Multimodal Connectivity-based Cortical Segmentation with Graph Neural Networks

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2 ABSTRACT

Due to the significant amount of time and expertise needed for manual segmentation of
the brain cortex from magnetic resonance imaging (MRI) data, there is a substantial need
for efficient and accurate algorithms to replace the need for human involvement. In this work,
we explore the capabilities of Graph Neural Networks (GNNs) to segment the brain surface
based on structural brain connectivity. We train three different GNN architectures, the Graph
Convolutional Network (GCN), the Graph Attention Network (GAT), and the Graph U-Net, and
evaluate their performances when trained on silver-standard cortical region labels created by
FreeSurfer. We take a multimodal approach to brain segmentation by examining the influence of
the structural connectivity values inferred from diffusion MRI (dMRI) in addition to using values
from structural MRI (sMRI). Our results demonstrate the utility of GNN models, particularly the
GAT architecture, which achieved Dice scores competitive to those reported in the literature with
non-graph methods. Additionally, structural connectivity derived from dMRI revealed significant
value in improving automatic segmentation, as models trained on combined attributes from dMRI
and sMRI outperformed those trained only on sMRI. Finally, we compared the GNN-based and
the FreeSurfer segmentations in their ability to predict demographic/clinical data, where neither of
the two approaches was statistically significantly superior to the other.

Keywords: cortical segmentation, structural brain connectivity, connectome-based prediction, diffusion MRI (dMRI), FreeSurfer, graph
neural networks

1 INTRODUCTION

Development of *in vivo* imaging techniques such as Magnetic Resonance Imaging (MRI) has given
neuroscientists an unprecedentedly detailed and non-invasive view of the human brain. However, as the
brain is a highly complex structure consisting of billions of neurons, interpreting MRI images remains a
challenge. Brain segmentation provides a valuable way of reducing dimensionality by dividing the brain
into a limited number of regions of interest (Gallardo Diez, 2018; Wang et al., 2018; Desikan et al., 2006).
Further, segmentation greatly aids medicine and neuroscience by helping to advance our understanding of
neuroanatomy and providing deeper insight into the connection between brain structure and human clinical
and behavioral data (Gallardo Diez, 2018).

Manual brain labeling is a tedious and time-consuming process (Roy et al., 2018). As a result, there has
been substantial research to fully automate the process. The vast majority of published methods use only
structural MRI (sMRI) images as input, which provide important information about brain anatomy and
allow measurements such as cortical thickness and curvature (Roy et al., 2018; Henschel et al., 2020, 2022;
Fischl et al., 2004; Zhang et al., 2024). However, recent studies indicate that multimodal segmentation can
provide novel insights and improve the utility of surface segmentation (Wang et al., 2018; Zhang et al.,
2024). Specifically, the relationship between structural connectivity and cortical morphology has been
exploited to leverage structural connectivity to segment (Zhang et al., 2024; Eschenburg et al., 2021; Wang
et al., 2018) and align (Petrović et al., 2009; Isaev et al., 2017; Cole et al., 2025) the cortex. Functional
connectivity obtained from functional MRI has also been used for such purposes (Wang et al., 2018; Conroy
et al., 2013). We explore here the impact of including structural connectivity, which is a measure of the
strength of physical white-matter connections between brain regions, to segment the cortex.

We train Graph Neural Networks (GNNs), such as the Graph Convolutional Network (GCN), the Graph
Attention Network (GAT), and the Graph U-Net architectures, based on information from sMRI alone as
well as combined sMRI and dMRI connectivity features, using the segmentation results obtained from
FreeSurfer (Fischl, 2012) as the *silver* standard. Doing so enables us to compare the segmentation quality of
a model trained on data from a single modality, in our case sMRI, with a model trained with the addition of
connectivity data derived from dMRI. Furthermore, we explore the accuracy of different GNN architectures,
as well as the influence of different sMRI-derived parameters on the final segmentation results.

