Predicting Brain Age using Transferable coVariance Neural Networks

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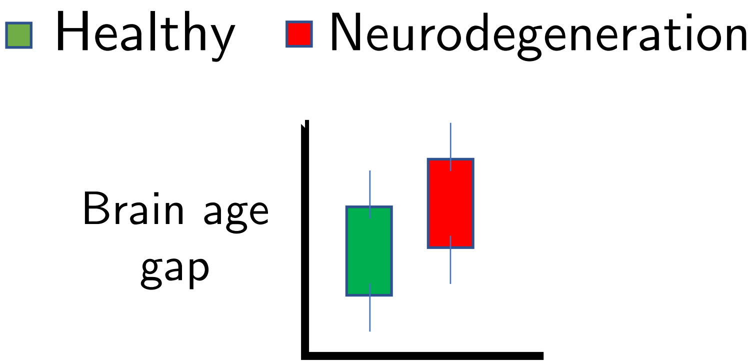
Introduction

- Individual rate of `aging’ is driven by a variety of factors, including environment, genetics, neurodegeneration

- Brain age provides a biological estimate of an individual’s age, derived from different brain imaging modalities

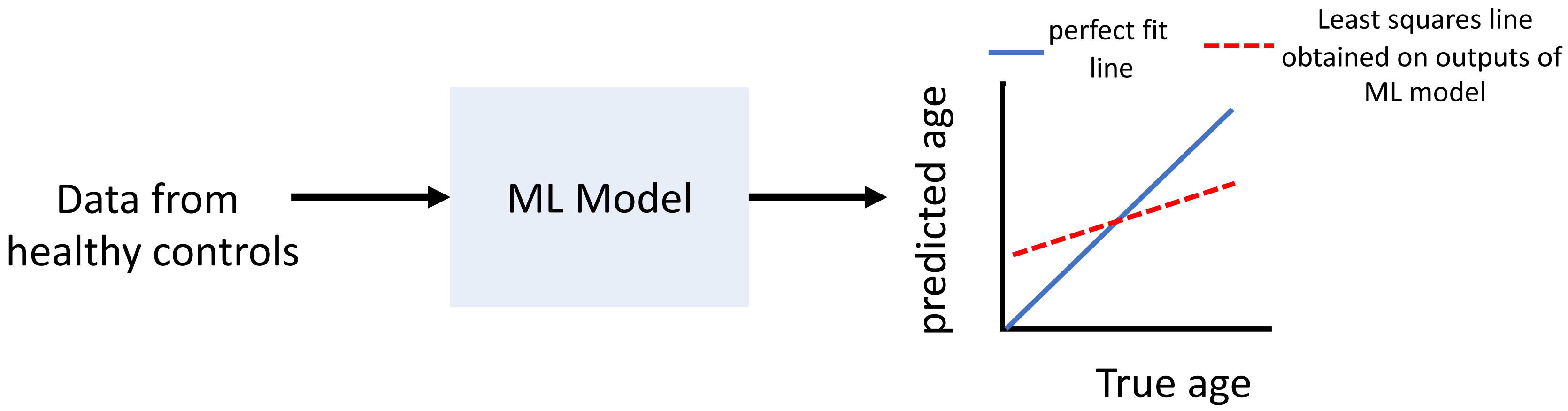
- Brain age gap: Deviation between brain age and chronological age (time since birth)



Brain age gap $\propto$ individual risks for neurological, neuropsychiatric and neurodegenerative diseases

Brain age gap evaluation using ML

Step 1. Train ML model to predict chronological age for healthy controls from cortical thickness features



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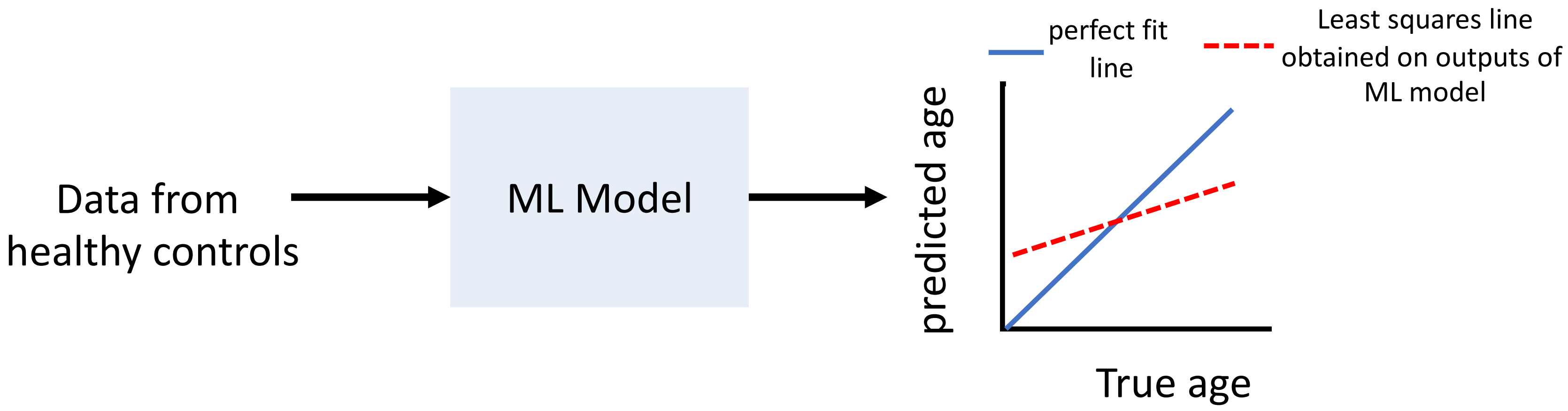

