PHYSICS-TRANSFER LEARNING: A FRAMEWORK TO ADDRESS THE ACCURACY-PERFORMANCE DILEMMA IN MODELING MORPHOLOGICAL COMPLEXITIES IN BRAIN DEVELOPMENT

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ABSTRACT

The development of theoretical science follows an observation-assumption-modeling approach, effective for simple systems but hindered by complexity in engineering. Artificial intelligence (AI) and machine learning (ML) offer a data-driven alternative for making inferences when direct solutions are elusive. Feature engineering extends dimensional analysis, revealing hidden physics from data. We present a physics-transfer (PT) framework to predict physics across digitally varied models, addressing the accuracy-performance trade-off in multiscale challenges. This is exemplified in modeling brain morphology development, essential for disease diagnosis and prognosis. Nonlinear deformation physics from basic geometries is encoded into a neural network and applied to complex brain models. Results agree with longitudinal magnetic resonance imaging (MRI) data, and learned variables correlate with physical descriptors, such as undetectable stress states and submicroscopic characteristics, demonstrating the effectiveness of PT in understanding multiscale problems.

1 INTRODUCTION

In engineering sciences, theoretical frameworks are traditionally built by following an observation-assumption-modeling pattern. From Galileo's studies on beam bending to Cauchy's formulation of continuum mechanics, this methodology has been effective for mechanics problems with a low-dimensional parameter space. In such scenarios, analytical models have often captured the complexity effectively. However, as scientific inquiry advances into the multiscale analysis of matter, the well-known 'curse of complexity' emerges. This presents significant challenges in capturing detailed physics solely via analytical methods.

A case in point is brain development, which encompasses gene expression, cellular dynamics, and mechanical fluctuations across multiple spatiotemporal scales, manifesting in dynamic morphologies (Llinares-Benadero & Borrell, 2019) (Fig. 1). First-principles theories, while providing high-fidelity models of molecular-level thermodynamics and kinetics, encounter scalability issues. At the structural level, finite element analysis (FEA) has proven to be an effective method for modeling deformation physics (Bayly, 2023). However, the complex morphology of brains presents significant modeling challenges. As a result, empirical models, noted for their efficiency, are limited by the constraints of assumptions and uncertainties in parameterization, necessitating validation against first-principles calculations or experimental observations. This dichotomy highlights the accuracy-performance conundrum in modeling the multiscale physics inherent in engineering sciences.

Recent advances in artificial intelligence (AI) and machine learning (ML) represent a promising data-driven alternative. Although often limited by data density and coverage, this emergent methodology provides an increasingly potent end-to-end solution as data quality and quantity improve.

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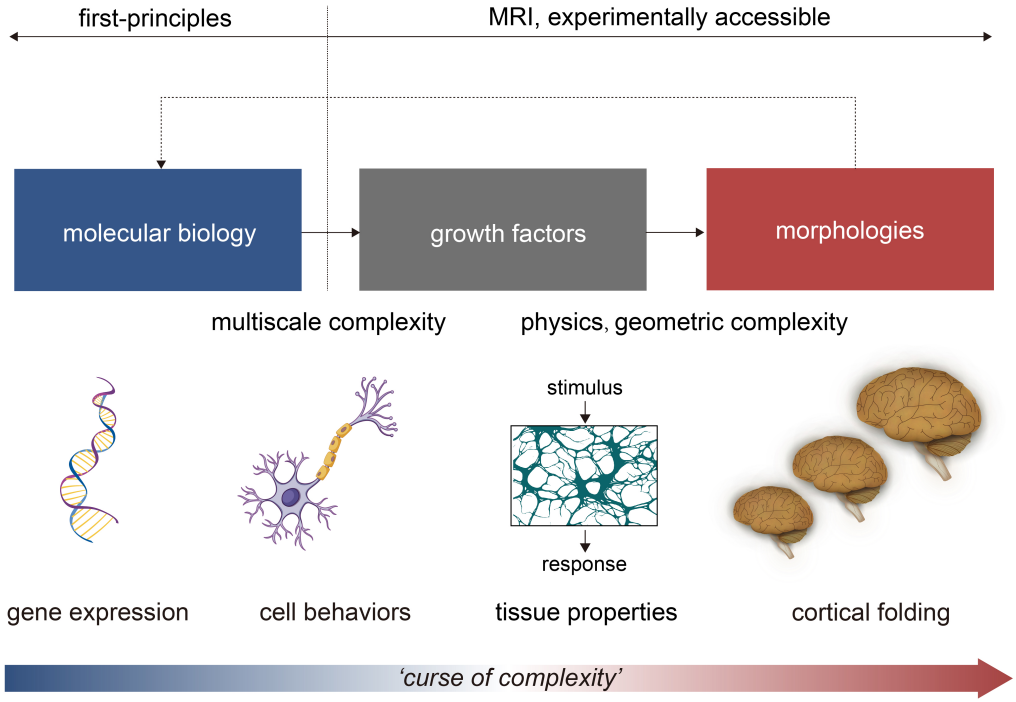