We also validate the best-performing model by examining its effectiveness in a downstream task, thereby
evaluating the applicability of the multimodal GNN and its possible improvement upon the silver-standard
training set. Given that FreeSurfer segmentation labels are created automatically, as opposed to manually,
they are not considered gold-standard ground truth (Fischl et al., 2004), and, as such, they might contain
errors. Overlap measures between the labels resulting from GNN and those of FreeSurfer, therefore, cannot
gauge any potential improvement over the training labels, as a perfect Dice score would only indicate that
the model has learned to perfectly reproduce the FreeSurfer results. Conversely, disparities between the two
results could indicate either an error on the part of the trained model or possibly an improvement upon the
FreeSurfer segmentation, something that cannot be estimated with silver-standard labels alone. Evaluating
the usefulness of the final segmentation when applied to a downstream task, such as age prediction, however,
provides us with a surrogate measure to compare the two segmentation methods.

We describe our methods in Section 2, provide our experimental results in Section 3, and discuss them
and conclude the paper in Section 4.

2 METHOD

The basis of our cortical graph structure is the pial surface automatically created with FreeSurfer (Fischl,
2012) from the T1-weighted 3D MRI image. The final result is in the form of a triangular mesh
approximating the pial surface, which is shown in Fig. 1 for one of the test subjects. The resulting
graph is unweighted. A feature vector is assigned to each vertex (node) in the graph and can contain a
combination of the characteristics derived from sMRI and dMRI.

Data collected from sMRI that we incorporated in the feature vector include (x, y, z)-coordinates of the
node, cortical thickness, and curvature values. Thickness is defined as the distance between the white and
pial surfaces, and curvature is defined as the inverse of the radius of the circle tangent to the surface at
the position of the corresponding vertex (mean curvature was used, which is the average of the curvatures

corresponding to the smallest and the largest tangent circles). Thickness and curvature are scalar values,
and the coordinates are a vector of length 3. The curvature is negative in a gyrus and positive in a sulcus.
The features were min-max normalized.

73 To compute structural connectivity of each vertex to the other vertices from dMRI, we used a conductance-
based method (Frau-Pascual et al., 2019). This approach models white-matter pathways within the brain
based on a combination of differential Maxwell's equations and Kirchoff's circuit laws. A high conductance
(i.e., low resistance) value computed between two regions represents a high degree of connectivity between
them. This method accounts for both direct and indirect brain connections and has been shown to predict
age and dementia (Frau-Pascual et al., 2021). We applied this method to sMRI and dMRI of 97 subjects
of the "100 Unrelated Subjects" group of the Human Connectome Project (HCP) Young Adult study,
which consists of healthy individuals aged 22-35 (Van Essen et al., 2013). Three subjects were omitted
due to failed connectivity computation. We were granted access to restricted HCP data, which contains,
among other sensitive information, the subjects' exact age, Mini-Mental State Exam (MMSE) scores,
and education level. During preprocessing, we transformed the data from the FreeSurfer uniform space,
fsaverage3, where the brain connectivity data had been computed, to the native space of every subject via
the *mris_apply_reg* command. The final connectivity map for each vertex was a feature vector of length 642
(the number of vertices in the hemisphere).

87 We used the following three different GNN architectures for segmentation:

88 • **Graph Convolutional Network (GCN)** is based on the Convolutional Neural Network concept, but
89  designed to work on graph structures. With each layer, the information from the neighboring nodes is
90  incorporated in the next layer's feature vector (Kipf and Welling, 2017).

91 • **Graph Attention Network (GAT)** allows to assign a degree of usefulness to each neighboring node,
92  making it a more complex architecture than the GCN (Veličković et al., 2018).

93 • **Graph U-Net** is based on the U-Net model, a deep-learning architecture well suited for the
94  segmentation of biomedical images. It contains Graph Pooling layers, which down-sample the graph,
95  followed by Graph Unpooling layers, which expand it back to the original size (Gao and Ji, 2019).

3 RESULTS

96 We first report the outcomes of the GNN model training on the task of cortical segmentation with the
97 FreeSurfer segmentation as ground truth. Next, we detail the results of predicting the demographic/clinical
98 characteristics of the subjects based on the segmentation results, which compares the usefulness of the
99 model's and the FreeSurfer's outputs for a real-life task.

