

Intensity Normalization

Intensity normalization

- ▶ Conventional MRI intensities (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.

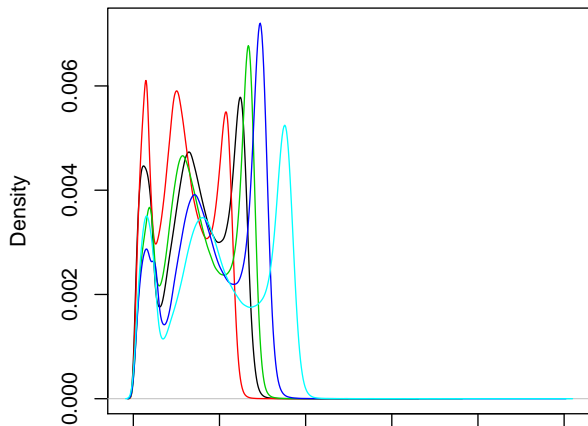
Goals of this tutorial

- ▶ 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).

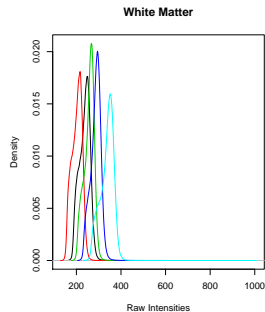
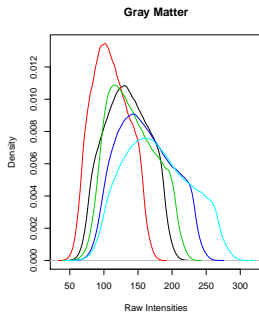
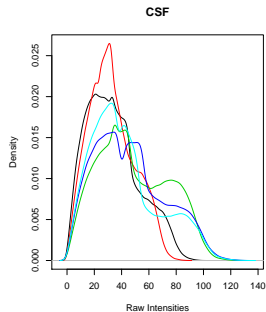
Visualizing whole-brain intensities

- ▶ 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.

Distribution of all Voxels in Brain Mask



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.

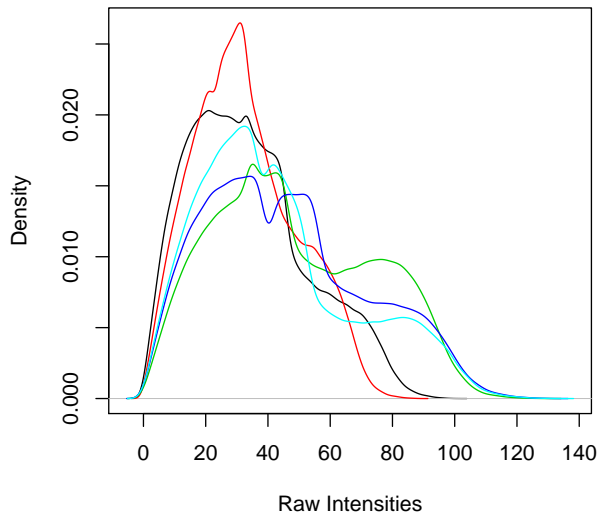
$$T1^{WB} = \frac{T1 - \mu_{WB}}{\sigma_{WB}}$$

- ▶ `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.

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

Whole-brain normalized intensities

CSF Before

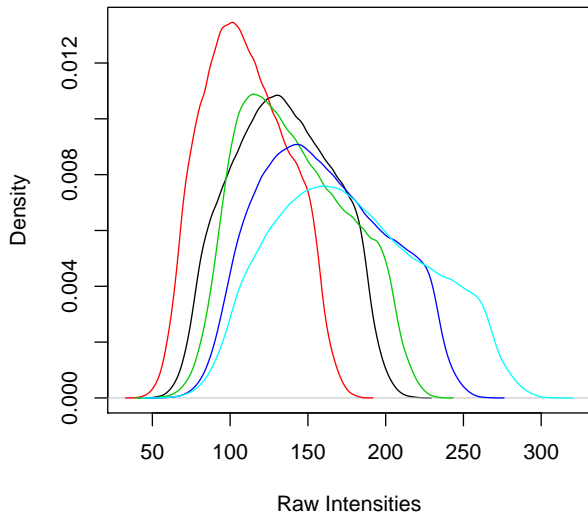


CSF After

Whole-brain normalized intensities

- Gray matter distributions are more comparable.