Step 2. Linear regression-based age-bias correct for outputs of ML model

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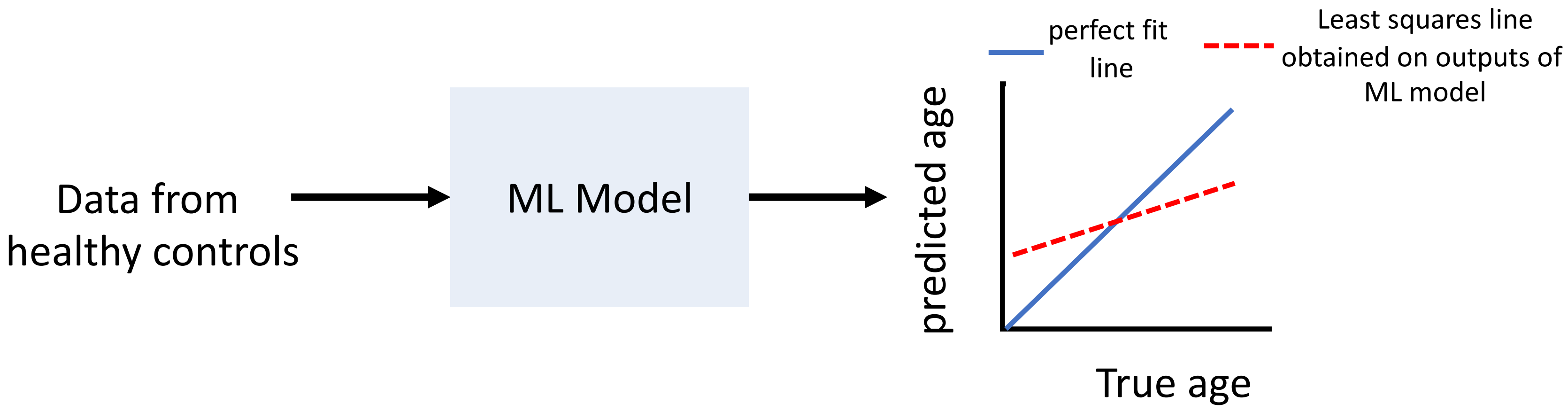
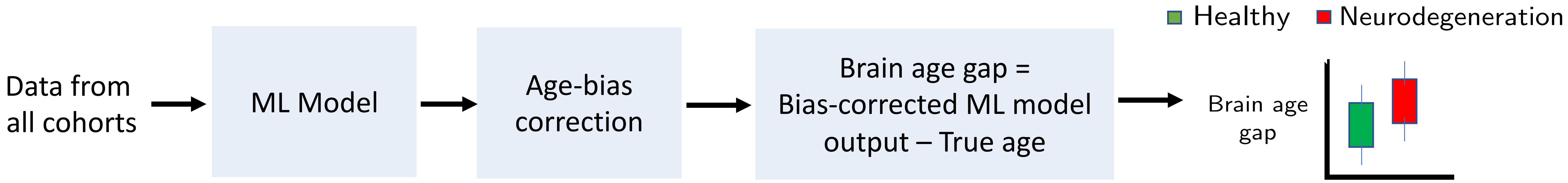
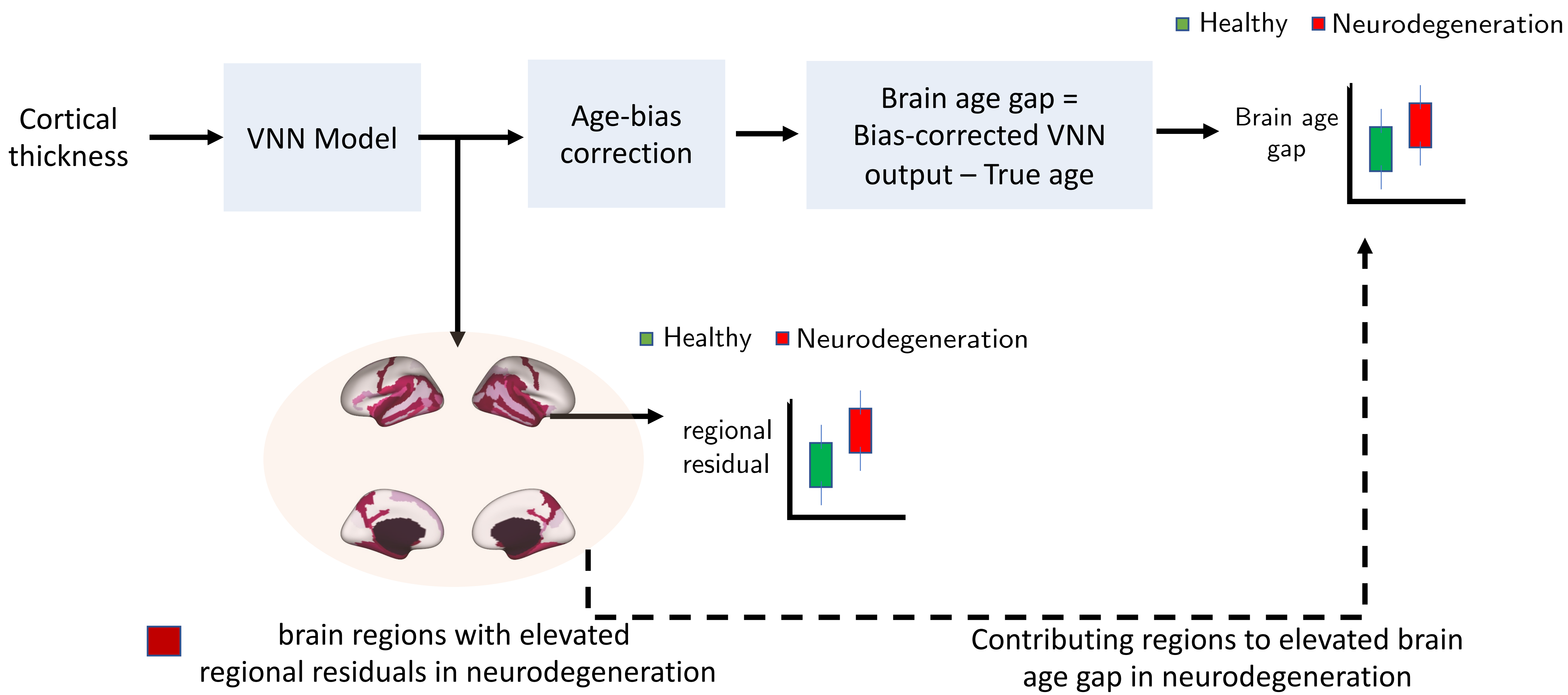


Step 2. Linear regression-based age-bias correct for outputs of ML model

Step 3. Obtain brain age gap for healthy controls and individuals with neurodegenerative condition.



coVariance neural networks (VNN) provide an anatomically interpretable brain age gap



Graph Filters and coVariance Filters

- Graph filter[a]

Graph signal $\mathbf{x} \longrightarrow \boxed{\mathbf{z} = \sum_{k=0}^{K} h_k \, \mathbf{S}^k \, \mathbf{x}} \longrightarrow \mathbf{z} = \mathbf{H}(\mathbf{S})\mathbf{x}$

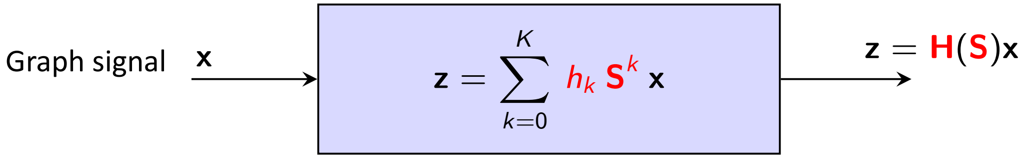
h_k: filter taps

Graph filter of order K supported on undirected graph $\mathbf{S} = \mathbf{R}\mathbf{F}\mathbf{R}^\mathsf{T}$

[a] Ortega, Antonio, et al. "Graph signal processing: Overview, challenges, and applications." *Proceedings of the IEEE* 106.5 (2018): 808-828.

