Tractmaps

Annotating tracts using cortical surface features

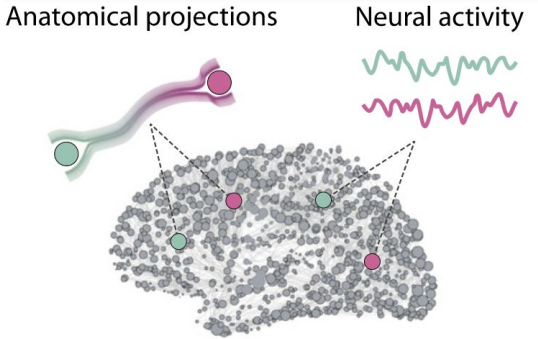
Lab meeting November 14, 2023

Joëlle Bagautdinova

Background

The question:

How does brain structure give rise to function?



Suárez et al., 2020, TICS

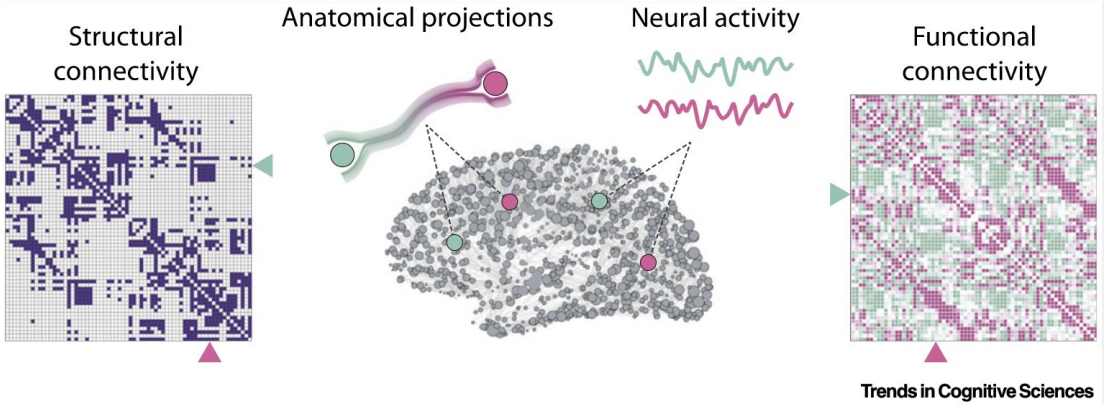
- Current thoughts:
  - structural connectivity gives rise to shared biological features on the cortical surface
  - cortical surface and white matter features mutually influence each other

Fornito et al., 2019, Alexander-Bloch et al., 2013, Hansen et al., 2023

Background

The question:

How does brain structure give rise to function?



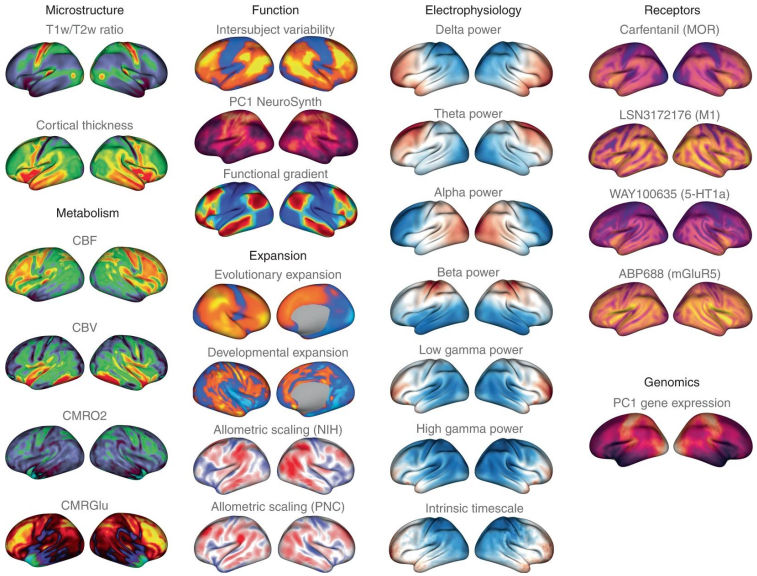
Suárez et al., 2020, TICS

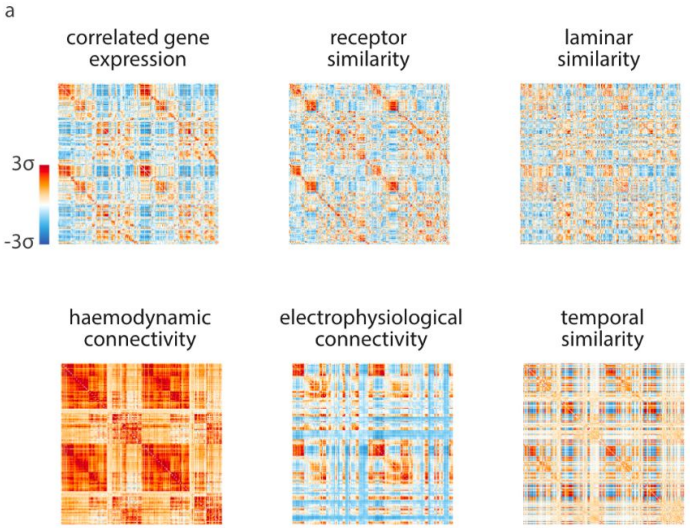
- Structure-function relationships are typically studied using **connectomics**
  - (regional nodes connected by structural and functional links)

Background

- Emerging efforts to annotate connectomes with surface features

  (Hansen et al., 2022; Markello et al., 2021)

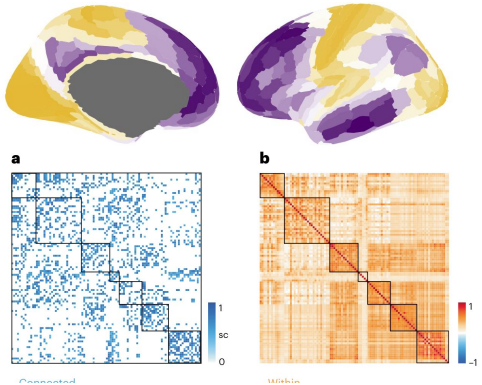




Gap

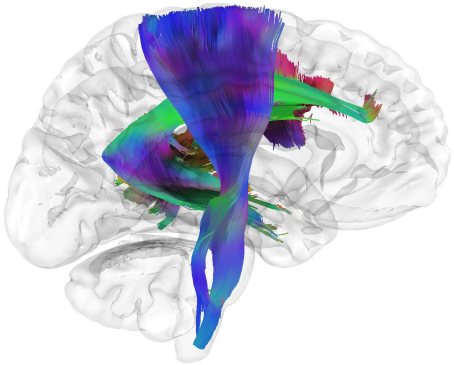
- Structural connectomes are oblivious to white matter tracts
  - They only tell you whether pairs of regions are structurally connected…
  - … not what tracts are connecting them!
- **Gap**: cortical surface features and white matter tracts have thus far been largely documented in separate literatures, precluding a comprehensive understanding of tract-to-surface relationships

Cortical surface features



OR…

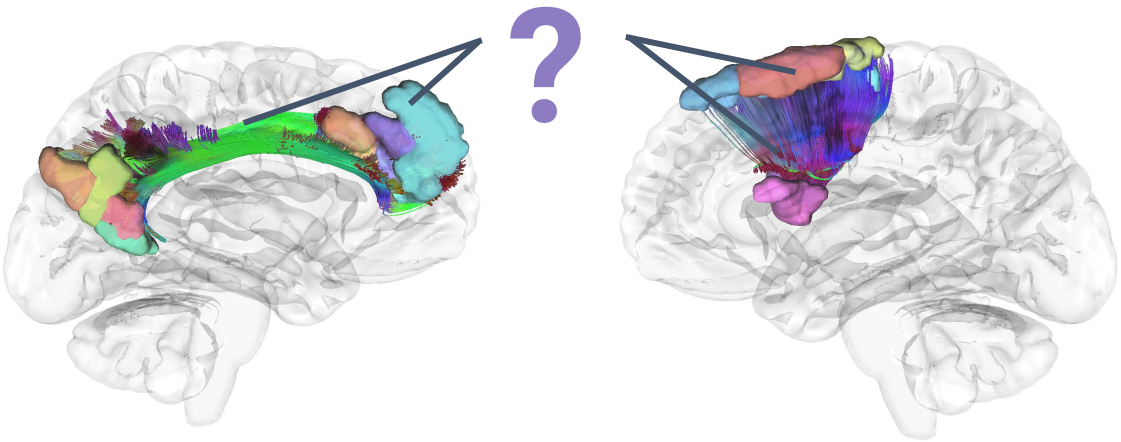
White matter tracts



Gap

Detailed surface features annotations… but how do they relate to white matter **tracts**?

