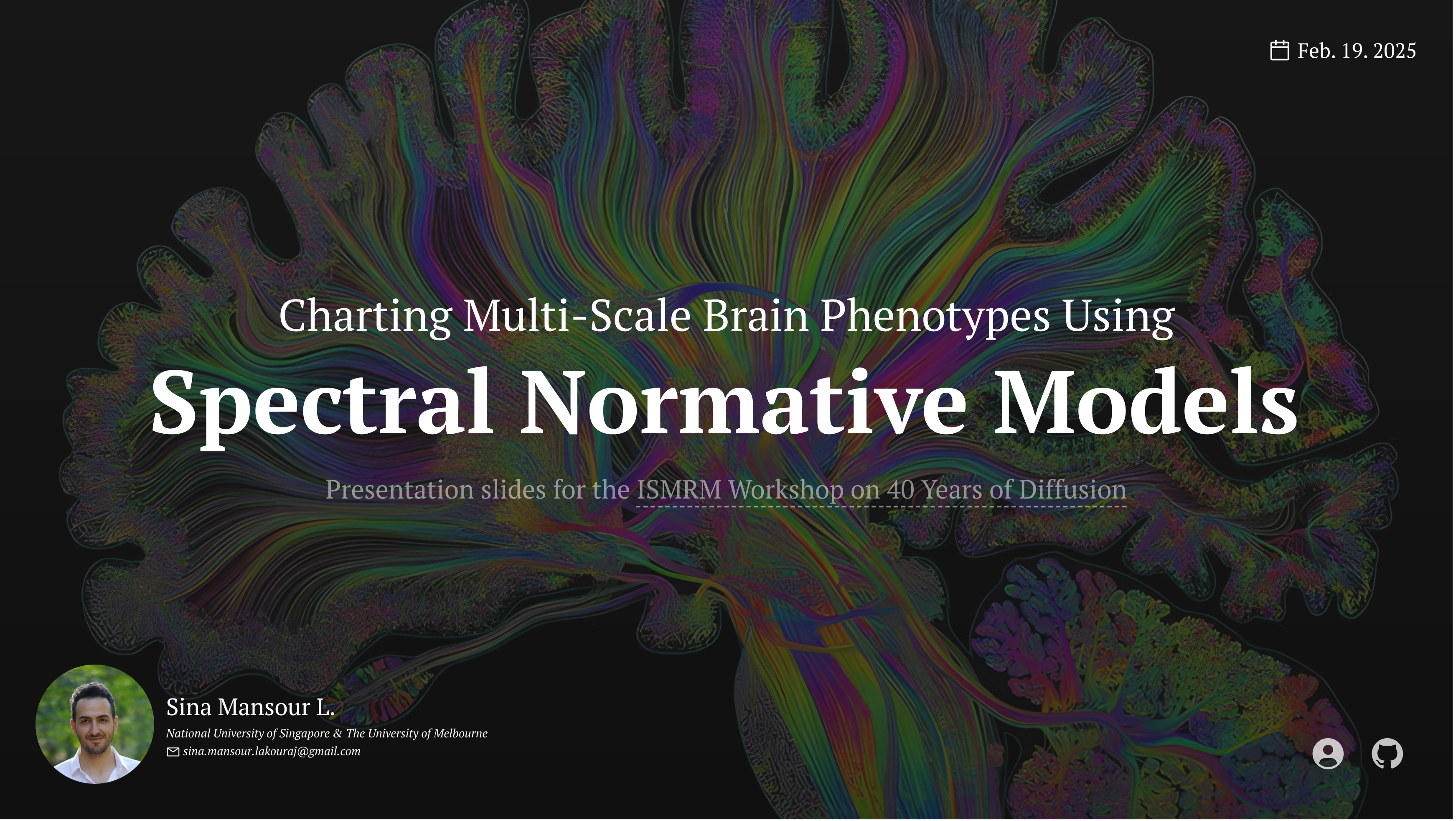

Feb. 19. 2025

Charting Multi-Scale Brain Phenotypes Using

Spectral Normative Models

Presentation slides for the ISMRM Workshop on 40 Years of Diffusion

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Declaration of Financial Interests or Relationships

Speaker Name: Sina Mansour L.

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

Overview

Big data in brain imaging, and the importance of dimensionality reduction

A primer on Graph Signal Processing (GSP)

Diffusion MRI and brain connectivity eigenmodes

Leveraging eigenmodes for Spectral Normative Modeling (SNM)

Empirical application: personalized brain charting of Alzheimer's Disease

→ Concluding remarks and future directions

Big data in brain imaging

Brain scans are inherently large files

Sample sizes are limited relative to exemplary AI models

→ Importance of dimensionality reduction for AI in neuroimaging

Graph Signal Processing (GSP)

