Segmenting thalamic nuclei from manifold projections of multi-contrast MRI

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1 Paper Summary

Introduction The thalamus is a gray matter structure located in the forebrain, whose main function is to relay sensory and motor signals within the brain. It can be divided into different clusters of densely packed neuronal cell bodies, called thalamic nuclei. These nuclei can atrophy or be affected by multiple diseases and, therefore, it is of utter importance to be able to segment and analyze them individually. The paper under study [1] addresses the problem of thalamic nuclei segmentation through manifold projection and clustering using multiple magnetic resonance imaging (MRI) modalities.

State of the Art (SOTA) and Main Contributions Positioning the methodology against SOTA is not straightforward as the dataset used is private, and no comparisons with standard benchmarks are presented.

Previous approaches to this problem differ in terms of (1) the input modality, and (2) the learning algorithm. For input modality, some methods use T1-weighed MRI [2, 3], others use diffusion MRI [4, 5, 6], while some use a combination of different modalities [7, 8, 9, 10, 11]. Algorithmically, we observe methods based on classical techniques such as bayesian networks [5], random forests [11] and spectral clutering [12], as well as deep learning techniques, primarily consisting of UNet derivatives [11, 7, 8, 10]. Some recent methods also employ a hybrid approach [13]. In general, their main limitations are: (1) they only consider a few clusters per hemisphere or they just report global metrics; and (2) they do not use the full range of available MRI contrasts as input, which is a problem as the thalamus and the nuclei tend to have low contrast on MRIs.

The main contribution of this work is using the full range of MRI contrasts (MPRAGE, FGATIR, T2-weighted, a 3D T1 map, DTI, and other derived values derived as connectivity maps) to overcome the low contrast problem. In terms of learning algorithms, they propose a novel approach capable of working with such high-dimensional input vectors, which consists of manifold projection using UMAP and *k-NN* clustering in the low-dimensional space.

Methodology To create the dataset, multi-contrast MRI images for 30 viable subjects are taken from a mild traumatic brain injury (mTBI) study. These images are registered and processed, and the 161 available features per voxel are combined to form five input vectors: Base (19D MR derived features), Coord (3D coordinates), Multi-TI (41D multi-parametric TI features), Conn6 and Conn98 (6D and 98D fiber connectivity). All data is normalized in an outlier-robust manner by linearly scaling the three - (0-2.5), (2.5-97.5), and (97.5-100) - percentile regions onto [0, 0.025), [0.025, 0.975], and (0.975, 1] values, respectively.

The label for each voxel is obtained by registering the Morel atlas [14] to the MPRAGE. Of the 19 original labels, the smaller ones are fused to keep only 13 labels. The registration results are manually corrected, and a thalamus mask is applied to eliminate the labels outside of its region. As the manual delineation is done per nucleus, some voxels remain unlabeled or might have with multiple labels.

The data is then used to train the UMAP algorithm, which determines key tissue signatures in a low dimensional space. During inference, each voxel is mapped into the embedding space and its classification is performed by applying a modified *k-NN* algorithm to also take multiple labels into consideration.

Validation and Results Training is performed using a five-fold cross-validation strategy with a 4:1 training to testing split. UMAP is trained in an unsupervised manner for 1000 epochs with no early stopping, only seeing the feature vectors of the 4 training sets. No information has been provided for the hyperparameter tuning methods neither for UMAP nor *k-NN*.

Two ablation studies were performed. First, to find the best combination of input feature vectors and, second, to find the optimal dimension for the latent space. Comparisons are done using Dice scores, reporting average score with standard deviation, as well as scores for individual nucleus.

The main results imply that adding connectivity information is not useful. Furthermore, the authors report a trade-off between performance and computational cost and conclude that projection into 2D space provides optimal results. Finally, when projecting to a 2D space, the average Dice score per nucleus ranges between **0.188** for the smaller ones and **0.860** for the larger ones.

2 Critical Assessment

Strengths The paper proposes a novel method for performing thalamic nuceli segmentation, that takes into account multiple information sources. The methodology is clear, easy to implement, and has a low computational complexity. Moreover, one big strength of this method is that both UMAP and *k-NN* are highly interpretable, and thus they are suitable for a sensitive field such as medical imaging.