What are the **surface features linked to major white matter tracts**?



Overarching Aim

Provide a comprehensive understanding of tract-to-surface relationships

Aims

Aim 1 Describe the cortical surface features of white matter tracts.

Aim 2 Determine whether the organization of surface features is dictated by white matter architecture.

Aim 3 Characterize the intrinsic organization of white matter tracts based on their surface features.

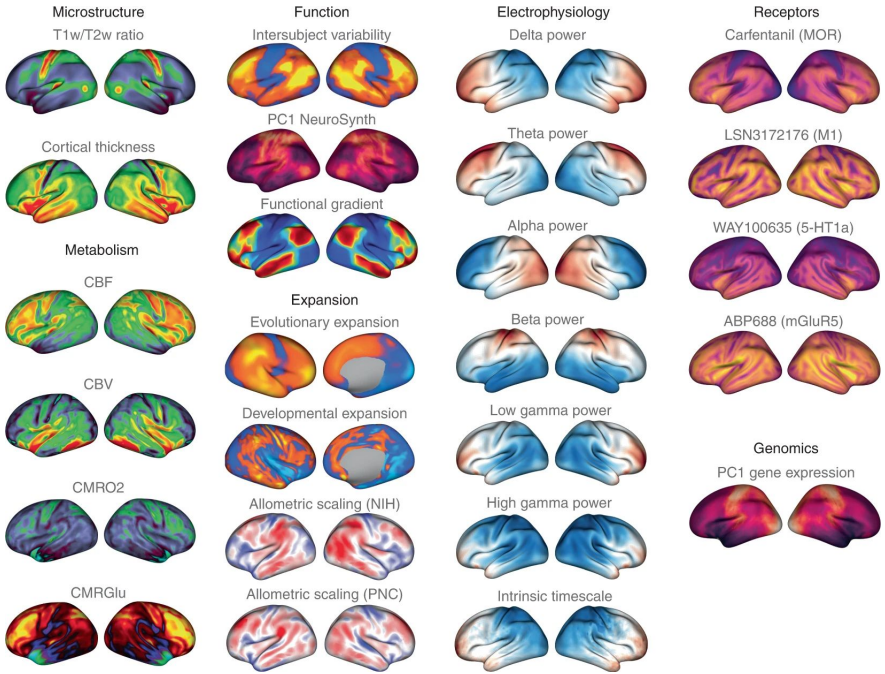
Methods: neuromaps

neuromaps: structural and functional interpretation of brain maps

Ross D. Markello, Justine Y. Hansen, Zhen-Qi Liu, Vincent Bazinet, Golia Shafiei, Laura E. Suárez, Nadia Blostein, Jakob Seidlitz, Sylvain Baillet, Theodore D. Satterthwaite, M. Mallar Chakravarty, Armin Raznahan & Bratislav Misic

Nature Methods **19**, 1472–1479 (2022) | Cite this article

- Repository: many different cortical surface features
- Transforms across multiple coordinate systems (volume, surface)
- Map-to-map comparisons (spins)



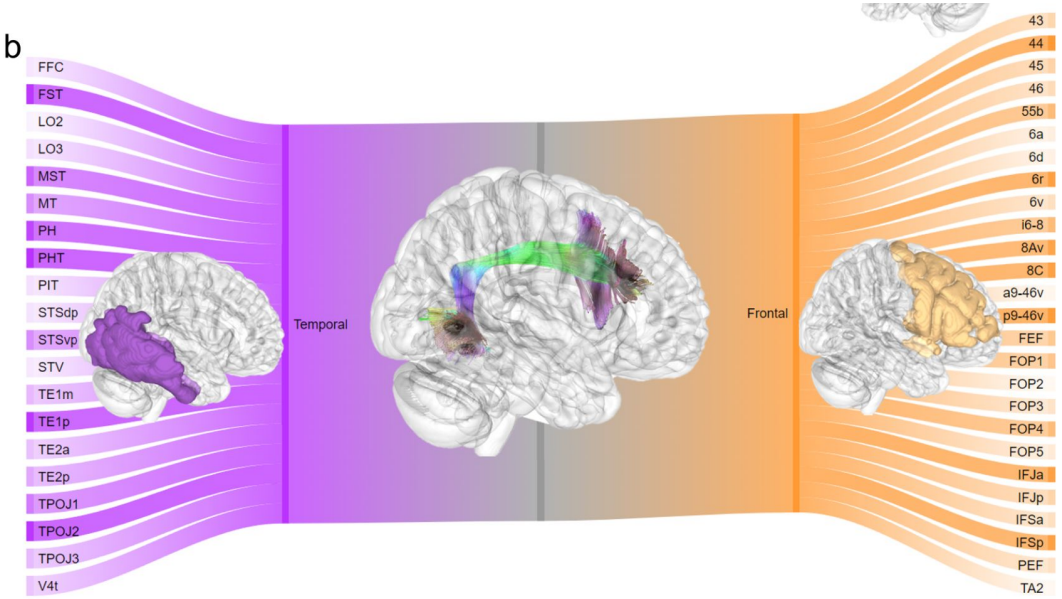
Methods: tract-to-region mapping

Population-based tract-to-region connectome of the human brain and its hierarchical topology

Fang-Cheng Yeh

Nature Communications **13**, Article number: 4933 (2022) | Cite this article

- Data: HCP (22-37 years), N=1065
- Population probabilities for each tract-to-region connection.
    - aka : in how many people did this connection exist
- Note: does not contain commissural tracts, brainstem, subcortical or cerebellar connections



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- Glasser parcellation
- Brain regions (360 rows) x tracts (50 columns)

Tracts

Brain regions

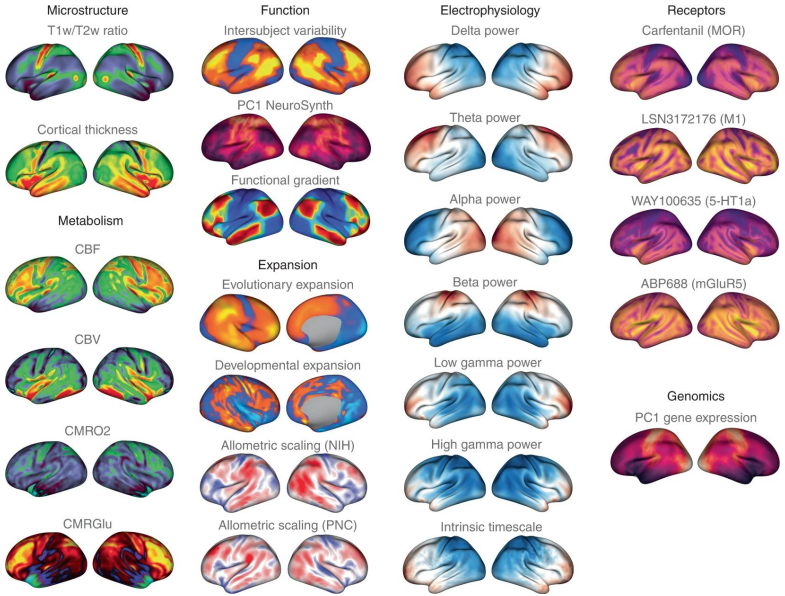
parcel_name	FAT_left	AF_left	PTAT_left	MdLF_left	SLF_III_left	SLF_II_left	SLF_I_left	C_FP_left	...
L_V1	0.0	0.000000	0.000000	0.0	0.0	0.0	0.0	0.0	...
L_MST	0.0	0.289202	0.931455	0.0	0.0	0.0	0.0	0.0	...
L_V6	0.0	0.000000	0.000000	0.0	0.0	0.0	0.0	0.0	...
L_V2	0.0	0.000000	0.000000	0.0	0.0	0.0	0.0	0.0	...
L_V3	0.0	0.000000	0.000000	0.0	0.0	0.0	0.0	0.0	...
...	...	...	...	...	...	...	...	...	...

Neuromaps + tract-to-region mapping = Tractmaps!

