POLYTECHNIQUE MONTRÉAL

A New Diffusion MRI Model for Brain Developmental Assessment and Injury Characterization

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Developer of the Diffusion Bubble Model (DBM)

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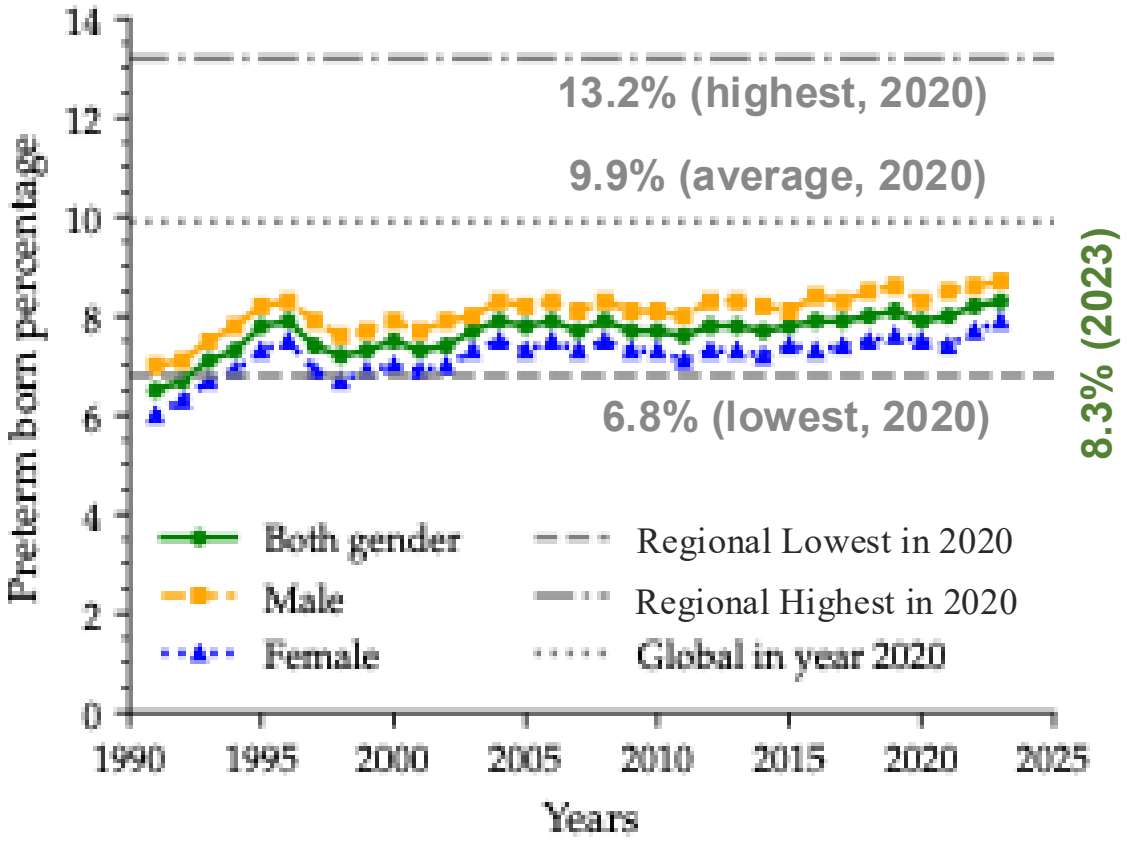
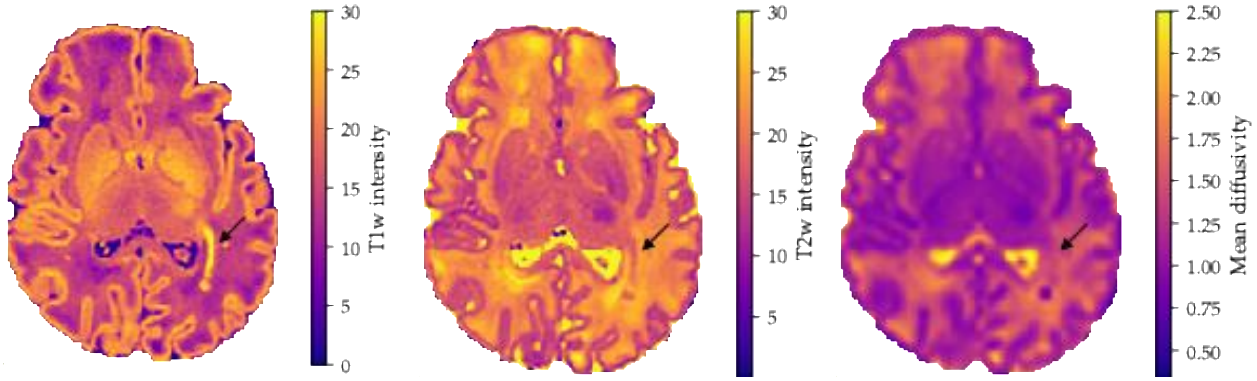
Introduction (Preterm birth & PWML)

Preterm birth rate in Canada



Preterm Births & Punctate white matter lesion (PWML)

- Preterm born: < 37 weeks of gestational age [1]
- Cases: 29.2 *k* (8.3% of total 0.35 M) [2]
- PWML definition: Small, non-cystic foci lesions in WM [3]
- Incidence: 18-35% in preterm [3]
- Outcomes: motor, cognitive deficits, behavioral problems



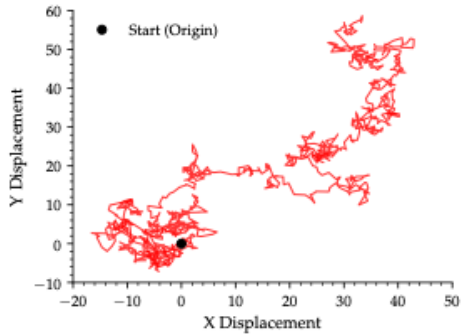
Challenge: heterogeneous appearance of a punctate white matter lesion (PWML) in medical images

1. **Healthy birth**: 37 to 42 weeks; **Preterm birth**: before 37 weeks; 2. **Data sources:** *Statistics Canada (1990–2023) and Ohuma et al., 2024 (global benchmarks).* **Figure generated from source data by the presenter.** 3. de-Bruijn2023-oe