A field of signal processing dedicated to analyzing signals on graphs

→ Generalization of discrete signal processing ideas to the realm of networks

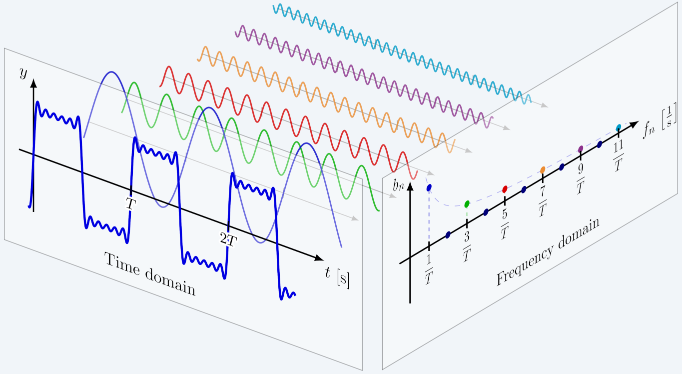
Inverse Discrete Fourier Transform

$$x_n = \frac{1}{N}\sum_{k=0}^{N-1} X_k e^{i2\pi kn/N}$$

Time domain

Frequency

Frequency



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domain

Graph Fourier Transform (GFT)

Analogous to DFT, but for graphs

GFT is defined using a graph shift operator

Graph Fourier basis via singular value decomposition of shift operator

Inverse Graph Fourier Transform

Graph signal domain

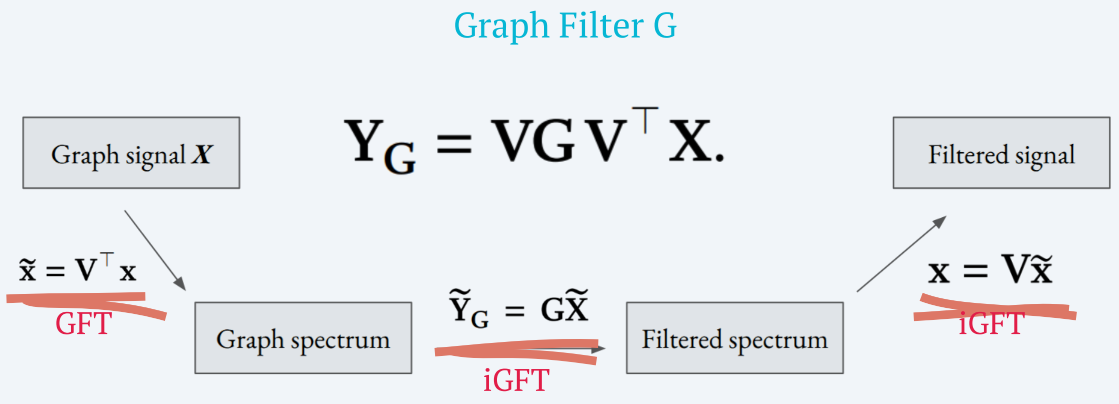
$$\mathbf{x} = \mathbf{V}\tilde{\mathbf{x}}$$

Graph frequency domain

Huang et al. (2018)

Graph Filters

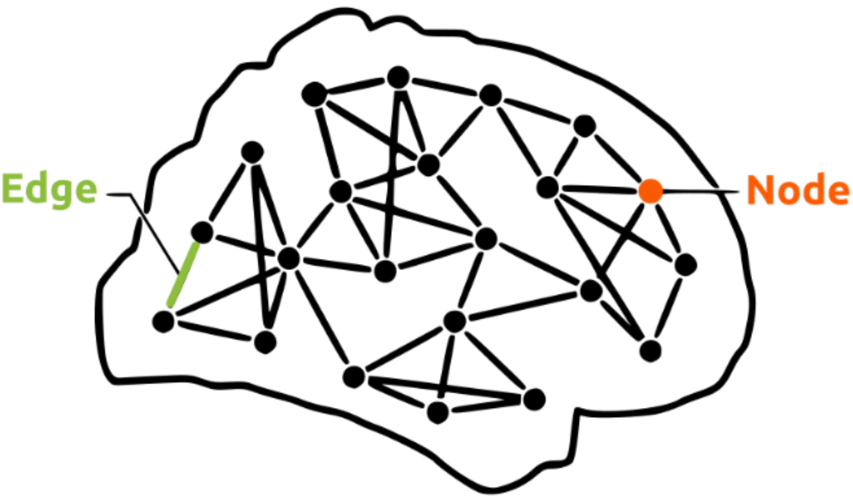
Idea: Reconstruct particular frequency bands of the signal

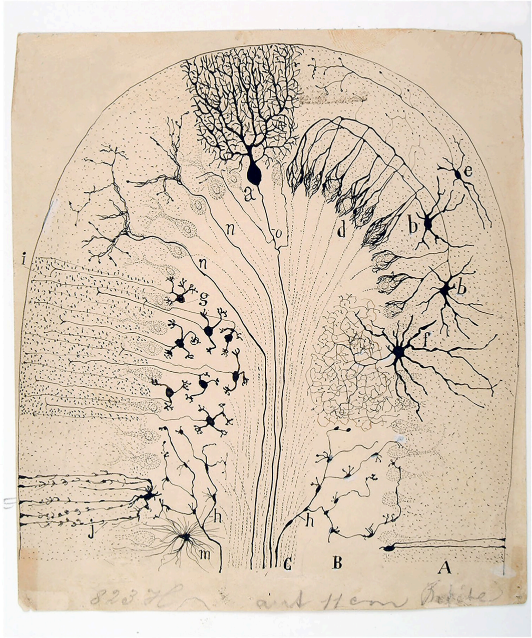


Huang et al. (2018)