Annotating white matter tracts with relevant cortical surface features

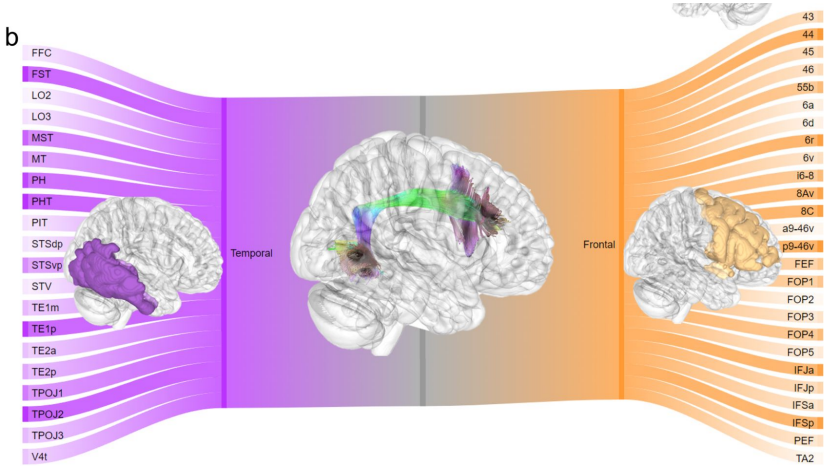
neuromaps: structural and functional interpretation of brain maps

Cortical properties



Population-based tract-to-region connectome of the human brain and its hierarchical topology

Tract-to-region connections



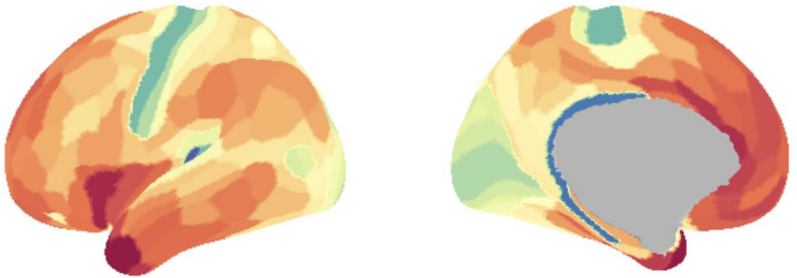
Neuromaps + tract-to-region mapping = Tractmaps!

Cortical properties

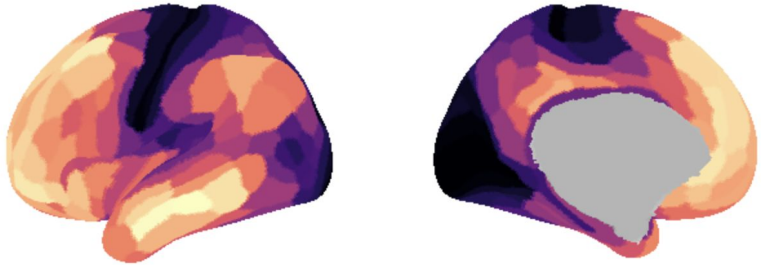
CBV	Cerebral blood volume
Areal scaling	Cortical areal scaling during development from the NIH dataset
FC	Diffusion map embedding gradient 1 of group-averaged functional connectivity
Expansion	Evolutionary cortical expansion
Metabolism	Glucose metabolism
Thickness	MRI cortical thickness from the Human Connectome Project S1200 release
Myelin	MRI T1w/T2w ratio from the Human Connectome Project S1200 release
Genes	PC1 of genes in the Allen Human Brain Atlas
GABA	PET and autoradiography informed GABAa benzodiazepine binding-site density
Serotonin 5-HT1a	PET tracer binding (Bmax) to 5-HT1a (serotonin receptor)
Serotonin 5-HT4	PET tracer binding (Bmax) to 5-HT4 (serotonin receptor)
Dopamine D1	PET tracer binding (BPnd) to D1 (dopamine receptor)
Dopamine D2	PET tracer binding (BPnd) to D2 (dopamine receptor)
Glutamate	PET tracer binding (BPnd) to mGluR5 (glutamate receptor)
S-A axis	Sensory-association mean rank axis

Step 1. Create parcellated maps

Intracortical myelination - Glasser 360 parcellation



S-A axis - Glasser 360 parcellation



Fetch the map

```
# load map of interest
myelin = fetch_annotation(source = 'hcps1200', desc = 'myelinmap',space = 'fsLR', den = '32k')
```

Parcellate!

```
# create parcellater object
glasser_parc = Parcellater(glasser, 'fsLR').fit()

# apply Glasser parcellation to surface maps of interest
myelin_glasser = glasser_parc.fit_transform(myelin, 'fsLR')
```

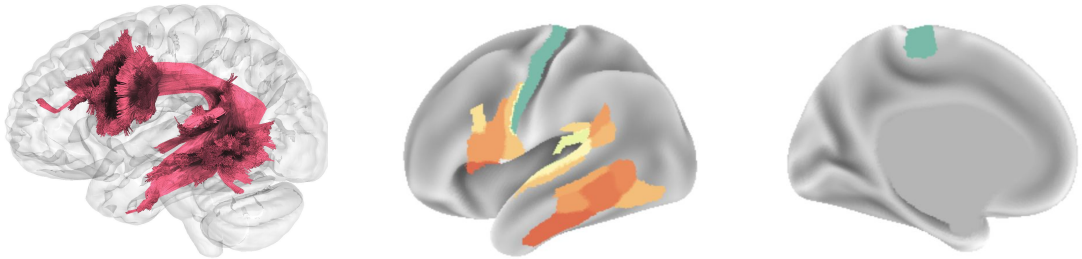
… and for many more maps!

Step 2. Link tract-to-region map to cortical properties

Intracortical myelination

```
tractmaps_utils.plot_parc_subset(brain_map = myelin_glasser,
                                 tract = 'AF_left',
                                 connection_threshold = 0.95,
                                 map_name = 'Intracortical myelination',
                                 tract_name = 'Left AF',
                                 colors = 'Spectral',
                                 mode = 'static')
```

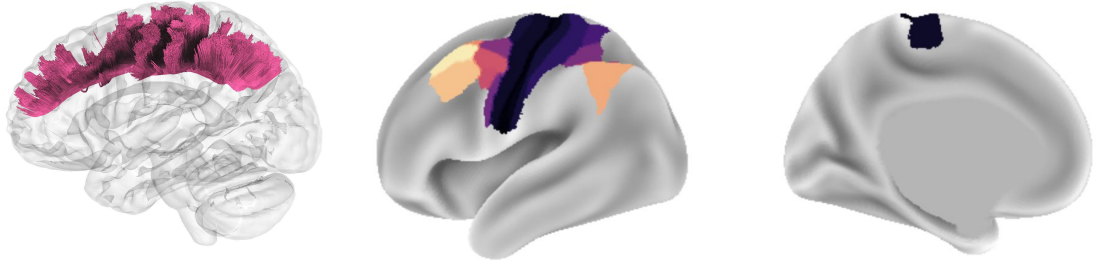
Intracortical myelination in 20 regions structurally connected to the Left AF



S-A axis

```
tractmaps_utils.plot_parc_subset(brain_map = sa_axis_glasser,
                                 tract = 'SLF_II_left',
                                 connection_threshold = 0.95,
                                 map_name = 'SA Axis',
                                 tract_name = 'Left SLF II',
                                 colors = 'magma',
                                 mode = 'static')
```

SA Axis in 17 regions structurally connected to the Left SLF II



Etc.

Aims

Aim 1 Describe the cortical surface features of white matter tracts.

Aim 2 Determine whether the organization of surface features is dictated by white matter architecture.

Aim 3 Characterize the intrinsic organization of white matter tracts based on their surface features.

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Aim 1 Describe the cortical surface features of white matter tracts.

H1 White matter tracts have both **shared and unique** cortical features in structurally connected regions, compared to unconnected regions.

