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# Learning Continuous- Time Trajectories of Adolescent Brain Structural Connectomes via Latent Graph Neural ODEs

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2025□ 12□ 15□

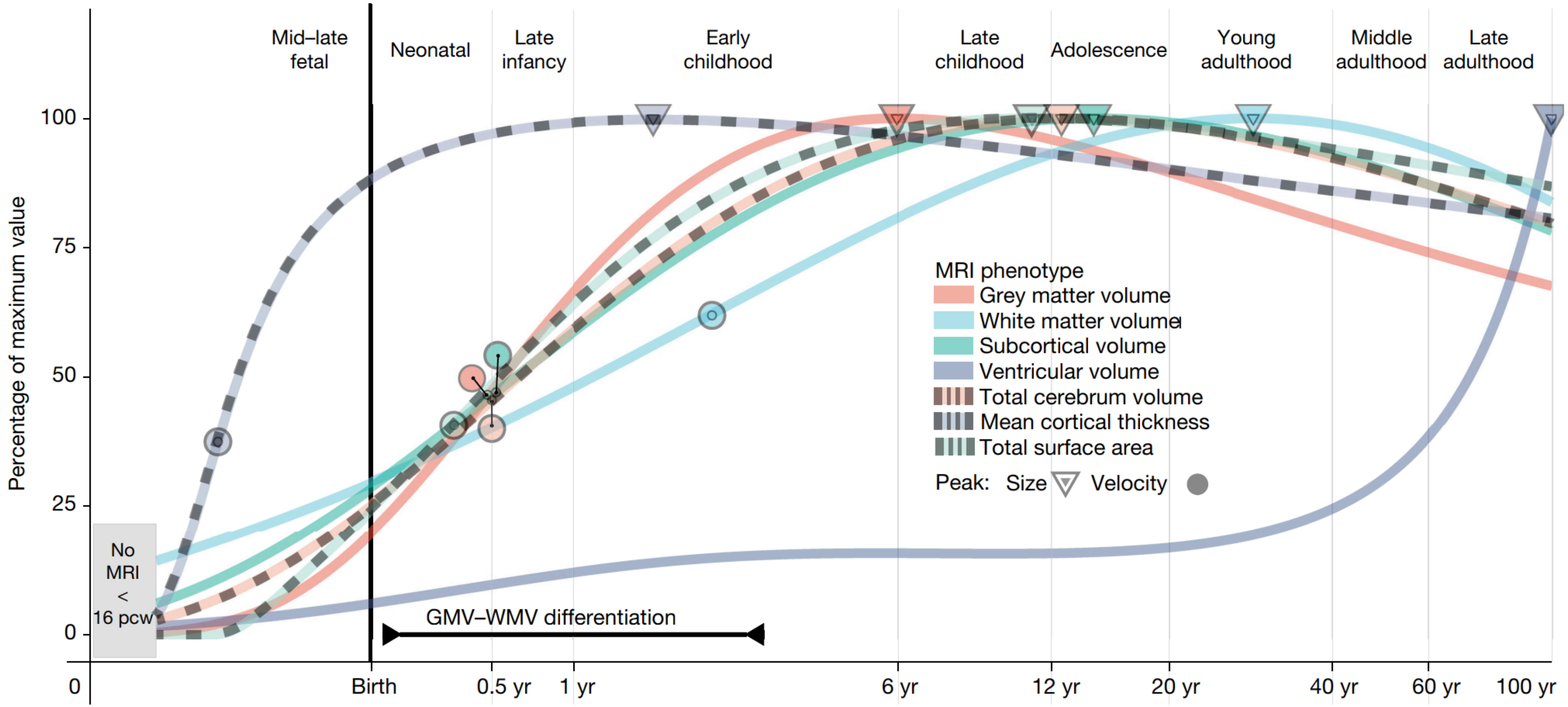