Network Neuroscience and GSP on brain graphs

Modeling anatomical brain networks





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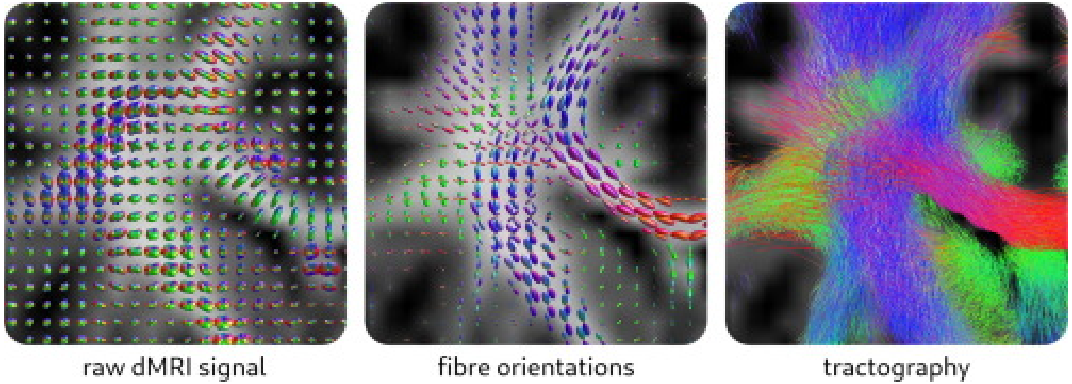
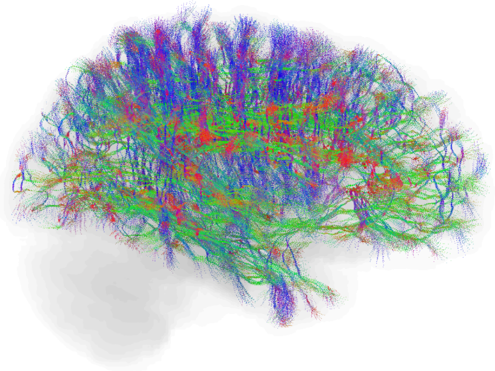
Diffusion MRI data

Enables mapping in-vivo anatomical wiring networks



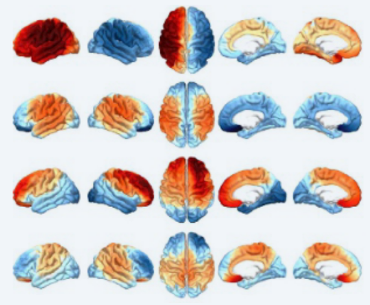


Tournier 2019

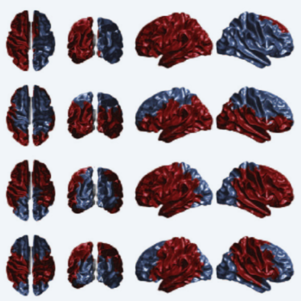
GSP in brain imaging

GSP methods have been used to study brain signals in the past decade

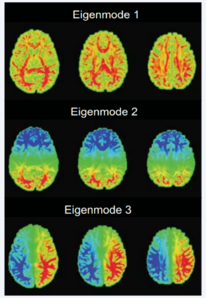
Different terminologies: harmonics, eigenmodes, gradients, …



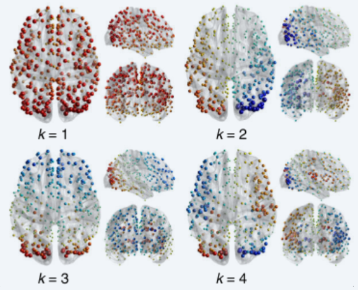
Atasoy et al. (2016)



Robinson et al. (2016)



Tarun et al. (2019)



Preti et al. (2019)

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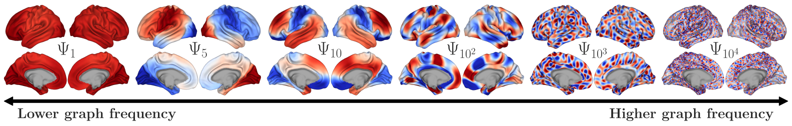
High-resolution connectome eigenmodes

Perform tractography over a large sample (e.g. HCP YA)

Map high-resolution connectomes (at the granularity of voxels or vertices)

Group-average connectome; shared anatomical connectivity backbone

→ Perform GSP; map graph Laplacian eigenmodes as an information basis



Signal $\leftarrow X = \sum_i \alpha_i \psi_i + \varepsilon = \hat{X} + \varepsilon$ Reconstruction