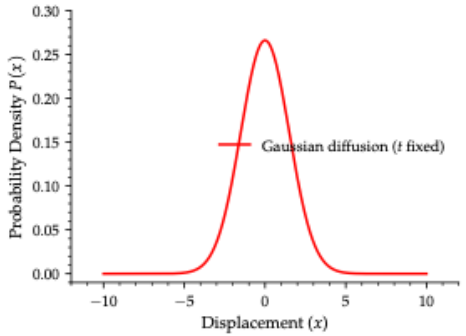
Diffusion Tensor Imaging

From water molecular thermal motion to DTI

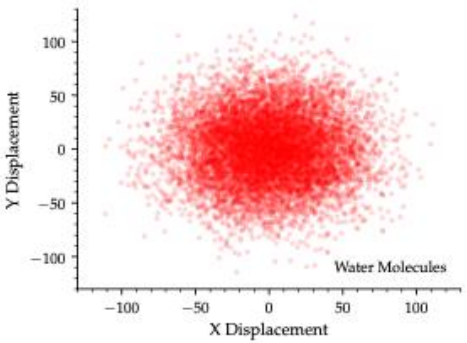
Free water molecular thermal motion



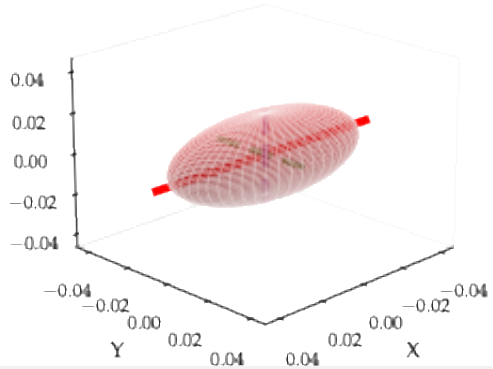
Free diffusion path



Gaussian diffusion profile

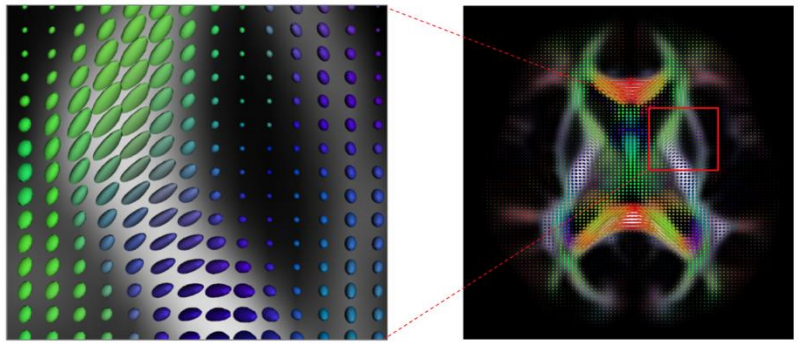


Water position cloud

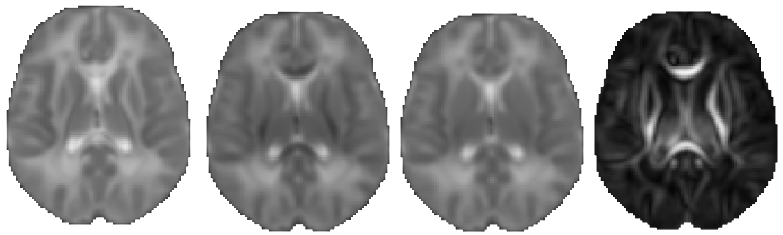


Gaussian diffusion ellipsoid

Diffusion Tensor Imaging

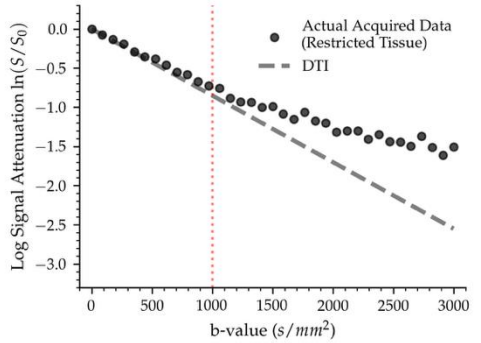


Tensor map (zoom-in and out)

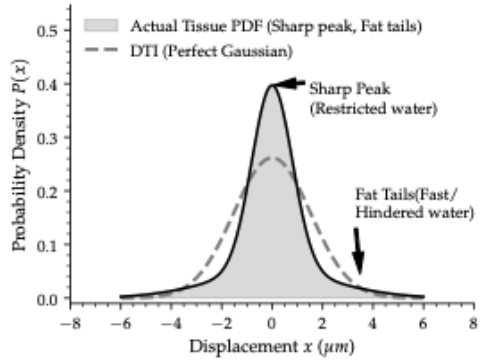


Metric maps derived from DTI [1]

