel method for *normalizing* the intensities within an image to best match those of a model distribution. The Kullback-Leibler divergence (KLD) is used

as a measure of how well a given intensity distribution matches a template distribution. We model the presence of unwanted intensity variation as $O = FI + n$ where O is the observed image, F is a multiplicative intensity corruption, n is acquisition noise and I is the desired "correct" image. For our purposes, n is considered to be of a high spatial frequency relative to F and of low magnitude relative to I . We therefore neglect the effect of n . Our desired result is therefore $I \approx F^{-1}O$. We necessarily constrain our estimates of F^{-1} to be of low spatial frequency. This provides a solution that improves the clustering of global image statistics while preserving the local contrast that defines the anatomical boundaries of interest and avoiding amplifying noise.

We solve for a field of intensity adjustment parameters F^{-1} such that the Kullback-Leibler divergence between the adjusted source and target data sets is minimized:

$$\arg \min_{F^{-1}} \sum_k p_k \log_2(p_k/q_k) \quad (1)$$

where p_k is the probability of occurrence of signal intensity state k in the corrected image $F^{-1}O$ and q_k is the probability of occurrence of signal intensity state k in the target model M .

2. METHODS

2.1. Overview

Because no closed-form solution for F^{-1} exists, we use an iterative solution. Since we constrain F^{-1} to be smoothly varying, we can solve for a sub-sampled version of the field, F_s^{-1} . We extend an iterative solver, described below, with a multi-resolution framework in order to increase performance and stability, while helping to enforce the smoothness constraint. We pick a subject whose intensity characteristics are appropriate for our application and generate the histogram of this subject's images as a model to which other subjects will be matched.

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2.2. Iterative Optimization

We use an iterative scheme in order to solve for our correction field. A typical $256 \times 256 \times 110$ voxel brain image data set with typical voxel size (0.9375 mm, 0.9375 mm, 1.5 mm) will result in a final subsampled correction field F_s that is $30 \times 30 \times 21$ values. Because of the large number of parameters being optimized, and because the objective function is reasonably expensive to calculate, we have chosen the Simultaneous Perturbation Stochastic Approximation (SPSA) method for optimization [1, 2]. SPSA calculates an approximation of the objective function gradient at each iteration and then adjusts the current solution estimate according to the gradient estimate. Finite differences are used in generating the gradient estimate and the SPSA method incorporates two “gain” sequences that serve to shrink, as the iterations progress, the distance over which the finite differences are calculated as well as the size of the adjustment step taken.

Spall notes [1] that, under proper conditions, SPSA performs with equivalent statistical accuracy to Keifer-Wolfowitz [3] FDSA finite-difference approximation, but requires only two evaluations of the objective function, regardless of the number of parameters being optimized. Keifer-Wolfowitz or Robbins-Munro methods generally require two evaluations for *each* parameter being optimized, so the computational cost savings of SPSA can be substantial. Spall also shows that with the proper choice of the perturbations utilized, this method is guaranteed to at least converge to a local minimum and can be modified to guarantee a global minimum.

SPSA generates a gradient estimate \hat{g}_i , at each iteration i , as follows:

$$\hat{g}_i(\hat{F}_s^{-1}) = \frac{\mathbf{u}(\hat{F}_s^{-1} + \mathbf{c}_i \Delta_i) - \mathbf{u}(\hat{F}_s^{-1} - \mathbf{c}_i \Delta_i)}{2\mathbf{c}_i \Delta_i} \quad (2)$$

here \mathbf{u} is the objective function. In our case, $u(\hat{F}_s^{-1}) = D(p(\hat{F}_s^{-1}O) \parallel p(M))$ where $p(\hat{F}_s^{-1}O)$ is the histogram of the adjusted image (the original image O multiplied by our current estimate of the adjustment field \hat{F}_s^{-1}), $p(M)$ is the model histogram to which we are matching, and D is the K-L divergence.

The gradient estimate is made across a perturbation of the parameter field \hat{F}_s^{-1} by $\pm \mathbf{c}_i \Delta_i$. It is the nature of Δ_i that guarantees convergence over a number of iterations. In [2], Spall suggests that sampling the elements of Δ_i from a Bernoulli ± 1 distribution with $+1$ and -1 equally likely and we have used this here. $\mathbf{c}_i \Delta_i$ is therefore a vector of $\pm c_i$.