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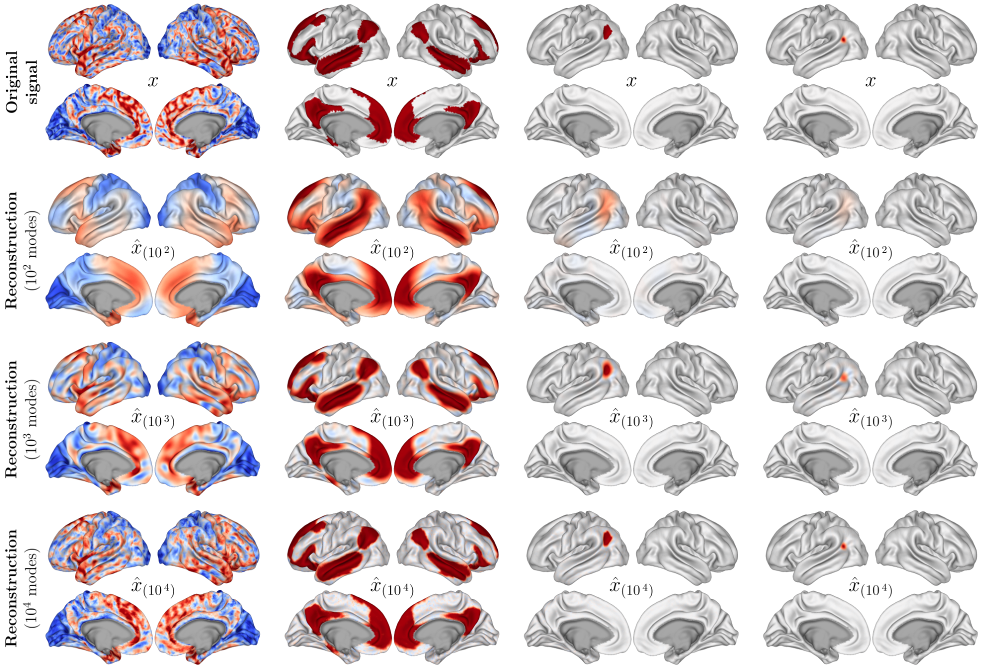
Signal reconstruction via eigenmodes:

Signal

$$X = \sum_i \alpha_i \psi_i + \varepsilon = \hat{X} + \varepsilon$$

Reconstruction



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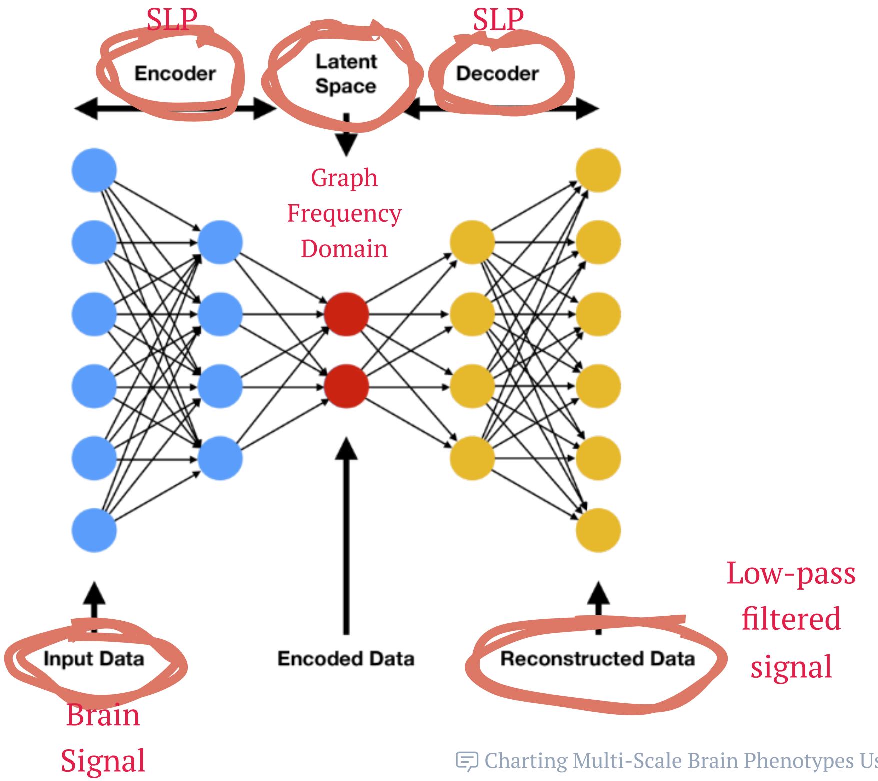
Conceptual analogy with autoencoders:



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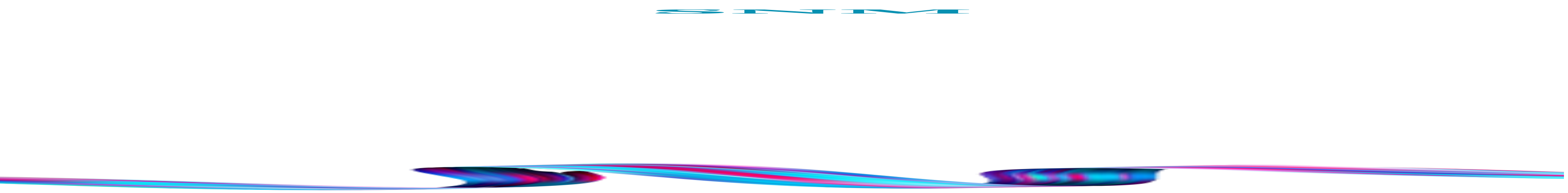
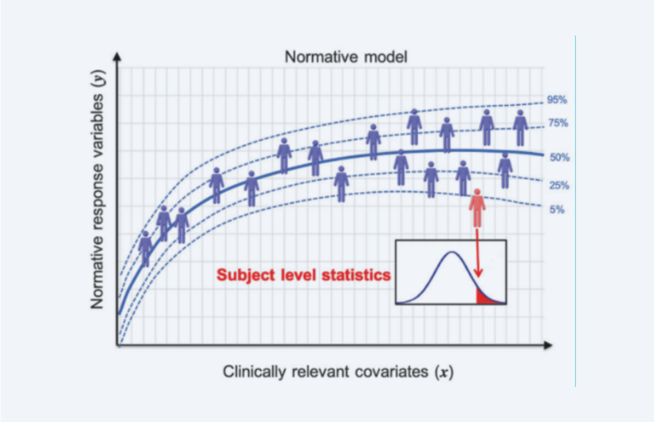
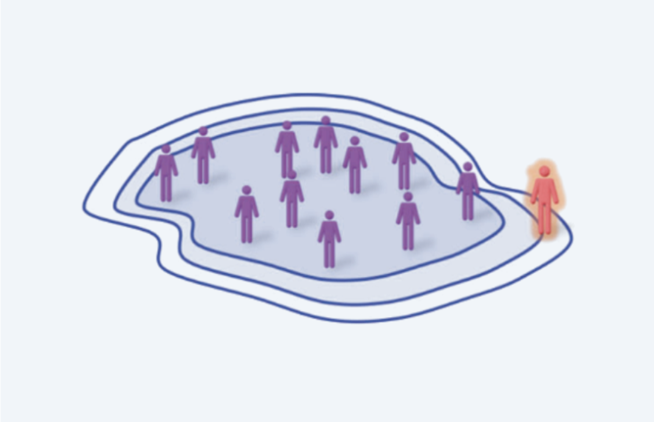
Spectral Normative Modeling



