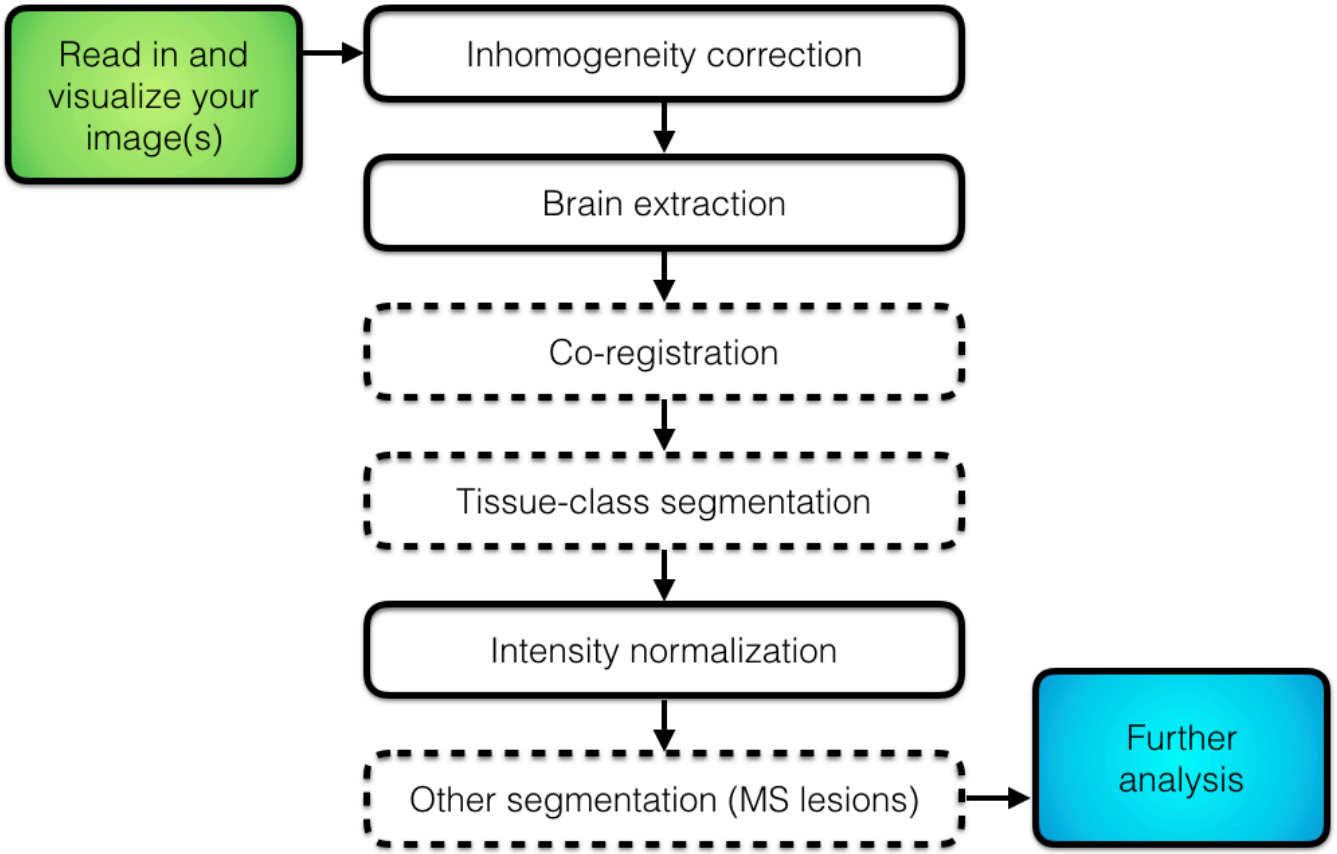
MS Lesion Segmentation

Overall Pipeline

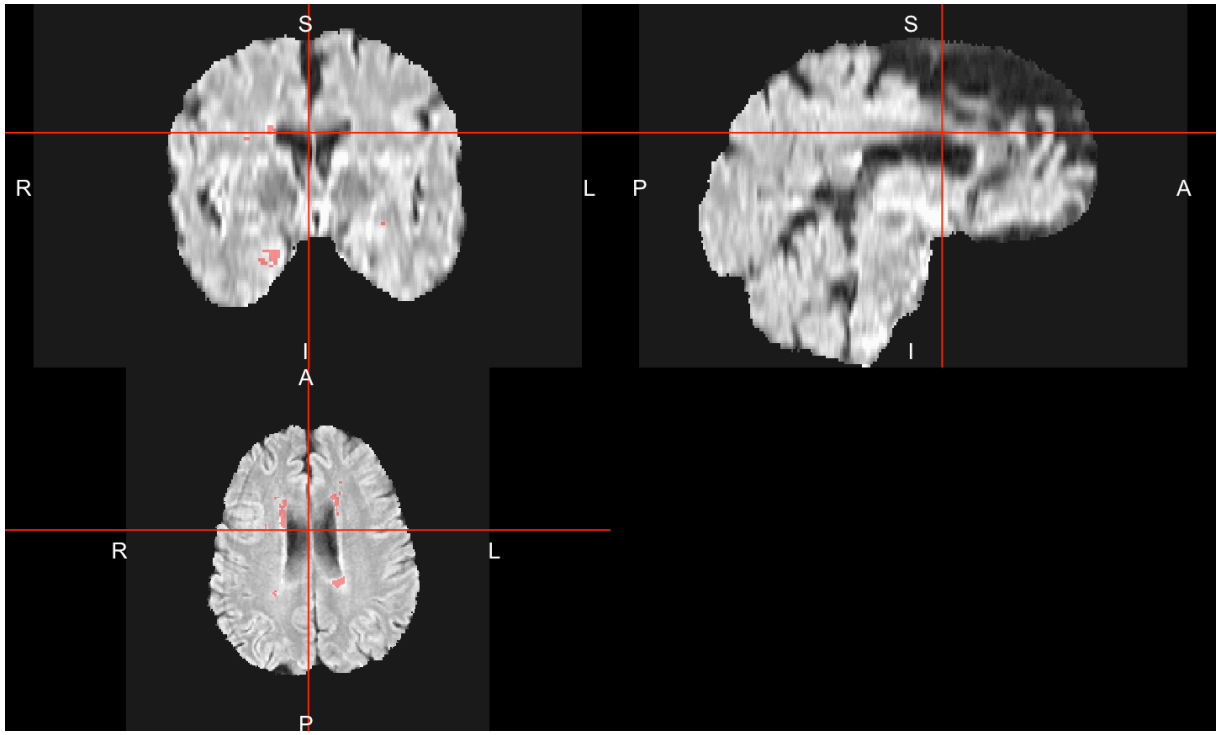


Background

- Obtaining manual lesion segmentations is often resource intensive.
- "Gold standard": Inter- and Intra-rater variability
- Accurate and efficient methods for automatic segmentation are necessary for scalability and research progress.
- In this tutorial, we will learn how to train and apply OASIS (Sweeney et al. 2013), an automatic lesion segmentation model, to obtain predicted lesion probability maps.
    - relies on intensity-normalized data

Visualization

- Here's the FLAIR volume for training subject 05 with a manual lesion segmentation overlayed.