Weaknesses To our view, the main weakness of this work relies on its reproducibility issues, as neither the code nor the data are publicly available. It is, therefore, impossible to replicate their results or compare the method experimentally with other state of the art techniques.

Moreover, having additional information regarding the dataset is necessary in order to evaluate its generalization capacity. For example, MR images tend to have very different characteristics depending on the parameters used for the acquisition, and are susceptible to inter-individual anatomical variability because of population demographics. Moreover, it should be tested on data outside of a mTBI test. Another point where more information would be needed is on the registration method used both for the labeling and for the prediction, as the performance of the model relies heavily on its accuracy.

With regards to the training, it is unclear how the hyperparameter tuning is performed. In particular, if the cross-validation test folds were used, then it would be important to clarify that the tables presented are only validation metrics, and not real test metrics.

Furthermore, on their conclusion the authors state that "*Our performance on several nuclei is higher than other works: [...]*". This claim is unfounded, as the cited papers use other data for training and evaluation, with a different labeling method. They also write that "*A higher accuracy can be achieved using a higher order latent space, but the embedding time will increase*". However, the accuracy of the model is not reported, just the Dice score. We think that this is just a case of term misuse.

Lastly, on a more general note, the method relies on a vast array of data, which is not available in general clinical MRI acquisition protocols [15]. This limits the proposed method's usability in practical settings.

Recommendations From the validation table, we can see that the performance is really uneven for different nuclei. In particular, the method performs poorly for smaller nuclei such as CM. While this is expected, as there are fewer labeled voxels for these classes, it could be interesting to explore some balancing techniques, such as data augmentation per class. Moreover, the utility of adding more clusters has to be evaluated against the decrease of average performance that they imply.

Moreover, the only reported metric is the Dice score, while literature also provide results for other metrics, in particular Volumetric Similarity (VS). Both scores show strong correlation when the overlap is significant. However, when there is non-optimal alignment, which is a possible scenario due to registration among modalities and semi-manual labeling, VS shows a strong divergent correlation [16]. We believe this could help unearth issues with the pipeline and improve the method.

Lastly, the overlap between labels can be a reasonably easy-to-solve source of problems, and further exploration on the usefulness of connectivity maps could be performed.

References

[1] Chang Yan, Muhan Shao, Zhangxing Bian, Anqi Feng, Yuan Xue, Jiachen Zhuo, Rao P Gullapalli, Aaron Carass, and Jerry L Prince. Segmenting thalamic nuclei from manifold projections of multi-contrast mri. In *Medical Imaging 2023: Image Processing*, volume 12464, pages 714–721. SPIE, 2023.

[2] Adolf Pfefferbaum, Edith V Sullivan, Natalie M Zahr, Kilian M Pohl, and Manojkumar Saranathan. Multi-atlas thalamic nuclei segmentation on standard t1-weighed mri with application to normal aging. *Human brain mapping*, 44(2):612–628, 2023.

[3] Julie P. Vidal, Lola Danet, Patrice Péran, Jérémie Pariente, Meritxell Bach Cuadra, Natalie M. Zahr, Emmanuel J. Barbeau, and Manojkumar Saranathan. Robust thalamic nuclei segmentation from t1-weighted mri using polynomial intensity transformation. *medRxiv*, 2024.

[4] Rémi Patriat, Tara Palnitkar, Jayashree Chandrasekaran, Karianne Sretavan, Henry Braun, Essa Yacoub, Robert A. McGovern, Joshua Aman, Scott E. Cooper, Jerrold L. Vitek, and Noam Harel. Dimani: diffusion mri for anatomical nuclei imaging—application for the direct visualization of thalamic subnuclei. *Frontiers in Human Neuroscience*, 18, 2024.

[5] Henry F.J. Tregidgo, Sonja Soskic, Juri Althonayan, Chiara Maffei, Koen Van Leemput, Polina Golland, Ricardo Insausti, Garikoitz Lerma-Usabiaga, César Caballero-Gaudes, Pedro M. Paz-Alonso, Anastasia Yendiki, Daniel C. Alexander, Martina Bocchetta, Jonathan D. Rohrer, and Juan Eugenio Iglesias. Accurate bayesian segmentation of thalamic nuclei using diffusion mri and an improved histological atlas. *NeuroImage*, 274:120129, 2023.