# 01

# Research Background

# Background

## Brain Charts

Bethlehem, R. A. I., et al. (2022). *Nature*

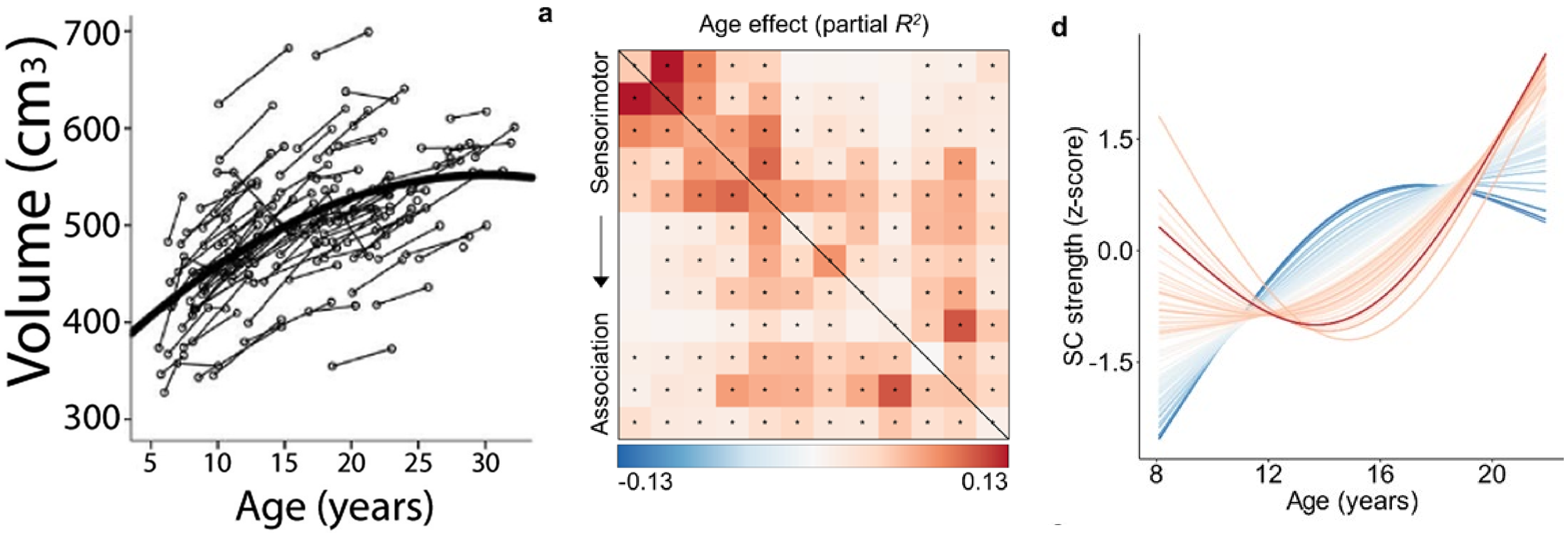



- Static
- Group-average
- Single-variable

Cannot sufficiently capture individual developmental dynamics and variation over time.