MS Lesion Segmentation with OASIS

- **O**ASIS is **A**utomated **S**tatistical **I**nference for **S**egmentation (Sweeney et al. 2013).
- OASIS takes FLAIR, T1, T2, and PD images.
  - Produces OASIS probability maps of MS lesion presence.
  - These can be thresholded into a binary lesion segmentation.
- The OASIS model is based on a logistic regression.
- Regress binary manual segmentation labels on the images, smoothed versions of the images, and some interaction terms (e.g., supervised learning).
- Performed well compared to common machine learning models (Sweeney et al. 2014)

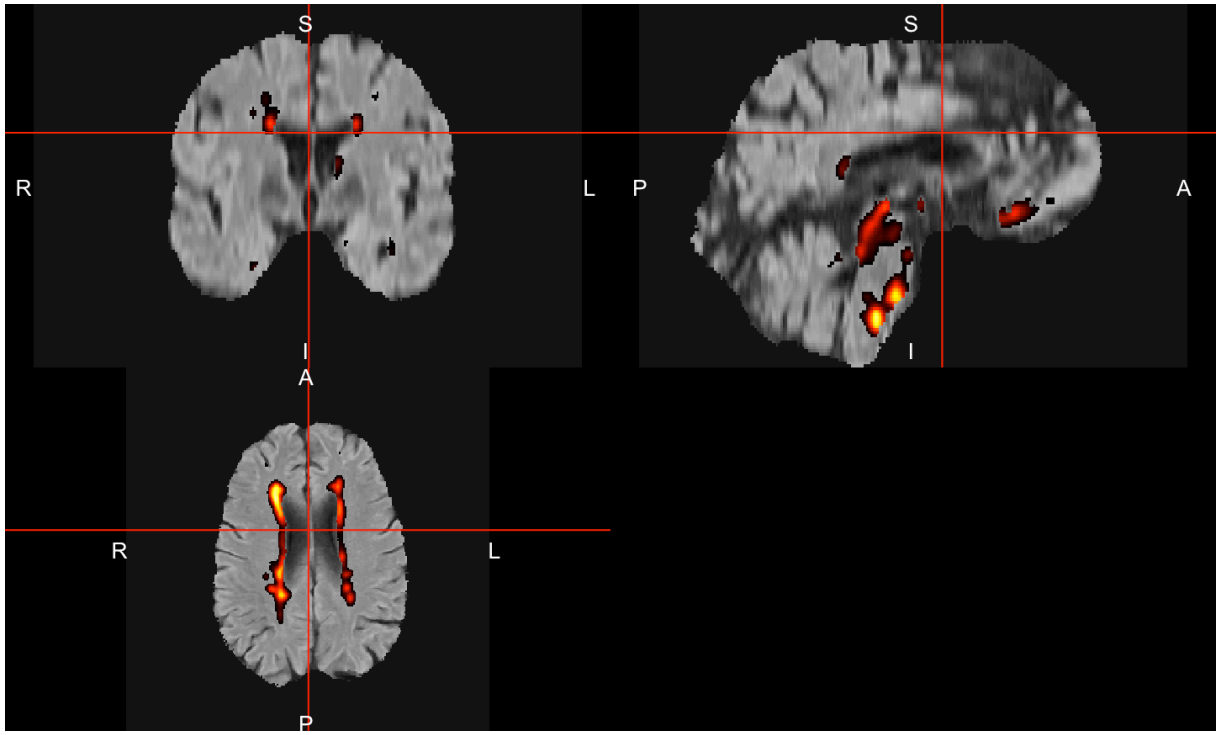
Default OASIS Model

- The OASIS library comes with default parameters that can be used to generate probability maps for new test subjects.
- The default model was trained on approximately 100 MS subjects and 30 healthy subjects with manual segmentations.
- Here we apply `oasis_predict` with the default model to obtain OASIS probability maps for the test subjects.

```
library(oasis)
default_predict_ts = function(x){
  res = oasis_predict(
      flair=ts_flairs[[x]], t1=ts_t1s[[x]],
      t2=ts_t2s[[x]], pd=ts_pds[[x]],
      brain_mask = ts_masks[[x]],
      preproc=FALSE, normalize=TRUE,
      model=oasis::oasis_model)
  return(res)
}
default_probs_ts = lapply(1:3, default_predict_ts)
```

Vizualization of probability map

- Here's the probability map for test subject 01 (no gold standard):