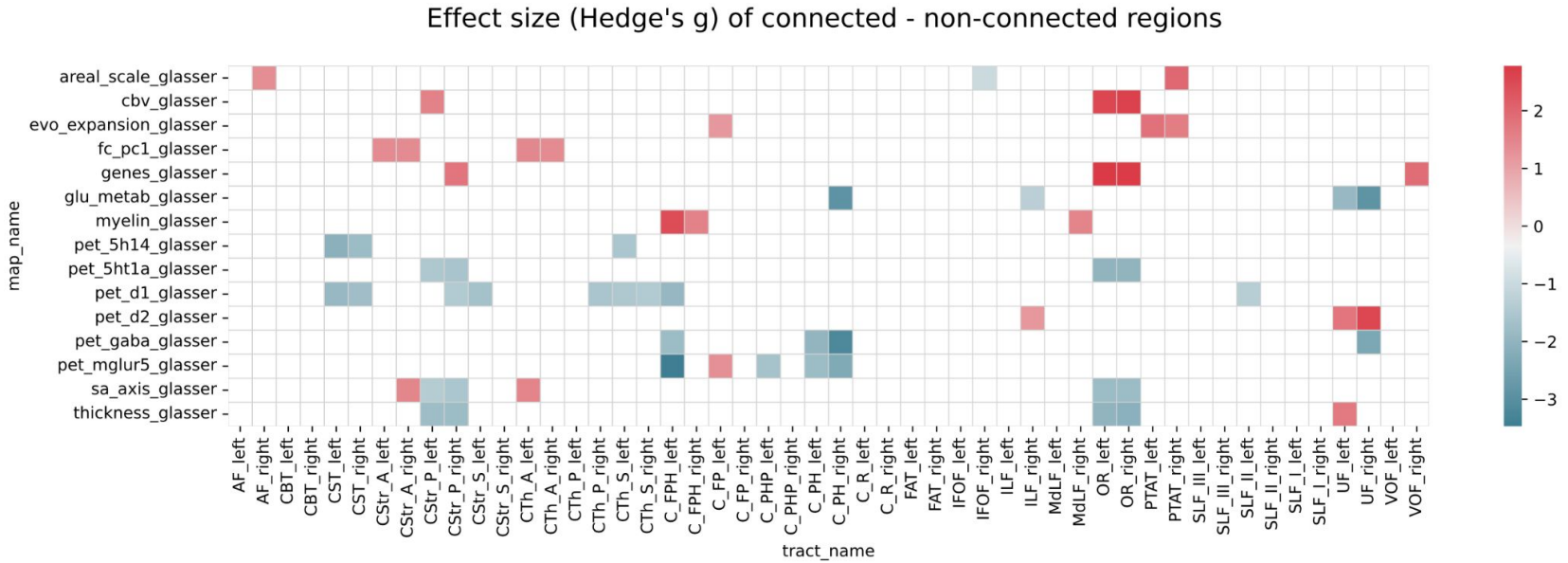
Aim 1: Describe the cortical surface features of white matter tracts

Aim 1 **H1** White matter tracts have both **shared and unique** cortical features in structurally connected regions, compared to unconnected regions.

Approach

- t-tests comparing cortical features in connected vs unconnected regions
- Comparison against shuffled surface feature maps (Alexander-Bloch, 2014 spin test)
- Significant result = surface features linked to this tract are unique
    - aka distinct from surface properties of non-connected brain regions

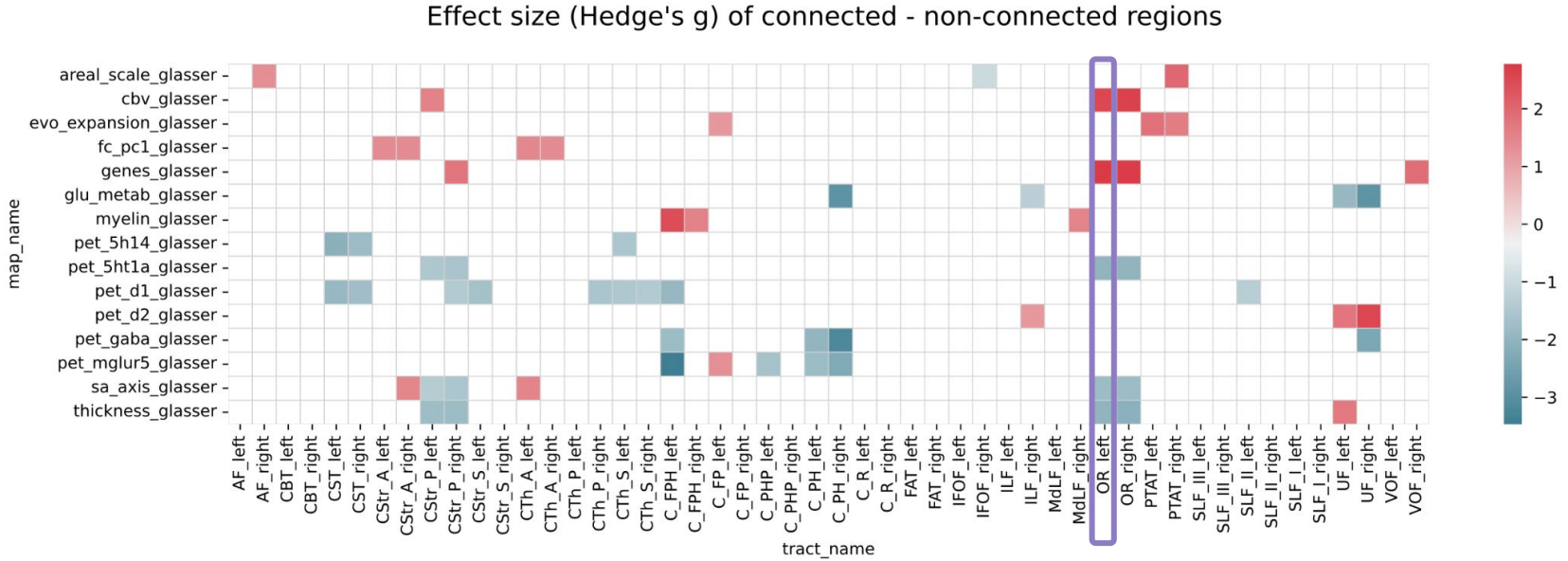
Aim 1: Describe the cortical surface features of white matter tracts



Colors = spin based significant effects

Aim 1: Describe the cortical surface features of white matter tracts

- What cortical features best describe a given **tract**?
- Relevant for researchers interested in unique cortical characteristics of a specific tract



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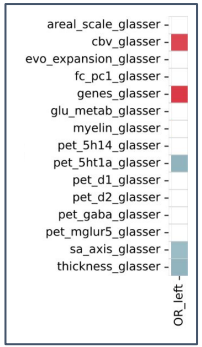
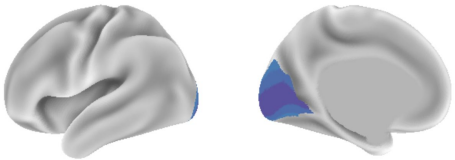
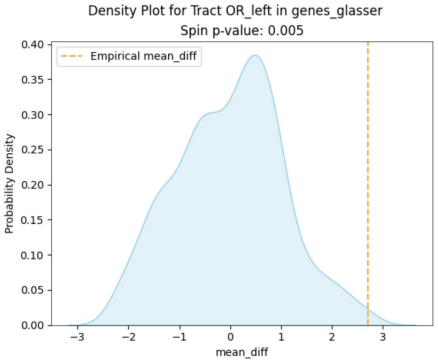
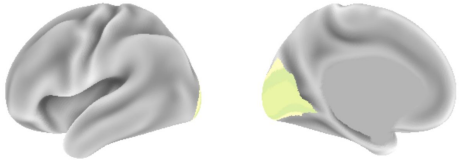