# Background

## The "Rewiring" Brain



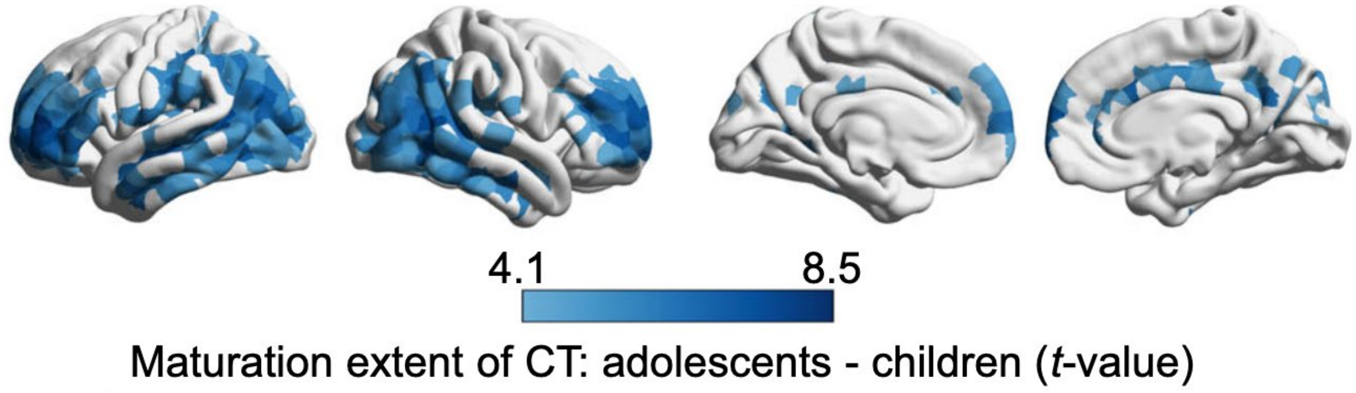

Structural Reorganization

- Pruning
- Myelination

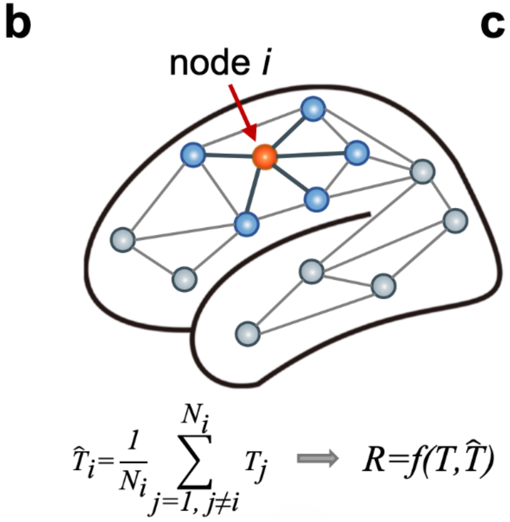
Development follows complex "Inverted-U" or asymptotic curves, not simple linear growth.

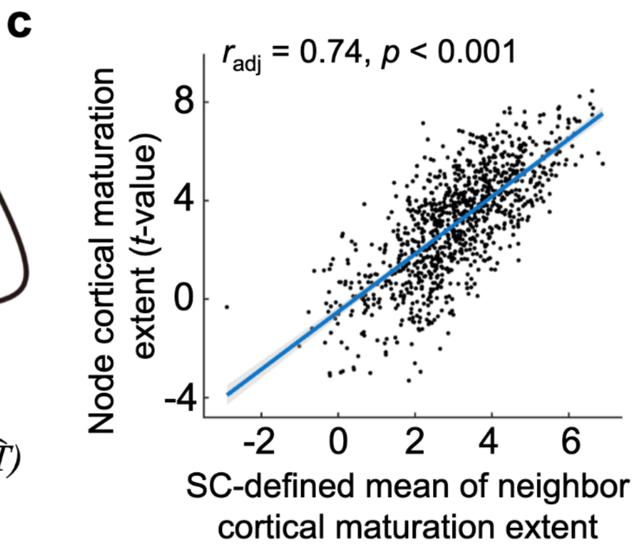
# Background

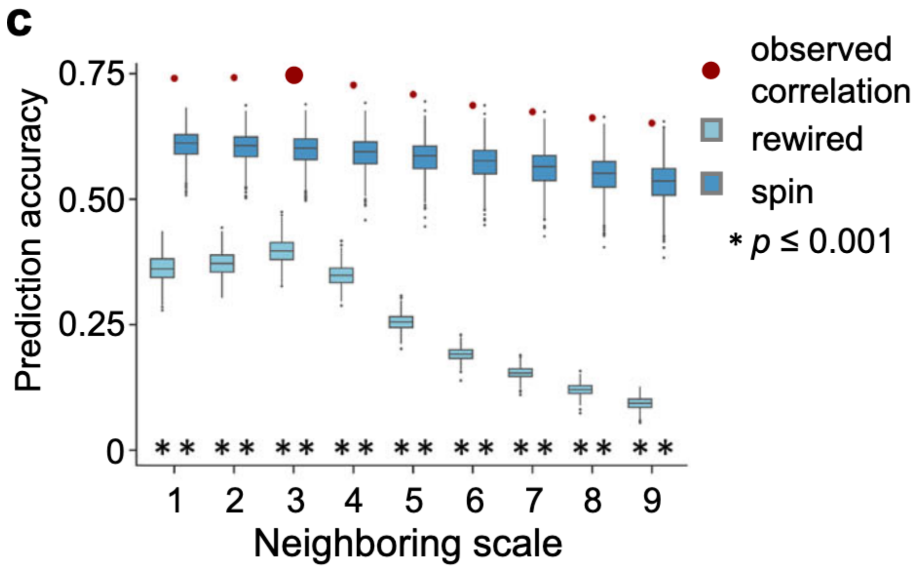
## Shape and Connection are Linked




Liang, X. et al. (2024). *Nat Commun*.




Cannot sufficiently capture individual developmental dynamics and variation over time.

# Background

## Challeges

**Irregular Sampling**

- Issue: Clinical visits are rarely perfectly.
- Limitation: Discrete models (RNNs) require rigid binning or imputation, introducing noise and bias.

**Lack of Mechanistic Coupling**

- Biology: Morphology drives white matter reorganization, and vice versa.
- Limitation: Existing models often treat nodes and edges as independent variables or static features.

