Intensity Normalization

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Intensity normalization

- Conventional MRI intensites (T1-w, T2-w, PD, FLAIR) are acquired in arbitrary units, making the images not comparable across scanners and visits.
- Intensity normalization brings the intensities to a common scale.

Goals of this tutorial

- ▶ Visualize the intensities using boxplots and densities
- ▶ Apply the WhiteStripe intensity normalization (Shinohara et al. 2014)

Reading in the images

- For the moment, we will work with the T1-w images from the training data.
- `vals` below is restricting to T1-w voxels that are within the brain mask.

```r
library(ms.lesion)
library(neurobase)
library(WhiteStripe)
fnames = get_image_filenames_list_by_subject(group = "trai
  type = "coregistered")
t1s = lapply(fnames, function(x) readnii(x["MPRAGE"]))
tissues = lapply(fnames, function(x) readnii(x["Tissue_Clas
masks = lapply(fnames, function(x) readnii(x["Brain_Mask"])

vals = mapply(function(t1, mask){
  mask_vals(t1, mask)
}, t1s, masks, SIMPLIFY = FALSE)
```

Code for plotting the data

```r
plot_densities = function(dens, xlab = "Raw Intensities",
                          main = "Whole Brain") {
  range_x = sapply(dens, function(d) range(d$x))
  range_x = range(range_x)
  range_y = sapply(dens, function(d) range(d$y))
  range_y = range(range_y)
  plot(dens[[1]], xlim = range_x, ylim = range_y,
       xlab = xlab, main = main)
  for (idens in 2:length(dens)) {
    lines(dens[[idens]], col = idens)
  }
}
plot_boxplots = function(vals,
                         main = "Whole Brain") {
  boxplots <- lapply(vals, boxplot, outline = FALSE, plot =
  boxplots = lapply(boxplots, function(x) x$stats)
  boxplots <- do.call(cbind, boxplots)
  boxplot(boxplots, main = main)
```
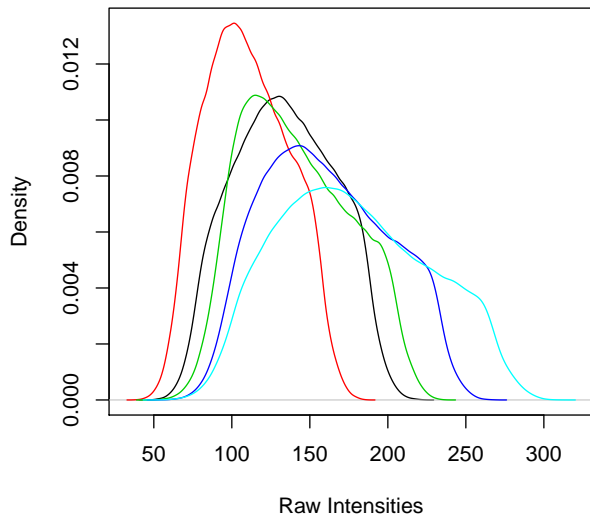
Visualizing the intensities

▶ Full brain densities are mixtures of the tissue class distributions.

```
plot_densities(dens)
```

Whole Brain
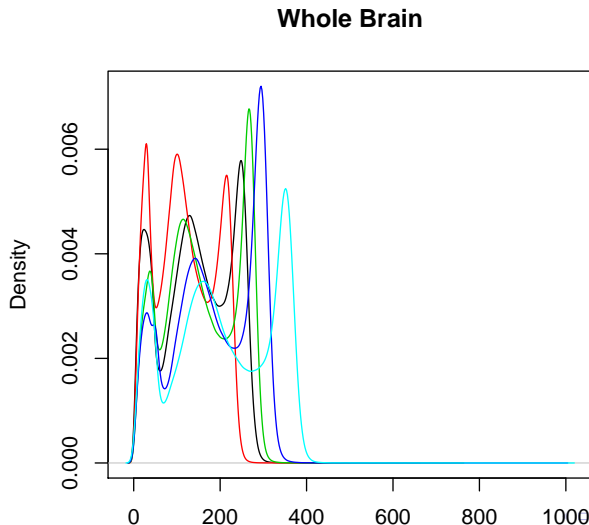
Visualizing the intensities by tissue class
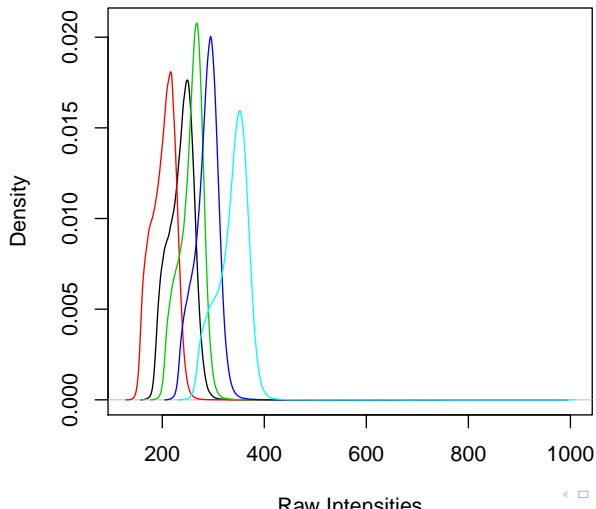

Gray Matter

Visualizing the intensities by tissue class

▶ Notice the complete non-overlap between some subjects' white matter distributions.