Figure 1: The accuracy-performance dilemma in multiscale modeling of brain morphological development.

The enhanced capabilities of interpolation and extrapolation can augment traditional theoretical approaches when direct solutions are impractical or intractable (Zhang et al., 2018; Li et al., 2022). Furthermore, feature engineering in ML parallels dimensional analysis, offering a systematic approach to identifying and exploiting internal correlations within complex datasets (Xu et al., 2022b). This analogy implies that ML, through its data-driven methods, has the potential to extract and transpose physical insights across digital models with varying levels of fidelity and complexity.

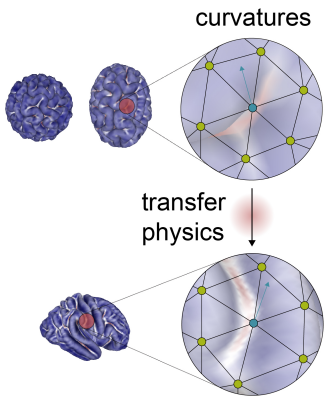

Figure 2: The physics-transfer (PT) framework that learns physics across models of varying complexities.

Inspired by these thoughts, we propose a physics-transfer (PT) framework designed to learn physics across digital models of varying complexities (Fig. 2). This learned physics is used for scientific inference, ensuring high accuracy and performance to address the challenge inherent in modeling complexity. The framework is demonstrated through the study of brain development, where organs exhibit complex morphologies and nonlinear deformation physics dictated by underlying multiscale processes. Initially, the physics of bifurcation in brain morphologies is learned using spherical and ellipsoidal models with simple geometries, which is then applied to predict the evolutionary behaviors of and human brains. We validate these predictions against experimental data obtained by magnetic resonance imaging (MRI), acknowledging the scarcity of such data in the current literature. The proposed framework offers considerable potential for enhancing our comprehension of complex multiscale challenges and for linking modeling insights with experimental observations.

2 PHYSICS-TRANSFER LEARNING FRAMEWORK

Models with varying complexities ($\mathcal{C}$) in multi-scale modeling show different parameter distributions, denoted as $p(\theta|\mathcal{C})$, where θ are the model parameters and $p(\cdot|\cdot)$ represents the conditional probability. The parameter distributions $p(\theta|\mathcal{D})$ in a specific ML context typically depend on data complexities ($\mathcal{D}$). Generally, data with low ($\mathcal{D}_{\mathrm{L}}$) and high ($\mathcal{D}_{\mathrm{H}}$) complexities can exhibit different distributions, that is

$$p(\theta|\mathcal{D}_{\mathrm{L}}) \neq p(\theta|\mathcal{D}_{\mathrm{H}}), \tag{1}$$

which limits the transferability and extrapolation of models trained on data with different complexities.

In certain situations, the physics ($\mathcal{P}$) underlying the dataset ($\mathcal{D}$) can facilitate extrapolation through a *physics-transfer* approach. If such a physical relationship exists between the features ($\mathbf{x}$) and the target ($\mathcal{O}$) in $\mathcal{D}$, then we have

$$\mathbf{x} \xrightarrow{\mathcal{P}} \mathcal{O}, \tag{2}$$

$$\mathbf{x} \cap \mathcal{O} = \mathcal{D}^{'} \subset \mathcal{D}, \tag{3}$$

where $\mathcal{D}^{'}$ represents a space of reduced dimensions. Specific ML models ($h \in \mathcal{H}$) can be designed to learn the underlying physics of the data. Models trained on data of varying fidelities tend to share a similar parameter distribution, meaning that

$$p(\theta|\mathcal{D}_{\mathrm{L}}^{'}) \approx p(\theta|\mathcal{D}_{\mathrm{H}}^{'}), \tag{4}$$

which makes the transferability and extrapolation of these ML models possible.