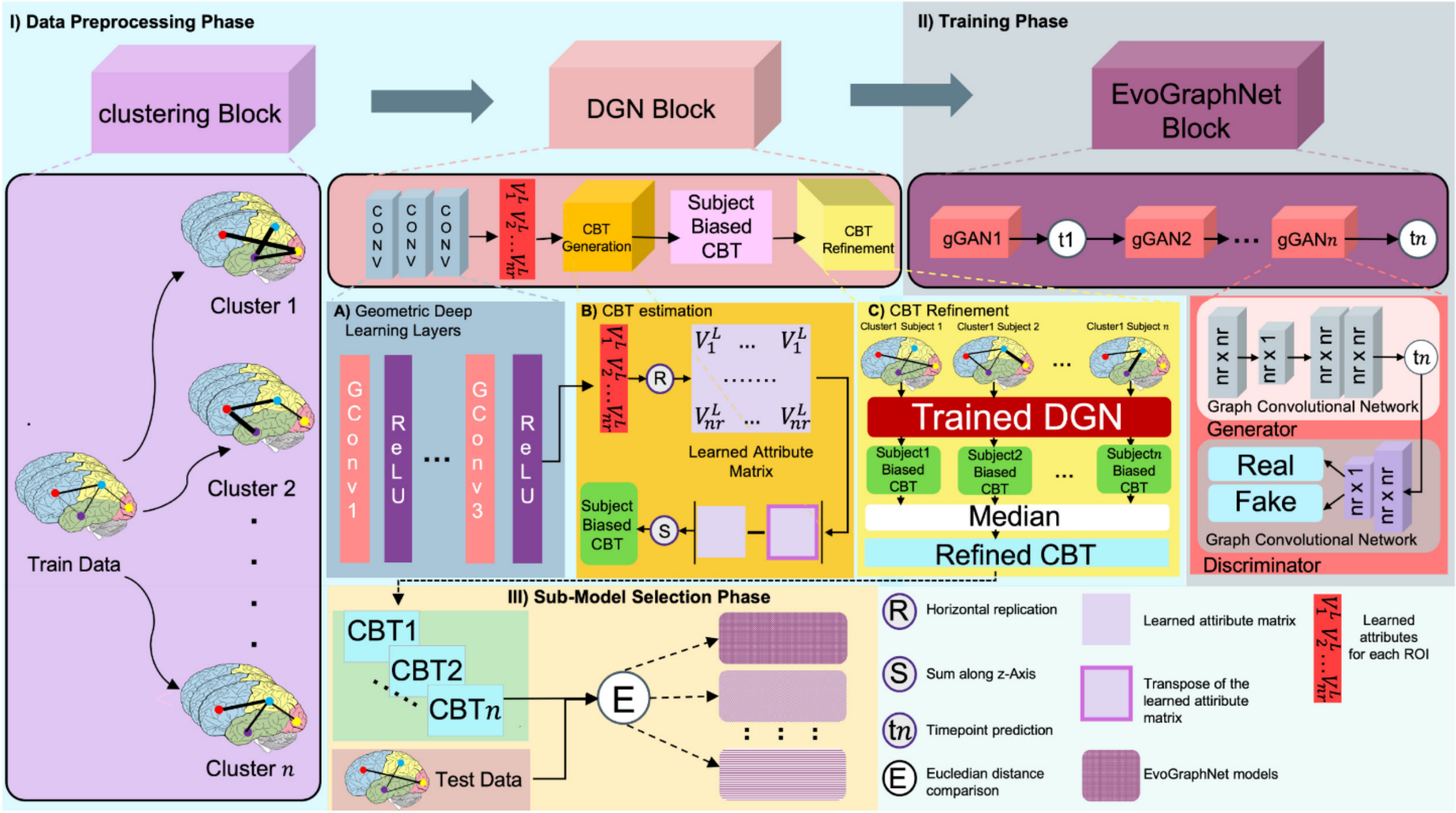
**Topological Invalidity**

- Issue: MSE-based loss functions produce "blurry," fully-connected average graphs.
- Limitation: Generated brains fail to preserve the "Small-Worldness," "Modularity," and specific cycle structures (Betti numbers) of real human brains.

# Background

## FLAT-Net

Guris O, et al. (2021). *MICCAI*.



