

# A Hybrid Approach to Intensity Normalization of Brain MRI based on Gaussian Mixture Model and Histogram Matching

Xiaofei Sun<sup>1</sup>, Lin Shi<sup>2,3</sup>, Yishan Luo<sup>1</sup>, Winnie CW Chu<sup>1</sup>, and Defeng Wang<sup>1,4</sup>

<sup>1</sup>Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, <sup>2</sup>Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, <sup>3</sup>Chow Yuk Ho Technology Centre for Innovative Medicine, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, <sup>4</sup>Department of Biomedical Engineering and Shun Hing Institute of Advanced Engineering, The Chinese University of Hong Kong, Shatin, NT, Hong Kong

## Introduction

Quantitative analysis of MR images (registration, segmentation and volumes statistics) is based on the assumption that corresponding anatomical locations have a similar intensity level, which is very difficult to guarantee especially in large-scale multi-center MRI-based neuroscience studies due to the inconsistent acquisition conditions such as various scanners and imaging parameters. Therefore, intensity normalization is a critical issue to guarantee that the MRI data collected at various acquisitions are comparable. In this study, a new method to normalize intensity in MR images is proposed. This new method does not require spatial alignment with existing atlas or template. The results show that the intensity normalization significantly improves the accuracy of the tissues segmentation results.

## Subjects and Methods

**Image acquisition and image preprocessing.** Eleven adult subjects (4 males, and 7 females) were scanned at two time points using T1-weighted fast field echo (FFE) pulse sequence in Siemens Sonata 1.5T scanner and T1-weighted inversion recovery multiplanar reformatting (IR-MPR) pulse sequence at Philips Achieva 3.0T MRI scanner, respectively with an interval of 8-12 minutes. All MRI images underwent skull removal operation using the FSL (FMRIB's Software Library) toolbox. Besides, image quality assessment was achieved using Aja-Fernández's histogram estimator model [1], and the high-quality image of every subject taken as a reference was selected to perform intensity normalization of low quality image.

**Intensity normalization using Gaussian Mixture Model and Histogram Matching.** The method basically consists of two steps: (I) estimating a mixture of Gaussian that approximates the intensity histogram. Given two brain MR images  $M_1$  and  $M_2$ , and their histograms  $h_1$  and  $h_2$ , then we utilize an intensity normalization function  $f$  so that each tissue of  $f(M_2)$  has the similar intensity level with corresponding tissue of  $M_1$ , without registering  $M_1$  and  $M_2$ . The intensity normalization function  $f$  should be consistent in corresponding tissues, i.e. the intensity of grey matter of  $f(M_2)$  should match the intensity of grey matter of  $M_1$ . To ensure this consistence of corresponding tissue, a mixture of  $n$  Gaussian distribution that models the two histograms  $h_1$  and  $h_2$  with the Expectation-Maximization (EM) algorithm is estimated and utilized. The EM algorithm is well adapted in this study because of its high convergence rate and relative insensitivity to initialization. In this study, we use three Gaussian distributions that model the main classes: white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF). The Gaussian mixture has proved to be relevant for fitting MR T1-weighted histograms [2]. For each tissue  $t$ , we achieve the center of the distribution  $\mu_t$  (respectively  $\nu_t$ ) for image  $M_1$  (respectively image  $M_2$ ).

(II) Computing the intensity normalization that aligns the mean intensity of tissues with histogram parameter. As this step is to normalize the intensity of the tissues and to interpolate smoothly the normalization, we choose a piecewise linear function. The histogram  $h_2$  of  $M_2$  is stretched, and shifted in order to cover all the gray scale levels in the histogram  $h_2$  of  $M_2$  as follows:

$$f(M) = \begin{cases} \left[ \mu_t + (M_2 - \mu_i) \frac{I_{low} - \mu_s}{S_1 - \mu_i} \right], & m_1 \leq M_2(x, y, z) \leq \nu_i \\ \left[ \mu_t + (M_2 - \mu_i) \frac{I_{high} - \mu_s}{S_2 - \mu_i} \right], & \nu_i \leq M_2(x, y, z) \leq m_2 \end{cases}$$

where  $\lceil \cdot \rceil$  denotes the "ceiling" operator,  $m_1$  and  $m_2$  are the mean values of each tissue of image  $M_1$  and image  $M_2$ , respectively.  $S_1$  and  $S_2$  stand for the left and right shoulder mode respectively.  $I_{low}$  and  $I_{high}$  are denoted as minimum and maximum values of each tissue in  $M_1$ .

## Results

We evaluated this new approach on different MR acquisitions for each of the 11 subjects. The qualitative result of intensity normalization is shown in Fig. 1. The original intensity disparity between the source image (Fig. 1 (A)) and reference image (Fig. 1 (C)) was greatly reduced after applying the proposed hybrid intensity normalization approach (Fig. 1 (B)). In this experiment, we used three Gaussian distributions to model the 3 tissue types (i.e., WM, GM and CSF) and the proposed parametric normalization function for histogram matching. The effectiveness of the proposed method in improving the tissue segmentation results of WM, GM, and CSF can be quantitatively reflected by the Dice Similarity coefficients (DSC) (Table 1) between segmentations of the three major tissues, WM, GM, and CSF, and their weighted average on 11 sets of MR images. The tissue classification was performed using fuzzy C-means [3].

## Conclusions

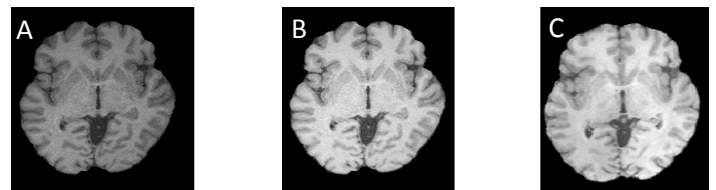
This study described a MR intensity normalization framework based on Gaussian Mixture Model and histogram matching that can normalize scans acquired on different scanners or with different acquisition parameters. We validated our method on real scan of the same cohort of subjects by normalizing the low quality to the high quality image of the same subject, and showed that it increased the consistency of the tissue classification results. These results showed that intensity normalization could achieve better image analysis performance without spatial registration, and relevant intensity information of each corresponding tissue must also be incorporated. A major strength of the current study is that intensity normalization approach is applied in the field of a large-scale, multi-centric dataset of MRI and other MR modalities (e.g. fMRI).

**Table1** Average DSC values of tissue segmentations are obtained from 22 scans, before and after normalization

Tissue	DSC before normalization	DSC after normalization
WM	0.8092±0.0180	0.8918*±0.0169
GM	0.6700±0.0494	0.7981*±0.0426
CSF	0.5225±0.0349	0.6658*±0.0249
Mean	0.6678	0.7901

\*Statistically significantly larger than before normalization (p-value < 0.05)

**Reference** [1]Aja-Fernández S, et al. Noise estimation in single-and multiple-coil magnetic resonance data based on statistical models. Magn. Reson. Imag. 2009; 27(10):1397-1409. [2]Kovacevic N, Lobaugh N J, Bmnskill M J, et al. A robust method for extraction and automatic segmentation of brain images. Neuroimage. 2002; 17(3):1087-1100. [3]Bezdek J C. A convergence theorem for the fuzzy ISODATA clustering algorithms. IEEE Trans. Patt. Anal. Machine Intell. 1980; 2(1): 1-8.



**Fig. 1.** Effect of the intensity normalization on T1-MR images. (A) Source image; (B) intensity normalized source image; (C) reference image.