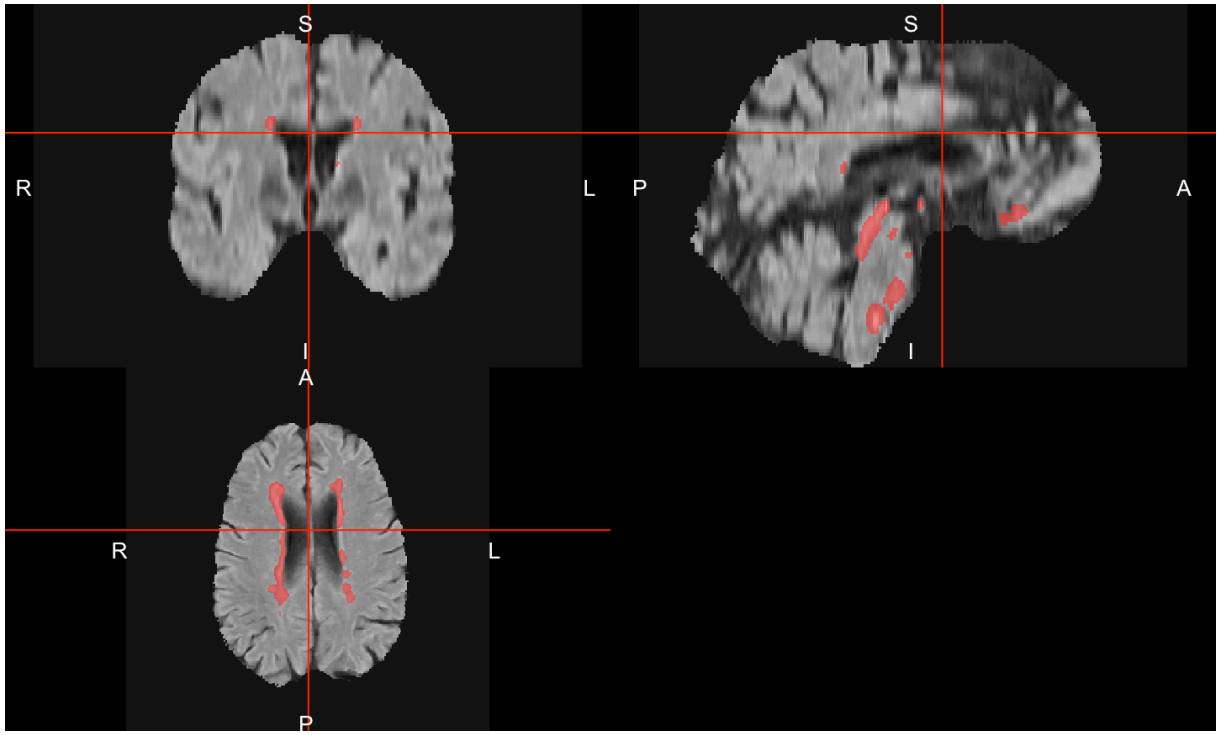


Thresholding: Getting a binary map

- We must choose a cutoff to binarize the OASIS probability maps.
- The `binary` argument in the `oasis_predict` function is FALSE by default, resulting in the output being the probability map.
  - Setting `binary=TRUE` will return the thresholded version, using the input to the `threshold` argument (default = 0.16).
  - 0.16 was obtained via a validation set allowing for a 0.5% false positive rate.
- In practice, we might want to use a grid search over thresholds and cross validation to choose the cutoff.