# Background

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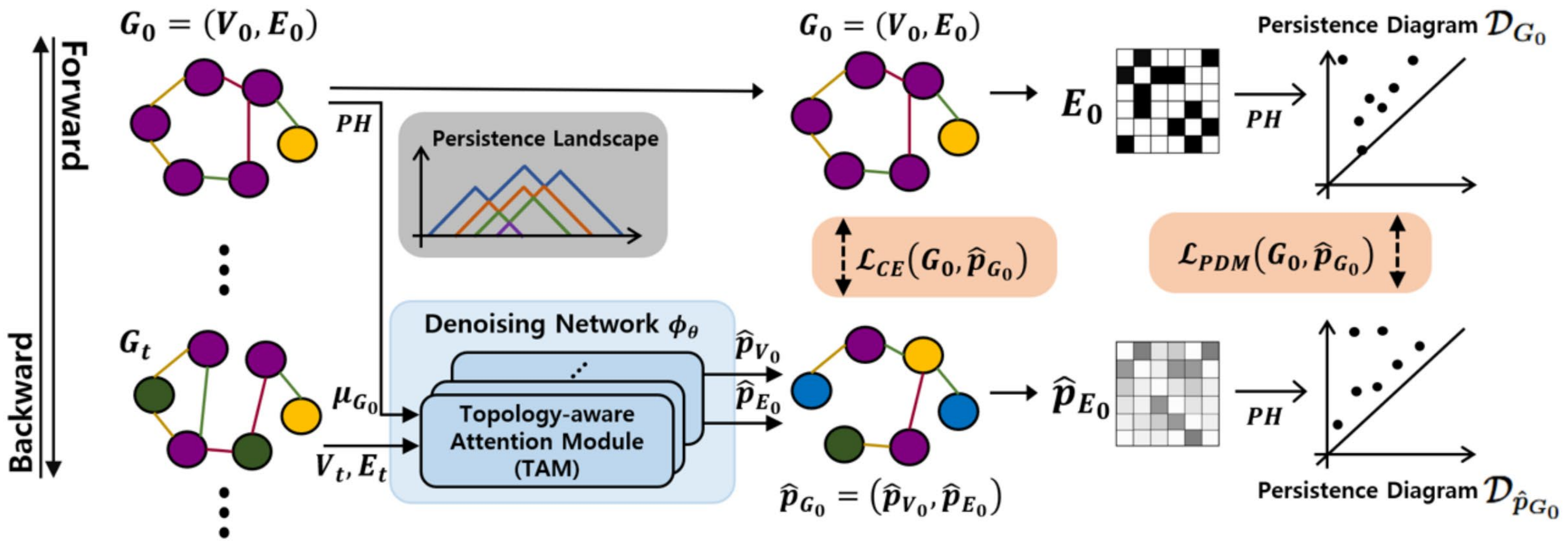
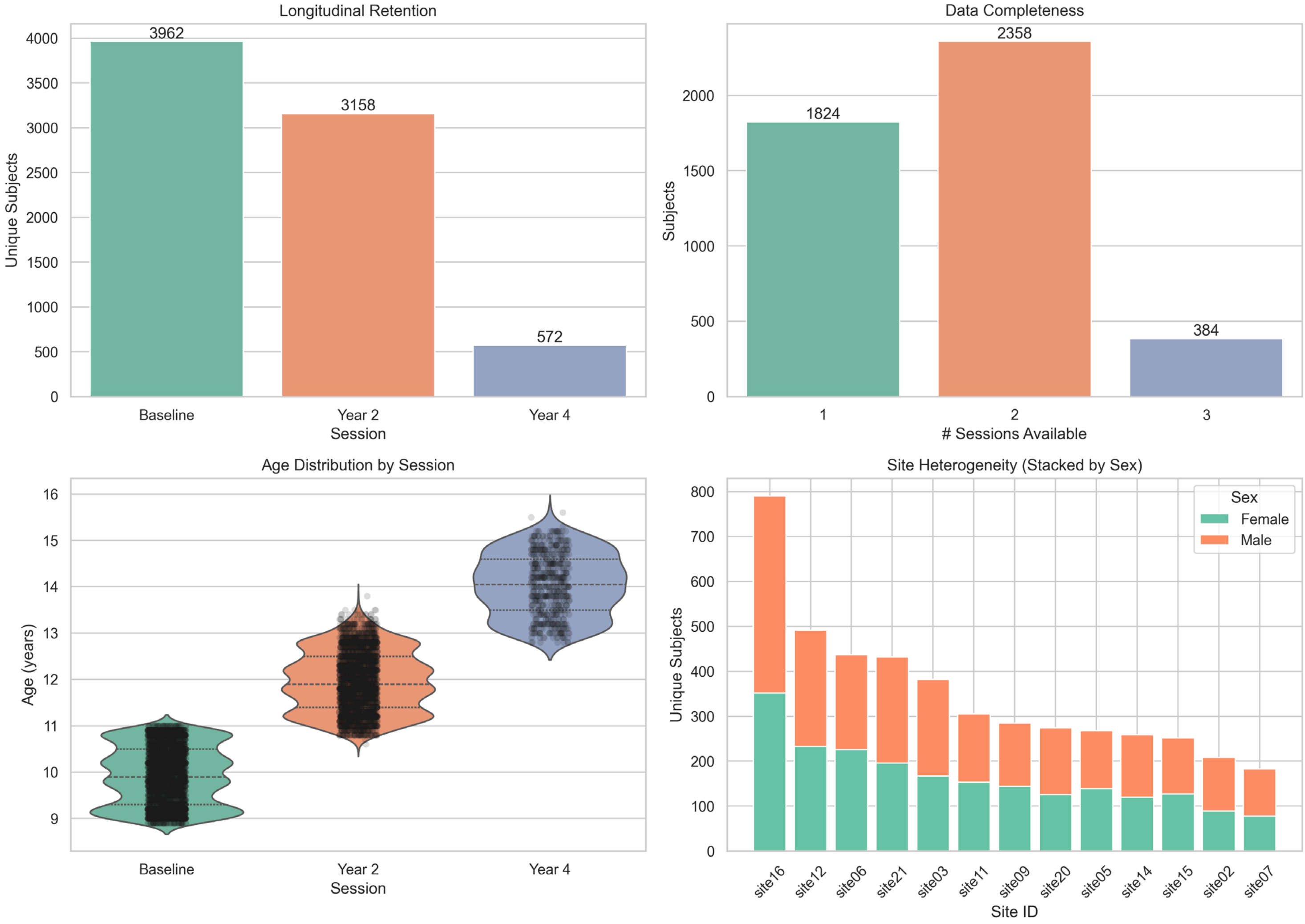
Chen Y, Gel Y. (2025). *ICLR*.