Normative Modeling

→ Characterizes population-level phenotype distribution to detect individual deviations from the norm.

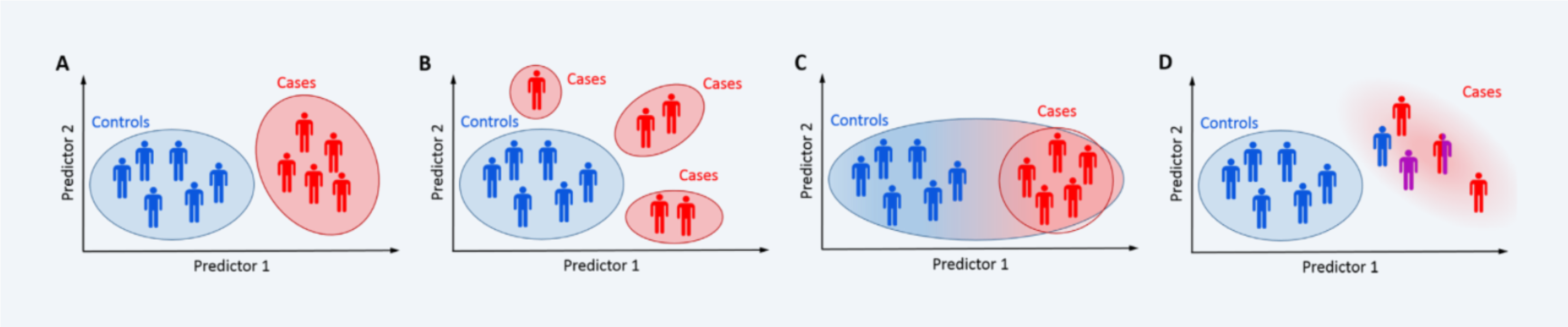




Marquand et al. (2019)

Normative Modeling & Personalized Medicine

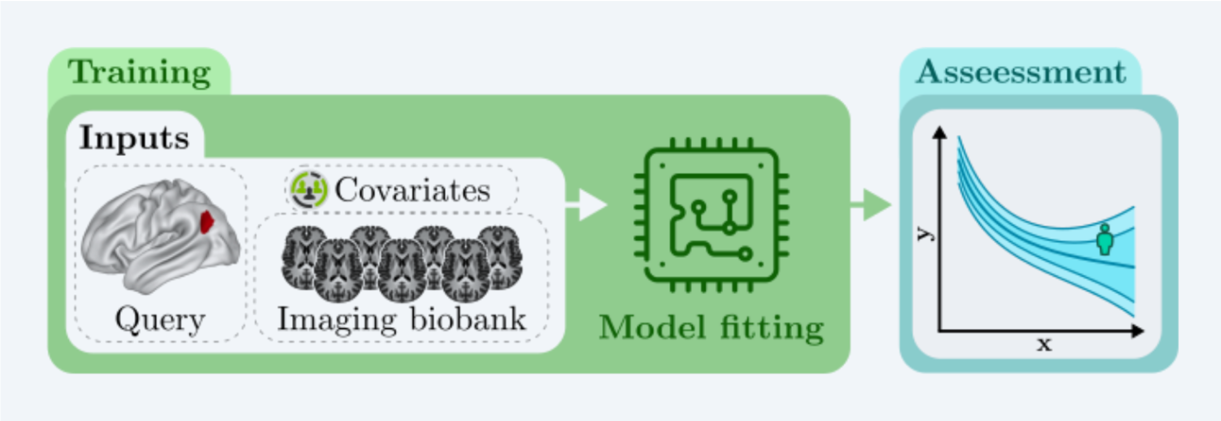
→ Enables exploration of individual-level differences and heterogeneity of pathological deviations.