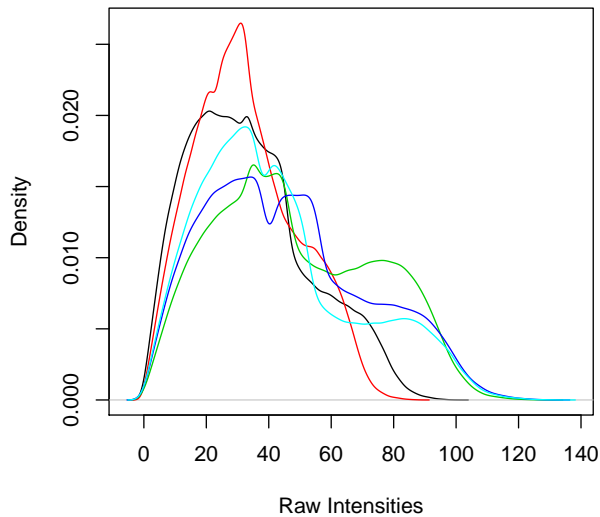

White Matter

Visualizing the intensities by tissue class


CSF

Whole-brain normalization

- Let's Z-score each voxel using mean and standard deviation computed from all voxels in the brain mask.
- `zscore_img` is a function in `fslr` that does this.

```
t1_norm = mapply(function(img, mask){
  zscore_img(img = img, mask = mask, margin = NULL)
}, t1s, masks, SIMPLIFY = FALSE)
```

Whole-brain normalized intensities

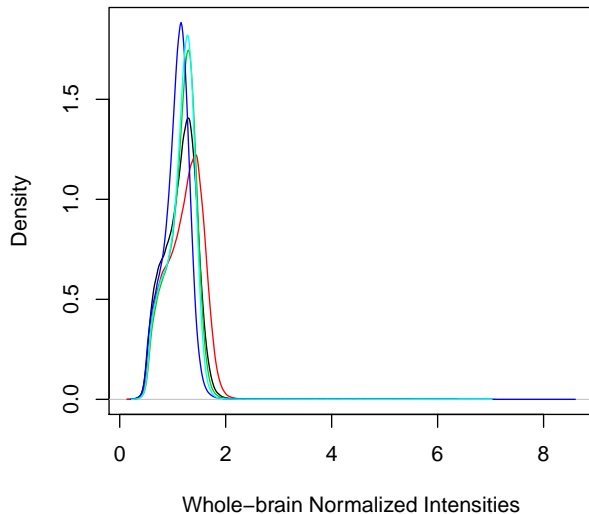- Gray matter distributions are more comparable.

Gray Matter
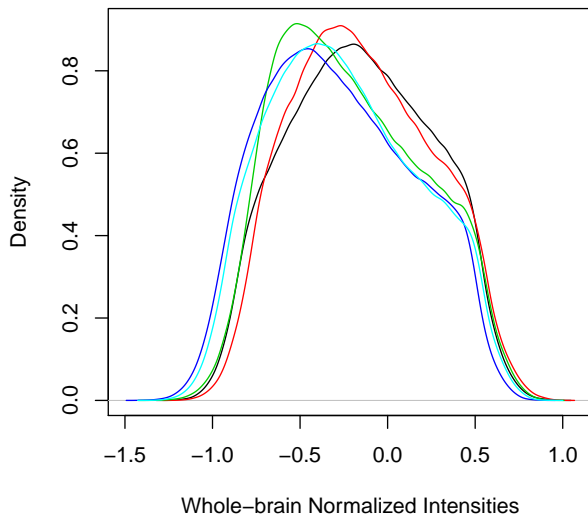
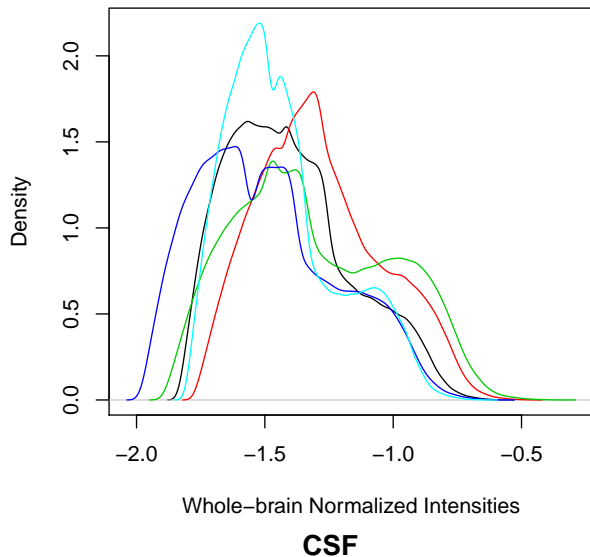**Gray Matter**

Whole-brain normalized intensities

▶ White matter distributions are more comparable.