# 02
# Methods

# Methods

## data




**Dataset:** ABCD Study (Adolescent Brain Cognitive Development).

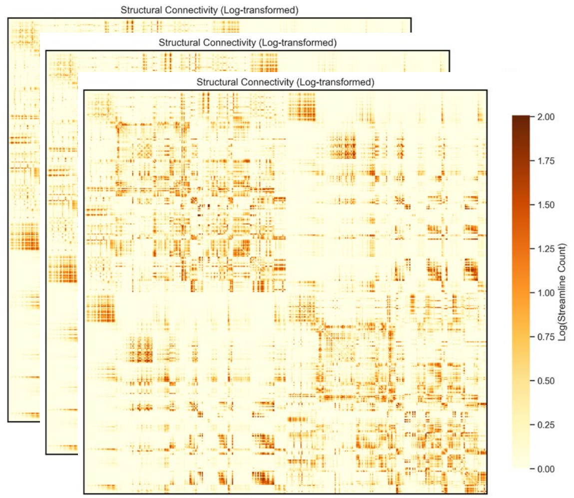
**Sample Size: 3,962** unique subjects (9-10 years baseline).

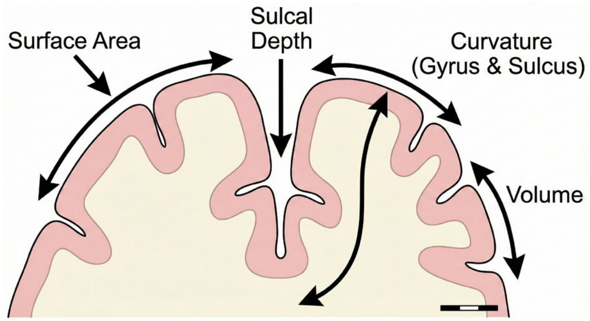
**Data Tiering Strategy:**

- Tier 1 (3+ timepoints): **384** subjects, used for learning non-linear acceleration.
- Tier 2 (2 timepoints): **2,358** subjects, used for learning velocity fields.
- Tier 3 (1 timepoint): **1,824** subjects, used for learning manifold distribution.