Marquand et al. (2016)

Conventional Normative Models (Direct Models)

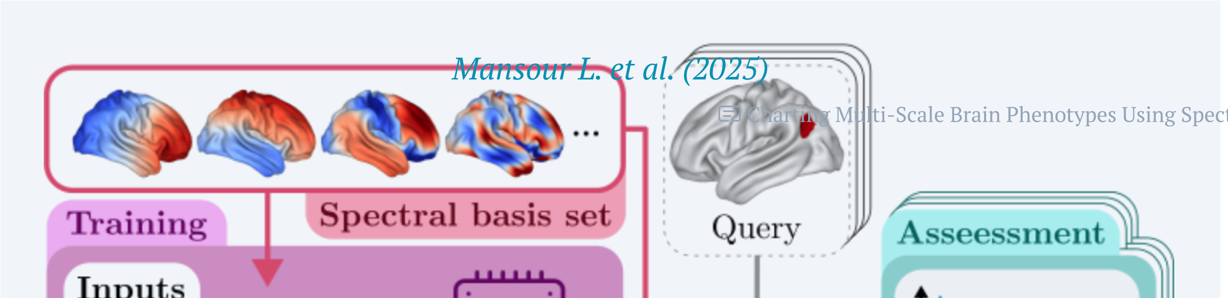
Trained to infer normative ranges of a **predefined fixed phenotype (y)** from a set of covariates (X).



Mansour L. et al. (2025)

Spectral Normative Modeling (SNM)

Idea: Use GSP as means to compress and reconstruct normative ranges.



Mansour L. et al. (2025)

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SNM performance

→ With at least **1000 modes** SNM achieves comparable estimates to that of a direct model.

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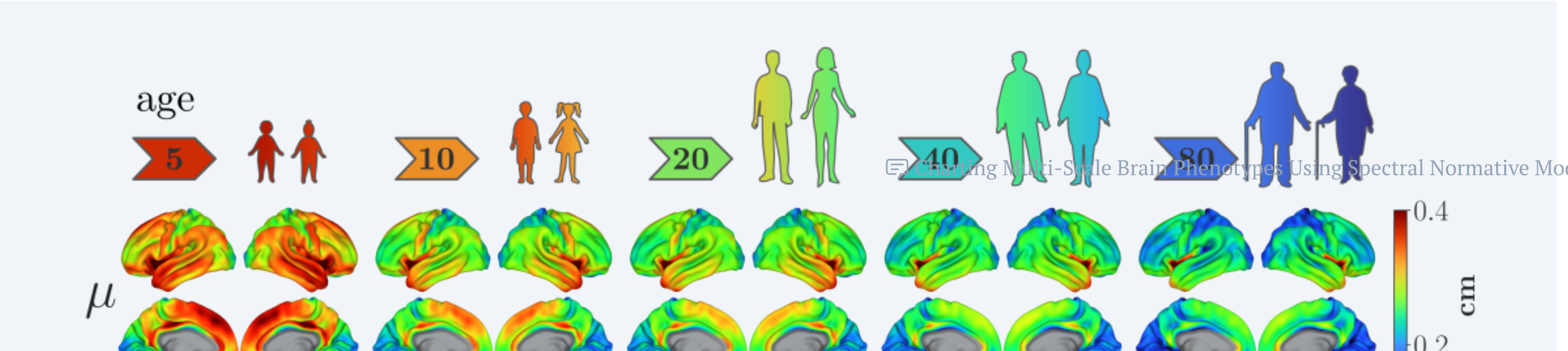
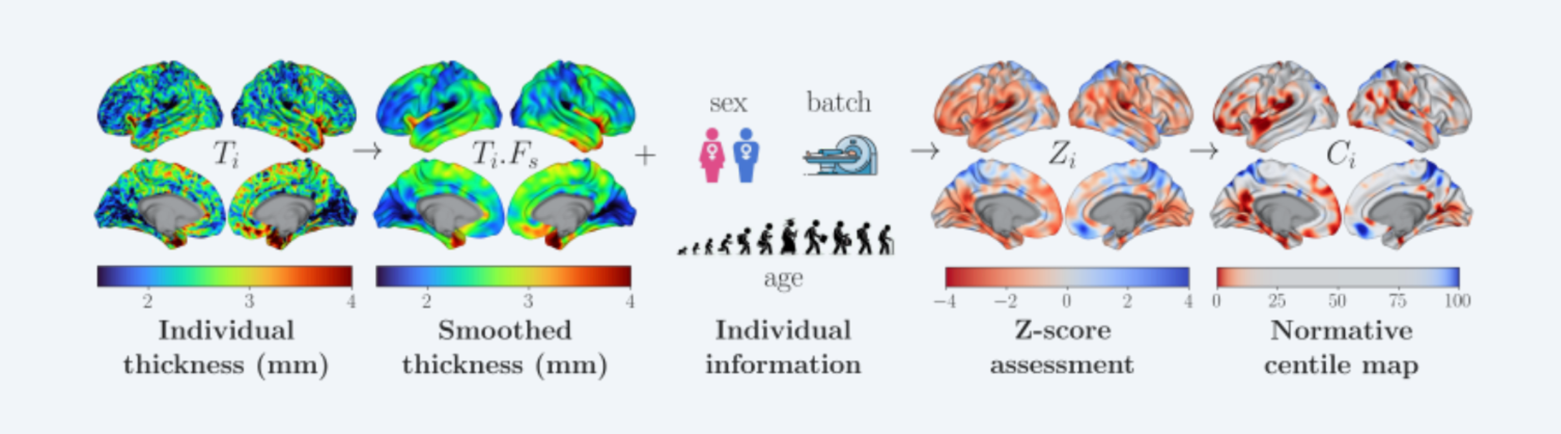
High-resolution normative modeling

→ Efficiently estimate charts at **vertex-resolution** across human lifespan.