3.1 Graph-based cortical segmentation

101 All three models were evaluated on 97 subjects of the "100 Unrelated Subjects" group of the HCP Young
Adult dataset. We held out 8 subjects as the final validation set, and the remaining 89 subjects were included
in a 5-fold cross-validation. We monitored the training process in each split by examining the Dice scores
of the model applied to both the training and the validation sets of the fold. In each fold, once training
concluded, we applied the trained model to the final validation set (8 subjects). The mean Dice score on
the final validation set over the five splits is reported and used as the primary metric to compare different
models in the following.

For GNN model training, the Adam optimization algorithm and the *ReduceLRonPlateau* scheduler were
used. The starting learning rate was $lr = 0.01$, and all models were trained for 100 epochs. Due to GPU
constraints, a batch size of 1 was chosen. Gaussian noise was added to the input features during training
for data augmentation.

Table 1 shows the final average Dice scores for the three model architectures and six different feature
vectors, for the right and left hemispheres. For ease of reading, the model trained on coordinates,
thickness, and curvature will be referred to as the "fully structural" model, and the model trained on
all possible attributes, that is, coordinates, thickness, curvature, and structural connectivity, will be called
the "multimodal" model.

3.1.1   Influence of the Feature Vector

As can be seen in Table 1 for both hemispheres, using only (x, y, z) coordinates of the vertex produced the
lowest Dice scores. Adding either the thickness or curvature scalar value slightly improved the results, with
thickness often slightly more helpful than curvature. Adding them both further increased the final score,
suggesting non-overlapping information by them. The most notable finding is the results by the multimodal
model (when the connectivity values are added), where the Dice score is considerably increased, e.g. up to
a cross-hemisphere mean of 0.923 for the GAT model. Worth pointing out is also that the model trained on
the combination of (x, y, z) + conductance still outperformed all models trained on data solely from sMRI.

3.1.2   Comparison of the model architectures

In terms of model performance, GAT outperformed GCN in nine out of the twelve feature combinations,
including all that include connectivity values. Among models only trained on structural data, GCN either
outperformed the GAT model or scored slightly below it. Graph U-Net achieved the lowest final scores in
all examined cases.

Two-sided paired *t*-tests across the results on the final validation set revealed the subject-mean Dice
scores from the multimodal model to be significantly higher for GAT as compared to GCN ($p = 2 \times 10^{-5}$
and $p = 10^{-6}$ for the left and right hemispheres, respectively) and Graph U-Net ($p = 7 \times 10^{-9}$ and
$p = 3 \times 10^{-6}$ for the left and right hemispheres, respectively).

3.1.3   Influence of the number of parameters on the model performance

As detailed in Section 3.1.1, the addition of connectivity values to the feature vector considerably
improved the segmentation results. For a fair comparison, the depth and width of the models were kept
constant regardless of the size of the feature vector. However, as shown in Table 2, the connectivity data
increase the size of the feature vector by 642, in turn increasing the number of trainable weights in our
multimodal models, whereas thickness and curvature each only add a single scalar value per vector. In
other words, when the sizes of the rest of the layers are kept constant, the number of trainable parameters
will increase with the length of the input feature vector. For example, for the GCN architecture, the number
of weights increases for a model trained solely on coordinates from 144k to 145k for a model trained on
a combination of coordinates, thickness, and curvature, and finally up to 474k for a model trained on all
available attributes.

It is worth pointing out that due to the possibility of overfitting, increasing the number of trainable
parameters does not always lead to enhanced performance. Having more parameters is therefore not
necessarily an advantage for a model trained on the connectivity values. However, for the sake of
completeness, we trained a GCN model with an increased width of the second layer on a feature vector

solely including attributes from sMRI, to see how much it would affect its performance. As can be seen in
Table 2, the final Dice score of the fully structural model is still significantly lower than the multimodal
model, even with more trainable weights in the former than in the latter. When the number of features in
the fully structural model is doubled relative to the original size, the score increases by 0.0223. However,
upon increasing the size again, the result plateaus.

3.2 Downstream task

155 We further evaluated the performance of the GNN model by employing it in a downstream task, which
156 tests the usefulness of the final segmentation results. As the multimodal GAT was the best-performing
157 model in both hemispheres in Section 3.1.2, we chose this model for the downstream task.