DTI Problems



Actual data vs. DTI



Actual PDF vs. DTI PDF

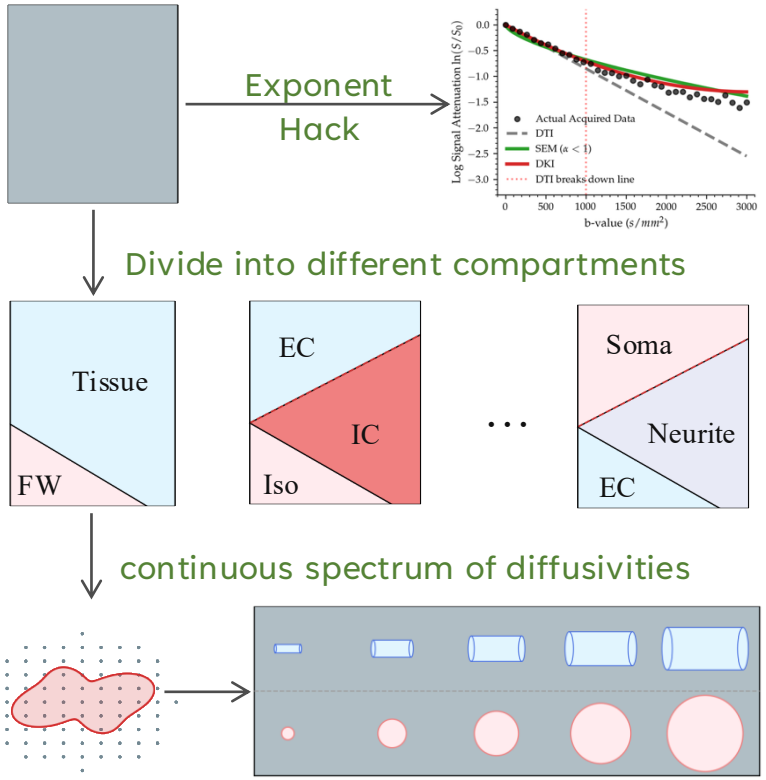
DTI

- DTI assumes one diffusion tensor (ellipsoid) in each voxel
- It is simple and stable

[1] Created based on infant template (created by author) with gestational age 37 weeks

Diffusion MRI Models

From DTI to statistical, compartment, and spectrum-based models

Names	Equations	Improvement	Type
DTI Pierpaoli (1996)	$e^{-b_k \mathbf{g_k^T D g_k}}$		Statistical
SEM Bennett (2003)	$e^{-(b\times DDC)^{\alpha}}$		
DKI Jensen (2003)	$e^{-b\sum_{i,j=1}^{3} D_{ij}g_ig_j+\frac{1}{6}b^2D_{\text{avg}}^2\sum_{i,j,k,l=1}^{3} W_{ijkl}g_ig_jg_kg_l}$		
FWE White (2013)	$(1-f_{\text{iso}})e^{-b_k \mathbf{g_k^T D g_k}}+f_{\text{iso}}e^{-b_k D_{\text{iso}}}$		Compartment
NODDI Zhang (2012)	$f_{\text{ic}}\cdot e^{-bD_{\text{ic}}(\theta\cdot\mathbf{n})^2}\cdot \text{Watson}(\kappa)+f_{\text{ec}}\cdot e^{-bD_{\text{ec}}}+f_{\text{iso}}\cdot e^{-bD_{\text{iso}}}$		
SANDI Palom. (2020)	$f_{\text{neurite}}\cdot e^{-b_{\text{neurite}}}+f_{\text{soma}}\cdot\left(\frac{\sin(qa)}{qa}\right)^2+f_{\text{ec}}\cdot e^{-bD_{\text{ec}}}$		
DSI Wedeen (2005)	$S(q,\Delta)=\int P(\mathbf{R},\Delta)e^{-2\pi\mathbf{q}\cdot\mathbf{R}}d^3\mathbf{R}$		Spectrum
DBSI Wang (2011)	$\int_a^b f(D)e^{-\lvert b_k\rvert D}dD+\sum_{i=1}^{N_{Ani}} f_i e^{-\lvert\vec{b}_k\rvert\lambda_{\perp i}}e^{-\lvert b_k\rvert(\lambda_{\parallel i}-\lambda_{\perp i})\cdot\cos^2\psi_{ik}}$		
RSI White (2013)	$\sum_{i=1}^{M} f_{D_i}e^{-bD_i}$		

Spectrum-based model

- **Definition:** Spectrum-based models extend multi-compartmentalization into a mathematical continuum or a densely sampled discrete set of basis functions—ordered by diffusivity or restriction scale
- Dimensionality Reduction: From Unconstrained 3D ODF to 1D Ordered Basis Spectrum

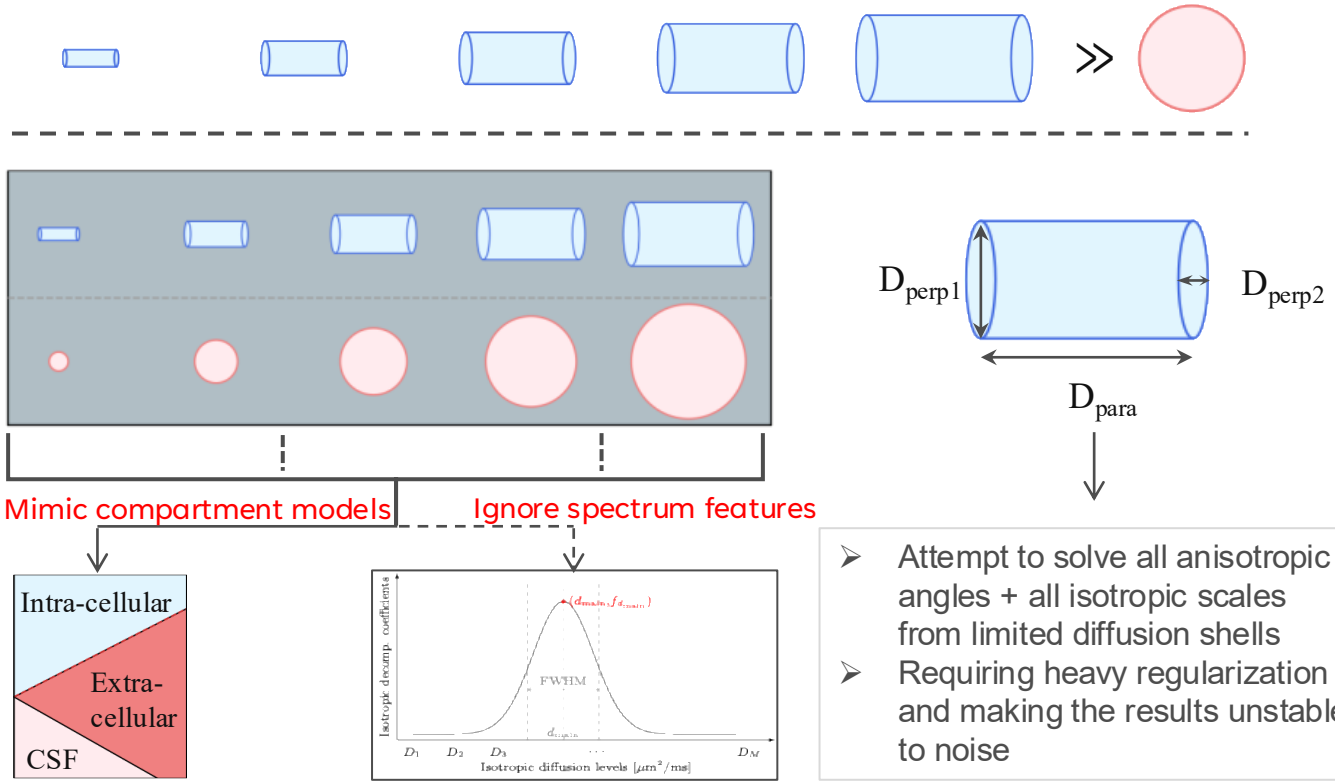
[1] ODF: Orientation Distribution Function