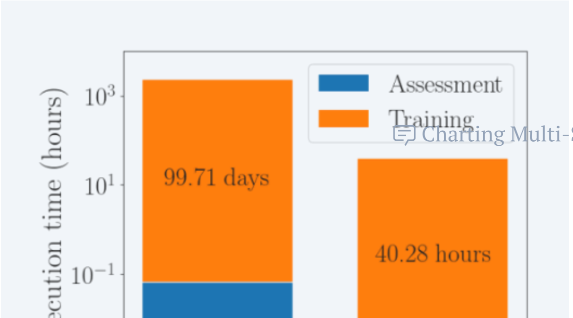
High-resolution normative modeling

→ Enables derivation of **individualized** vertex-resolution abnormality scores.



High-resolution normative modeling

→ For vertex-resolution NMs, SNM achieves **100x to 10,000x** speedup.



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Clinical application: AD dementia

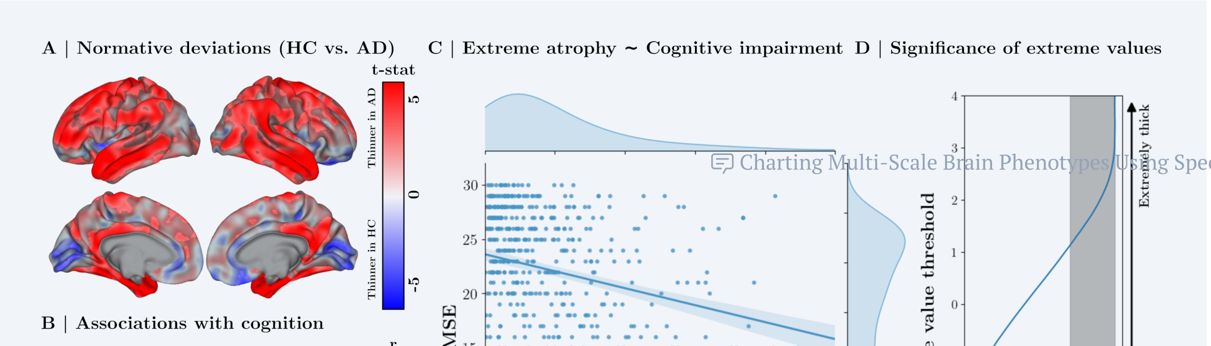
Train SNM on a healthy normative sample (HCP Lifespan)

Transfer learning: freeze demography covariates, fine-tune site effects (harmonization)

→ Clinical data: Healthy Controls (HC), Mild Cognitive Impairment (MCI), & Alzheimer's Disease (AD)