Graph Filters and coVariance Filters

- Graph filter

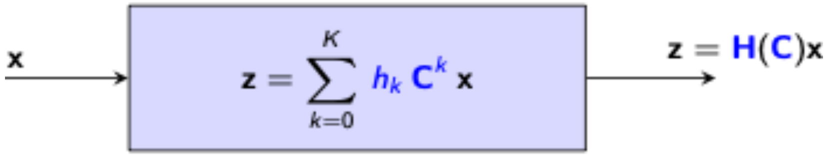


h_k: filter taps

Graph filter of order K supported on undirected graph $\mathbf{S} = \mathbf{RFR}^\mathsf{T}$

- coVariance filter [b]

For an m-dimensional dataset of n samples, $\mathbf{x}_n \in \mathbb{R}^{m \times n}$,
sample covariance matrix $\mathbf{C} = \frac{1}{n}(\mathbf{x}_n - \bar{\mathbf{x}}_n)(\mathbf{x}_n - \bar{\mathbf{x}}_n)^\mathsf{T}$



coVariance filter of order K supported on sample covariance matrix $\mathbf{C} = \mathbf{UWU}^\mathsf{T}$

[b] Sihag et al. "coVariance Neural Networks", NeurIPS 2022.

Graph Filters and coVariance Filters

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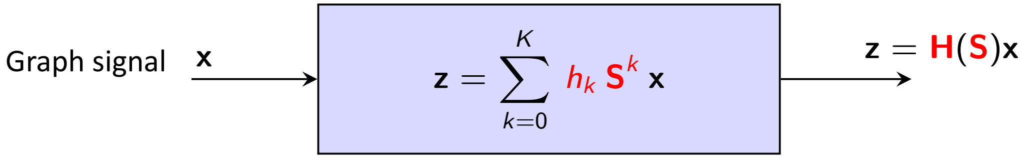

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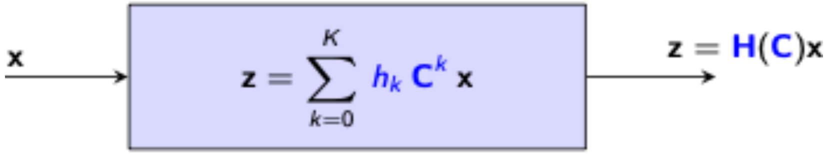


coVariance filter of order K supported on sample covariance matrix $\mathbf{C} = \mathbf{U}\mathbf{W}\mathbf{U}^{\mathsf{T}}$

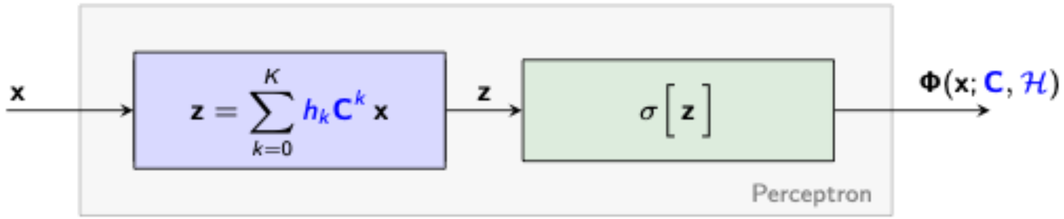
- Spectral representation of coVariance filter $\mathbf{H}(\mathbf{C})$

$$\mathbf{U}^{\mathsf{T}}\mathbf{H}(\mathbf{C})\,\mathbf{x} = \sum_{k=0}^{K} h_k \mathbf{W}^k\,\mathbf{U}^{\mathsf{T}}\mathbf{x} = h(\mathbf{W})\,\mathbf{U}^{\mathsf{T}}\mathbf{x} \rightarrow \text{PCA!!}$$

[b] Sihag et al. "coVariance Neural Networks", NeurIPS 2022.

VNN Architecture

- coVariance perceptron



$\sigma(\cdot)$: pointwise non-linearity function (e.g. ReLU, $\tanh$)

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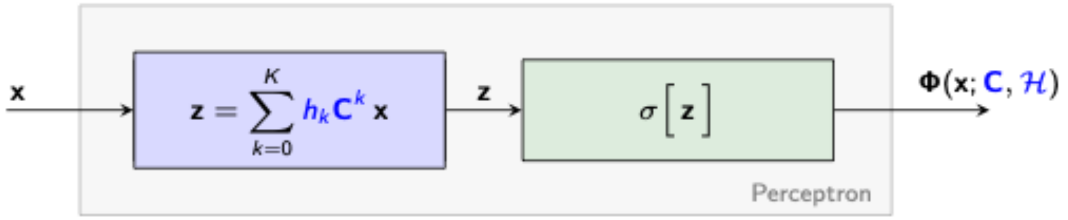