3 EXPERIMENTS

In predicting brain morphology, ML models are trained using data from simple geometries, such as spheres, followed by zero-shot extrapolation on brain data, direct modeling of which requires significantly higher computational costs to capture both the overall geometry (structure, shape, size) and local features (the cortex, subcortical structures, and ventricles). Sampling from the morphological development space of simple geometries proves more efficient than that of brain tissues. Simple geometries offer high density and comprehensive coverage, and their spatiotemporal similarities to brain morphological development enable robust generalization. Verified predictive accuracy and validation with experimental data demonstrate success of the PT approach in resolving the accuracy-performance dilemma, which arises from the multiscale complexities in geometry.

3.1 THE CONCEPT OF PHYSICS TRANSFER TO ADDRESS MORPHOLOGICAL COMPLEXITIES

Brain development involves complex multiscale physics, encompassing gene expression, protein folding, and cellular behaviors such as cell division, differentiation, and migration, as well as macro-

scopic morphological instabilities (Llinares-Benadero & Borrell, 2019). Continuum modeling incorporating growth tensor parameters is widely used to describe the morphological evolution of tissue growth (Tallinen et al., 2016; Striedter et al., 2015; Darayi et al., 2022; Budday & Steinmann, 2018; da Costa Campos et al., 2021; Alenyà et al., 2022). These growth tensor parameters are linked to micro-scale cellular behaviors, providing a multiscale modeling framework for modeling morphological instabilities. However, modeling brain morphological development is challenging due to the geometrical nonlinearity, leading to low computational efficiency and poor convergence in FEA (Tallinen et al., 2016). Consequently, there are limited studies directly modeling brain morphology. Most studies focus on simplified geometries such as 2D shell substrates or 3D spheres and ellipsoids (Darayi et al., 2022; Budday & Steinmann, 2018; da Costa Campos et al., 2021; Wang et al., 2021). Notably, these shapes reflect spatiotemporal characteristics similar to brain morphology, such as ridge-valley networks and bifurcation behaviors.

By designing neural network architectures ($h \in \mathcal{H}$), one can capture the physics of bifurcation and morphological features from simple geometries with low complexity. Models trained on these data, characterized by parameter distributions $p(\theta|\mathcal{D}'_{\mathrm{L}})$, can then be extrapolated to predict brain morphological development with a much more complex geometry.

3.2 Digital libraries from continuum mechanics modeling

We then construct digital libraries of morphological patterns involving spheres, ellipsoids, and human brains with increasing geometrical complexities (Fig. S1). For spheres and ellipsoids with simpler geometries, a representative core-shell model is used (Tallinen et al., 2014; Wang et al., 2021; Xu et al., 2022a; Yin et al., 2008), as implemented to explore the mechanical instability in cortical folding (Tallinen et al., 2016; Striedter et al., 2015; Darayi et al., 2022; Budday & Steinmann, 2018; da Costa Campos et al., 2021; Alenyà et al., 2022). The outer spherical shell represents the cerebral cortex (gray matter), and the inner core for the white matter. The core and shell structures are modeled as modestly compressible hyperelastic Neo-Hookean material with different growth rates (Tallinen et al., 2016). Following experimental evidence (Fischl & Dale, 2000; Chang et al., 2007; Xu et al., 2010; Dervaux & Amar, 2008; Budday et al., 2015), the cortical thickness ranges from $0.03-1.63\ \mathrm{mm}$ according to the abnormal and normal human cerebral cortex measurements and the scale factor (Fischl & Dale, 2000; Chang et al., 2007), and the relative shear modulus ($G_{\mathrm{grey}}/G_{\mathrm{white}}$) ranges from $0.65-1$ (Xu et al., 2010; Dervaux & Amar, 2008; Budday et al., 2015). The tangential growth (TG) model is used to simulate the cellular mechanisms that create the growth stresses and lead to the pattern evolution (Tallinen et al., 2014; 2016; Llinares-Benadero & Borrell, 2019).

3.3 Architecture and Model Setup

In FEA, morphological data are meshed into discretized tetrahedral elements. The representation can be directly translated into graphs, where the nodes correspond to the vertices of the elements, and the edges correspond to the edges of the elements. Graph neural networks (GNN) can then be constructed to extract key features from the graphs. We utilize an encoder-decoder architecture to learn the complexity of morphological development (Fig. S2). The input to the model is a graph representation of the morphology, with node features such as the coordinates and normal directions. The output is the local curvatures. The 3D coordinates of the morphologies and global features such as the gyrification index are used to constrain the model through the loss function.