# Methods

## Framework




**Input Representation:**

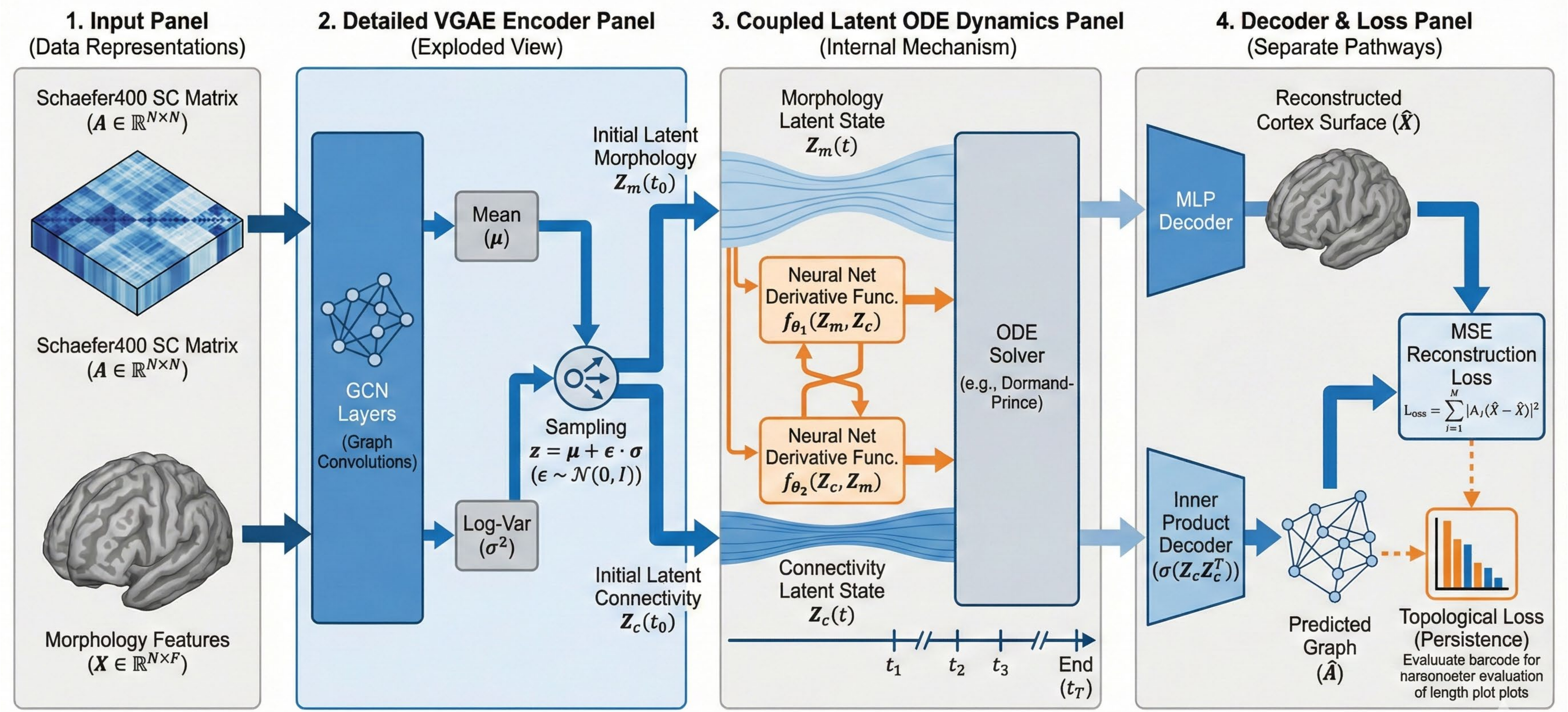
- Multi-Modal Data: $G_t = (A_t, X_t, C)$
- $A_t$(Structure): Structural Connectivity (SC). Pre-processing: Log-Euclidean mapping to respect the SPD manifold.
- $X_t$(Morphology): Cortical Thickness, Volume, Myelination maps.
- $C$(Covariates): Continuous Age, Sex, and Site_ID (critical for de-confounding).

**Latent Encoding:**

- Latent Morphology: $Z_{morph} \in \mathbb{R}^{N \times d}$
- Latent Connectivity Wiring: $Z_{conn} \in \mathbb{R}^{N \times d}$

# Methods

pipeline



# Methods

## Coupled Differential Equations

$$\begin{cases} \dfrac{dZ_{\text{morph}}}{dt} = f_{\theta_1}\left(Z_{\text{morph}}, Z_{\text{conn}}, t, C\right) \\ \dfrac{dZ_{\text{conn}}}{dt} = f_{\theta_2}\left(Z_{\text{conn}}, Z_{\text{morph}}, t, C\right) \end{cases}$$

**Morphology Evolution:** The rate of cortical thinning is regulated by current connectivity strength/intensity.

**Connectivity Evolution:** The pruning rate of connectivity is driven by the morphology of local brain regions.

Solver: odeint_adjoint (Dormand-Prince), allowing for adaptive step sizes to handle stiff dynamics during rapid developmental phases.