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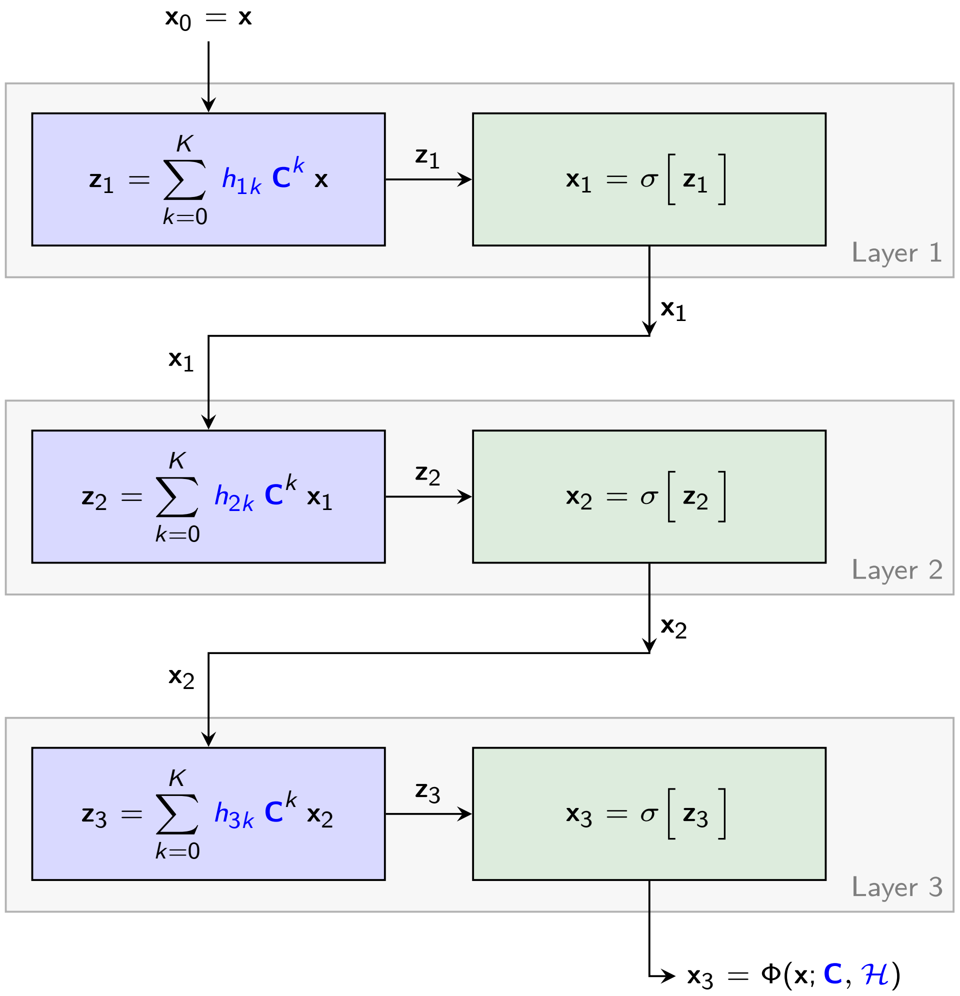
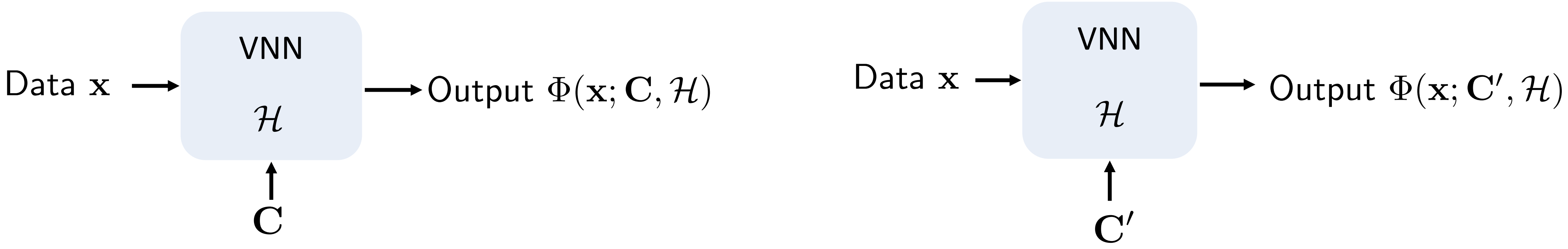
- coVariance Neural Networks (VNN)



Advantages offered by VNNs

- Stability to perturbations in sample covariance matrix, overcome limitations of PCA



Provably stable: $\|\Phi(\mathbf{x}; \mathbf{C}; \mathcal{H}) - \Phi(\mathbf{x}; \mathbf{C}'; \mathcal{H})\|$ is bounded [b]

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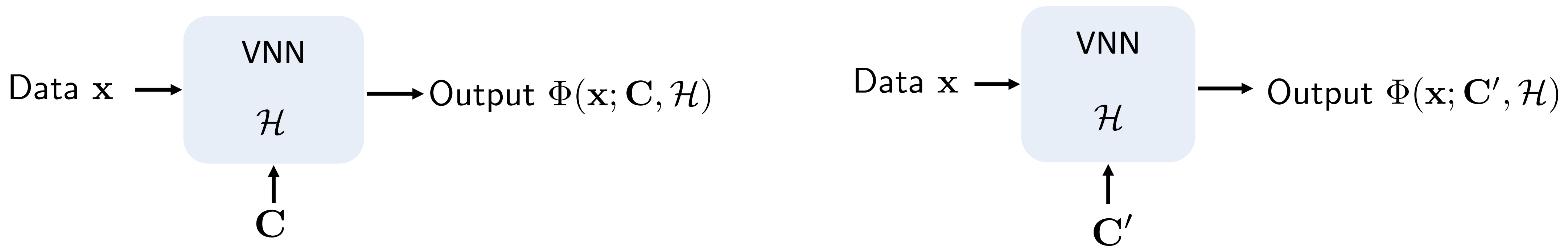

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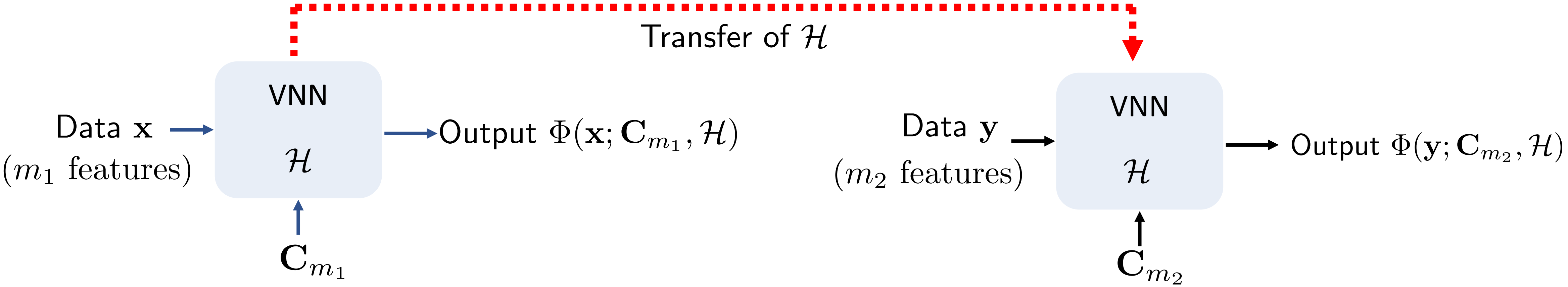
- Transferability of learnt parameters to datasets of different dimensionalities



