Introduction

The work presented here implements the algorithm described in [1] and [2]. The method involves learning the intensity scale parameters from a set of images in a training dataset, which are then used to define a reference scale. This reference distribution is derived by averaging key statistical parameters from the training images. Once established, the reference landmarks are applied to scale all images in the dataset, ensuring consistent intensity normalization across the dataset.

Main Work

The code consists in several steps:

1. NIfTI image Downloading of 12 subjects.
   As part of the downloading, a data structure called *imageData* is created which contains the 12 images, their respective NIfTI metadata information, their subject description and if they are part of the training dataset.

2. The landmarks, percentiles or other statistical orders, referenced through the code as '*peak'*, are defined in two functions setUpPercentiles and setUpPeaks. The landmarks are used in the standardization step if the image is part of the training set and for all the images in the transformation step.
   The minimum; $m_{1,}$ and maximum image pixel intensities; m_2, minimum, p1 and maximum, p2 pixel intensity percentiles are computed. In addition, of m_1, m_2, p_1 and p_2; the authors recommend using at least one more landmark, *w*, the shoulder of the background hump when the histogram is unimodal and μ, the second mode of the histogram when it is bimodal.
   The histogram-specific parameters landmarks of each image are manually determined (Table 1):
   - Each image's histogram is plotted, highlighting the locations of m_1, m_2, p_1, p_2, and additional user-selected landmarks. These landmarks are determined based on the height of the bins, which represent the total number of pixels at each intensity level in the image.
   - The function findNthLargestBinsIntensity identifies the peak intensity values by analyzing the histogram. It selects the intensity corresponding to the n^{th} largest bin, where bins are sorted by the number of pixels (bin counts).
   - plotHistogramWithLandmarks plots a histogram with all its landmarks: m_1, m_2, p_1, p_2, and other mode related landmarks (Fig. 1).

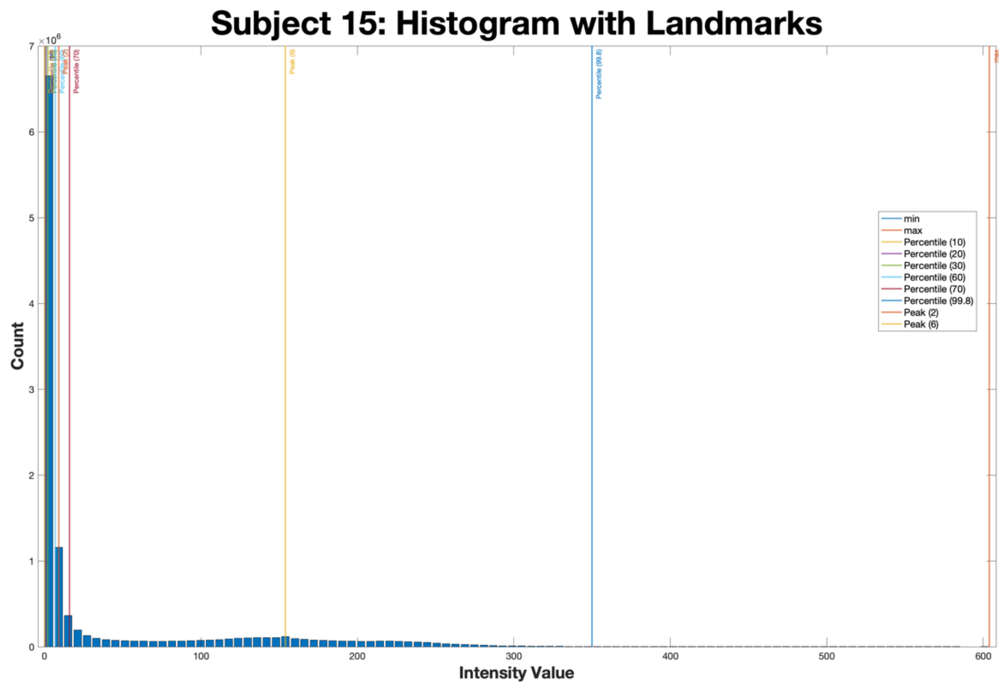

Fig. 1: Subject 15 Histogram with its landmarks

Subject	pc_1	pc_2	Mode1 (bin n^o)	Mode 2 (bin n^o)
2	10	99.8	2	5
3	10	99.8	2	20
4	10	99.8	2	20
5	10	99.8	2	20
6	10	99.8	2	41
7	10	99.8	2	6
9	10	99.8	2	6
10	10	99.8	2	10
11	10	99.8	2	6
12	10	99.8	2	6
13	10	99.8	2	6
15	10	99.8	2	6

Table 1: Subjects with their major landmarks.