3.4 Experimental datasets constructed from MRI

We collect experimental data of human brain to validate our PT approach. The data of human brain morphologies are rare, especially for the sequences of individual brain morphologies (Fig. S1) (Bethlehem et al., 2022; Ciceri et al., 2024). We collect high-resolution MRI data of brain anatomy from open-source brain structural atlases (Ciceri et al., 2024), which are then translated to 3D model geometries using a pipeline involving cortical and sub-cortical volume segmentation and cortical surface extraction (Makropoulos et al., 2018).

3.5 RESULTS

We train our models on spherical data, applying them to the morphological development of ellipsoids and human brains. As an ablation study, we removed features related to normal directions, retaining only morphological data. This approach is termed statistical learning since curvatures, which encapsulate the essential physics of bifurcation processes, are pivotal in nonlinear elasticity studies.

Our results demonstrate that for inferring data from spheres, both traditional statistical ML methods and PT can accurately estimate local curvature metrics, calculated as $|H| + |K|$, where H and K represent the mean and Gaussian curvatures, respectively (Fig. 3a). However, when these models, trained on spherical data, are applied to ellipsoids and human brain models obtained from experimental MRI images, PT learning significantly outperforms, while statistical ML does not perform as well (Figs. 3b and 3c). This validation using model ellipsoidal data and experimental brain data underscores the outstanding generalizability provided by the coded physical principles within the network.

Once the model learns the physics of bifurcation and geometrical representations in discrete curvatures, the vertex-ridge network naturally forms (Fig. 4a). From these reduced-dimension representations, metrics can be established to monitor the evolutionary dynamics of brain morphology (Figs. 4b and 4c). Additionally, there is potential to derive the underlying dynamic equations, which we plan to investigate in future work.

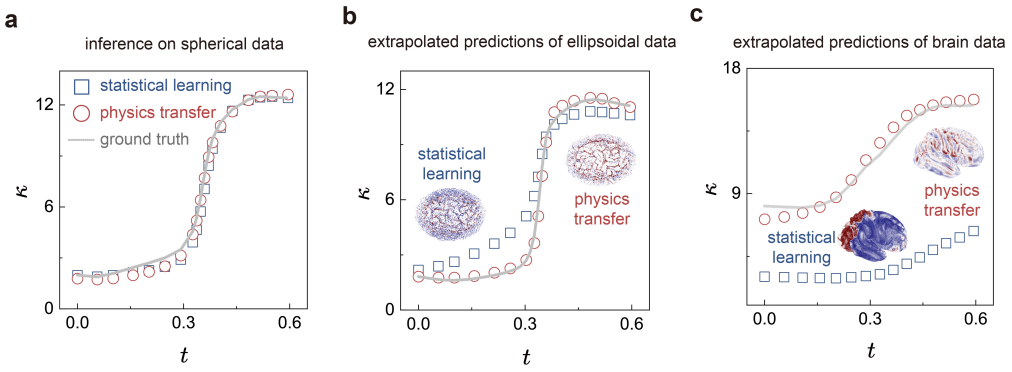

Figure 3: Brain morphology development prediction using the PT approach and statistical learning. **(a)** Interpolative predictions for spherical data. **(b, c)** Extrapolative predictions for ellipsoidal data **(b)** and the development of brain morphologies **(c)**. The insets are colored by the local curvature metrics, $|H|+|K|$, where H and K are the mean and Gaussian curvatures, respectively.

3.6 NEURAL NETWORK ANALYSIS

Our work digitizes the traditional observation-assumption-modeling approach in engineering sciences by employing neural network representations. As ML models learn physics from data, physical features organically emerge within the neural networks (Figs. 5a and 5b). In studying brain morphologies, the ML model employing PT shows a similar weight distribution ($p(\theta|\mathcal{D}_{\mathrm{L}}^{'}) \approx p(\theta|\mathcal{D}_{\mathrm{H}}^{'})$), evaluated through the mean value μ of the neural network weights across different layers, after learning from both spherical and ellipsoidal data (Fig. 5b). Conversely, the ML model based on statistical learning using the morphology data demonstrates a noticeable difference in parameter distribution ($p(\theta|\mathcal{D}_{\mathrm{L}}) \neq p(\theta|\mathcal{D}_{\mathrm{H}})$) as compared to PT learning (Fig. 5a). The consistent features in weight distribution across data with varying complexity reflect the generalizability.