Spectrum-Based Models: Gaps and Solutions

Three Critical Gaps of spectrum model

1. Anisotropic Bias

Over-allocate mathematical bandwidth to resolving anisotropic fibers

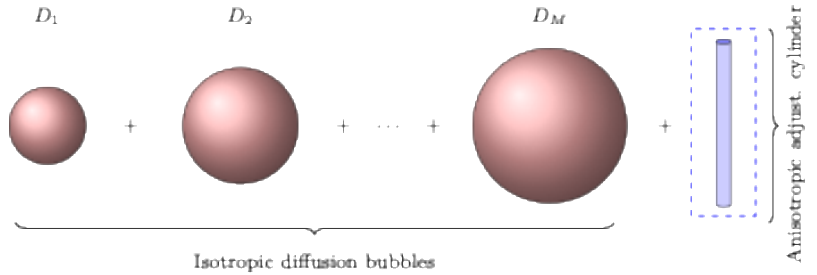


2. Discretization Trap

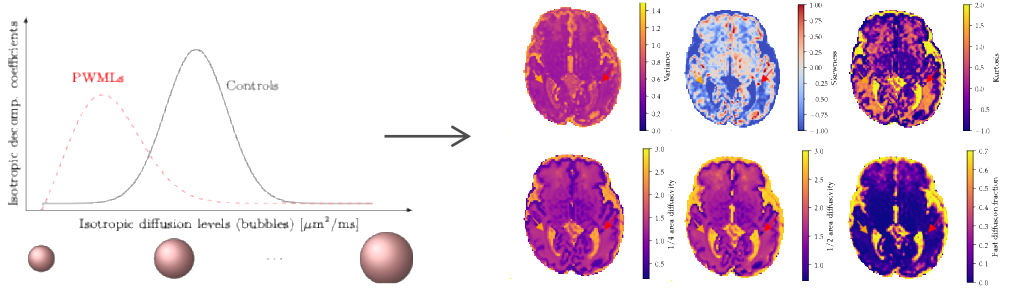
- Attempt to solve all anisotropic angles + all isotropic scales from limited diffusion shells
- Requiring heavy regularization and making the results unstable to noise

3. Ill-Posed "Universal Solver"

Our Diffusion Bubble Model



$$S_k/S_0 = \sum_{i=1}^{M} f_{D_i} e^{-b_k \mathbf{g_k^T D_i g_k}} + \sum_{j=1}^{N} f_{D_j} e^{-b_k \mathbf{g_k^T D_j g_k}} + \epsilon_k$$



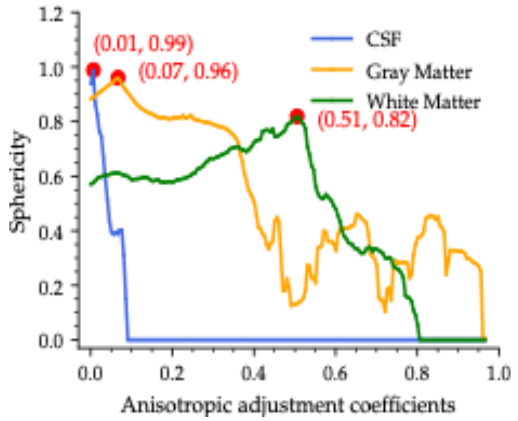
From diffusion spectrum curve to metric maps

[1] Zhang2025-va

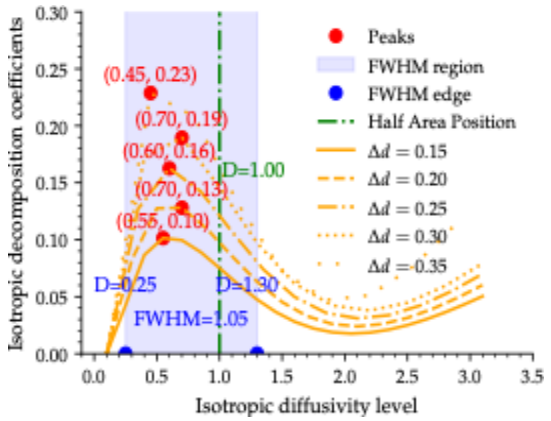
Algorithms of DBM

Algorithm 1 (DBM): A Two-Step Heuristic Decomposition

Step 1: Anisotropy adjustment

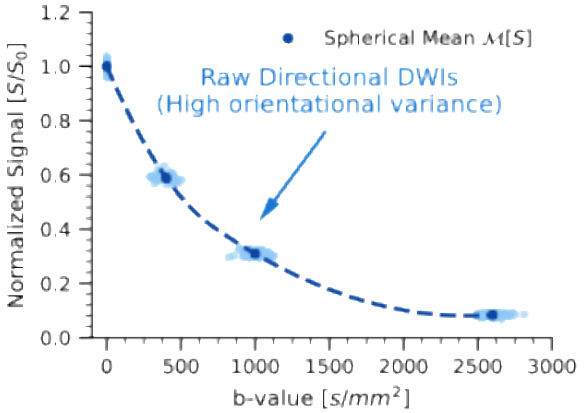


Step 2: Spectrum fitting (NNLS)