3.2.1 Statistical correlation

To examine the applicability of the segmentation outputs of the trained model and FreeSurfer, we
correlated region-wise imaging attributes, namely average cortical thickness and average conductance,
with demographic/clinical characteristics such as age, MMSE score, and education level. Specifically,
we calculated the average thickness/conductance value for every segmented cortical region for both the
FreeSurfer and the GAT model segmentations, and then determined how the resulting values correlated
with the subjects' age/MMSE/education.

When correlating the average of all within-region mean thickness values with age, for FreeSurfer
segmentation, the left hemisphere showed statistical significance with $r = -0.35$ and $p_{ave}^{FS} = 0.002$. The
negative linear correlation is consistent with what is reported in the literature (Aycheh et al., 2018). For the
right hemisphere, the values are slightly less significant, with $r = -0.23$ and $p_{ave}^{FS} = 0.02$. Model-based
segmentation performed similarly to FreeSurfer-based segmentation; for the left hemisphere, $r = -0.31$
and $p_{ave}^{model} = 0.002$, and for the right hemisphere $r = -0.23$ and $p_{ave}^{model} = 0.02$.

In region-wise correlation, four FreeSurfer regions passed the Bonferroni-corrected threshold ($\alpha_B =$
$0.05/35 = 0.0014$) in the left hemisphere and two in the right hemisphere. For model-based segmentation,
five regions fulfilled the threshold for the left hemisphere, and two for the right hemisphere. Table 3
shows the p-values for the specific regions in which at least one of the segmentation sources passed the
significance threshold α_B. While this shows certain regions' strong correlation with cortical thickness,
the model and FreeSurfer performed similarly, as a paired Wilcoxon signed rank test on the region-wise
p-values revealed no statistically significant difference ($p_W = 0.16$ and $p_W = 0.88$ for the left and right
hemispheres, respectively).

No correlation between other brain attributes in a brain region and/or other demographic/clinical features
passed the α_B significance threshold.

3.2.2 Age prediction

For the prediction task, we combined regions from both hemispheres, resulting in an input vector of length
70. We used seven available machine learning models from the MATLAB Regression Learner Toolbox. We
also trained different-sized Multi-Layer Perceptrons (MLPs). The performance was determined with the
root mean square error (RMSE), which should be at the very least below the standard deviation of the label
data, $\sigma_{age} = 3.70$ years, in order to show any form of utility.

FreeSurfer segmentation outperformed the GAT segmentation, achieving a lower RMSE for four out of
seven models when using thickness as a brain characteristic and for all models when using conductance.
However, the results for both methods were not satisfactory enough for a clear conclusion - the lowest

reported RMSE was 3.44, i.e. only 0.26 below σ_{age}, for the Regression Trees when using the FreeSurfer
segmentation and the average conductance.

MLP showed poor training results, either indicating over- or underfitting, and a large variation in the
RMSE between different validation splits. This significant training instability suggests that the model was
not capable of properly generalizing on the dataset, making the comparison between the two segmentation
methods difficult to interpret. As such, no strong conclusions could be drawn from the final results.

4 DISCUSSION

We demonstrated that GNNs are a suitable network architecture for the task of cortical surface segmentation,
comparable to the non-deep-learning based algorithms such as the one employed by FreeSurfer. While
the direct comparison with other methods in the literature is limited due to the difference in datasets and
cortical atlases used, the final reported scores of 0.768 for the model solely trained on sMRI-derived data
and, especially, 0.927 for the model trained by including connectomic data are comparable to the currently
reported state-of-the-art results (Henschel et al., 2020, 2022; Roy et al., 2018; Wu et al., 2019; Cucurull
et al., 2018; Eschenburg et al., 2021).

The considerable increase in the final Dice scores for the model trained in a multimodal fashion indicates
the significant utility of structural connectivity in the task of brain segmentation. Notably, the model trained
on the combination of (x, y, z) and conductance outperformed models trained on all available features
from sMRI, which suggests that connectivity values provide more useful information than the thickness or
curvature, even though those are the parameters that are utilized by the FreeSurfer segmentation algorithm
(Fischl et al., 2004).

