Thalamic Parcellation From Multi-modal Data Using Random Forest Learning

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Goal: *Thalamus nuclear segmentation from random forest learning on MR/DTI - derived multi-modal features.*

1. Motivation

- The thalamus is involved in numerous neurodegenerative diseases (Alzheimer's, Multiple Sclerosis, Parkinson's).
- It is composed of neuronal clusters called nuclei, which are responsible for communication between various cerebral cortex and midbrain regions. The nuclei are *differentially affected* in disease.
- While there is minimal contrast in conventional MR, DTI shows promise (diffusion tensor imaging):
  - Fractional Anisotropy (FA) shows thalamus boundary
  - Changes in Principal Eigenvector (PEV) through Knutsson edge map show inter-nuclear boundaries (see 2.2).
- Others have used spatial location and tensor statistics [Wiegell], connectivity [Behrens], tensor homogeneity [Jonasson, Rittner] to differentiate among nuclei.
- No one has attempted to reproduce manual results without prior information on the target.

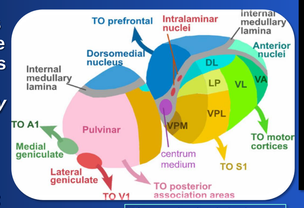
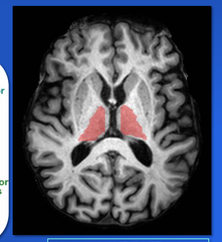
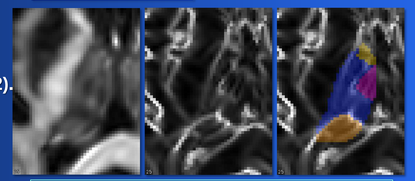


Diagram showing thalamic nuclei and associated cortical and midbrain connectivity.



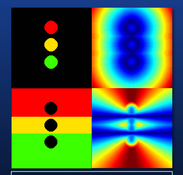
Axial view in MP-RAGE, with left and right thalamus highlighted.



Close-up of example thalamus. Left: in fractional anisotropy (FA), showing the thalamus boundary. Middle: the Knutsson edge map, showing changes in PEV. Right: left thalamus nuclear delineation (manual) from the Knutsson edge map image: anterior nucleus [yellow], medialdorsal [red], ventral group [blue], and pulvinar [orange].

2. Method

- Our goal is to automatically segment the thalamic nuclei using learned patterns in multi-modal features. We integrate potentially discriminating features used in prior work, such as spatial coordinates, the Knutsson map, and other DTI-based and structural MRI information.
  1. Training: we form a **multi-dimensional feature per voxel**, which we associate with a nucleus label from a manual rater.
  2. **Random Forest** classification to discriminate thalamus from background and thalamic nuclei from each other, using all the multi-contrast data at our disposal.
  3. Target: random forest learners, when applied to a target case, inform the external forces of the **MGDM method**:
     - Multiple-object Geometric Deformable Model: level set method enforcing topology constraints [Bogovic].
     - Allows ***per-boundary*** forces and object-relative image appearance: nucleus-nucleus, nucleus-background. This allows the random forest learners to push individual shared boundaries.



Toy example of MGDM distance map and decomposition.

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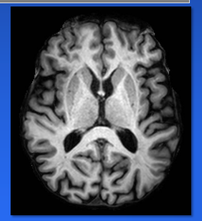
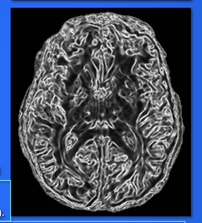
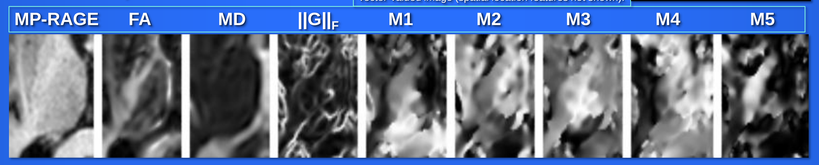
2.2 Feature Selection

- We integrate 12 potentially discriminating features from structural and diffusion-derived imaging data.
  - MP-RAGE (magnetization-prepared rapid acq. with grad. echo) – improved contrast for MS lesions.
  - FA (fractional anisotropy) – non-uniformity of diffusion computed using the eigenvalues of the diffusion tensor.
  - MD (mean diffusivity) – average eigenvalue of tensor.
  - The PEV is the unit vector associated with the largest eigenvalue of the diffusion tensor. Since opposing vectors in Cartesian coordinates should represent the same orientation, there is a sign ambiguity in defining a difference measure between PEV's. The **Knutsson mapping accounts for this ambiguity** [Knutsson]:
    $M([x,y,z]) = \{x^2 - y^2,\ 2xy,\ 2xz,\ 2yz,\ (2z^2 - x^2 - 2y^2)/\sqrt{3}\}$
  - Knutsson edge map $||G||_F$ – rapidity of change in orientation
  - Spatial location