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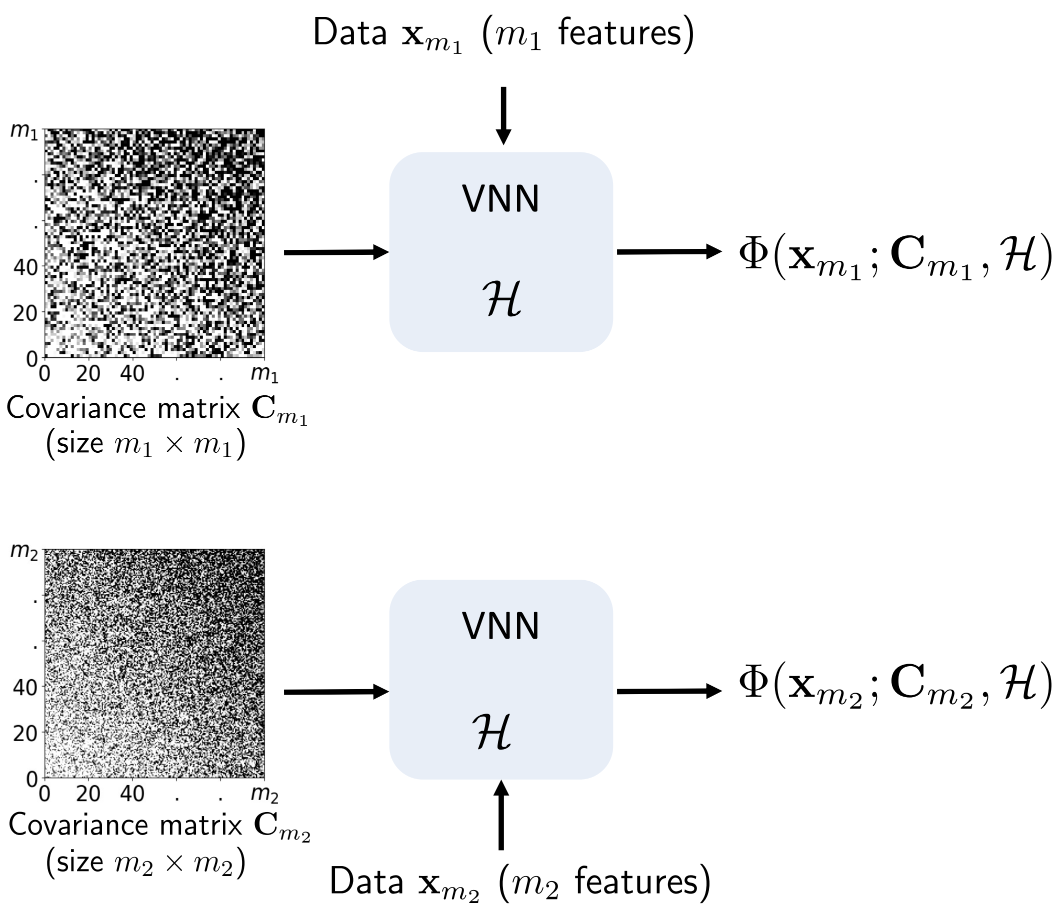
VNN performance is transferable across different covariance matrices derived from same covariance function



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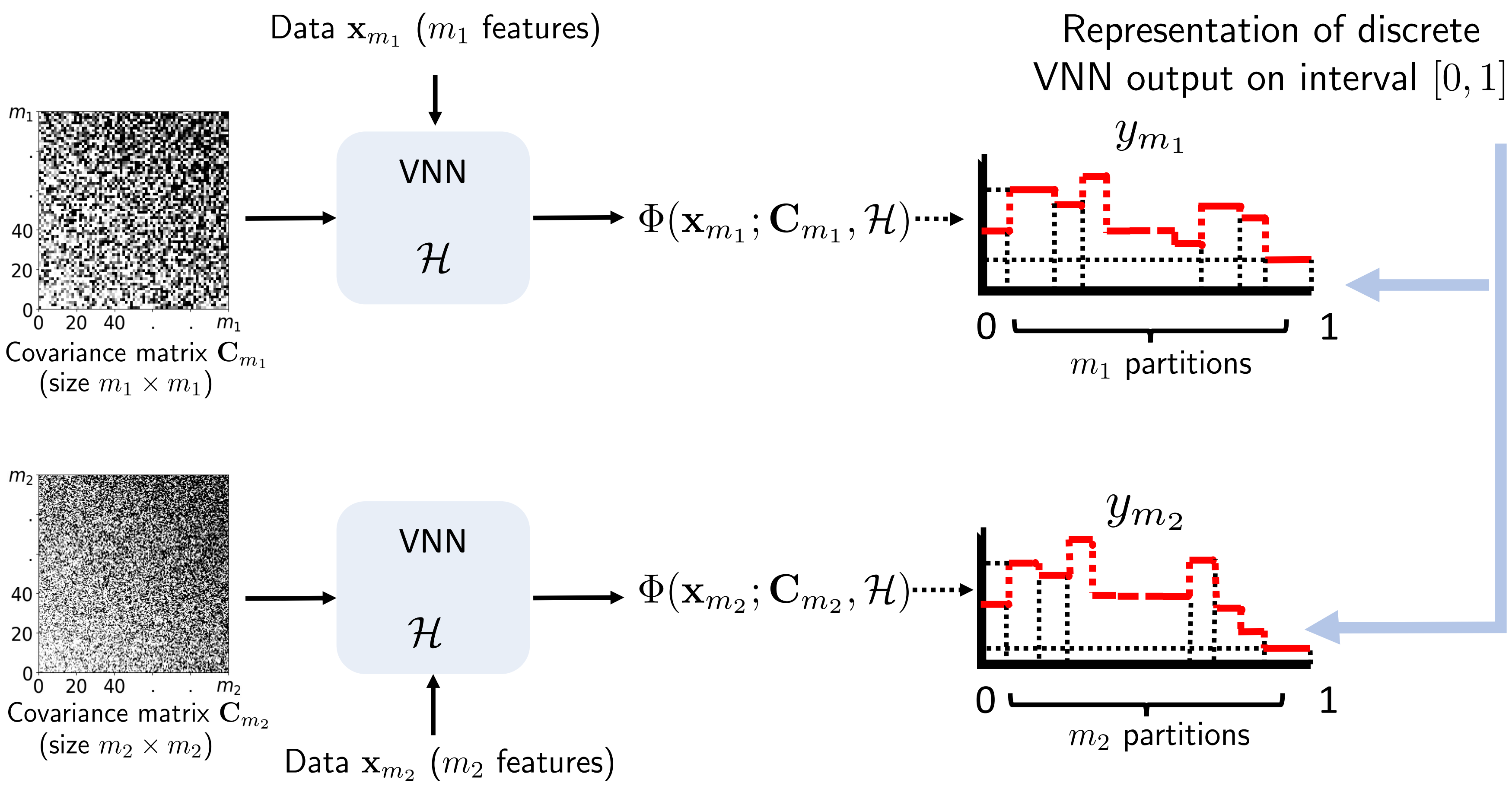