Gray Matter Before

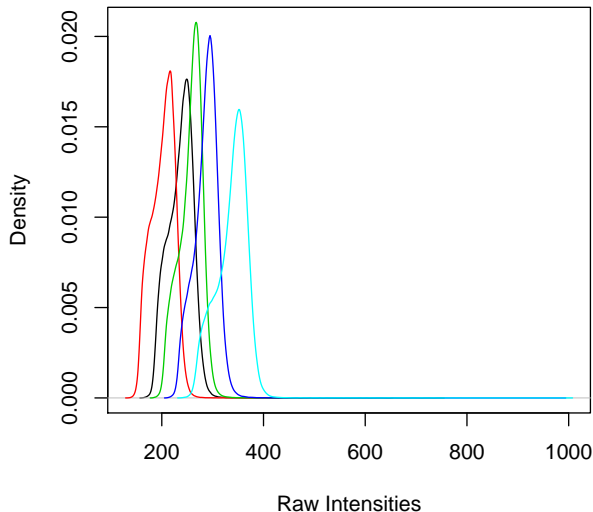


Gray Matter After

Whole-brain normalized intensities

- ▶ White matter distributions are more comparable.

White Matter Before



White Matter After

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.

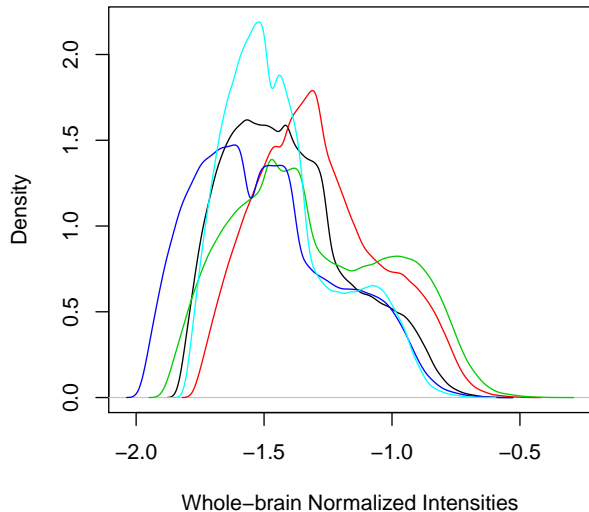
White Stripe normalization code

```
ind = whitestripe(img = t1, type = "T1", stripped = TRUE)$v  
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 indices 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 indices from a call to `whitestripe` and returns the White Stripe normalized image as a `nifti`.

WhiteStripe normalized intensities

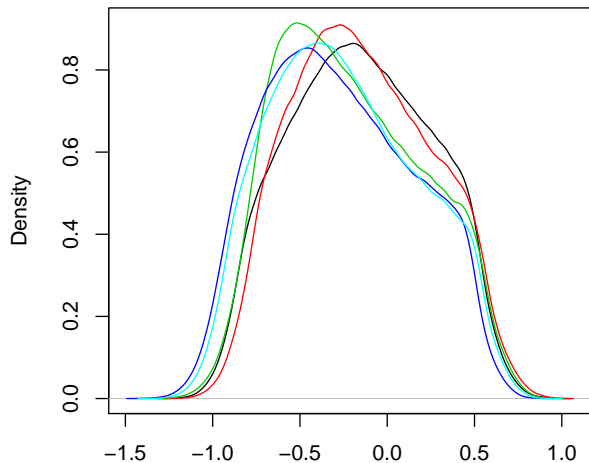
Whole-brain: CSF



White Stripe: CSF

WhiteStripe normalized intensities

Whole-brain: Gray Matter

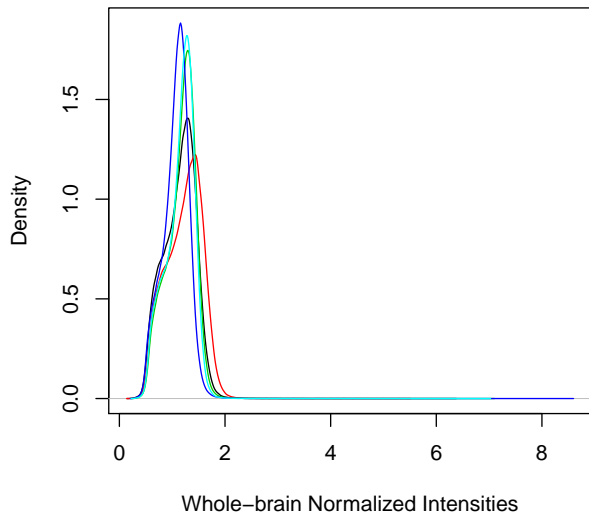


Whole-brain Normalized Intensities

White Stripe: Gray Matter

WhiteStripe normalized intensities

Whole-brain: White Matter



White Stripe: White Matter

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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 intensities 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.