Vizualization of binary map

- Here's the binary mask for test subject 01, using the default 0.16 threshold:



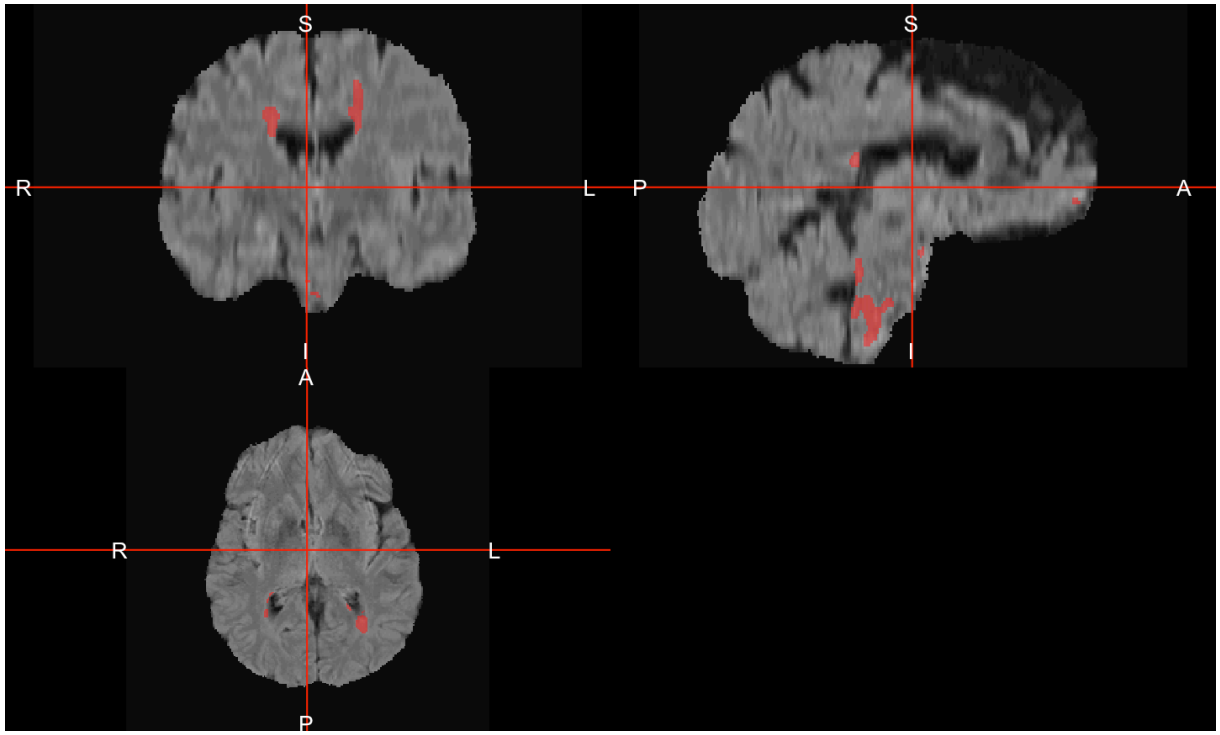
Default OASIS Model

- To evaluate how the default model performs, we need to compare the predictions to a gold standard.
- Let's therefore obtain OASIS probability maps for our training subjects.
- We will use the default threshold to binarize.

```
default_predict_tr = function(x){
  res = oasis_predict(
      flair=tr_flairs[[x]], t1=tr_t1s[[x]],
      t2=tr_t2s[[x]], pd=tr_pds[[x]],
      brain_mask=tr_masks[[x]],
      preproc=FALSE, normalize=TRUE,
      model=oasis::oasis_model, binary=TRUE)
  return(res)
}
default_probs_tr = lapply(1:5, default_predict_tr)
```

Default OASIS Model Results

- Here's the FLAIR volume for training subject 05 with the OASIS segmentation overlayed.