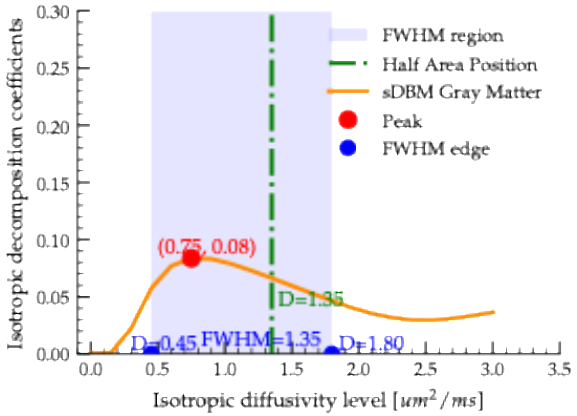


Algorithm 2 (sDBM): An Analytical Spherical Mean Solver

Step 1: Spherical mean



Step 2: Spectrum fitting (ElasticNet Inversion)



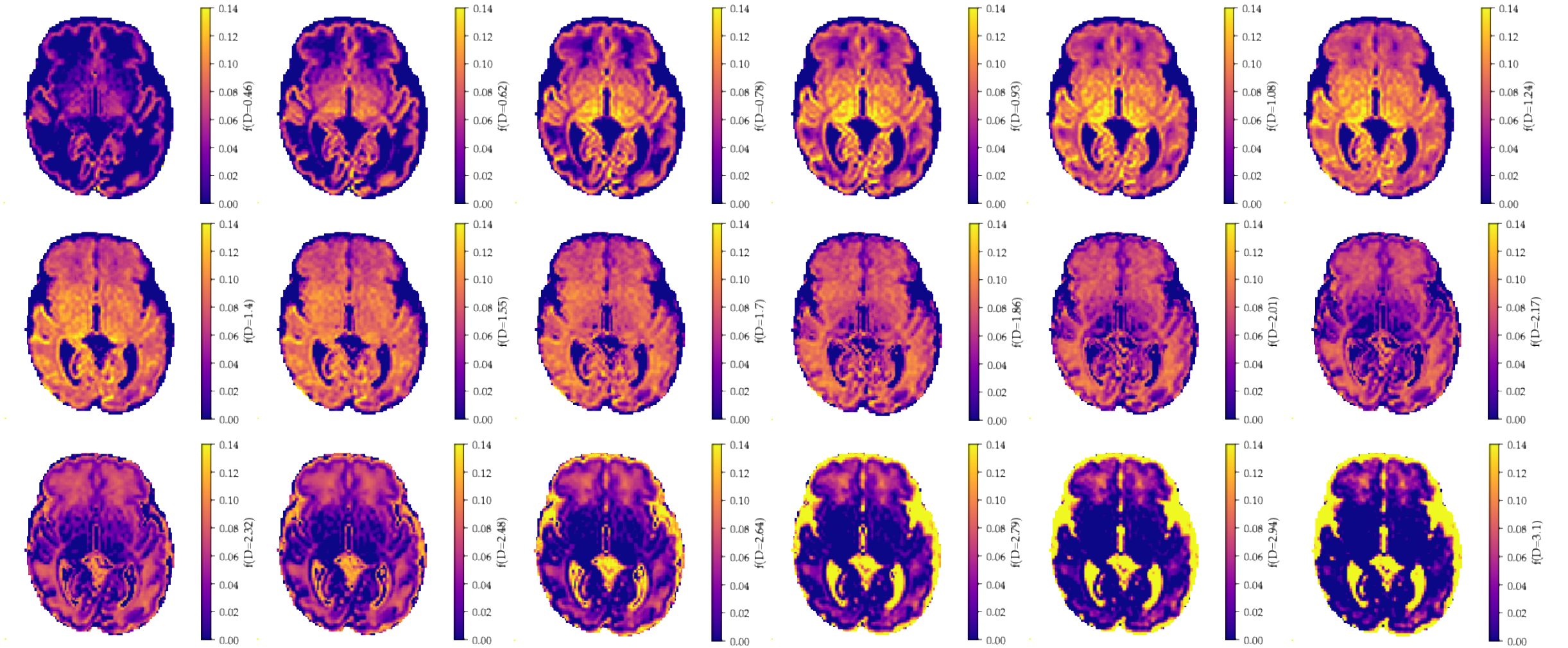
	Non-shell (DWI) data	**Multi-shell (DWI) data**
Goal	Isolate orientation dependence to reconstruct isotropic spectrum	Analytically extract isotropic spectrum from sparse clinical data
Prior	Fixed healthy cylinder & smooth continuous bubbles	
Method	Heuristic iterative search + followed by NNLS	Spherical mean decoupling + Elastic Net inversion
Output	A continuous isotropic spectrum	

Two paths, one spectral philosophy: Adapting the mathematical engine to the acquisition domain (Dense DSI vs. Sparse Multi-shell)

[1] source data: gray matter in slice 31 of a neonatal DWIs (sub-CC00147XX16, ses-48500)

