Intensity Normalization

Intensity normalization

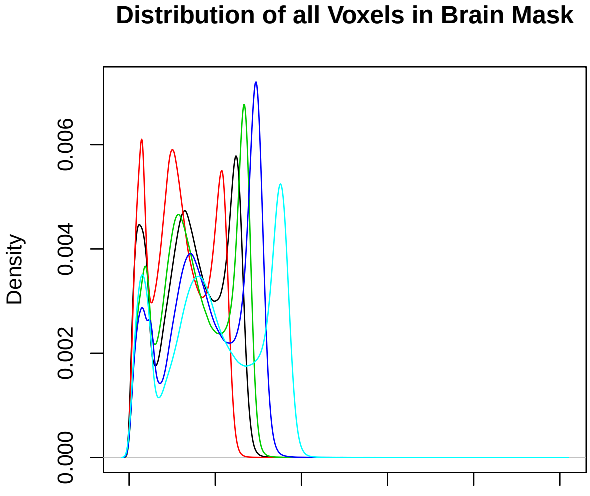
- Conventional MRI intensites (T1-w, T2-w, PD, FLAIR) are acquired in arbitrary units
- Images are not comparable across scanners, subjects, and visits, even when the same protocol is used.
  - This affects algorithm performance, prediction, inference.
  - Even simple things like thresholding an image
- Intensity normalization brings the intensities to a common scale across people.
- We will discuss subject-level intensity normalization.

Goals of this tutorial

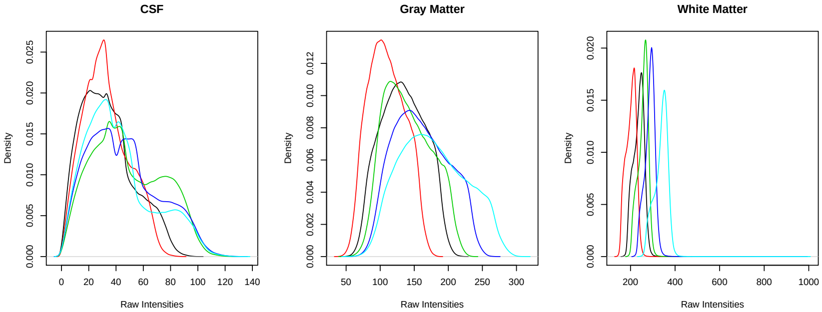
- Visualize intensity distributions from different subjects and tissue classes.
  - Because MS lesions are in the white matter, comparable white matter distributions are the target goal
- Apply the White Stripe intensity normalization (Shinohara et al. 2014).

Visualizing whole-brain intensities

- For the moment, we will work with the T1-w images from the training data.
- Full brain densities are mixtures of the three tissue class distributions.



Visualizing the intensities by tissue class



Whole-brain normalization

- Let's Z-score each voxel using mean μ_{WB} and standard deviation σ_{WB} computed from all voxels in the brain mask.

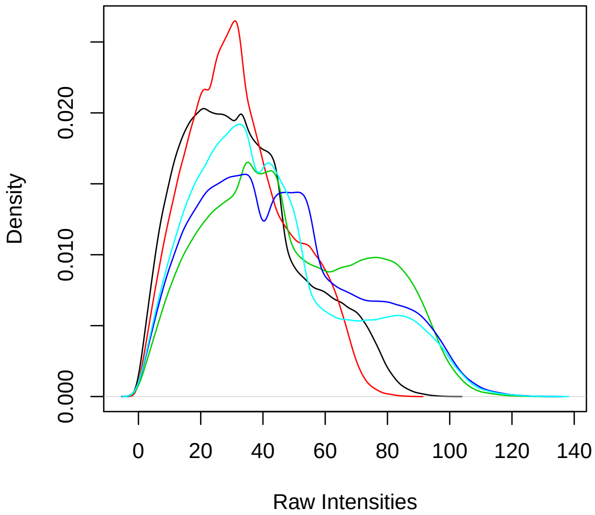
$$T1^{WB} = \frac{T1 - \mu_{WB}}{\sigma_{WB}}$$

- `zscore_img` is a function in `neurobase` that does this.
- It takes an image and a binary mask. The default is to use all voxels in the brain mask.