- pc_1 is set to 10% and not 0 because most of the largest peak in the histogram of the images correspond to the background pixels with 0 intensity.
- Other percentiles used are: 20% 30% 60% 70%.

3. S1 and S2 are computed, S1 is set to 1, s2 to the maximum of all the pixel intensities of the whole dataset of images (finds1s2).

4. The landmarks of each inage are standardized following the standardization algorithm (Fig. 2). Independently of an image being in the training dataset or not, the landmarks of all the images are computed. This provides the flexibility to select different reference landmarks for the mean landmarks if decision is made to use another set of images as part of the training set.

If the minimum of an image intensities is less than pc_1 it is set to pc_1 and similarly if the maximum of an image intensities is greater than pc_2 it is set to pc_2. Tuning of these minimums or maximums could be further refined in future iterations of the algorithm (functions: applyStandardizationToLandmarks, applyStandardizations and standardize).

5. A matrix is created which has for rows the landmarks of the images of the training datasets (all subjects but 13 and 15). The means of these landmarks are computed column-wise and stored in each image metadata structure. (Fig. 2)

Algorithm 2: Standardization

Input : A set of images V_j ($j = 1, \dots, N$) and histogram parameters pc_1, pc_2, s_1, s_2 and landmark points $\mathcal{L} \in \{L_1, L_2, \dots, L_M\}$

Output: $\{\mu_{\mathrm{ks}} \mid 1 \leqslant k \leqslant n\}$

for $j = 1$ **to** N **do**
  Compute H_j of V_j;
  Determine P_{1j} and P_{2j} corresponding to pc_1 and pc_2 and find $\mu_{1j}, \mu_{2j}, \dots, \mu_{Mj}$ in H_j;
  Map $[p_{1j}, p_{2j}]$ of H_j to $[s_1, s_2]$ (linear map);
  Find the new mapped landmarks;
  Given $\mu_j \in [P_{1j}, P_{2j}]$;
  $\mu'_j = s_1 + \frac{\mu_j - P_{1j}}{P_{2j} - P_{1j}}(s_2 - s_1)$;
end
Calculate rounded means using all subjects j mappings:

$$\mu'_{1s}, \mu'_{2s,\dots}, \mu'_{Ms}$$

$$\mu_{ks} = \left\lfloor \frac{1}{N} \sum_{j=1}^{N} \mu'_{kj} \right\rfloor \text{ for } k = 1, \dots, M$$

Fig. 2: Standardization Algorithm.

6. Each image is then transformed including subject 13 and 15 which were not part of the training datasets using the mean of the standardized landmarks (based on the training dataset images) following the transformation algorithm (Fig. 3). The histograms of the transformed images are also computed and stored for further access (transformImages, transformImage).

Algorithm 3: Transformation

Input : An Image $V_i \in V_{PD}$, $pc_1, pc_2, s_1, s_2, \mu_{1s}, \mu_{2s}, \ldots, \mu_{ms}$
Output: Transformed image V_{si} or LUT that stores intensity transformation

Begin:

1. Compute $H_i = (G_i, h_i)$ of V_i
2. Determine P_{1i}, P_{2i} corresponding to pc_1, pc_2.
3. Map sections of the scale of H_i linearly to the standard scale (see Fig. 4)
4. Map the intensity value of every voxel

Fig. 3: Transformation algorithm.