White Matter

White−brain Normalized Intensities

Whole-brain normalized intensities

CSF

Whole−brain Normalized Intensities

CSF

Why White Stripe?

- Whole-brain normalization may reduce signal in the higher intensities, i.e., less contrast between lesion intensities and normal appearing white matter.
- White Stripe normalization is based on parameters obtained from a sample of normal appearing white matter.
- The idea is to make normal appearing white matter comparable across subjects while preserving high lesion intensity contrast to aid automatic segmentation algorithms.
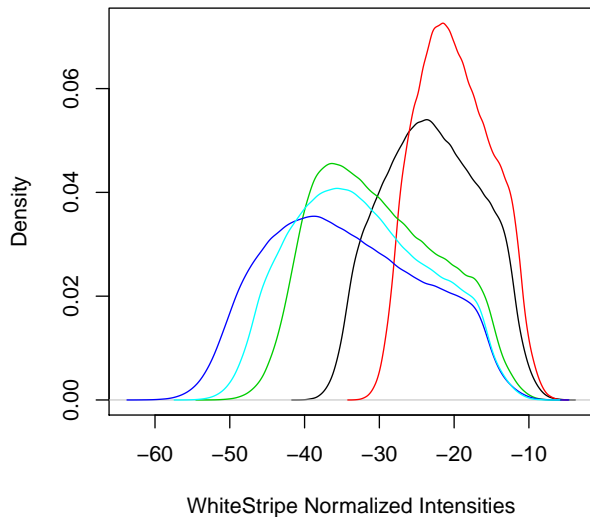
White Stripe normalization

- We normalize each voxel using the mean and standard deviation computed from normal appearing white matter voxels.
- Thus, normal appearing white matter will have a standard normal distribution.
- Units will correspond to variability (standard deviation) of normal appearing white matter.
- Gray matter and CSF distributions, however, may not be comparable across subjects.

```
ws_norm = function(t1) {
  ind = whitestripe(img = t1,
                    type = "T1",
                    stripped = TRUE)$whitestripe.ind
  whitestripe_norm(t1, indices = ind)
}
t1_ws_norm = lapply(t1s, ws_norm)
```

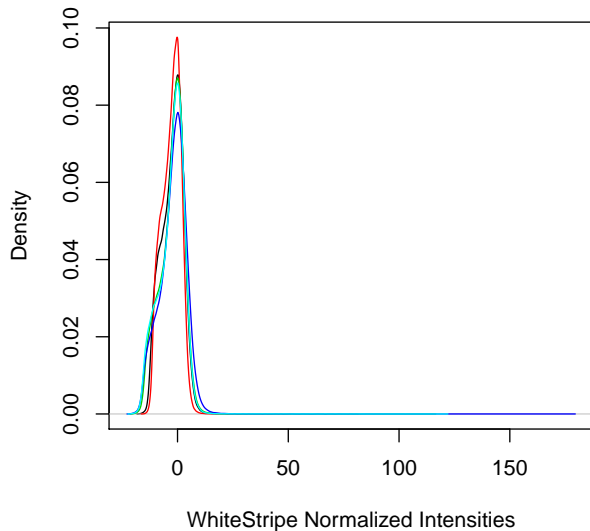# WhiteStripe normalized intensities

Gray Matter

Gray Matter
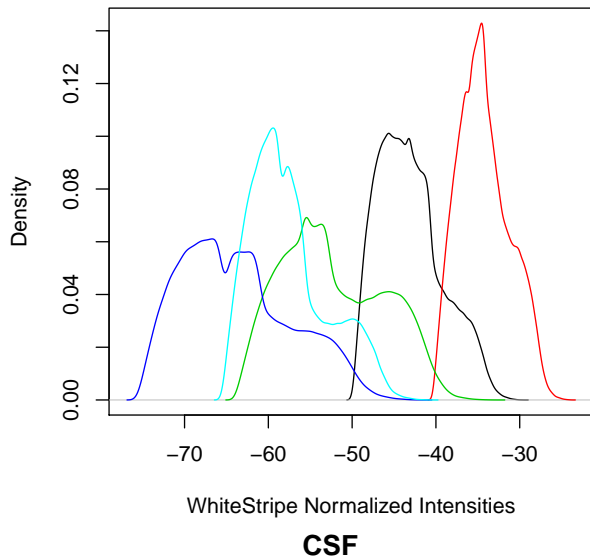
WhiteStripe normalized intensities

White Matter

WhiteStripe normalized intensities

CSF

Density vs WhiteStripe Normalized Intensities

CSF

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 for subsequent lesion segmentation algorithms or analysis.
- Newer methods exist, such as RAVEL, which extends WhiteStripe to make intensites comparable across subjects for all tissues (Fortin et al. 2016).

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.