Spatial Decoding of the Continuous Spectrum

From cortex to white matter transition

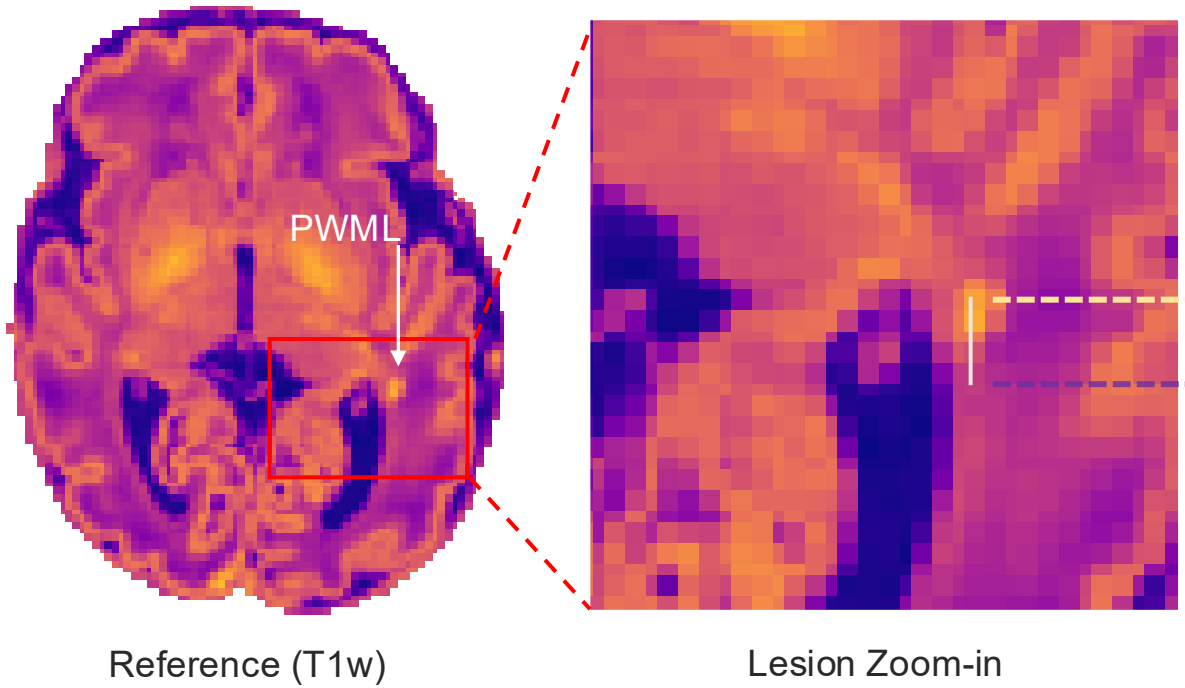


From white matter to CSF transition

[1] source data: gray matter in slice 31 of a neonatal DWIs (sub-CC00147XX16, ses-48500)

Mapping pathological gradient: from edge to core

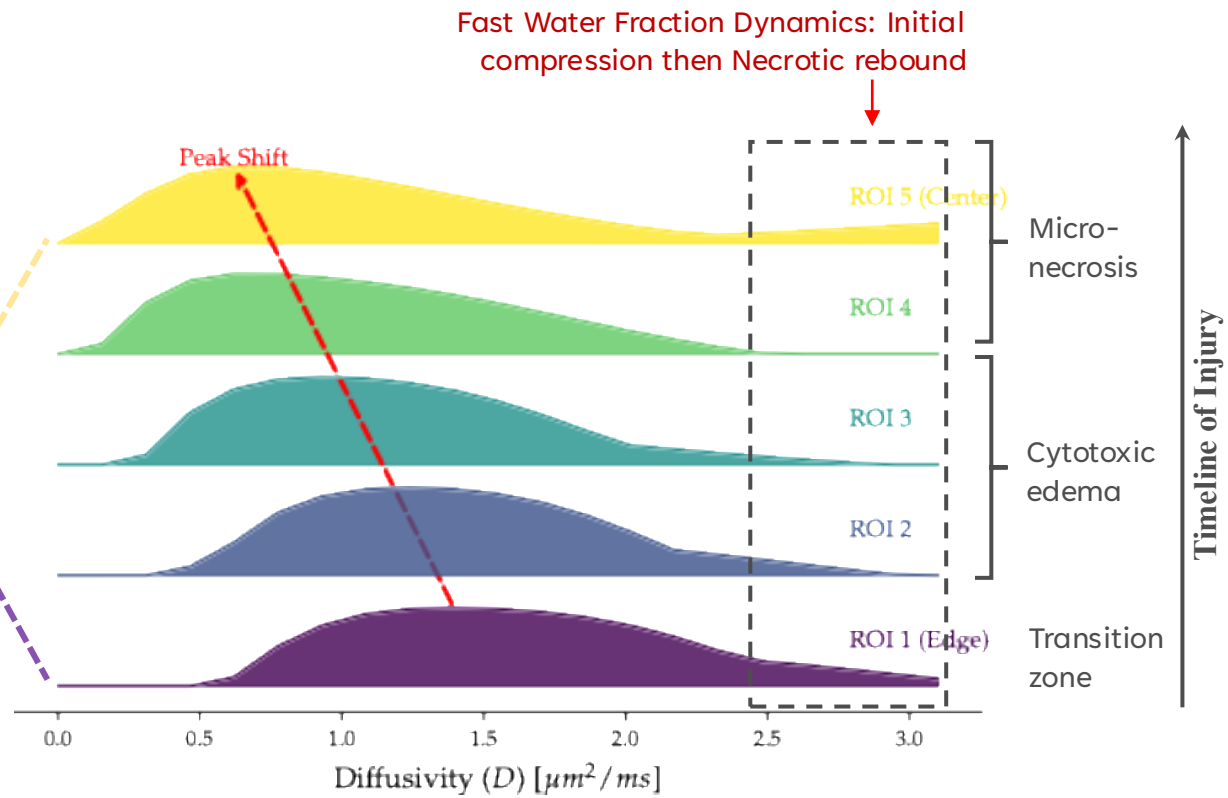
Anatomical Localization (PWML on right optic radiation)



Reference (T1w)

Lesion Zoom-in

Spectral Evolution (apply DBM to 3-shell dMRI data)

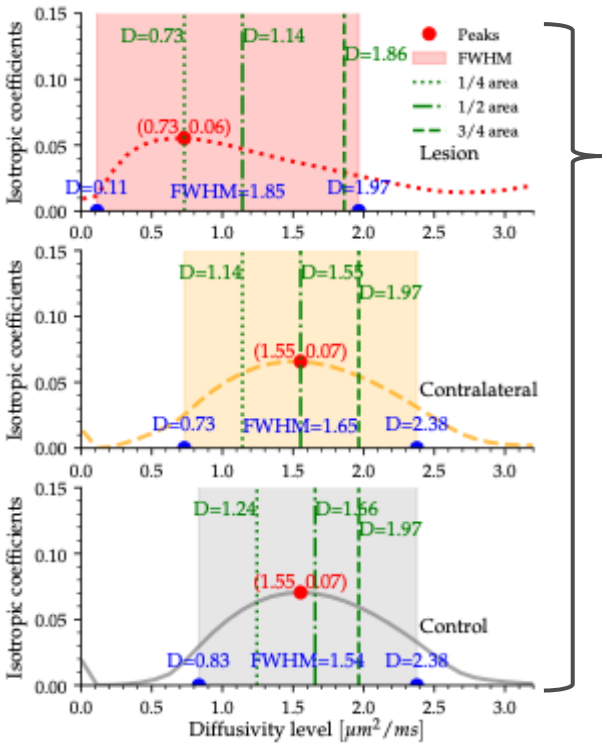


The continuous spectrum captures the pathological gradient: from restricted cytotoxic swelling to heterogeneous micro-necrosis.