Evaluation

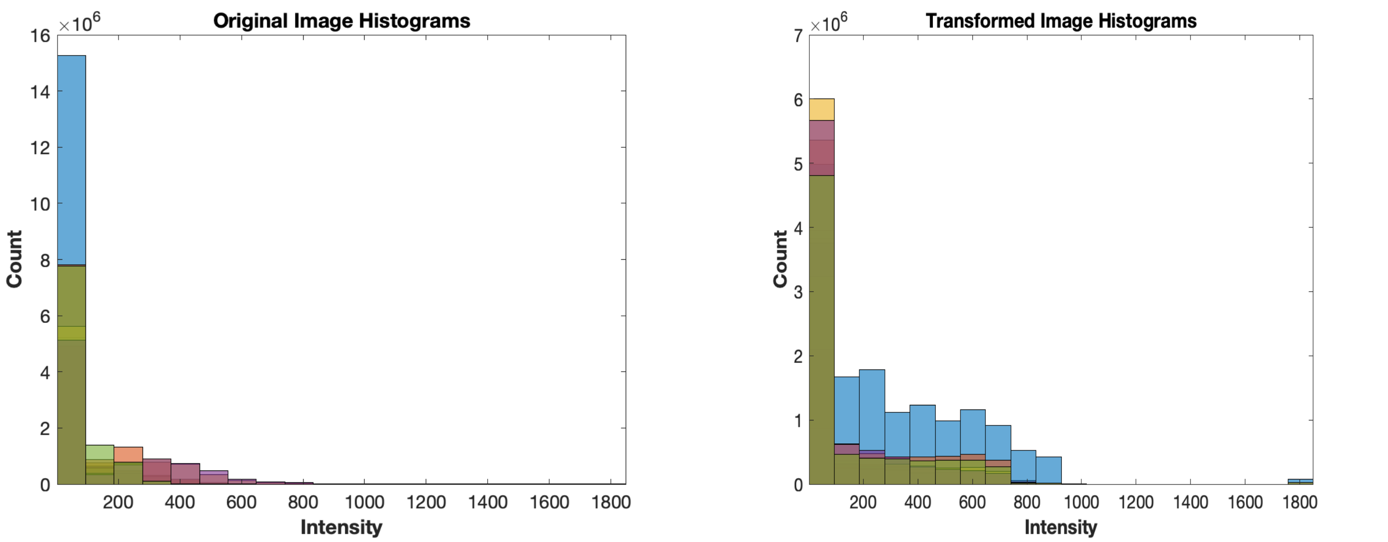

Fig. 4: Subject MRI Image Histograms before and after Scale Standardization.

From the provided histograms, the following observations can be made regarding the image histograms **before** and **after transformation** (plotBothHistograms, Fig. 4):

Before Transformation (Original Image Histograms):

1. **High Intensity Concentration at Low Values**:
   - A significant proportion of the pixel intensities are concentrated at lower intensity values (between 0 and 200), as seen from the tall bar around these values.
   - This suggests that the original images have a limited range of pixel intensity values, with most pixels clustered in the lower intensity range.

2. **Sparse Distribution at Higher Intensities**:
    - The histogram shows a sparse distribution of pixel counts as intensity values increase beyond 200.
    - Very few pixels have intensities higher than 600, indicating that the images may have poor contrast or very low dynamic range in the higher intensity regions.

After Transformation (Transformed Image Histograms):

1. **More Even Distribution Across Intensity Range**:
    - The transformed image histogram shows a more even spread of pixel intensities, with fewer pixels concentrated at the lower intensity values compared to the original images.
    - There are a more gradual distribution of pixel counts across a wider intensity range, suggesting the transformation has redistributed the intensities more evenly across the scale.
2. **Improved Dynamic Range**:
    - The pixel intensities now span a larger portion of the intensity spectrum (from 0 to around 1000). This suggests that the transformation has improved the dynamic range of the images, enhancing the contrast.
3. **Peak Distribution Shift**:
    - The transformation has shifted the location of intensity peaks (previously concentrated at very low values) toward a more balanced intensity range.
    - This can indicate that the transformation algorithm has stretched the intensity values to make the image more interpretable and balanced.