# Methods

## Topology-Aware Decoder

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**Morphology Reconstruction:** $\hat{X}_t = \mathrm{MLP}(Z_{morph}(t))$

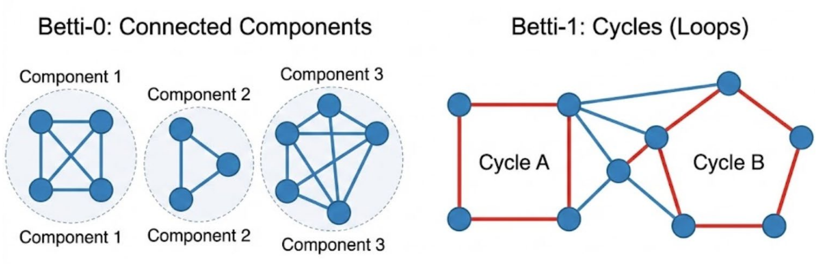
**Connectivity Reconstruction:** $P_{ij} = \sigma(Z_{conn} Z_{conn}^T)$

Dynamic Sparsification: Instead of a fixed threshold, we apply Top-K filtering or L1 Regularization.

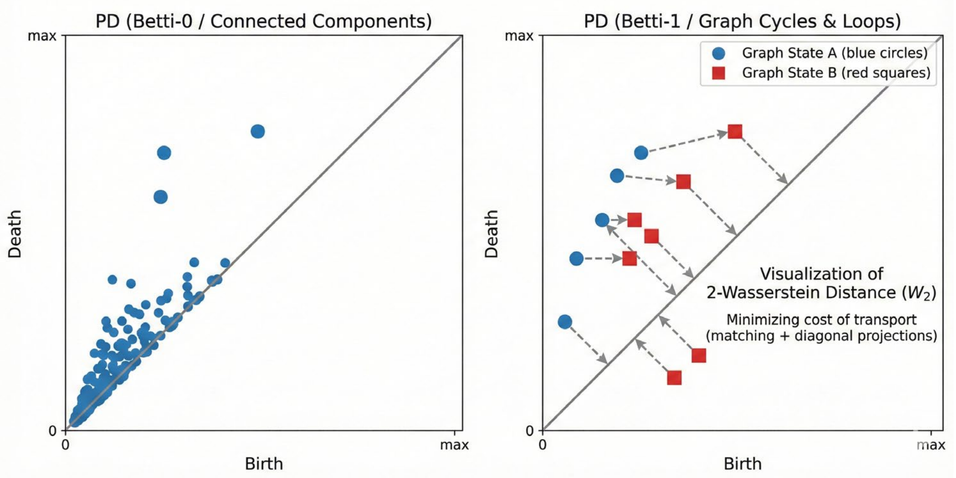
This allows the model to simulate **Synaptic Pruning**—the network naturally becomes sparser and more efficient over time (simulating the transition from child to adult).

# Methods

## The "Realism" Loss Landscape




**Loss Function:** $\mathcal{L} = \mathcal{L}_{Recon} + \lambda_1 \mathcal{L}_{KL} + \lambda_2 \mathcal{L}_{Topo} + \lambda_3 \mathcal{L}_{Smooth}$




$\mathcal{L}_{Recon}$ Standard MSE/BCE for node and edge reconstruction.

$\mathcal{L}_{KL}$ Variational constraint for the latent space.

$\mathcal{L}_{Topo}$ Preserves Betti numbers (connected components and cycles).

- Computes Persistence Diagrams (PD) for Ground Truth and Generated graphs.
- Minimizes the Wasserstein Distance between them.

$\mathcal{L}_{Smooth}$ Prevents chaotic jumps, enforcing smooth biological development.

# Results

## Results

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| MSE/Corr | Identity map | Vector lstm | GraphRNN | ours |
|---|---|---|---|---|
| 2-year | 66.10 / 0.734 | 63.77 / 0.7414 | | |
| 4-year | 73.60 / 0.703 | 62.09 / 0.7460 | | |
| mean | 67.32 / 0.729 | 63.55 / 0.7420 | | |

More topological metrics……

Maximum Mean Discrepancy of the distribution:

- Degree
- Clustering
- Orbit

# Key Analysis

## Validation Metrics

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Irregular Sampling Robustness:

- Test: Randomly mask time points.
- Metric: Accuracy of the ODE solver in interpolating the missing scans compared to RNN imputation.

Developmental Trend Recovery:

- Test: Plot average connectivity strength vs. Age.
- Metric: Does the model recover the population-level Inverted-U or Pruning curves?

Individual Fingerprinting:

- Test: Can we identify Subject A at Year 4 using the generated Year 4 graph?
- Metric: Identification Accuracy. High accuracy proves we preserved individual traits and didn't just learn the "average brain."


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