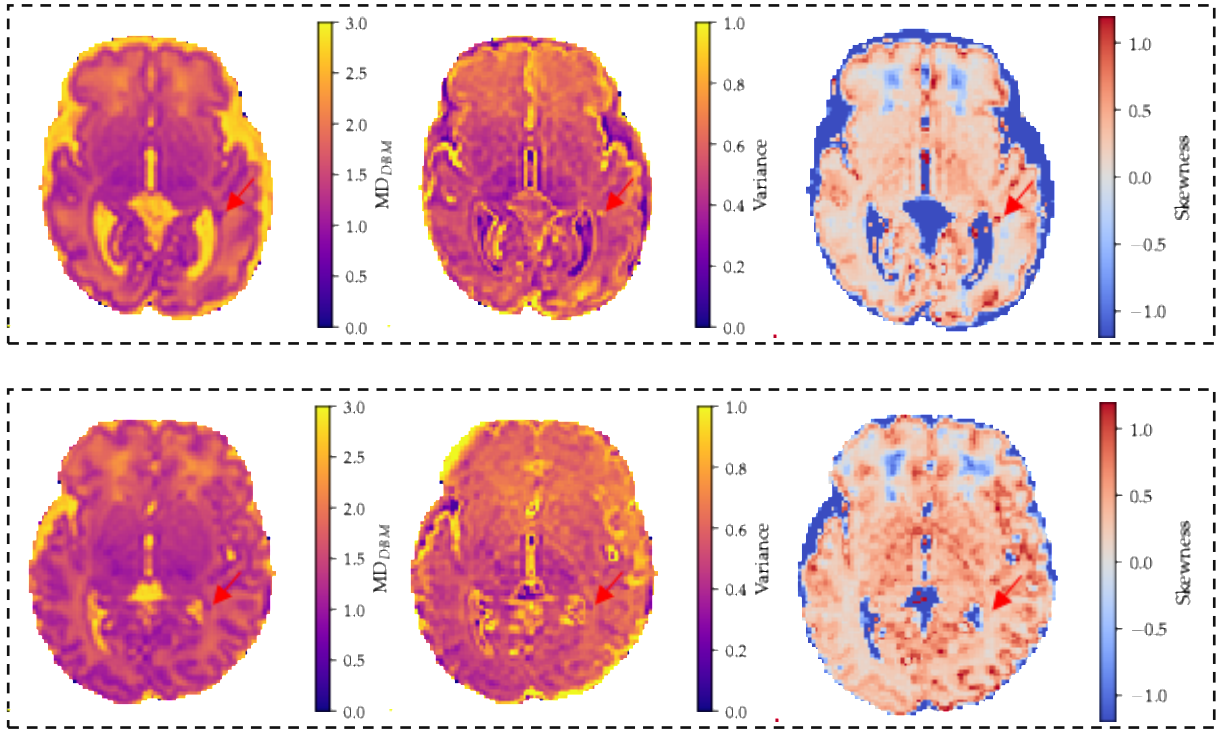
* Subject: 35 weeks GA, Neonate; 3-shell clinical dMRI (b=400, 1000, 2600 s/mm^2)

In Vivo Detection and Subtyping of Neonatal PWML

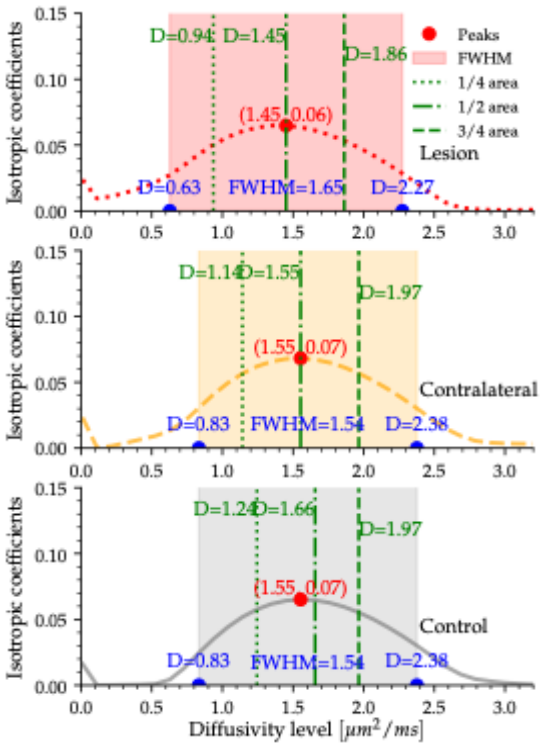
Type I (Necrotic): Wet-type



Derived Metric Maps From DBM



Type II (cytotoxic): Dry-type



Biophysical Phenotypes

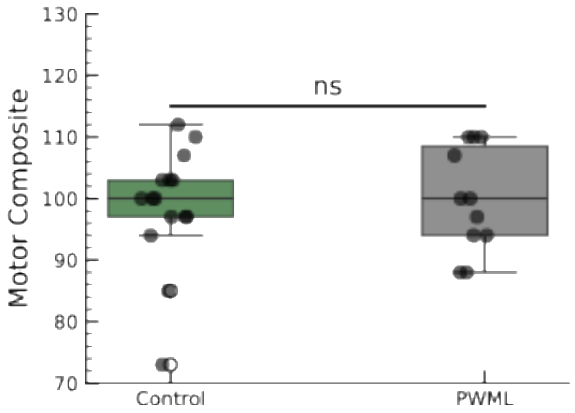
- **Type I (Wet):** Cytotoxic swelling followed by focal necrosis (Left-shift + Fast-water rebound)
- **Type II (Dry):** Pure cytotoxic swelling without membrane rupture (Left-shift only)

[1] Zhang et al., NeuroImage (2025); Cohort: 20 Neonates with unilateral optic radiation PWML vs. 20 Matched dHCP Controls (Age & Sex matched)