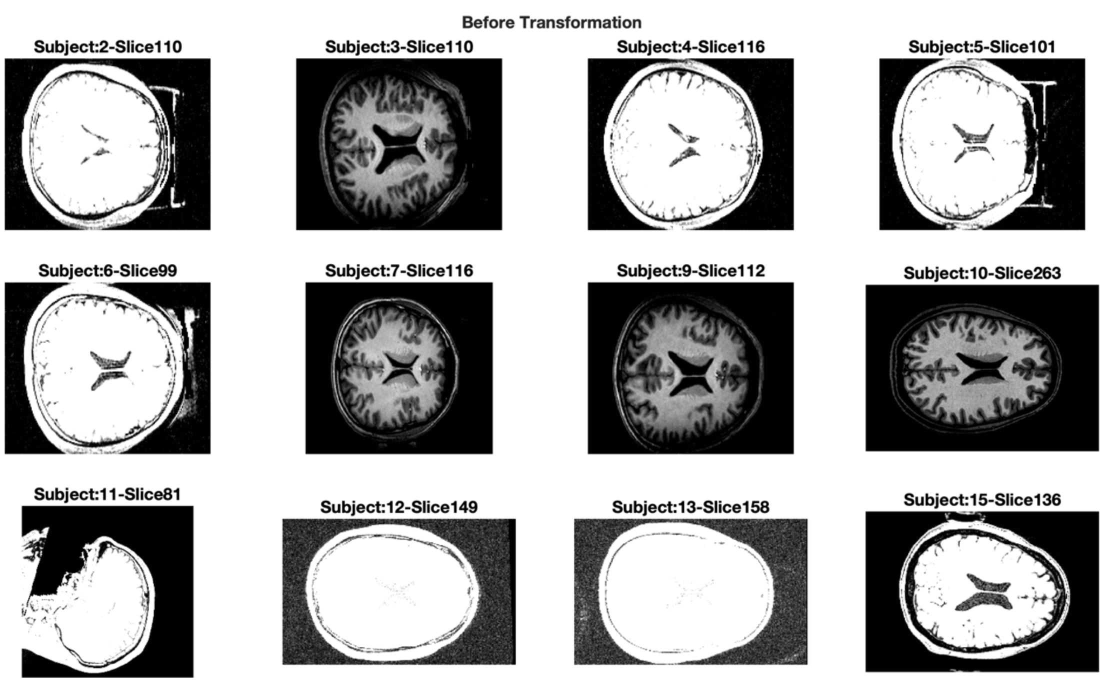

Fig. 5: Similar Brain MRI Slice cross subjects before transformation

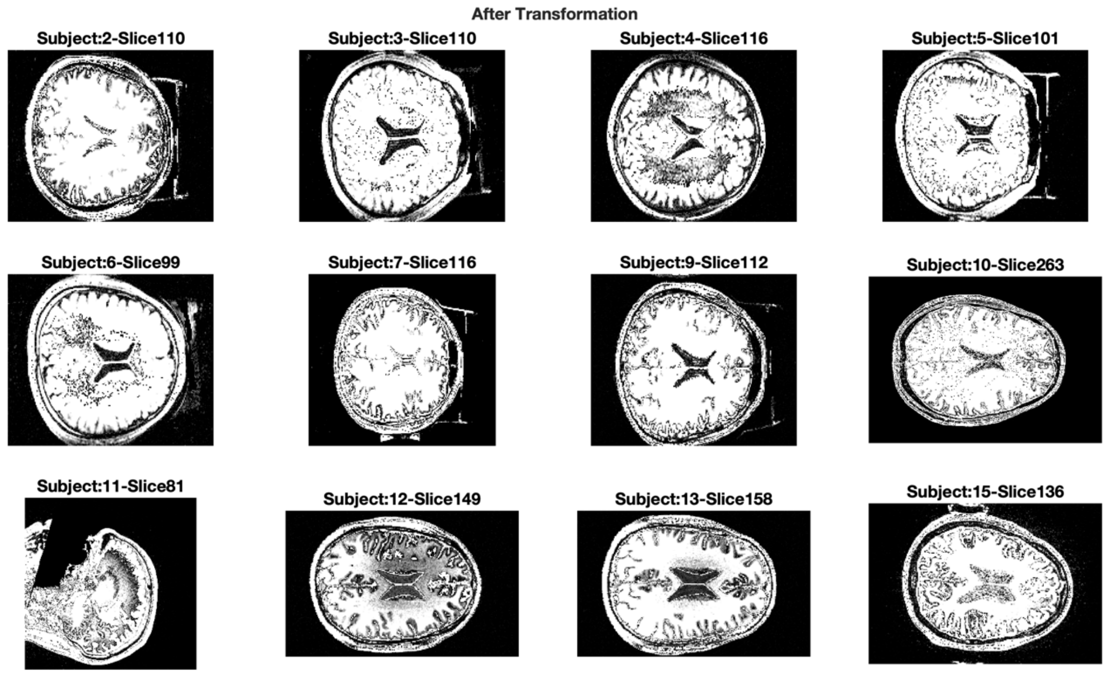

Fig. 6: Similar Brain MRI Slice cross subjects after Scale Standardization.

Observations from the same slice across subjects before and after scale standardization (Fig. 5 and 6, plotSliceCrossSubjects):

Before Standardization (Fig. 5):

1. **Variability in Contrast**:
   - There is significant variability in contrast between subjects. Some slices appear overexposed (too bright), such as those from Subject 2 and Subject 4, while others, like those from Subject 3 and Subject 9, display better contrast.
   - This variability can make cross-subject analysis difficult, as intensity values are not consistent across all images.
2. **Detail Visibility**:
   - For some subjects (e.g., Subject 6), structural details are less visible due to very high or low intensity levels, leading to saturation or darkened images.
   - The lack of consistent intensity scaling means that fine details, such as brain tissue structure, are difficult to compare across subjects.
3. **Inconsistent Dynamic Range**:
   - Different subjects exhibit varying intensity ranges. For example, the images from Subject 12 and Subject 13 are washed out, indicating an uneven dynamic range and possibly poor contrast settings in the original images.

After Standardization (Fig. 6):

1. **Improved Contrast Consistency**:
   - After scale standardization, the contrast between subjects has improved. Most images have a similar brightness and contrast level, with clear structures visible in each slice (e.g., ventricles and brain tissue boundaries).
   - Subjects such as 2, 4, and 6, which previously showed overexposed regions, now exhibit better intensity distribution, making structural details more apparent.
2. **Enhanced Detail**:
   - The details in the brain anatomy are more uniformly visible across subjects. For example, previously washed-out slices from Subject 12 and Subject 13 now have clearer definitions of brain structures.