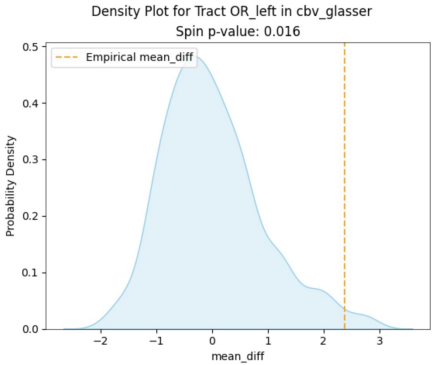
1. Gene expression



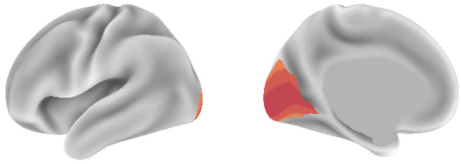


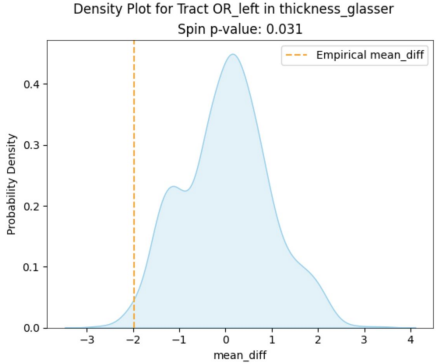
2. Cerebral Blood Flow





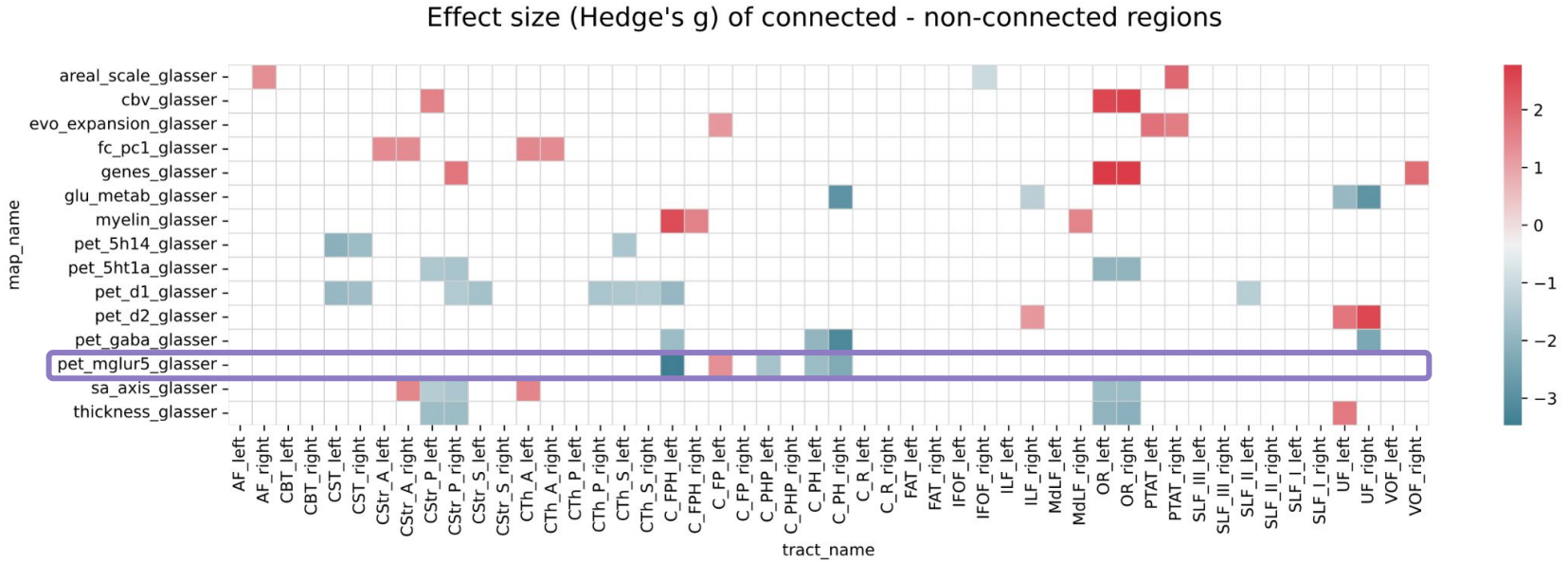
3. Cortical thickness





Aim 1: Describe the cortical surface features of white matter tracts

- What tracts have the most unique values within a given **cortical feature**?
- Relevant for researchers interested in understanding which tracts are uniquely linked to a cortical map of interest



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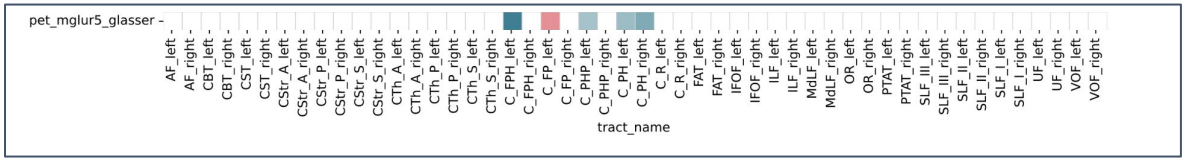
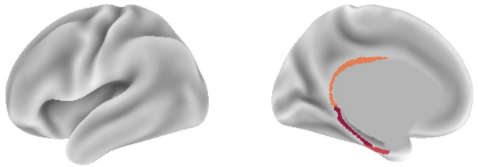
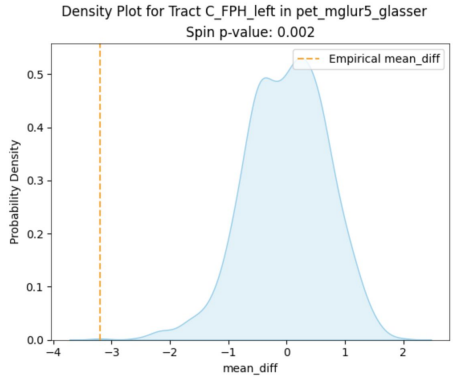
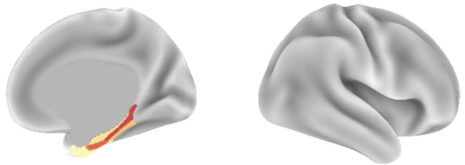


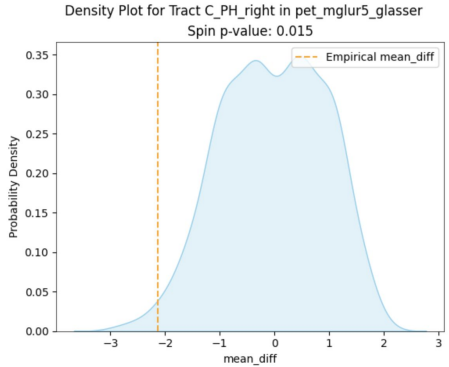
1. Cingulum, frontal parahippocampal





2. Cingulum, parahippocampal





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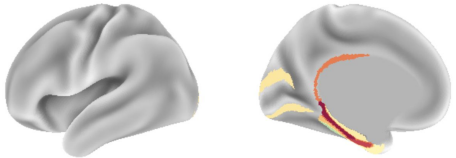
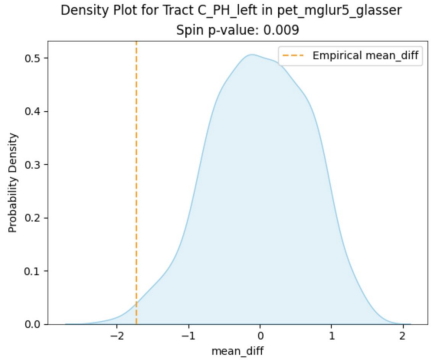
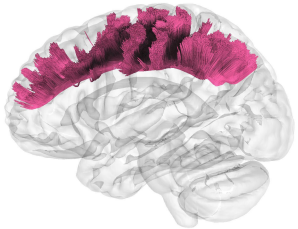


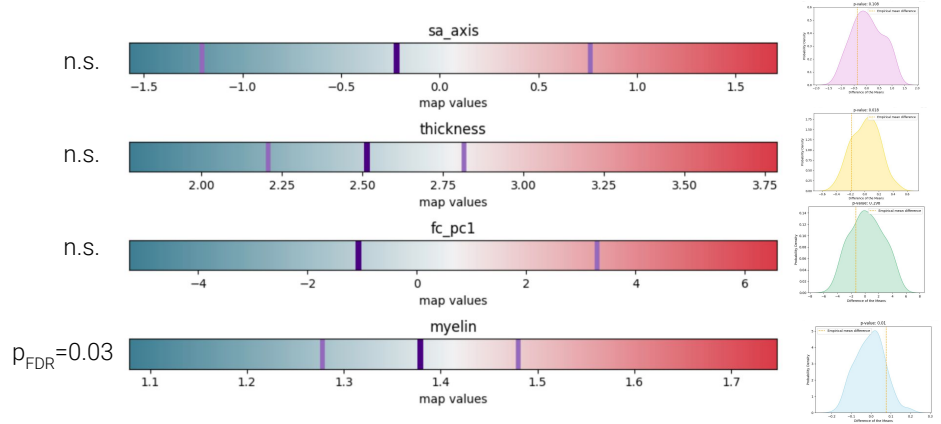


Aim 1: Describe the cortical surface features of white matter tracts

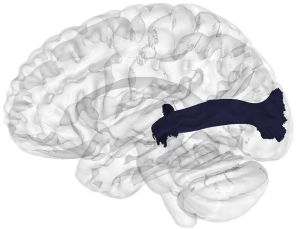
- Describe the cortical properties associated with a tract-of-interest