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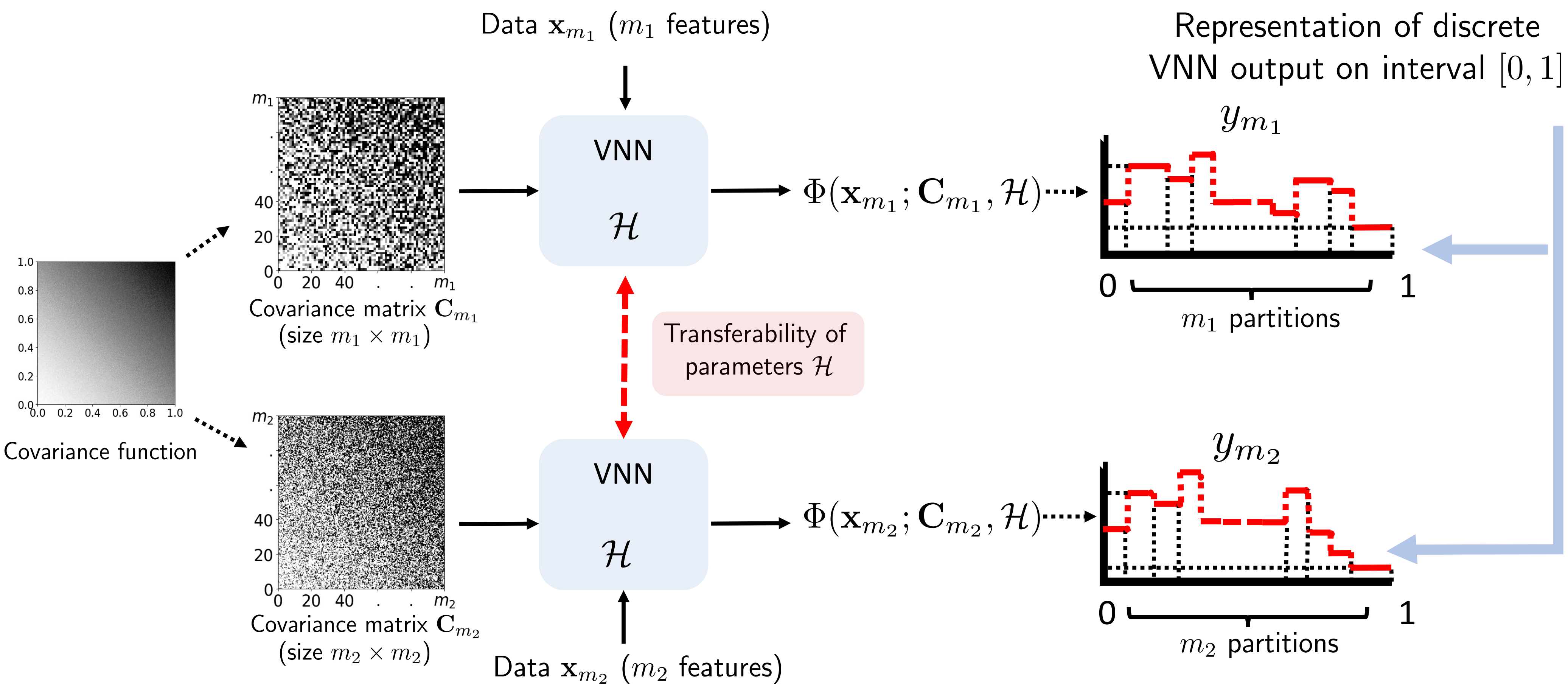
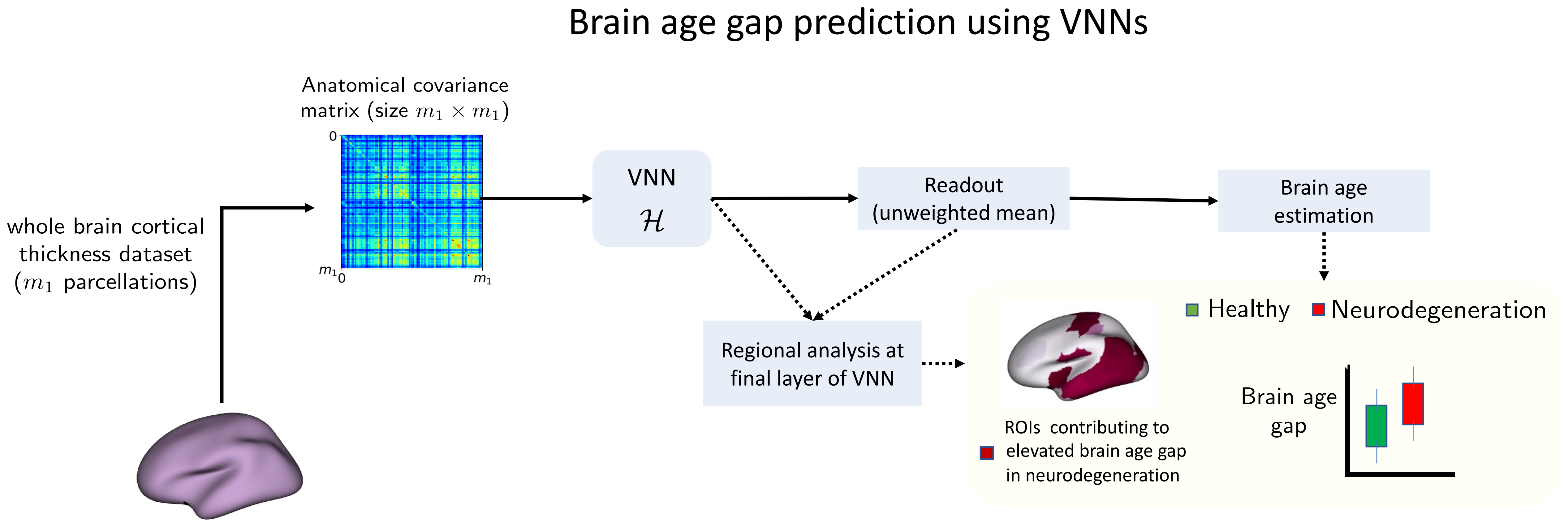