The gain sequences are defined as follows:

$$c_i = c/i^\gamma \quad (3)$$

$$a_i = a/(i + A)^\alpha \quad (4)$$

where c_i controls the distance over which the gradient estimate is made and a_i controls the size of the resulting step taken. A is an added parameter that allows for a more aggressive value of a , while avoiding instability during early iterations. The decay parameters, α and γ , are set to 0.602 and 0.101, which was the starting point recommended in [2].

After each iteration, the estimate of the solution parameter field \hat{F}_s^{-1} is updated as:

$$\hat{F}_s^{-1} = \hat{F}_s^{-1} - \mathbf{a}_i \hat{g} \quad (5)$$

3. RESULTS

3.1. Segmentation of a cohort of subjects using a single model subject

Our primary goal is to enable more efficient segmentation of brain images. To illustrate the effect of normalization on the segmentation process, we took a pool of seven subjects, chose a single model subject, and normalized the other six subjects to the joint intensity characteristics of this model. We used a fast k NN classification algorithm [4], without any other filtering or removal of extra-cerebral structures, and segmented the images into four tissue classes: background, grey matter, white matter, and cerebrospinal fluid (csf). We trained the k NN classification algorithm using data from the model subject.

Figure 1 shows the result of this process. The left image shows the derived classification when the technique is applied, without per-subject training, to each of our six test scans. Due to the intensity differences between subjects, and between locations within a subject’s scan, the segmentation is quite poor. The image on the right shows more expected results when the technique is applied, again without per-subject training, to images that have been normalized to the model subject.

3.2. Correction of intensity artifact using joint intensity information

Figure 2 shows a plot of joint and marginal densities from some of our neonatal data. The joint histogram on the left shows the initial state of a dataset that suffered from a severe intensity artifact within the SPGR channel. The histogram in the middle shows the result after successfully normalizing the image to the subject model shown at right. Graphing of specific features within the images showed that the intensity artifact was removed from the SPGR channel and the T2 channel was also modified, slightly, to better agree with the model distribution. Additionally, we normalized syn-

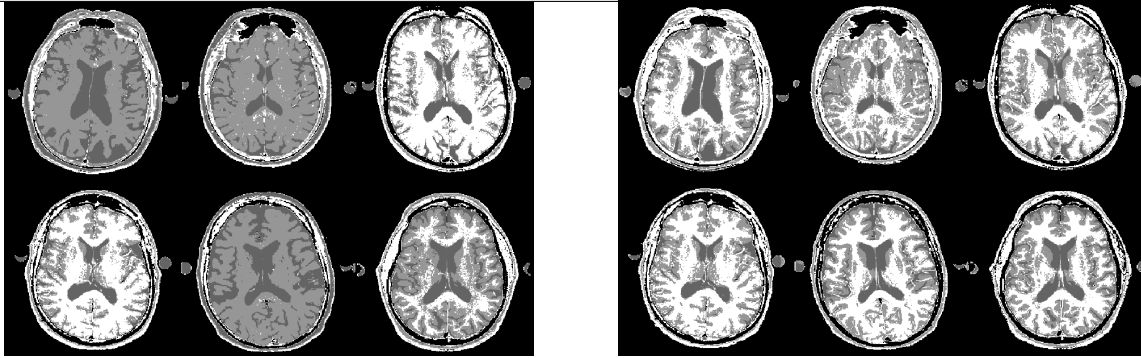


Fig. 1. Segmentation of axial PD MR images, from six different subjects, into tissue classes. Left is the result without per-subject training of the classifier. Right is the corresponding images resulting from single-subject training of the classifier and normalization of the remaining images to the single model subject.

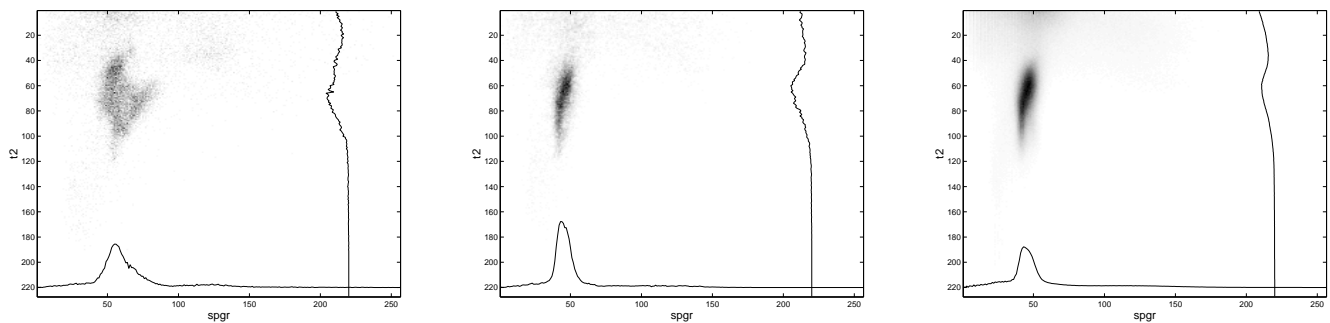


Fig. 2. joint (scatter) and marginal histograms (line). left: initial subject data; middle: corrected subject data; right: model data

thetic images with added defects and found good agreement between the derived correction and the applied defect.