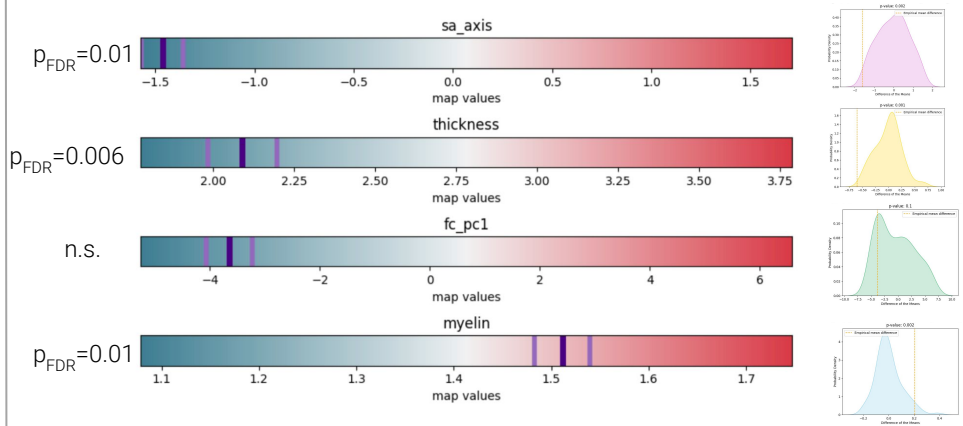
Left superior longitudinal fasciculus





Left optic radiation





Aims

Aim 1 Describe the cortical surface features of white matter tracts.

Aim 2 Determine whether the organization of surface features is dictated by white matter architecture.

Aim 3 Characterize the intrinsic organization of white matter tracts based on their surface features.

Aims

Aim 2 Determine whether the organization of surface features is dictated by white matter architecture.

H1 The topographical organization of cortical surface features is **dictated by the underlying structural connections**, whereby different tracts are differentially linked to surface features.

Aim 2: Determine whether the organization of surface features is dictated by white matter architecture

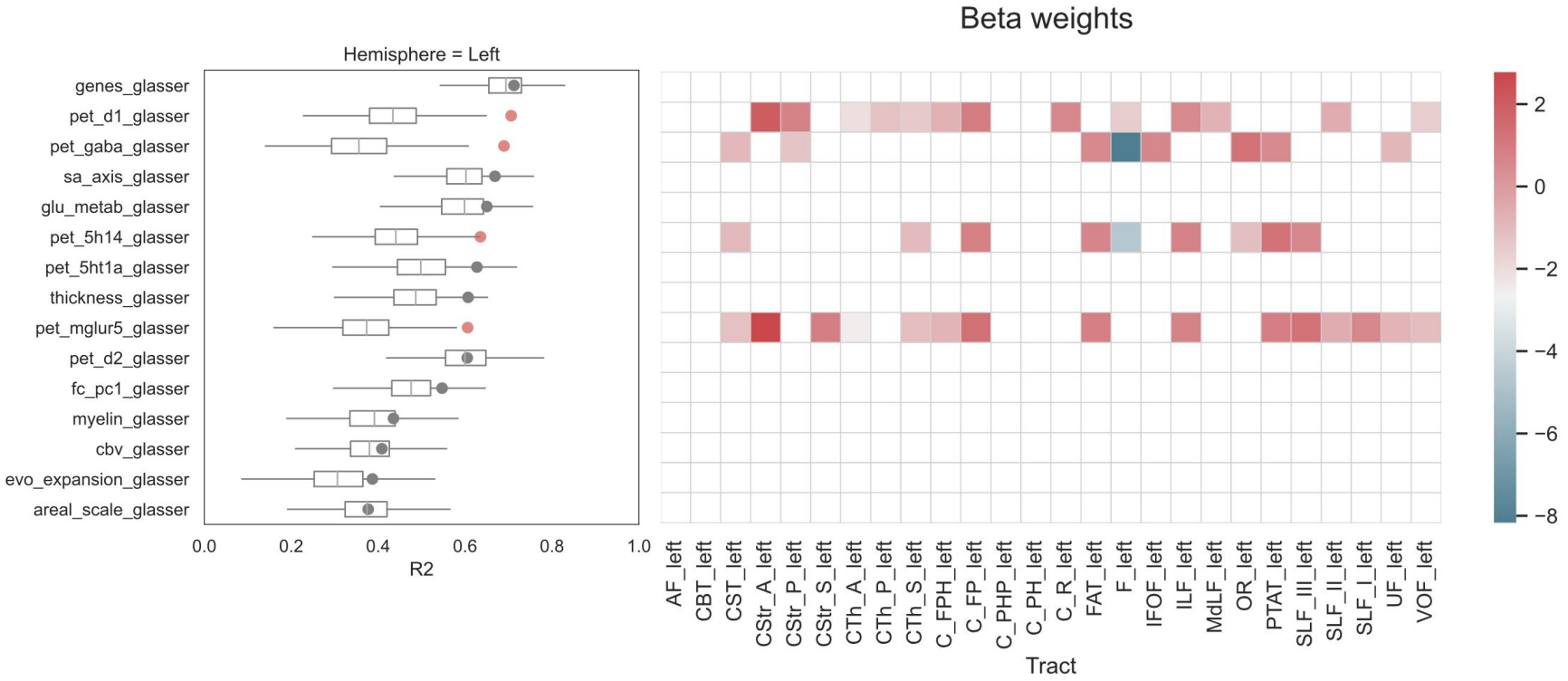
Aim 2 **H1**

The topographical organization of cortical surface features is **dictated by the underlying structural connections**, whereby different tracts are differentially linked to surface features.

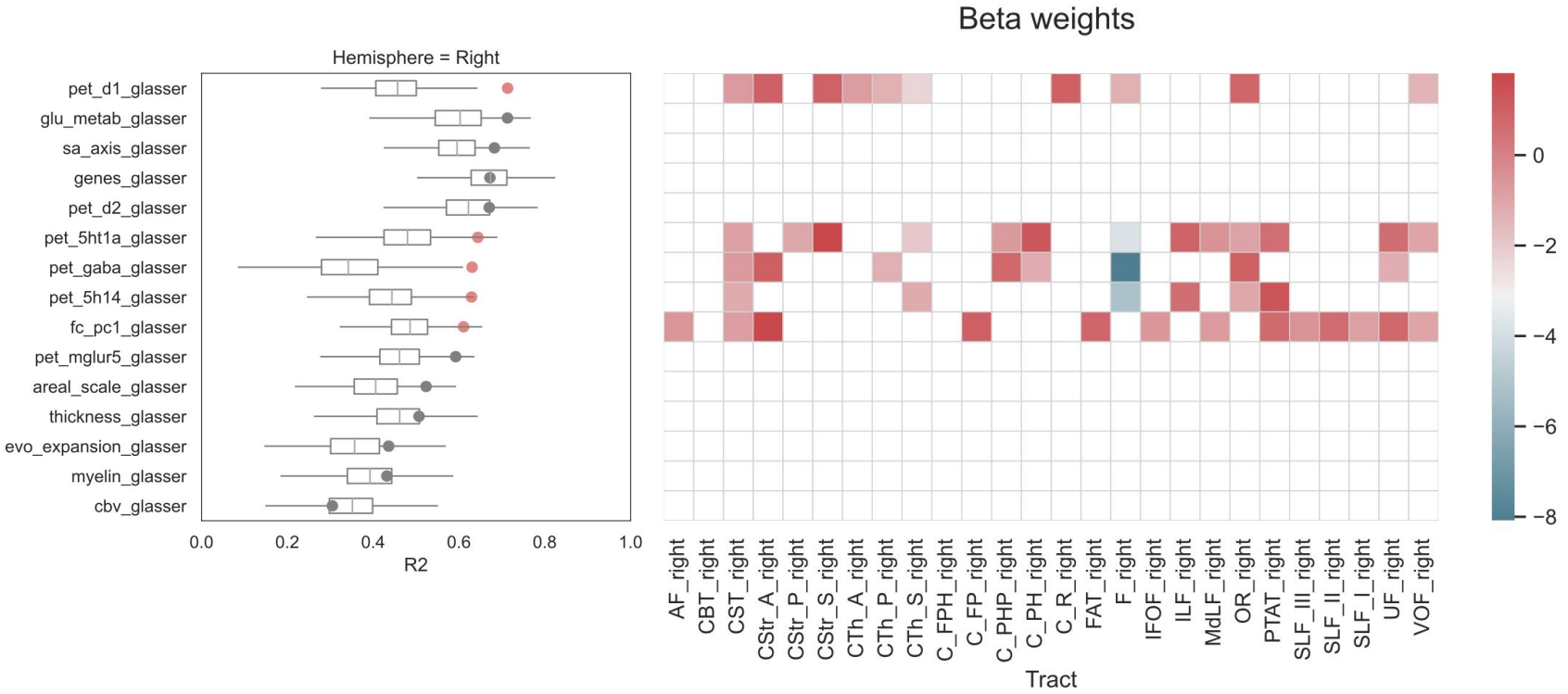
Approach

- Multiple linear regression
  - tract-to-region probability maps used to predict a given surface map
  - Surface feature ~ tract1 + tract2 + tract3 + … + tract52
- Compare the results to randomly shuffled surface features
- If we find a close correspondence between surface features and tract-to-region connectivity, this would suggest that spatial topographies of tract connectivity patterns may drive the patterning of surface features

Aim 2: Determine whether the organization of surface features is dictated by white matter architecture



Aim 2: Determine whether the organization of surface features is dictated by white matter architecture



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Aims

Aim 3 Characterize the intrinsic organization of white matter tracts based on their surface features.