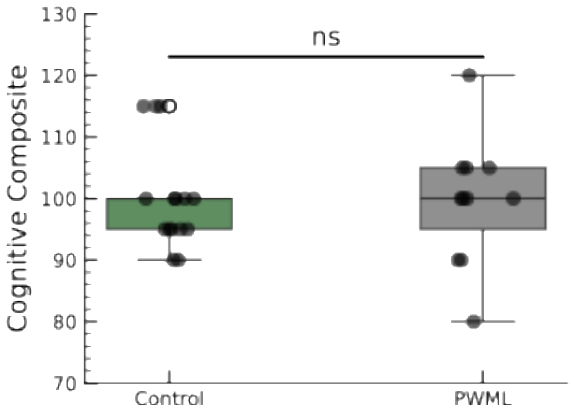
Prognostic Value: Subtyping Unmasks Hidden Neurodevelopmental Deficits

Conventional Grouping (All PWMLs)

No significant deviations from healthy controls



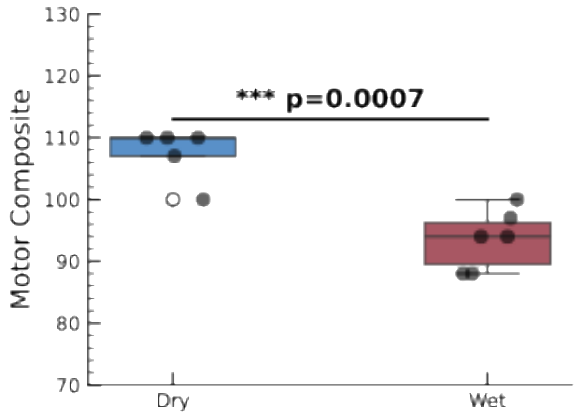
Baseline Motor



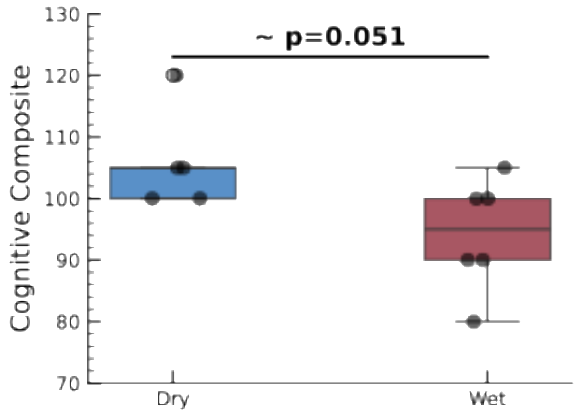
Baseline Cognitive

DBM Stratification (Microstructural Phenotypes)

The 'Wet' (necrotic) phenotype specifically drives severe developmental delays



DBM Motor (Dry vs Wet)



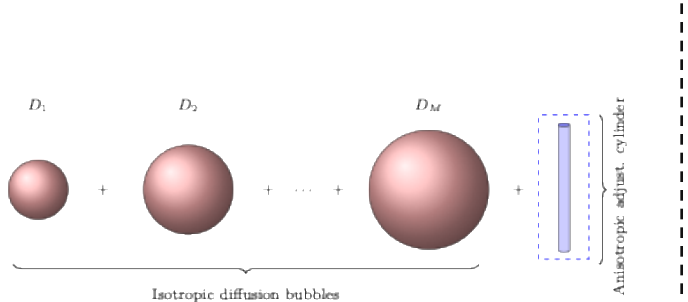
DBM Cognitive (Dry vs Wet)

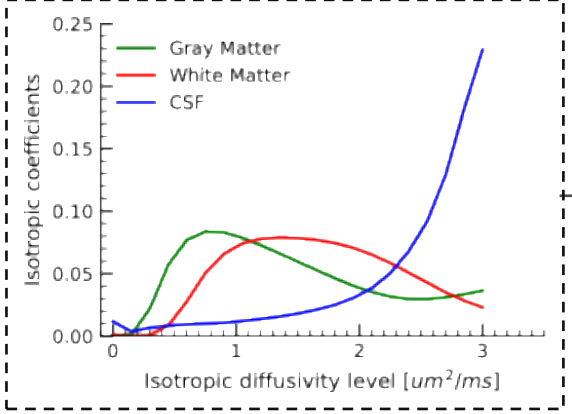
Clinical Impact	➢ **Beyond detection: DBM subtyping transforms a silent, non-specific MRI finding into a highly sensitive predictor of long-term neurodevelopment.**

[1] Longitudinal cases with evolving pathology were assigned the phenotype at maximum scan age to prevent subject duplication (Wet n=6, Dry n=5)

Summary and Future Work

Summary

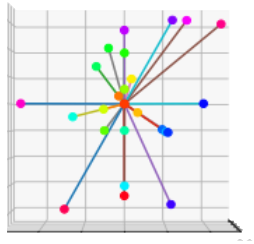




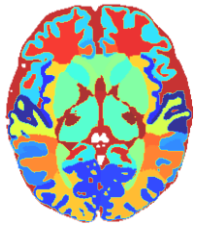
- **Methodological Innovation**: Developed the DBM, a robust continuous spectral solver capable of blind microstructural parcellation without prior anatomical assumptions
- **Pathological Discovery**: Discovered and biophysically defined two distinct PWML phenotypes ("Wet" necrotic vs. "Dry" edematous) previously masked in conventional MRI
- **Clinical Translation**: Demonstrated that spectral subtyping effectively predicts long-term motor and cognitive developmental trajectories

Future work

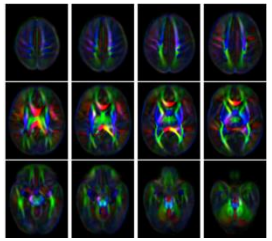
Algorithmic Evolution & Target-Specific Modeling



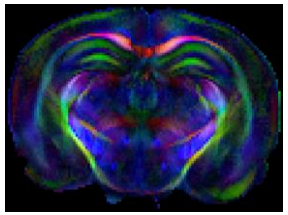
Tissue and lesion segmentation



4D Fetal-to-Neonatal Spatiotemporal Atlas



Translational Expansion Beyond the Brain



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