Analyzing neuron activation states helps explain the extrapolation performance of PT learning (Figs. 5c and 5d), aligning with the curvature mapping in (Fig. 3c). For models trained on spherical data, PT models show neuron activation patterns similar to those for brain morphology data (Fig. 5d). In

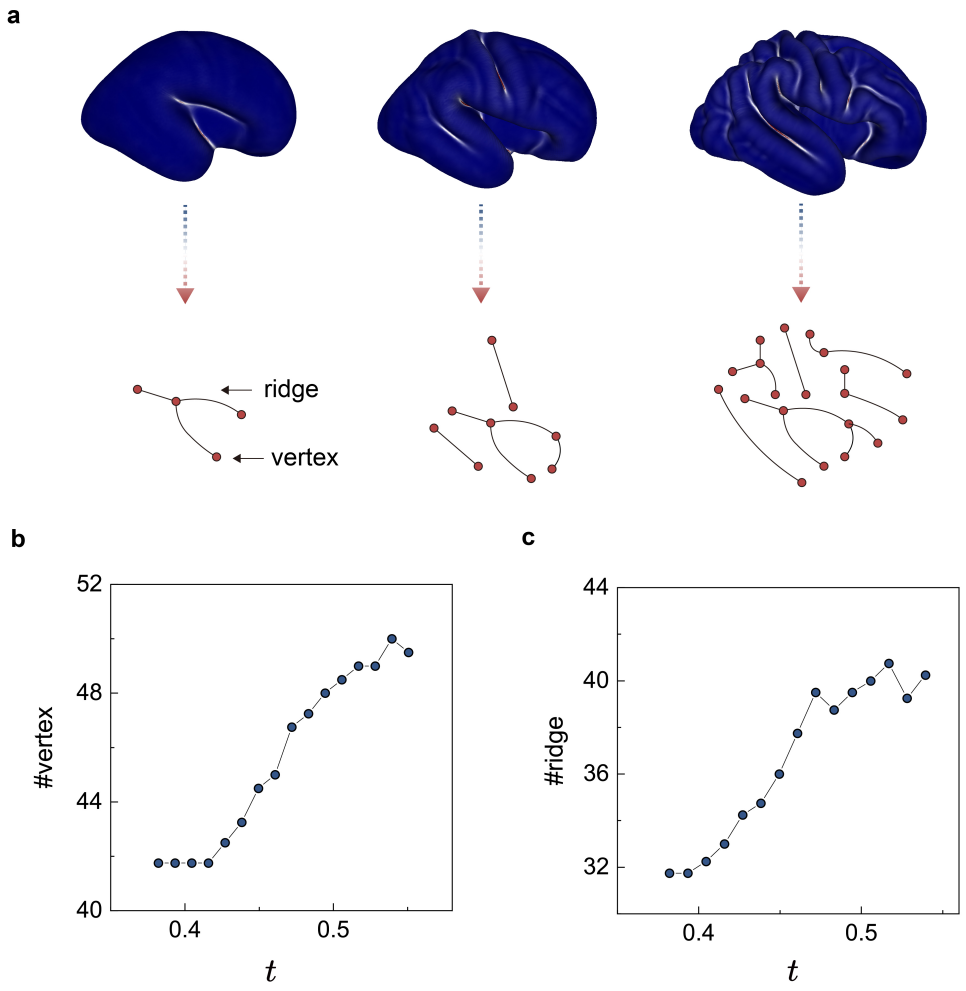

Figure 4: Dimension-reduction representation of brain morphological development. **(a)** The vertex-ridge network emerging from the machine learning (ML) model. **(b, c)** Dimension-reduction metrics used to track the evolutionary dynamics in brain morphological development, which include the number of the vertices **(b)** and the number of ridges **(c)**.

contrast, the activation patterns of statistical learning models differ significantly between spherical and brain data (Fig. 5c).

3.7 Discussion

The deformation physics in the digital library stems from prior investigations into the constitutive relationships in brain morphological development. However, these relationships come with complexity and uncertainty (Darayi et al., 2022). Our framework stands to benefit from a deeper understanding of brain constitutive relationships. Further advances in theoretical, experimental, and ML-based constitutive models could enhance the accuracy of deformation physics descriptions (Linka et al., 2023). Similarly, the concept extends to the growth factor that is directly associated with biomolecular kinetics (Darayi et al., 2022; Llinares-Benadero & Borrell, 2019). By extending current work through data at the intersection of first-principles simulations and constitutive modeling, we might complete our understanding of the multiscale complexity in brain morphology development.