   - Darker images like Subject 12's slice are also better balanced after transformation, revealing more details that were previously obscured.
3. **Harmonized Dynamic Range**:
   - The intensity scaling has effectively harmonized the dynamic range across all subjects, allowing for a more meaningful comparison of structural features.
   - The transformation process successfully normalized the intensity values, allowing similar intensities across different subjects to be comparable in a more meaningful way.

Challenges

- The initial challenge was understanding how to collect and aggregate the data to enable an efficient and accurate implementation of the standardization and transformation algorithms.
- The minimum and maximum scaling values, which are applied during standardization for each image, appear to be computed during the transformation process, but this approach may not be sufficient.
- Additionally, verifying the correctness of the algorithm implementation was difficult due to the absence of ground truth.

Future Directions

- Outliers in image intensities can skew the mean of the landmarks and should be identified and removed.
- The algorithms can be applied to slices from the same brain view to ensure consistency and the slices of the same brain view are transformed using the landmarks computed for these types of slices.
- To streamline the process of determining key landmarks, intensity ranges can be used to focus on bins with the highest intensities.
- Additionally, quality metrics or annotated images can be employed to refine the selection of images for the training dataset, ensuring that only high-quality images contribute to the computation of the transformation scale parameters.

Reference:
[1] Laszlo G, Nyul and Jayaram K. Udupa, “On Standardizing the MR Image Intensity Scale”, Magnetic Resonance in Medicine 42:1072-1081 (1999)
[2] Laszlo G, Nyul and Jayaram K. Udupa, “New Variants of a Method of MRI Scale Standardization”, IEE Transactions on Medical Imaging, VOL.19. N).2, Feb 2000.