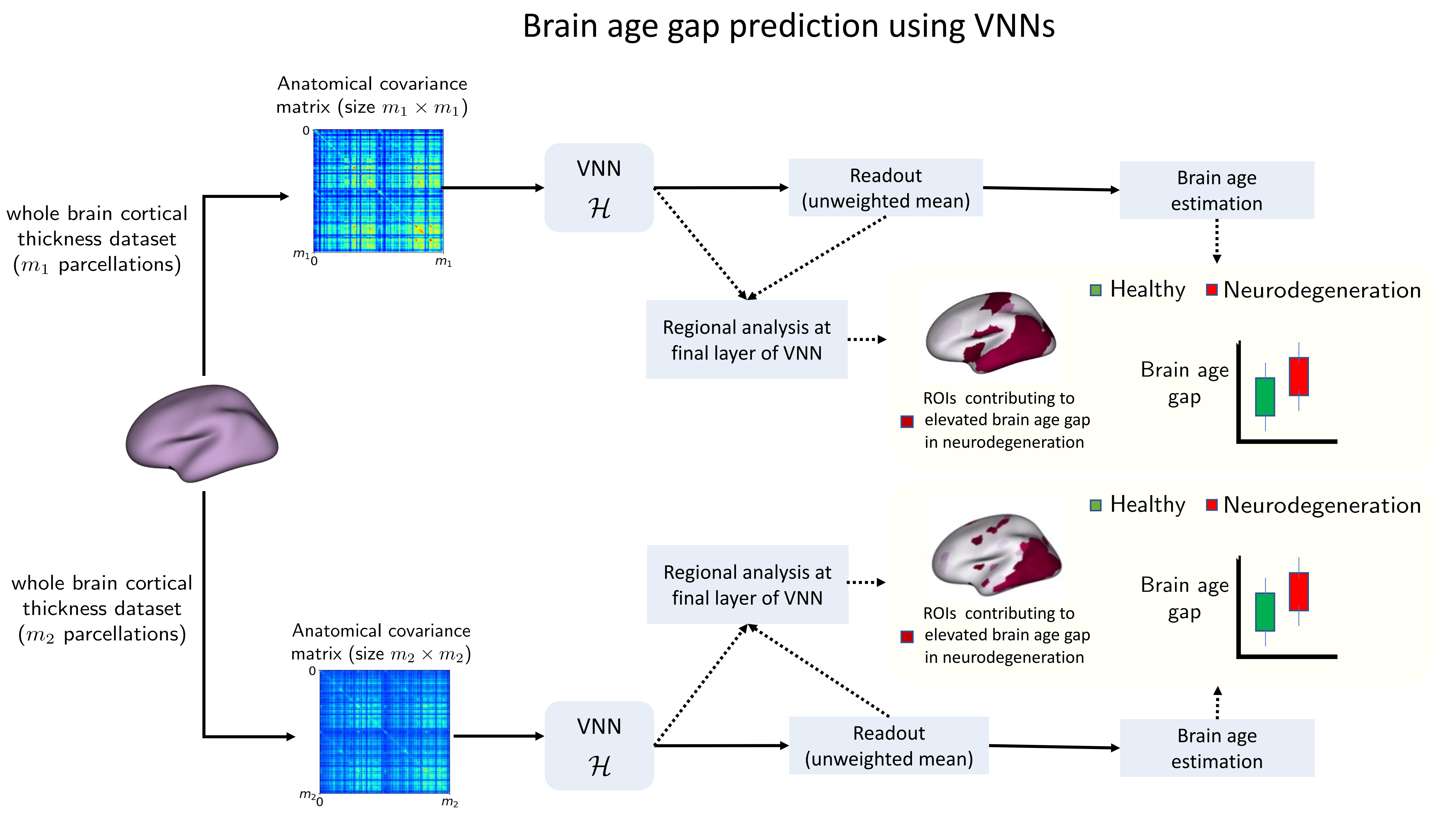
Theoretical guarantees (Theorem 3 in [c])

$$\|y_{m_1} - y_{m_2}\| \propto \mathcal{O}\left(\frac{1}{m_1^{3\zeta/2-1}} + \frac{1}{m_2^{3\zeta/2-1}}\right), \text{ for } \zeta \in (2/3, 1]$$

[d] Sihag et al. " Transferability of coVariance Neural Networks and Application to Interpretable Brain Age Prediction using Anatomical Features ", arxiv:2305.01807



Brain age gap prediction using VNNs
Anatomical covariance matrix (size $m_1 \times m_1$)
0
m_1
0
m_1
whole brain cortical thickness dataset (m_1 parcellations)
VNN
$\mathcal{H}$
Readout (unweighted mean)
Brain age estimation
Regional analysis at final layer of VNN
Healthy
Neurodegeneration
ROIs contributing to elevated brain age gap in neurodegeneration
Brain age gap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whole brain cortical thickness dataset (m_2 parcellations)
Anatomical covariance matrix (size $m_2 \times m_2$)
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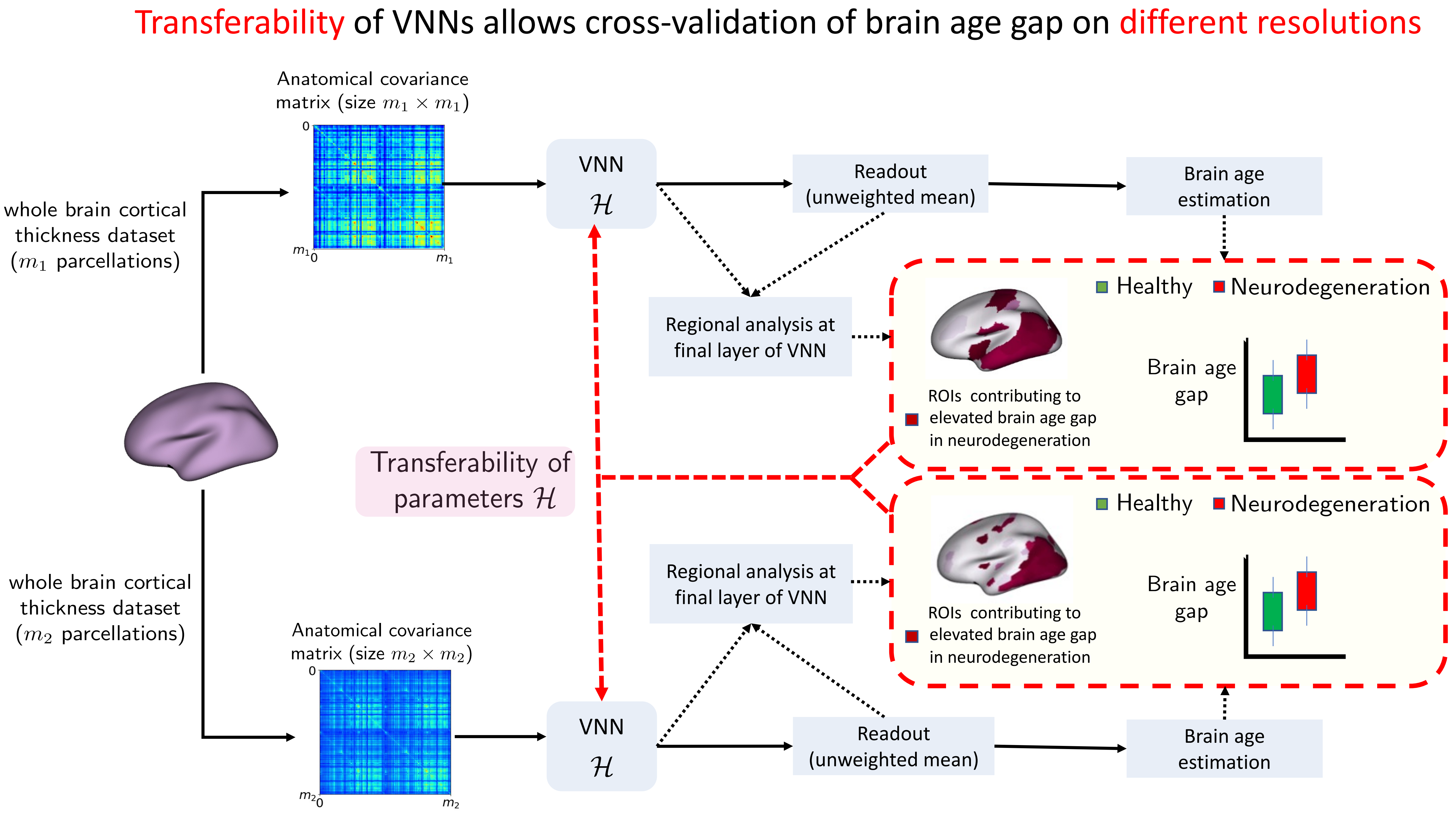