Default OASIS Model Results

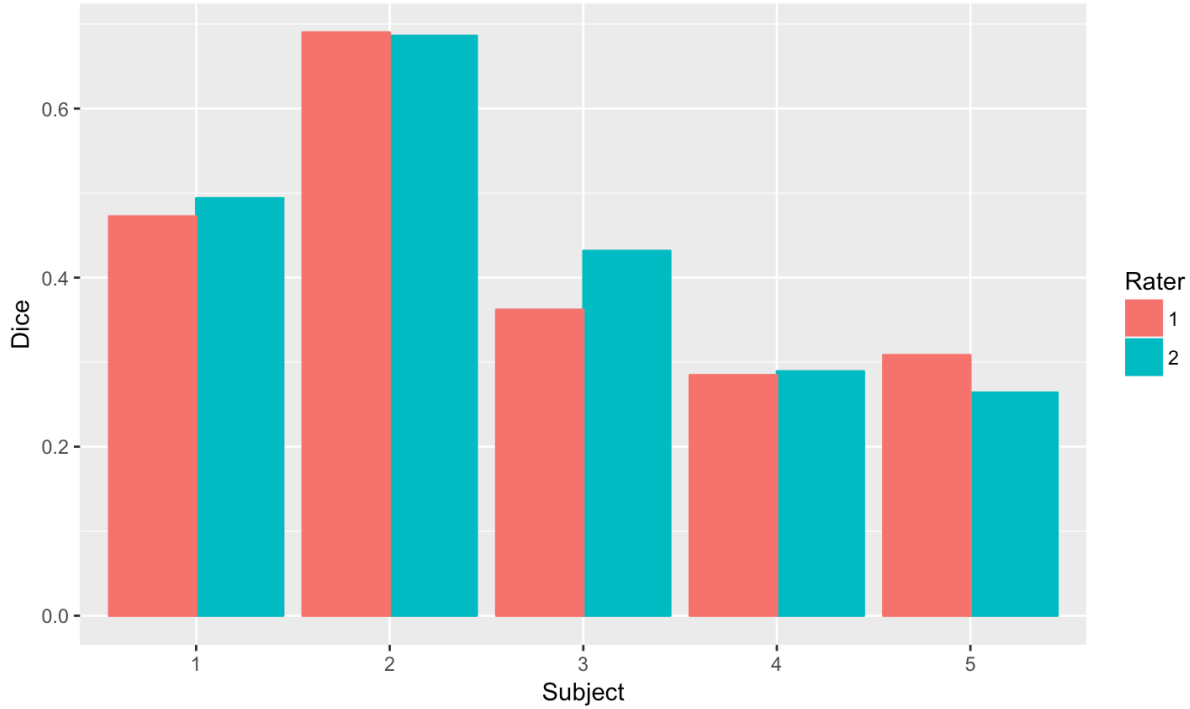
Sorensen–Dice coefficient

- Similarity measure between two samples
- Ranges from 0 to 1
- (TP) - true positive, (FP) - false positive, (FN) - false negative

$$D = \frac{2TP}{2TP + FP + FN}$$

Default OASIS Model Results

Dice coeffients for the training subjects compared to raters 1 and 2



Improving Results

- The default model is picking up a lot of false positives in the spinal cord.
- We might improve the results by re-training the OASIS model using our five training subjects.
- To re-train using new data, binary masks of gold standard lesion segmentations are needed and should be in T1 space.

Making OASIS data frames

- OASIS requires a particular data frame format, which we create using the function `oasis_train_dataframe`.
- Includes an option to preprocess your data (`preproc`), which does (1) inhomogeneity correction using `fsl_biascorrect` and (2) rigid coregistration using `flirt` to the T1 space.
- Includes an option to whole-brain intensity normalize (`normalize`).
- `make_df()` below is a helper function.

```
make_df = function(x){
  res = oasis_train_dataframe(
      flair=tr_flairs[[x]], t1=tr_t1s[[x]], t2=tr_t2s[[x]],
      pd=tr_pds[[x]], gold_standard=tr_golds2[[x]],
      brain_mask=tr_masks[[x]],
      preproc=FALSE, normalize=TRUE, return_preproc=FALSE)
  return(res$oasis_dataframe)
}
oasis_dfs = lapply(1:5, make_df)
```

Training OASIS

- The function `oasis_training` takes the data frames we made and fits a logistic regression using labels and features from a subset of voxels in each subject's brain mask (top 15% in FLAIR intensity).
- The function `do.call` is a useful R function that applies the function named in the first argument to all elements of the list specified in the second argument.