4. DISCUSSION

Viola first proposed the use of entropy of image intensities in order to correct RF field inhomogeneity artifacts in MR images in [5]. Viola observes that the corrupting artifact serves to increase pixel entropy and this can be seen in the histogram as a blurring together of the peaks from distinct tissue classes. Mangin presented an entropy-minimization method that uses a rapid simulated-annealing approach to solve for a correction field [6]. This seems to work quite well for the removal of smoothly varying intensity artifacts in single-band (e.g. single pulse-sequence MR) data.

We have extended the idea of using entropy as an intrinsic measure to characterize a corrupting spread in intensity distribution. The Kullback-Leibler divergence provides a measure of *relative* entropy and we exploit this to allow matching to a model intensity distribution. In the case of field-inhomogeneity artifact correction in single band data, our method appears to work as well as entropy minimiza-

tion, in our experience, given a model of the proper distribution. In our case, model generation is quite easy as it simply requires collection of statistics from suitable images and then the model can be reused. Our goal for this work, however, is to allow for the generation of representative data for a given subject population and then to train a statistical classifier on that model data. As we have shown, subsequent subjects from a similar population could then be corrected, using our method, and segmented by a statistical classifier that has been trained solely on the model data.

4.1. Relationship to Other Works and Conclusion

Several authors have proposed methods for normalizing or standardizing MR intensity values. Nyúl and Udupa proposed a method for generating a piecewise linear transformation of intensities across images [7]. This method requires choices regarding the shape of the expected histogram, however the authors note that in practice only one or two shapes occur. In a later publication, Madabhushi and Udupa provide evidence that correcting field inhomogeneity artifacts should be done prior to intensity normalization [8].

Christensen reported a method using even-order histogram derivatives to calculate characteristic values to which to normalize [9]. Both methods create a global intensity transformation that does not vary spatially throughout the image and also rely on some sort of tissue class model. Our technique differs in two key ways. First, we match to a supplied histogram model which can be generated by any representative subject. This allows us to proceed without assumptions about the shape of the histogram or the specific contribution of a given class of tissue. Secondly, since we solve for a spatially varying normalization field, it is not necessary for us to involve a separate step for field inhomogeneity correction. Our experience has been that this technique works well to remove inhomogeneity effects if normalization is done relative to an unaffected model image.

The algorithm of Wells et al. [10] provides a simultaneous estimate of tissue classification and estimation of a smoothly varying intensity inhomogeneity artifact. This important technique has been successful in several different applications. However, it requires the specification of the class conditional probability density functions (pdfs), and these are especially difficult to accurately specify in the scans of developing brains that we see. Also, if the intensity artifact is such that a class conditional pdf in a subject scan is closer to a different class conditional pdf in the statistical model, rather than being closest to the desired match, the initial segmentation estimate may be poor. The algorithm may then converge to an undesirable solution in which the intensities are adjusted to further push the wrong class conditional pdf to increase the match with the initially close but incorrect class conditional pdf of the model. In practice for our neonate MRI scans we have found it time consuming and challenging to accurately develop the statistical model required. The algorithm we have presented here may act as a substitute for, or operate in conjunction with, the algorithm of [10] by providing an initial correction field estimator which enables a good initial match of the class conditional pdfs.

We have a large set of neonatal brain image data which poses some unique challenges. A great deal of white matter myelination happens subsequent to delivery, so brain MR images of early neonates have vastly different intensity statistics than is seen in adults. One aspect of this difference is significant reduction in contrast between gray and white matter on an SPGR scan. For this reason intensity non-uniformity artifacts, such as those that result from the use of an external RF coil, are a significant problem when attempting to classify the tissue structure of these images. Furthermore, we are interested in automating the segmentation process and avoiding the per-subject training necessary with many successful segmentation algorithms. This method leads to fully automated segmentation of brain images.

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