Transferability of VNNs allows cross-validation of brain age gap on different resolutions
Anatomical covariance matrix (size $m_1 \times m_1$)
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Results

- Whole brain cortical thickness datasets on two populations
  1. healthy controls (**HC**, n =105, age = 62.6 ± 7.62 years, 57 females)
  2. individuals with mild cognitive impairment or Alzheimer's disease diagnosis
     (**AD+**, n = 67, age = 68.52 ± 9.29 years, 28 females)

- Three multi-scale datasets (organized according to different versions of Schaefer's atlas)

FTDC Datasets

- FTDC100 (number of features = 100) - FTDC300 (number of features = 300) - FTDC500 (number of features = 500)

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Objective: Regression of cortical thickness against chronological age for HC cohort

Mean absolute error

Training \ Testing	FTDC100 (HC)	FTDC300 (HC)	FTDC500 (HC)
FTDC100 (HC)	5.39 ± 0.084	5.5 ± 0.101	5.61 ± 0.132
FTDC300 (HC)	5.39 ± 0.193	5.41 ± 0.167	5.47 ± 0.169
FTDC500 (HC)	5.43 ± 0.2	5.38 ± 0.15	5.4 ± 0.169

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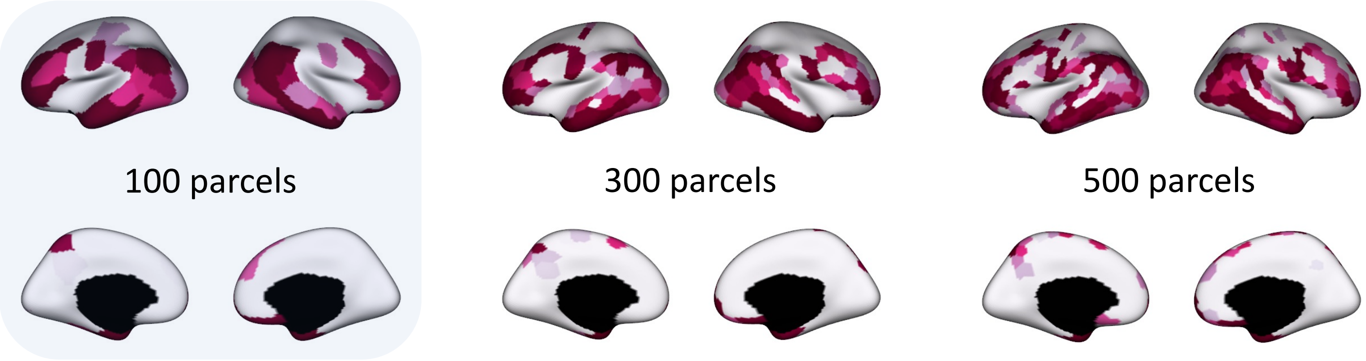
VNNs are transferable across datasets of dimensionalities 100, 300, and 500

Results

Objective: Brain age gap prediction in HC and AD+ cohorts from VNNs trained on FTDC100 dataset

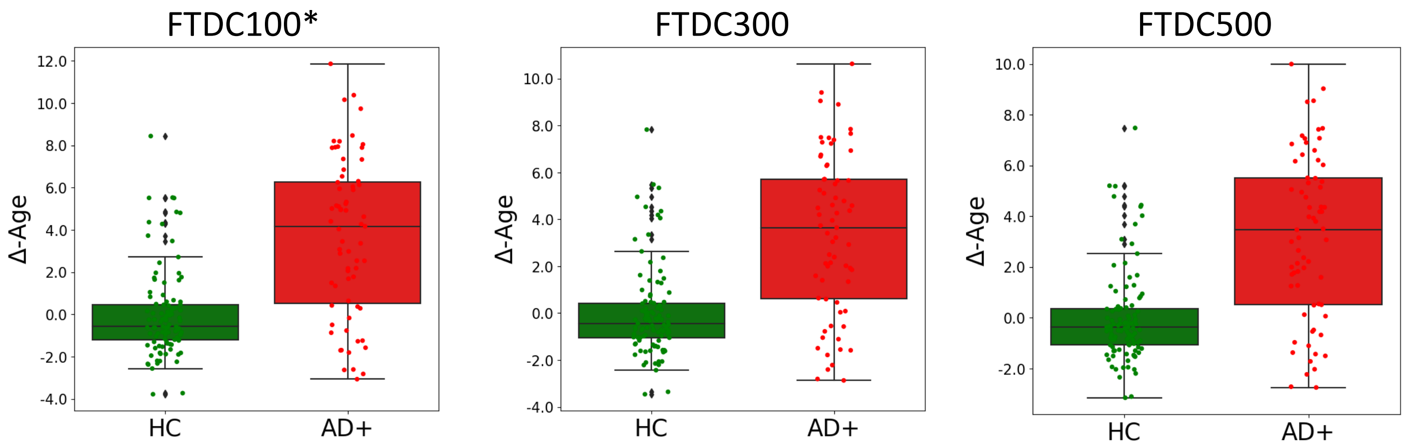
a



- ROIs contributing to elevated brain age gap in AD+ across different resolutions

b

Brain age gap (Δ-Age): HC vs AD+



- Brain age gap is elevated in AD+ w.r.t HC cohort in 100-feature dataset
- Results on brain age gap retained after transferring VNN to 300 and 500-feature datasets

Conclusions

- VNNs provide an anatomically interpretable perspective to brain age
- Transferability of VNNs help cross-validate interpretability across datasets of different dimensionalities
- VNN-derived brain age is a potential biomarker for early detection of neurodegeneration and disease monitoring