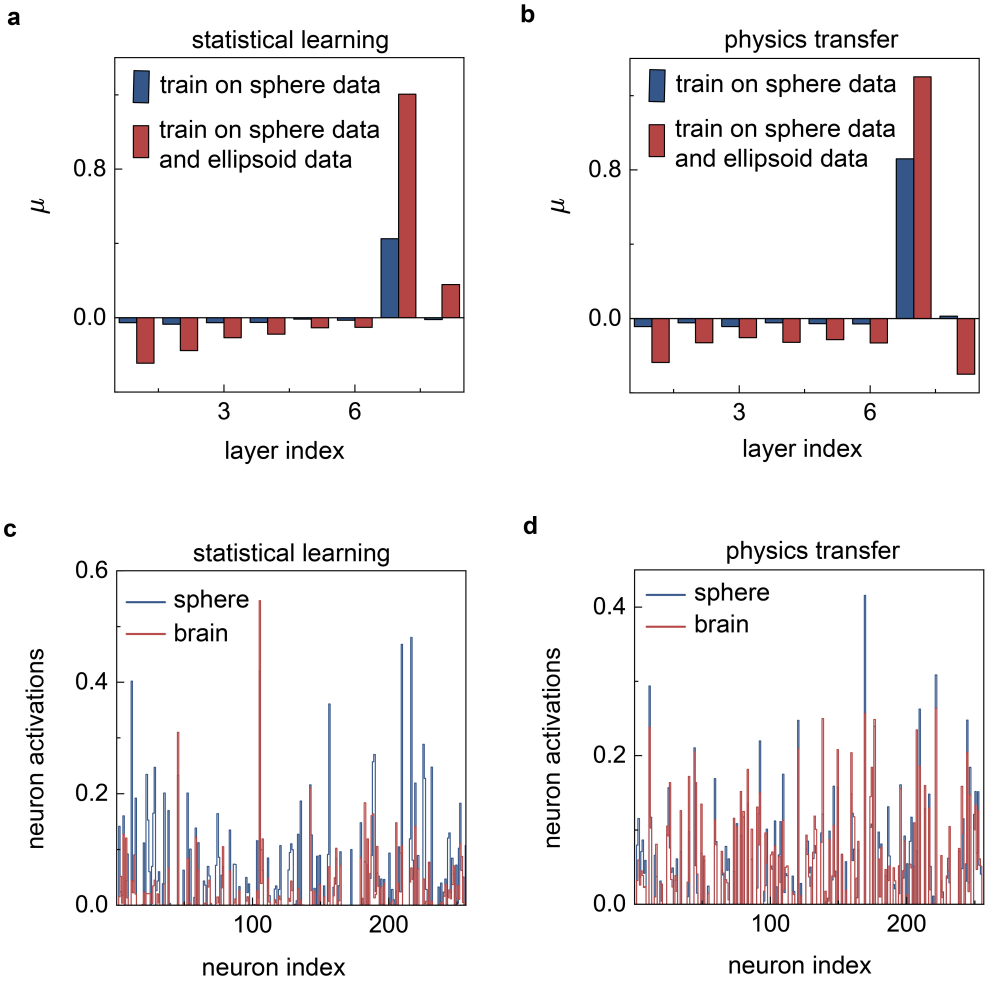

Figure 5: Analysis of neural network structures. **(a, b)** Weights parameters distribution of ML models trained on the spherical and ellipsoidal data for statistical learning **(a)** and PT learning **(b)**. **(c, d)** Neuron activations of the ML models trained on spherical data, when inference on both spherical and brain data for statistical learning **(c)** and PT learning **(d)**.

Nevertheless, the ability of the PT approach to model physics is constrained by the accuracy of digital libraries, which rely on the thoroughness of theoretical models and experimental data. To improve predictions of human brain morphologies, the scarcity of MRI data can be addressed by utilizing results from ongoing projects like the Developing Human Connectome Project (dHCP) (Makropoulos et al., 2018), or by incorporating animal data.

4 Related Work

Our PT framework shares similar concepts found in existing ML methods for combining multi-fidelity data (Ramakrishnan et al., 2015; Batra et al., 2019; Smith et al., 2019). Δ-learning aims to predict high-fidelity properties by assessing discrepancies between model predictions at various fidelity levels (Ramakrishnan et al., 2015). Objective properties are achieved by statistically correcting low-fidelity computations. Similarly, the low-fidelity as a feature (LFAF) method determines relations between properties from models of different fidelities. It predicts high-fidelity properties using objective properties and input parameters derived from low-fidelity models (Batra et al., 2019).