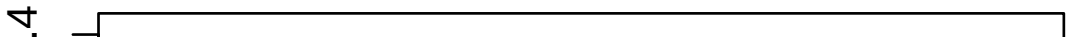
```r
zscore_img(img = img, mask = mask)
```

Whole-brain normalized intensities

CSF Before

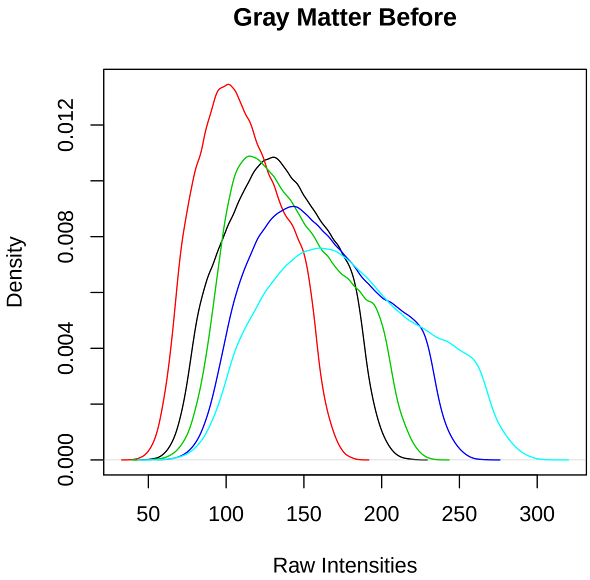


CSF After



Whole-brain normalized intensities

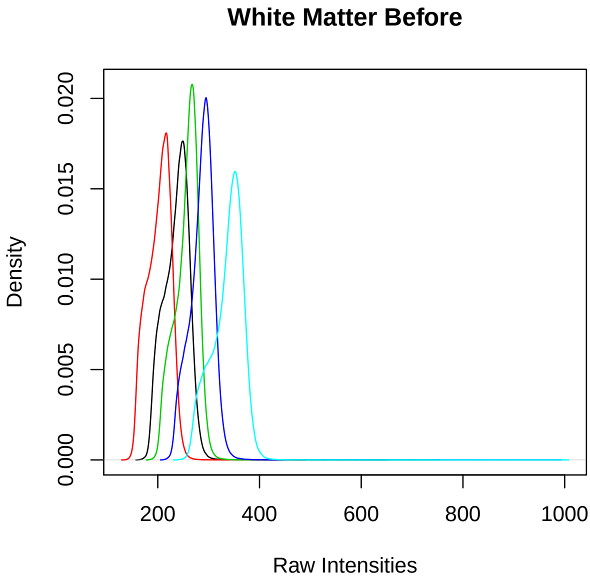
- Gray matter distributions are more comparable.



Gray Matter After

Whole-brain normalized intensities

- White matter distributions are more comparable.



Other Normalizations: White Stripe

- Whole-brain normalization may be sensitive to outliers.
- Lesions in MS can have very high intensities, which lead to bad estimates of mean/variance
  - Other more robust transformations may be used, such as using the median to center, IQR to scale, etc.
- White Stripe (Shinohara et al. 2014) is based on parameters obtained from a sample of normal appearing white matter (NAWM), which is robust to outliers.
  - The idea is to make normal appearing white matter comparable across subjects and visits.

White Stripe normalization

Procedure 1. Find white matter area on histogram

2. Estimate mean μ_{WS} and variance σ_{WS} of voxel intensities in that area
3. Normalize with those means/variances:

$$T1^{WS} = \frac{T1 - \mu_{WS}}{\sigma_{WS}}$$

- After normalization, NAWM will have a standard normal distribution and units will be in standard deviations of NAWM.
- Gray matter and CSF distributions may not be comparable after White Stripe.