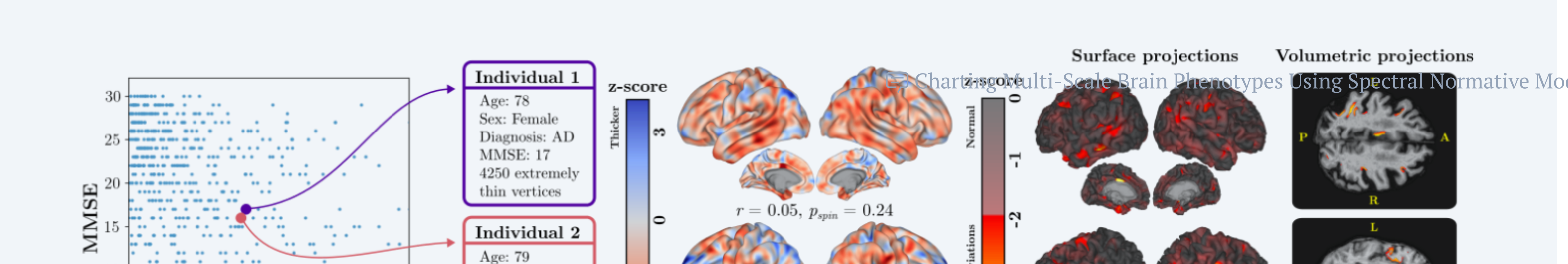
Clinical application: AD dementia

→ Population-level evaluations: Cortical correlates of cognitive decline



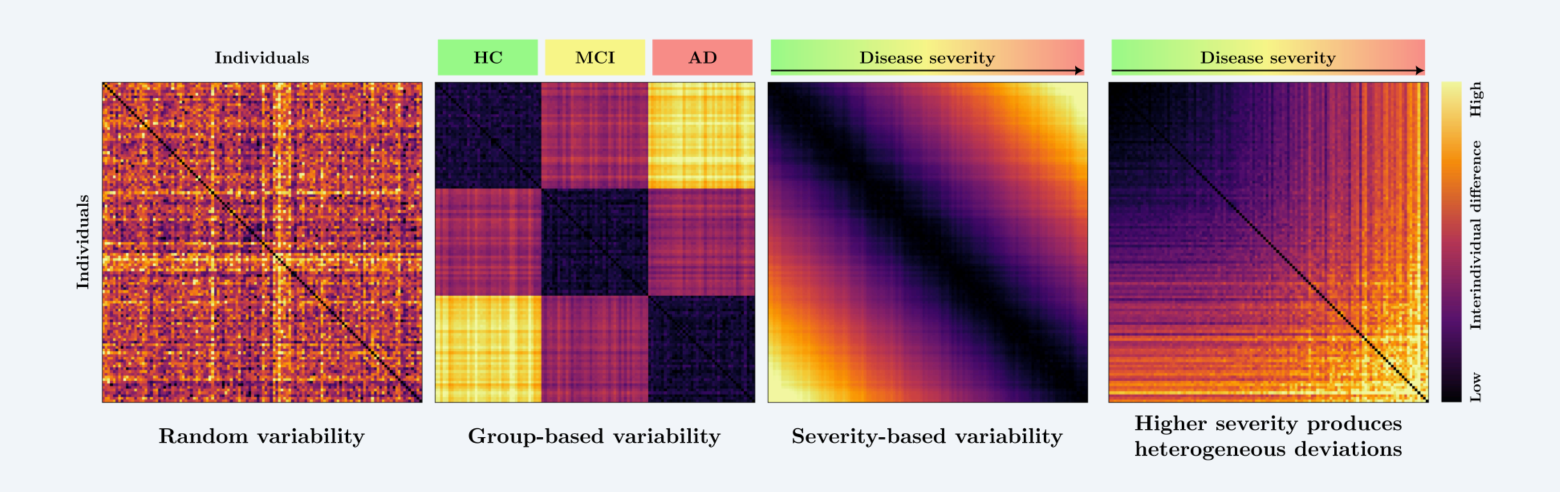
Clinical application: AD dementia

→ Individual-level evaluations: Heterogeneous landscape of dementia-induced cortical atrophy



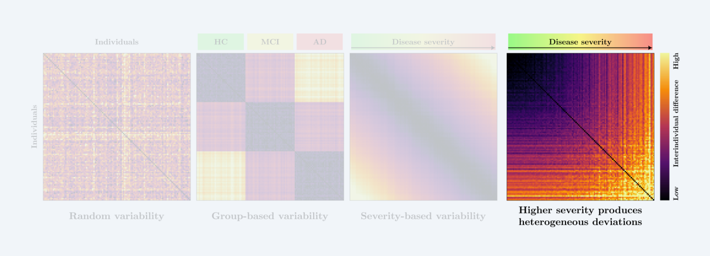
Clinical application: AD dementia

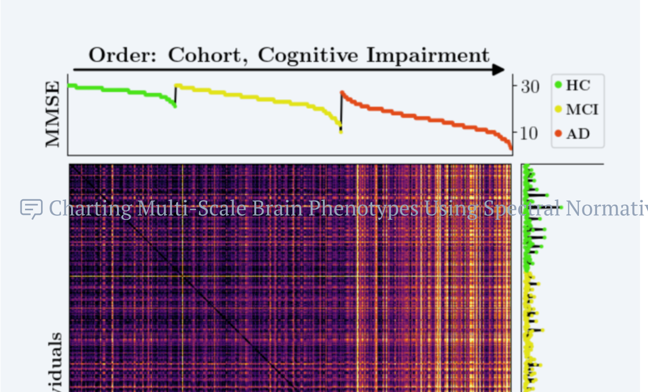
→ Hypothetical patterns of interindividual variability



Clinical application: AD dementia

→ Empirical variability





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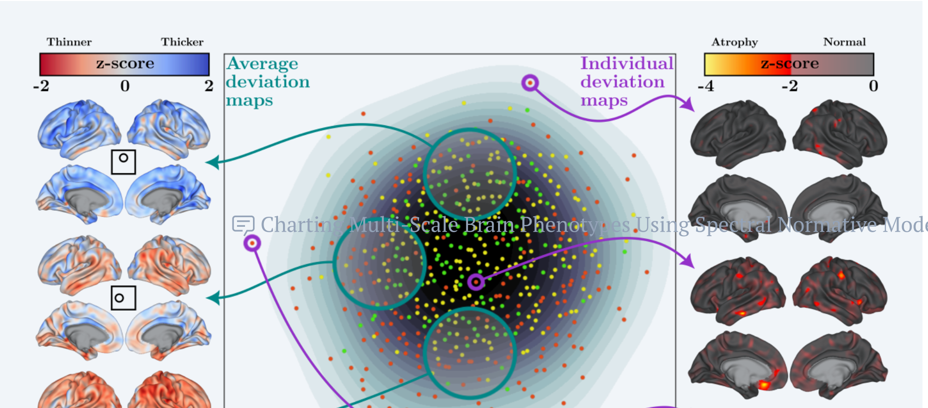
Clinical application: AD dementia

→ Individual heterogeneity



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Clinical application: AD dementia

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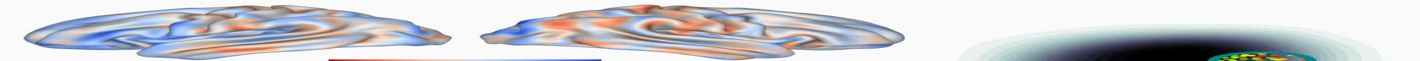

Clinical application: AD dementia

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