In transfer learning, neural networks are initially trained with low-fidelity data. Subsequently, the parameters are fine-tuned using high-fidelity data to ensure accurate predictions (Smith et al., 2019). However, these methods are statistical in nature and do not convey the physics carried by the data.

On the other hand, supervised learning requires labeling data from high-fidelity models during training, which is not always feasible. The scarcity of longitudinal MRI data of brains limits the application of traditional statistical learning methods for direct prediction of the development of human brain morphologies (Bethlehem et al., 2022; Ciceri et al., 2024). Our PT framework resolves this constraint from the accuracy-performance dilemma by going beyond the statistical approach and transferring the physics across models with different geometrical complexties.

ACKNOWLEDGMENTS

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APPENDIX

CONTINUUM MECHANICS MODELING FOR BRAIN MORPHOLOGY DEVELOPMENT

Brain development is regulated by genetic, molecular, cellular, and mechanical factors across multiple spatiotemporal scales (Klingler et al., 2021; Llinares-Benadero & Borrell, 2019), and the differential tangential growth hypothesis is commonly used (Tallinen et al., 2016; Klingler et al., 2021; Llinares-Benadero & Borrell, 2019). FEA can model morphological evolution during brain growth at the continuum level (Tallinen et al., 2016; 2014; Darayi et al., 2022; Budday & Steinmann, 2018; Wang et al., 2021). The tangential growth (TG) of the outer gray matter is faster than the inner white matter, known as the TG model (Tallinen et al., 2016). Compression resulting from the mismatch in deformation may then lead to mechanical instabilities of the brain surface, forming characteristic sulci and gyri structures (Tallinen et al., 2014; 2016; Striedter et al., 2015; Darayi et al., 2022; Wang et al., 2021; Budday & Steinmann, 2018; da Costa Campos et al., 2021).

In continuum modeling, the reference configuration can be mapped to the current one through the deformation gradient tensor as

$$\mathbf{F} = \mathbf{F}^{\mathrm{e}} \cdot \mathbf{G}, \tag{5}$$

where $\mathbf{F}^{\mathrm{e}}$ is the elastic deformation gradient and $\mathbf{G}$ is the growth term. In the TG model, the growth tensor $\mathbf{G}$ is

$$\mathbf{G} = g\mathbf{I} + (1-g)\hat{\mathbf{n}} \otimes \hat{\mathbf{n}}, \tag{6}$$

where $\hat{\mathbf{n}}$ is the surface normal of the reference configuration, $\mathbf{I}$ is the unit tensor, and

$$g = 1 + \frac{\alpha_t}{1 + e^{10(\frac{y}{T}-1)}} \tag{7}$$

is the growth coefficient, where α_t controls the magnitude of local cortical expansion. There is a smooth transition from the surface of the gray matter layer to the white matter layer with a gradually decreasing growth coefficient. y is the distance to the surface, and T is the thickness of the cortex. The brain is modeled as a nonlinear neo-Hookean hyperelastic material, where the strain energy density is

$$W = \frac{G}{2}[\mathrm{Tr}(\mathbf{F}^{\mathrm{e}}\mathbf{F}^{\mathrm{e}\mathrm{T}})J^{-2/3} - 3] + \frac{K}{2}(J-1)^2, \tag{8}$$

where G is the shear modulus, J is the determinant of Jacobian matrix, K is the bulk modulus.

For brain growth, a core-shell structure with a spherical geometry is used for its simplicity. The outer radius is 10 mm and the shell thickness ranges from 0.03 to 1.63 mm, which are determined from the measurements of abnormal and normal human cerebral cortices (Fischl & Dale, 2000; Wang et al., 2021). 4-node tetrahedral elements with a density of 10^6 tetrahedra/cm^3 for discretization with the convergence confirmed (Tallinen et al., 2016; Wang et al., 2021). The morphogenesis of brains is triggered by internal elastic stresses generated from differential core-shell growth. The interaction between surfaces is modeled with an energy penalty via vertex-triangle contact, which prevents the nodes from penetrating the faces of elements (Ericson, 2004). An explicit solver is used to minimize the total (elastic and contact) energy of the quasi-static system. The time step $\Delta t = 0.05a\sqrt{\rho/K}$ is set to ensure the convergence, where a is mesh size and ρ is mass density (Belytschko et al., 2014).