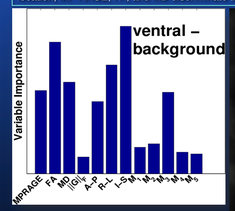
Above and right: whole brain axial view of MP-RAGE (top) and Knutsson edge map (right). Below: example vector-valued image (spatial location features not shown).

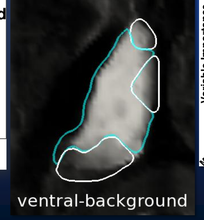


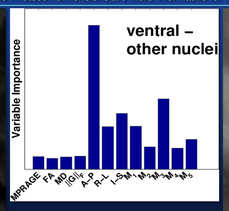
2.3 Random Forest Learning

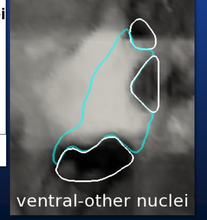
- Decision trees are constructed through random subsampling of the data and features [Breiman]. Here: single feature, minimum misclassification decision
- **Train** nucleus-nucleus and nucleus-boundary regions. For each region, output is a tree ensemble that, given a new observation, returns a putative class label for that observation and membership scores for that and the other (less likely) class labels.
- **Test**: apply the ensemble classifiers from the training cases to that subject's data, combining the associated membership scores.

Bar charts showing feature importance for typical nucleus-background (left) and nucleus-nucleus tree ensembles, and the associated target membership images. Spatial location, MP-RAGE, FA, and MD discriminate the thalamus with background, while the Knutsson dimensions are more informative for nucleus-nucleus discrimination.





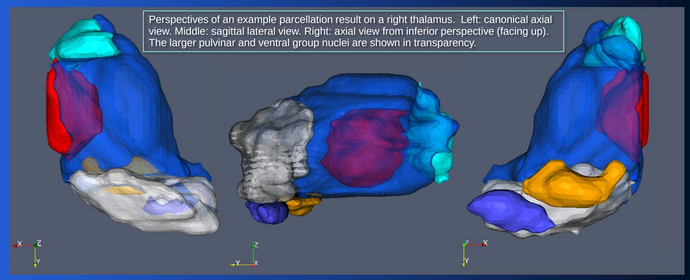




3. Experimental Results

- 22 MP-RAGE and DTI acquired on 3T MR scanner, resampled to .83mm isotropic
- Bagged cross-validation against manual delineations, 10 x train-on-5.
- Results exceed previously measured inter-rater variability; while the results on the lateral and medial geniculates are poor, those nuclei are also exceedingly small, potentially only two or three voxels in the original DTI resolution.
- Unlike previous work, these results were **achieved without requiring extensive prior knowledge** of the target's thalamus boundary.

Nucleus	Mean Dice	Median Dice
Anterior	0.576 ± 0.146	0.593
MedialDorsal	0.641 ± 0.142	0.664
Ventral Group	0.833 ± 0.074	0.838
Pulvinar	0.711 ± 0.102	0.725
Lateral Gen.	0.394 ± 0.202	0.405
Medial Gen.	0.489 ± 0.244	0.515

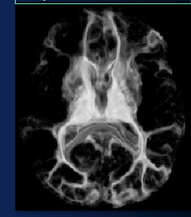


Perspectives of an example parcellation result on a right thalamus. Left: canonical axial view. Middle: sagittal lateral view. Right: axial view from inferior perspective (facing up). The larger pulvinar and ventral group nuclei are shown in transparency.

4. Conclusions, Future Directions

- Long-term goal is the large scale study of thalamic neuro-pathology using automated methods. In this paper we have extended thalamic parcellation to place us closer to that goal.
- We must improve accuracy, by training more specific (nucleus-everything) random forest learners and pooling results over a larger number of training cases.
- Compare Knutsson to other tensor/PEV dissimilarity measures.
- **Cortical connectivity** to combine global and local information.

Axial view of fiber counts given seeding within the thalamus. Using FSL Diffusion Toolbox.



Cortical surface colored by region, along with example connectivity-based parcellations of the left thalamus (axial view). These FSL-based results are consistent with those of [Behrens], and show a large variance in parcellation. Note the temporal versus occipital connectivity of the posterior areas.