When considering the network architecture, GAT was the strongest one when connectivity data were
included. However, GCN performed comparatively well when only sMRI values were considered. This is
possibly because the more complicated architecture of the GAT model performs better when it needs to
generalize on a more complex training set, and the GCN is not powerful enough to process the significantly
longer feature vector once the connectivity data are introduced, even when it has more training weights.
When the training data include only attributes from sMRI, a less powerful model such as a GCN might be
enough.

It is worth noting that the Graph U-Net layers needed to be kept narrower than those in the other two
architectures due to memory constraints, resulting in a much smaller number of training weights, 170403,
for a Graph U-Net, in comparison to 473705 for a GCN and 242863 for a GAT model (for a feature vector
of length 647). However, the fact that the GAT model, while having significantly fewer training weights
than the GCN model, still managed to outperform it, indicates that a suitable model architecture should
still be able to perform well with fewer trainable parameters. While GPU time and memory were limiting
during model training, they are often much less of a concern during inference (e.g., while applying a trained
model in a clinical setting), where even CPUs can be used to segment an image in a reasonable time.

The influence of trainable weights on the network performance was further explored in Section 3.1.3.
The results from Table 2 indicate that, as expected, simply increasing the training weights is not a suitable
alternative to introducing new attributes in the feature vector and adding new information to the training
set.

In the second part of this work, we aimed to examine whether the GNN model has the capability to
generalize upon FreeSurfer labels well enough to show higher utility in a downstream task posed. However,

the results failed to unequivocally prove an improvement in the GNN-based segmentation. The RMSE
from the MATLAB toolbox models did not show clear superiority of one method over the other, and the
MLP showed typical behavior of an overfitted model, suggesting that the model most likely simply learned
to memorize the input vector and their age labels, and did not have enough data to generalize on. It is
therefore not possible to state whether the model was able to improve upon the silver-standard labels it was
trained on.

One significant limitation of the study is the lack of manually labeled data, which could be used as
the gold standard during training, serving as more reliable labels than the silver-standard segmentation
created with FreeSurfer, and also as a benchmark for the evaluation of the final results. Training on more
subjects could also improve the performance of the model in the downstream task. Nonetheless, as graph
segmentation is intrinsically a node classification task, 97 subjects were enough for high training and
validation scores. For the model to improve upon FreeSurfer, however, it may require a larger amount of
data to be able to generalize upon the variation in the input. It is possible that with the amount of data
provided, the model was capable of matching FreeSurfer's segmentation, but not necessarily improving
upon it.

Furthermore, it would be beneficial to see if the models are equally capable of generalizing on a more
diverse group of subjects. As stated before, the brain surfaces used for training were all from a young and
healthy population. However, for neuroscientific research as well as in clinical settings, patients and elderly
individuals are often of more interest. Even more insightful would be to compare the influence of brain
connectivity on the segmentation of the brains of patients with neurological disorders that are known to
influence both the structure and connectivity of the brain, such as Alzheimer's disease.

Future work includes validating our approach on gold-standard manually annotated cortical labels,
attention-weight and node-importance analysis of the GAT architecture to explore which regions or
connectivity features drive improvements, and training an end-to-end segmentation model to optimize
downstream tasks (such as age prediction). Finally, more recent architectures, such as GCNs with an
added attention mechanism (Tan et al., 2025) or diffusion-based approaches (Zhu et al., 2024), have shown
great potential in the task of cortical surface segmentation. It would be worth exploring whether such
state-of-the-art architectures could also benefit from the inclusion of structural connectivity.

CONFLICT OF INTEREST STATEMENT

258 The authors declare that the research was conducted in the absence of any commercial or financial
259 relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

260 AŁ: Conceptualization, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing
261 – original draft, Writing – review & editing. AK: Conceptualization, Supervision, Writing – review &
262 editing. CP: Conceptualization, Supervision, Resources, Writing – review & editing. AFP: Data curation,
263 Resources, Writing – review & editing. IA: Conceptualization, Data curation, Funding acquisition, Project
264 administration, Resources, Supervision, Writing – review & editing.

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DATA AVAILABILITY STATEMENT

Magnetic resonance images were provided by the Human Connectome Project (HCP) (Van Essen et al., 2013), WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil): https://www.humanconnectome.org/study/hcp-young-adult.