White Stripe normalization

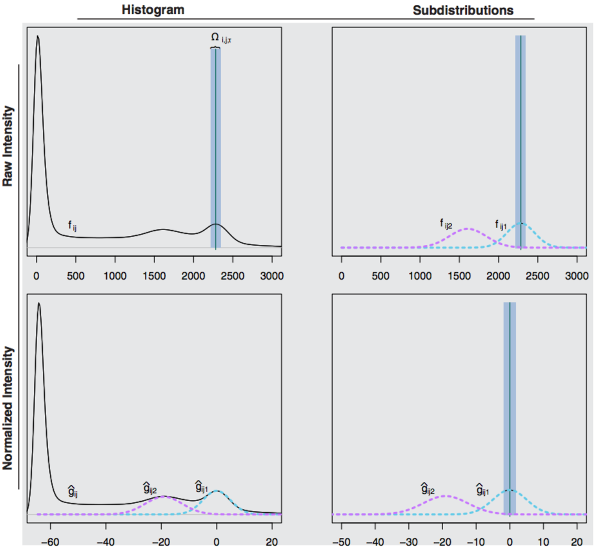


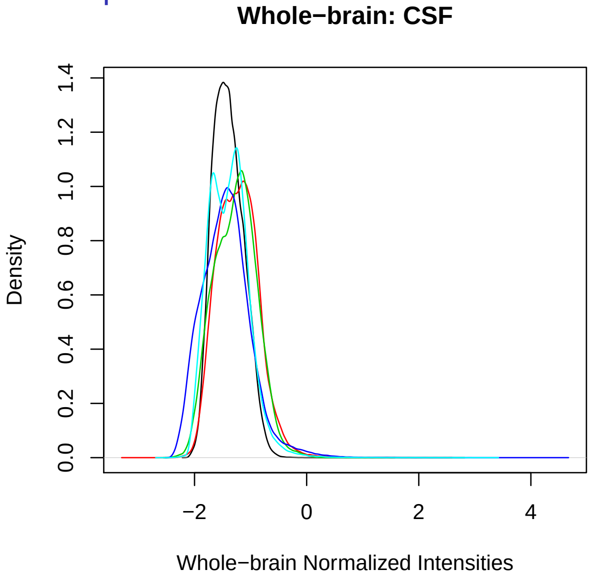
Figure 1: whitestripe

White Stripe normalization code

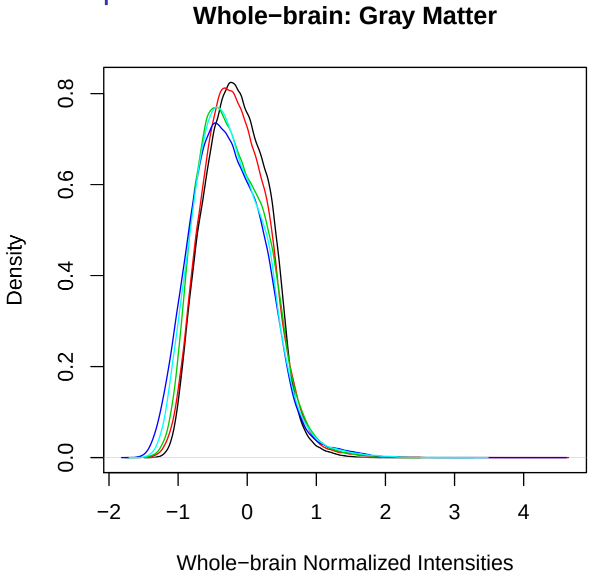
```
ind = whitestripe(img = t1, type = "T1", stripped = TRUE)$w
ws_t1 = whitestripe_norm(t1, indices = ind)
```

- The `whitestripe` function takes an image, image type (in our case T1), and a logical indicating whether the image has been skull stripped.
- The indicies of voxels in the NAWM used for estimating the normalization parameters are located in the list element `$whitestripe.ind`.
- The function `whitestripe_norm` takes an image and the indicies from a call to `whitestripe` and returns the White Stripe normalized image as a nifti.

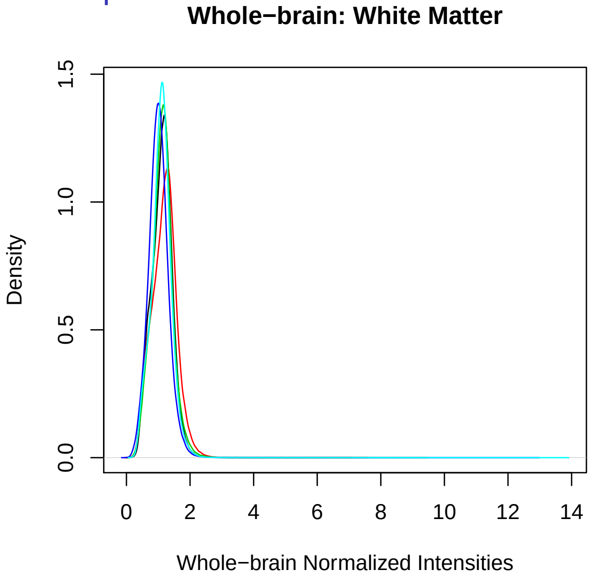
WhiteStripe normalized intensities



WhiteStripe normalized intensities



WhiteStripe normalized intensities



Conclusions

- Intensity normalization is an important step in any image analysis with more than one subject or time point to ensure comparability across images.
- White Stripe normalization may work better and have better interpretation than whole-brain normalization for subsequent lesion segmentation algorithms and analysis.
- Other intensity normalization methods that make intensites comparable across subjects for all tissues exist.
  - RAVEL, which is an extension of WhiteStripe is one example (Fortin et al. 2016).
  - Located at https://github.com/Jfortin1/RAVEL
  - This was shown to have better comparability than histogram matching

References

Fortin, Jean-Philippe, Elizabeth M Sweeney, John Muschelli, Ciprian M Crainiceanu, Russell T Shinohara, Alzheimer's Disease Neuroimaging Initiative, and others. 2016. "Removing Inter-Subject Technical Variability in Magnetic Resonance Imaging Studies." *NeuroImage* 132. Elsevier: 198–212.

Shinohara, Russell T, Elizabeth M Sweeney, Jeff Goldsmith, Navid Shiee, Farrah J Mateen, Peter A Calabresi, Samson Jarso, et al. 2014. "Statistical Normalization Techniques for Magnetic Resonance Imaging." *NeuroImage: Clinical* 6. Elsevier: 9–19.