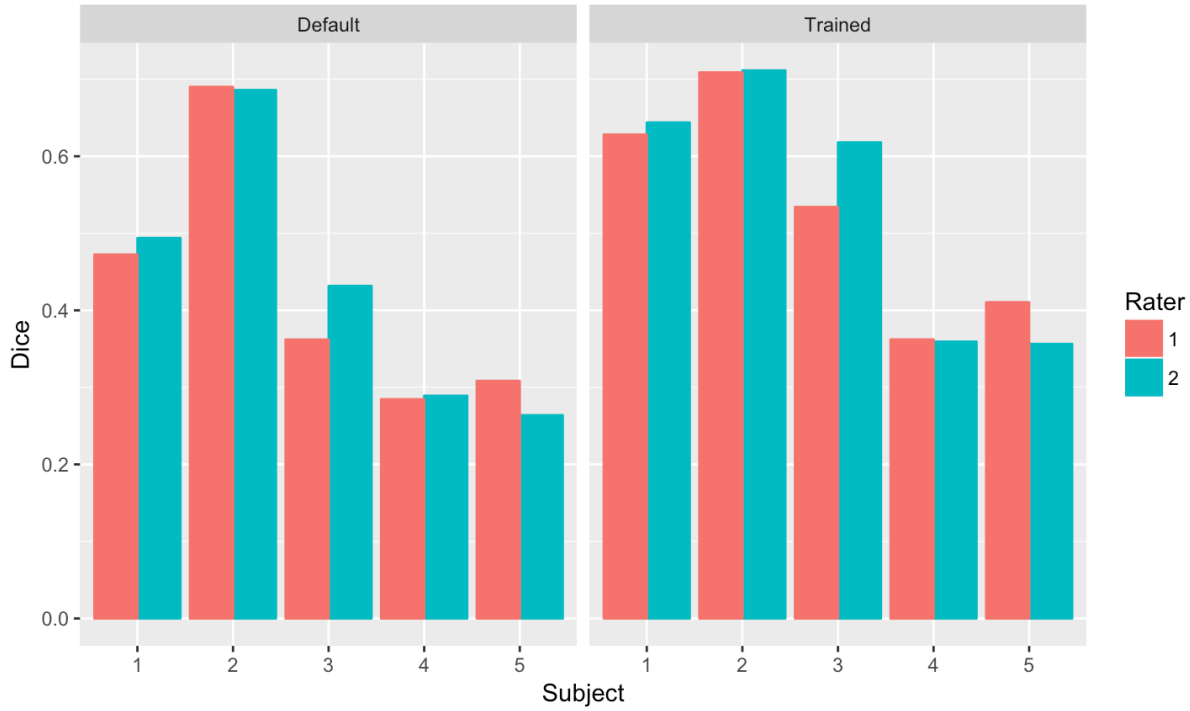
```
ms_model = do.call("oasis_training", oasis_dfs)
```

OASIS model object

```
print(ms.lesion::ms_model)

Call:  glm(formula = formula, family = binomial, data = train_vectors_multi)

Coefficients:
   (Intercept)        FLAIR_10           FLAIR        FLAIR_20
       -5.6939          4.1041          1.4076         -2.1562
         PD_10              PD          PD_20            T2_10
        4.7047          0.1739       -17.3328          9.9606
            T2           T2_20          T1_10              T1
        0.8376        -19.2016         12.5254          1.2533
         T1_20  FLAIR_10:FLAIR  FLAIR:FLAIR_20        PD_10:PD
      -27.9823         -1.0304         -3.4276          0.2922
      PD:PD_20        T2_10:T2        T2:T2_20        T1_10:T1
       -1.1567         -0.9565          1.5197         -1.3398
      T1:T1_20
        4.6929

Degrees of Freedom: 860824 Total (i.e. Null);  860804 Residual
Null Deviance:      491900
Residual Deviance: 243900   AIC: 243900
```