Assigning material models and parameters to brain tissue regions is challenging due to intra-regional variability and differences across individual brains. Additionally, properties change with development or aging. The alternative approach taken here, which is the current state of the art, involves assigning 'typical' properties for a tissue type and age, using experimental data that closely approximate the specific loading conditions. The bulk modulus of the core and shell is 5 times the shear modulus (Tallinen et al., 2016). Following the experimental evidence, the relative shear modulus ($G_{\mathrm{shell}}/G_{\mathrm{core}}$) ranges from 0.65 to 1 (Budday et al., 2015).

SUPPLEMENTARY FIGURES AND FIGURE CAPTIONS

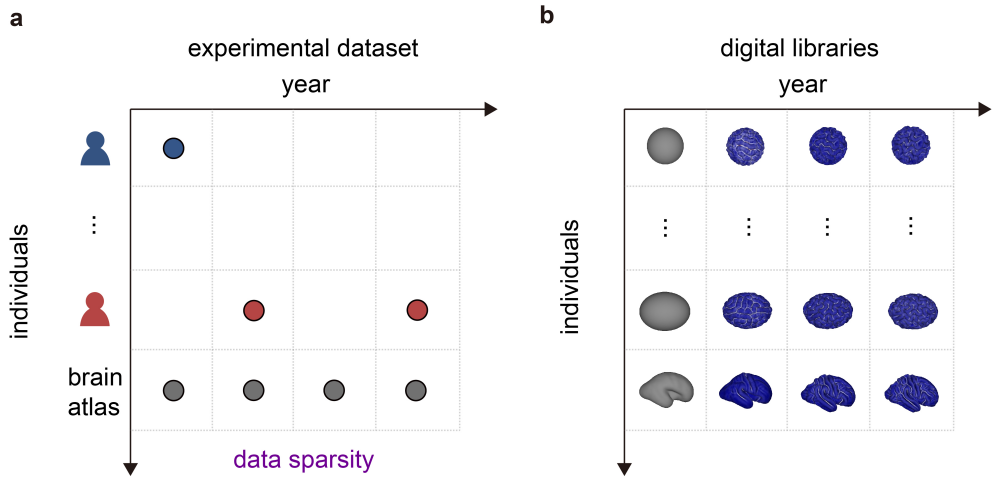

Figure S1: Experimental magnetic resonance imaging (MRI) datasets and finite element analysis (FEA) digital libraries of brain morphological development. **(a)** Experimental datasets collected from the literature (Ciceri et al., 2024). **(b)** Digital libraries constructed from our FEA.

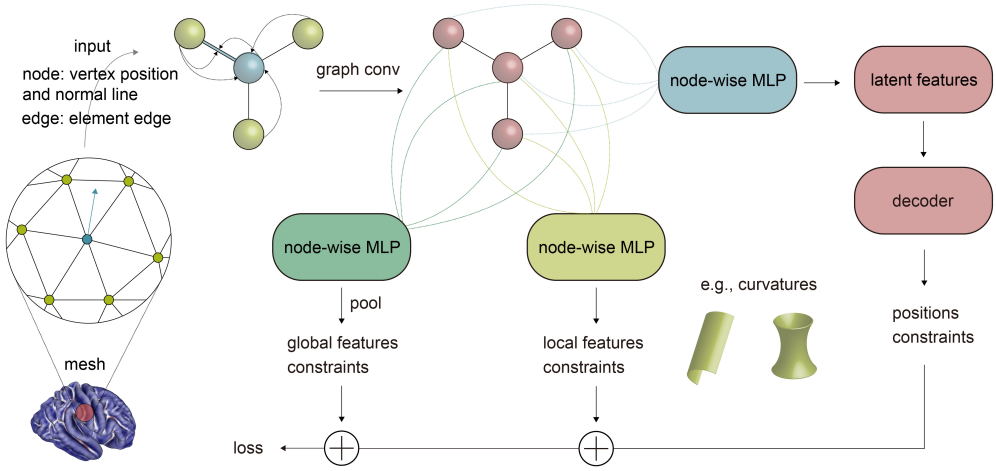

Figure S2: The neural network architecture. An encoder-decoder architecture is employed to capture the complexity of morphological development. The model takes as input a graph representation of the morphology, where node features include coordinates and normal directions. The output is local curvatures. Additionally, the 3D coordinates of the morphologies and global features, such as the gyrification index, are incorporated into the loss function to constrain the model.