[6] Giovanni Battistella, Elena Najdenovska, Philippe Maeder, Naghmeh Ghazaleh, Alessandro Daducci, Jean-Philippe Thiran, Sébastien Jacquemont, Constantin Tuleasca, Marc Levivier, Meritxell Bach Cuadra, et al. Robust thalamic nuclei segmentation method based on local diffusion magnetic resonance properties. *Brain Structure and Function*, 222:2203–2216, 2017.

[7] Marina Ruiz-Perez, Sergio Morell-Ortega, Marien Gadea, Roberto Vivo-Hernando, Gregorio Rubio, Fernando Aparici, Mariam de la Iglesia-Vaya, Thomas Tourdias, Pierrick Coupé, and José V. Manjón. Deepthalamus: A novel deep learning method for automatic segmentation of brain thalamic nuclei from multimodal ultra-high resolution mri, 2024.

[8] Lavanya Umapathy, Mahesh Bharath Keerthivasan, Natalie M Zahr, Ali Bilgin, and Manojkumar Saranathan. Convolutional neural network based frameworks for fast automatic segmentation of thalamic nuclei from native and synthesized contrast structural mri. *Neuroinformatics*, pages 1–14, 2022.

[9] Manojkumar Saranathan, Charles Iglehart, Martin Monti, Thomas Tourdias, and Brian Rutt. In vivo high-resolution structural mri-based atlas of human thalamic nuclei. *Scientific Data*, 8(1):275, 2021.

[10] Mohammad S. Majdi, Mahesh B. Keerthivasan, Brian K. Rutt, Natalie M. Zahr, Jeffrey J. Rodriguez, and Manojkumar Saranathan. Automated thalamic nuclei segmentation using multi-planar cascaded convolutional neural networks. *Magnetic Resonance Imaging*, 73:45–54, 2020.

[11] Joshua V Stough, Jeffrey Glaister, Chuyang Ye, Sarah H Ying, Jerry L Prince, and Aaron Carass. Automatic method for thalamus parcellation using multi-modal feature classification. In *Medical Image Computing and Computer-Assisted Intervention–MICCAI 2014: 17th International Conference, Boston, MA, USA, September 14-18, 2014, Proceedings, Part III 17*, pages 169–176. Springer, 2014.

[12] Ulas Ziyan, David Tuch, and Carl-Fredrik Westin. Segmentation of thalamic nuclei from dti using spectral clustering. In *Medical Image Computing and Computer-Assisted Intervention–MICCAI 2006: 9th International Conference, Copenhagen, Denmark, October 1-6, 2006. Proceedings, Part II 9*, pages 807–814. Springer, 2006.

[13] Anqi Feng, Yuan Xue, Yuli Wang, Chang Yan, Zhangxing Bian, Muhan Shao, Jiachen Zhuo, Rao P. Gullapalli, Aaron Carass, and Jerry L. Prince. Label propagation via random walk for training robust thalamus nuclei parcellation model from noisy annotations. In *2023 IEEE 20th International Symposium on Biomedical Imaging (ISBI)*, pages 1–5, 2023.

[14] Anne Morel, Michel Magnin, and Daniel Jeanmonod. Multiarchitectonic and stereotactic atlas of the human thalamus. *Journal of Comparative Neurology*, 387(4):588–630, 1997.

[15] Lavanya Umapathy, Mahesh Bharath Keerthivasan, Natalie M. Zahr, Ali Bilgin, and Manojkumar Saranathan. Convolutional neural network based frameworks for fast automatic segmentation of thalamic nuclei from native and synthesized contrast structural MRI. *Neuroinformatics*, 20(3):651–664, 2022.

[16] Abdel Aziz Taha and Allan Hanbury. Metrics for evaluating 3d medical image segmentation: analysis, selection, and tool. *BMC medical imaging*, 15:1–28, 2015.