Trained OASIS Model Results

- Using the same threshold of 0.16.
- Dice coeffients for default vs. re-trained OASIS model



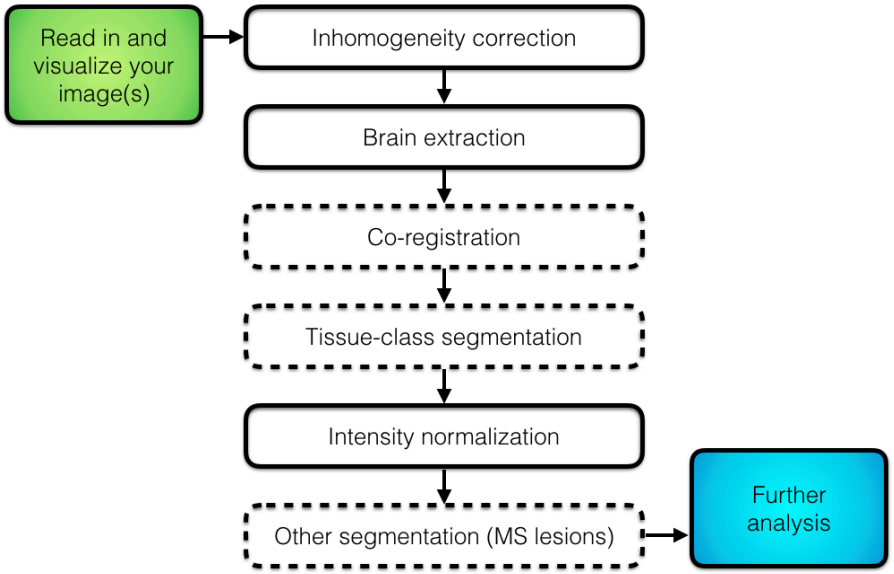
Improvement

- Percent improvement in dice over the default model:

ID	Rater 1	Rater 2
01	33	30.4
02	2.7	3.7
03	47.5	43.2
04	27.3	24.3
05	33.1	35.1

Wrap-up

- We've covered all (or most) image pre-procssing steps in a typical image pre-processing pipeline, starting with raw nifti images.
- Everything was done in R!



What we didn't cover

- fMRI: see `fmri` library
- Other imaging modalities, e.g., CT, PET
  - MALF segmentation is robust
- Voxel-wise testing: see `voxel` library
- Other population-level statistical inference:
- Statistical/machine learning: see `caret` library

What can you do next?

- Further modeling and statistical analysis.
- Register images to a template to do population inference.
- General R
  - Build your own R libraries for image analysis.
  - Rmarkdown for reproducible reports
  - R shiny apps

Resources

- Neurohacking tutorial on Coursera
- Neuroconductor: central repository for image analysis R libraries

Website

http://johnmuschelli.com/imaging_in_r

References

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References

Sweeney, Elizabeth M, Russell T Shinohara, Navid Shiee, Farrah J Mateen, Avni A Chudgar, Jennifer L Cuzzocreo, Peter A Calabresi, Dzung L Pham, Daniel S Reich, and Ciprian M Crainiceanu. 2013. “OASIS Is Automated Statistical Inference for Segmentation, with Applications to Multiple Sclerosis Lesion Segmentation in Mri.” *NeuroImage: Clinical* 2. Elsevier: 402–13.

Sweeney, Elizabeth M, Joshua T Vogelstein, Jennifer L Cuzzocreo, Peter A Calabresi, Daniel S Reich, Ciprian M Crainiceanu, and Russell T Shinohara. 2014. “A Comparison of Supervised Machine Learning Algorithms and Feature Vectors for MS Lesion Segmentation Using Multimodal Structural MRI.” *PloS One* 9 (4). Public Library of Science: e95753.