H1 White matter tracts are organized in a hierarchical manner based on their surface features.

Aim 3: Characterize the intrinsic organization of white matter tracts based on their surface features

Aim 3 **H1** White matter tracts are organized in a hierarchical manner based on their surface features.

Approach

- **Similarity Network Fusion (SNF)**
  - Goal: capture inter-tract similarity across many cortical map features
  - Unsupervised computational method that combines many different types of measurements for a given set of samples (e.g. patients, or here tracts)
  - SNF first constructs a similarity network for each of the data types and then iteratively integrates these networks using a novel network fusion method

Aim 3: Characterize the intrinsic organization of white matter tracts based on their surface features

Aim 3 **H1**

White matter tracts are organized in a hierarchical manner based on their surface features.

Approach

Similarity Network Fusion (SNF)

Cortical thickness

Brain regions

Tracts

	0	1	2	3	4	5	6	7	8	9	...
FAT_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.000000	0.000000	0.000000	...
AF_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.371427	0.000000	0.000000	...
PTAT_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.000000	0.000000	0.000000	...
MdLF_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.000000	0.000000	0.000000	...
SLF_III_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.371427	-0.834541	0.000000	...
SLF_II_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.371427	-0.834541	-0.440182	...

Intracortical myelination

Tracts

	0	1	2	3	4	5	6	7	8	9	...
FAT_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.000000	0.000000	0.000000	...
AF_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.371427	0.000000	0.000000	...
PTAT_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.000000	0.000000	0.000000	...
MdLF_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.000000	0.000000	0.000000	...
SLF_III_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.371427	-0.834541	0.000000	...
SLF_II_left	0.000000	0.0	0.000000	0.000000	0.000000	0.000000	0.0	0.371427	-0.834541	-0.440182	...

And more maps…

Cortical thickness

Tracts

Tracts

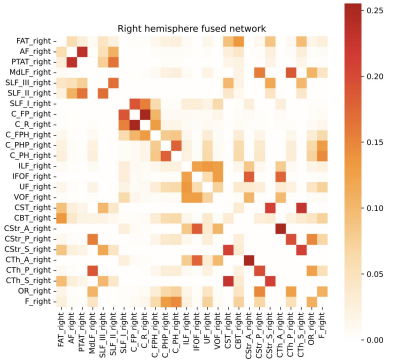
Intracortical myelination

Tracts

Tracts

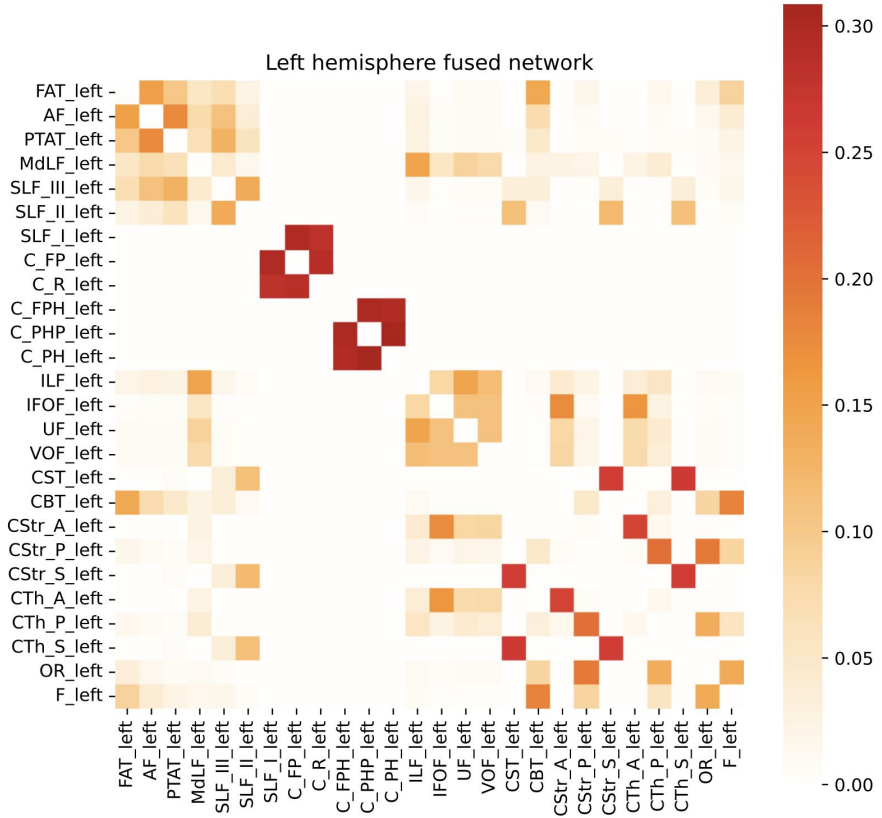
And more maps…

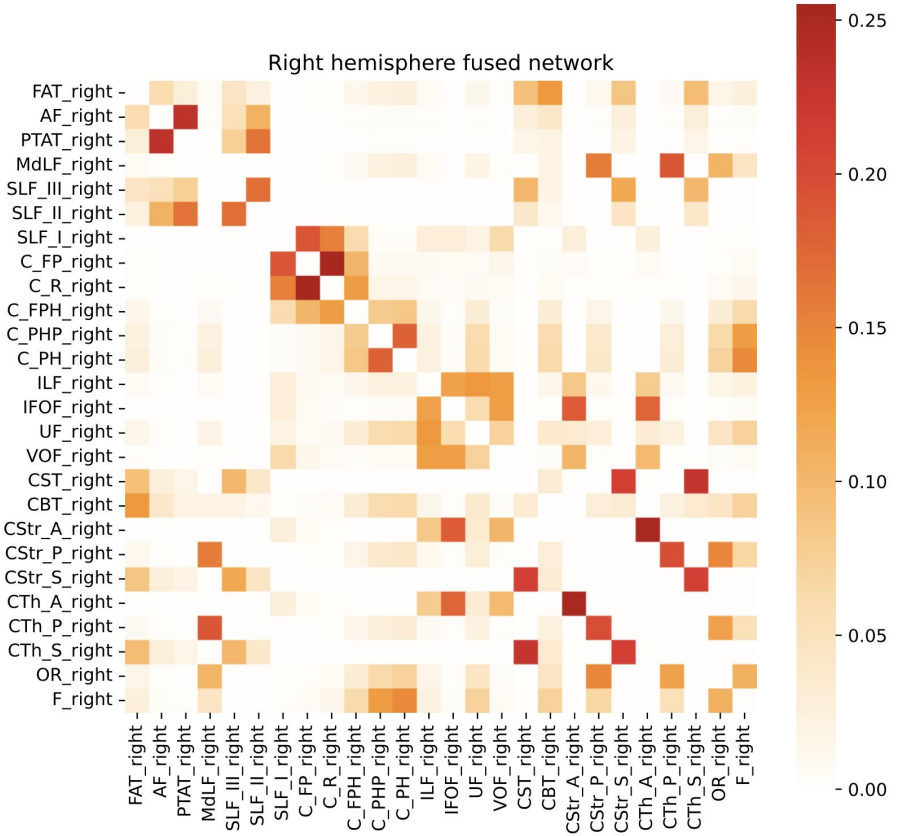
Fused network



Aka how similar tracts are based on their cortical surface features

Aim 3: Characterize the intrinsic organization of white matter tracts based on their surface features