The conductance model of structural brain connectivity (Frau-Pascual et al., 2019) was computed using our public toolbox at https://github.com/ainafp/FVT4DWI. FreeSurfer (Fischl, 2012) is publicly available at https://surfer.nmr.mgh.harvard.edu. The models employed here were built using the PyTorch Geometric library (Fey and Lenssen, 2019).

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Figure 1. Visualization of the pial surface of an example subject from the training dataset. The zoomed-in regions show the triangular tessellation of the surface in greater detail. Note that while the structure of the graph is that of the mesh, the positioning of the nodes in the 3D space (used here for visualization) is not part of the graph. The (x, y, z) coordinates are in fact used as part of the feature vector of each vertex.

Feature vector	GCN	GAT	Graph U-Net
Left hemisphere			
(x, y, z) coordinates	0.712 ± 0.009	0.707 ± 0.017	-
(x, y, z) coordinates + thickness	0.743 ± 0.003	0.744 ± 0.005	-
(x, y, z) coordinates + curvature	0.742 ± 0.003	0.745 ± 0.007	-
(x, y, z) coordinates + thickness + curvature	0.761 ± 0.008	0.768 ± 0.005	0.744 ± 0.003
(x, y, z) coordinates + thickness + curvature + conductance	**0.9104 ± 0.0008**	**0.927 ± 0.003**	**0.882 ± 0.003**
(x, y, z) coordinates + conductance	0.8930 ± 0.0006	0.914 ± 0.003	-
Right hemisphere			
(x, y, z) coordinates	0.708 ± 0.005	0.711 ± 0.004	-
(x, y, z) coordinates + thickness	0.735 ± 0.004	0.728 ± 0.008	-
(x, y, z) coordinates + curvature	0.725 ± 0.006	0.722 ± 0.009	-
(x, y, z) coordinates + thickness + curvature	0.753 ± 0.007	0.760 ± 0.003	0.734 ± 0.004
(x, y, z) coordinates + thickness + curvature + conductance	**0.900 ± 0.001**	**0.918 ± 0.002**	**0.876 ± 0.009**
(x, y, z) coordinates + conductance	0.886 ± 0.002	0.904 ± 0.002	-

Table 1. Dice scores (mean ± StD) on the final validation dataset for GCN, GAT, and Graph U-Net architectures for both left and right hemispheres. The highest value in each row is highlighted in green. The row with the highest values is in bold. Graph U-Net was trained only for two types of input feature vectors due to the significantly longer training time required and poor initial results.

(x, y, z) **coordinates + thickness + curvature**	
Number of parameters	**Dice Score**
145001	0.7410 ± 0.0013
285801	0.7633 ± 0.0031
499201	0.7630 ± 0.0017
(x, y, z) **coordinates + thickness + curvature + conductance**	
Number of parameters	**Dice Score**
473705	0.9104 ± 0.0008

Table 2. The influence of the number of model parameters on the final Dice score for a GCN model.

Region	FreeSurfer	GAT Model
Left Hemisphere		
Superior frontal gyrus	$p = 0.002,$ $r = -0.332$	$p = 0.0008,$ $r = -0.334$
Inferior frontal gyrus, Pars triangularis	$p = 1.86e - 07,$ $r = -0.500$	$p = 9.3e - 07,$ $r = -0.474$
Inferior parietal cortex	$p = 0.002,$ $r = -0.315$	$p = 0.001,$ $r = -0.321$
Superior temporal gyrus	$p = 0.001,$ $r = -0.321$	$p = 0.0009,$ $r = -0.332$
Banks of the superior temporal sulcus	$p = 7.0e - 05,$ $r = -0.392$	$p = 7.7e - 05,$ $r = -0.390$
Right Hemisphere		
Middle frontal gyrus, Rostral division	$p = 0.0011,$ $r = -0.325$	$p = 0.0009,$ $r = -0.332$
Middle frontal gyrus, Caudal division	$p = 0.0001,$ $r = -0.383$	$p = 0.0002,$ $r = -0.366$

Table 3. Brain regions with mean cortical thickness statistically significantly correlated with age (by at least one method), for FreeSurfer and GNN-based (GAT) segmentation.