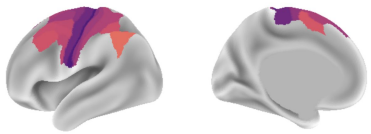




Aim 3: Characterize the intrinsic organization of white matter tracts based on their surface features

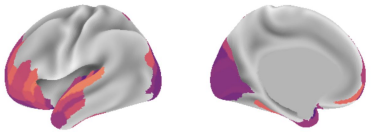
Left hemisphere

mGluR5 in 23 regions connected to Cluster 1



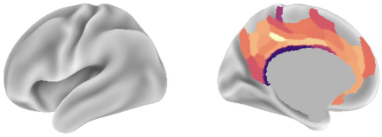
'SLF_II_left', 'CST_left', 'CStr_S_left', 'CTh_S_left'

mGluR5 in 56 regions connected to Cluster 2



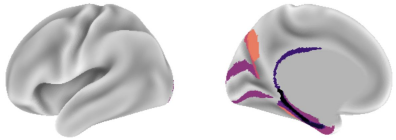
'MdLF_left', 'ILF_left', 'IFOF_left', 'UF_left', 'VOF_left', 'CStr_A_left', 'CTh_A_left'

mGluR5 in 27 regions connected to Cluster 3



'SLF_I_left', 'C_FP_left', 'C_R_left'

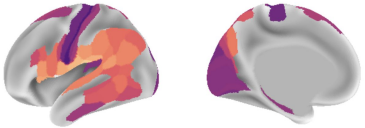
mGluR5 in 10 regions connected to Cluster 4



'C_FPH_left', 'C_PHP_left', 'C_PH_left'

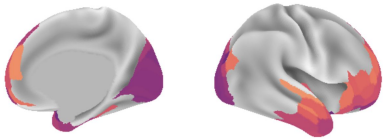
mGluR5 in 52 regions connected to Cluster 5

'FAT_left', 'AF_left', 'PTAT_left', 'SLF_III_left', 'CBT_left', 'CStr_P_left', 'CTh_P_left', 'OR_left', 'F_left'



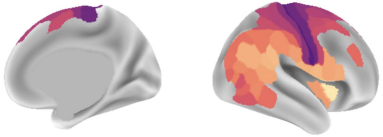
Right hemisphere

mGluR5 in 50 regions connected to Cluster 1



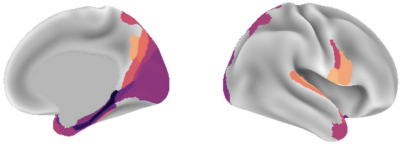
'ILF_right', 'IFOF_right', 'VOF_right', 'CStr_A_right', 'CTh_A_right'

mGluR5 in 48 regions connected to Cluster 2



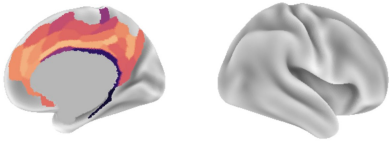
'FAT_right', 'AF_right', 'PTAT_right', 'SLF_III_right', 'SLF_II_right', 'CST_right', 'CStr_S_right', 'CTh_S_right'

mGluR5 in 34 regions connected to Cluster 3



'MdLF_right', 'C_PHP_right', 'C_PH_right', 'UF_right', 'CBT_right', 'CStr_P_right', 'CTh_P_right', 'OR_right', 'F_right'

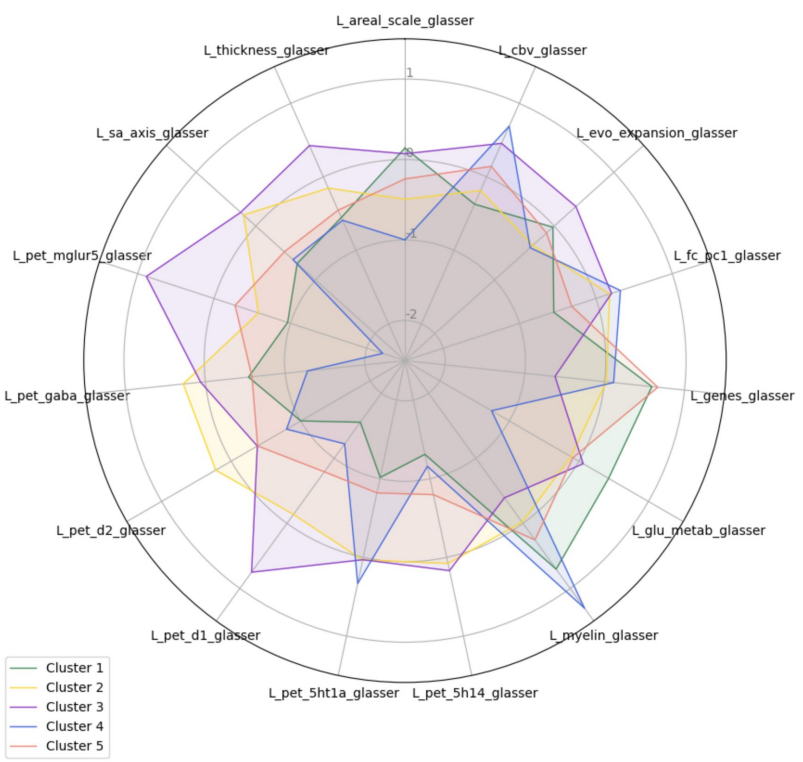
mGluR5 in 29 regions connected to Cluster 4



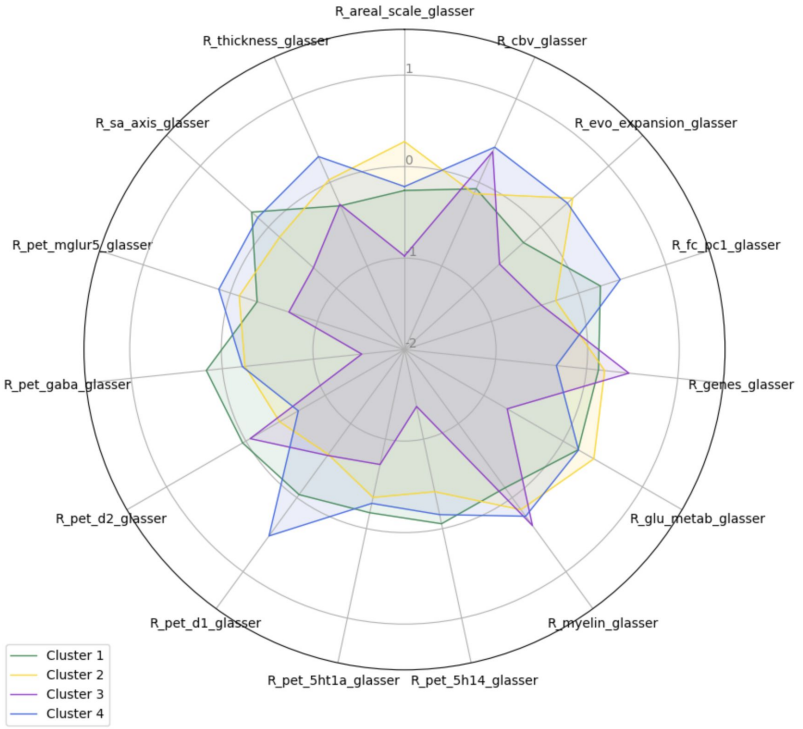
'SLF_I_right', 'C_FP_right', 'C_R_right', 'C_FPH_right'

Aim 3: Characterize the intrinsic organization of white matter tracts based on their surface features

Left hemisphere



Right hemisphere



In summary

Aim 1	H1	White matter tracts have both shared and unique cortical features in structurally connected regions, compared to unconnected regions.	✓
Aim 2	H1	The topographical organization of cortical surface features is dictated by the underlying structural connections, whereby different tracts are differentially linked to surface features.	✓ For receptor maps
Aim 3	H1	White matter tracts are organized in a hierarchical manner based on their surface features.	? Maybe??

What I learned

- Linking (and testing!) cortical surface features and white matter tracts is easier said than done
- More (correction - **a lot more**) Python
- Working with surface features, neuromaps, spin testing
- Dominance analysis (ongoing)
- Similarity Network Fusion
- Team work makes the dream work… and dream work is team work!!

Thank you PennLINC!

Ted Satterthwaite
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Maggie Pecsok
Valerie Sydnor
Arielle Keller
Taylor Salo
Et al.!!!