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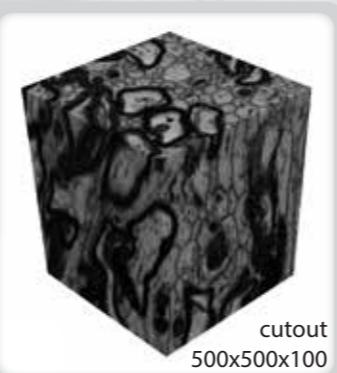
BACKGROUND

- The application of microstructure techniques in diffusion imaging (e.g. axon diameter¹ and membrane permeability estimation²) are often validated using Monte Carlo simulations.
- The geometric substrates are usually highly simplified cylindrical models that have a limited number of compartments.

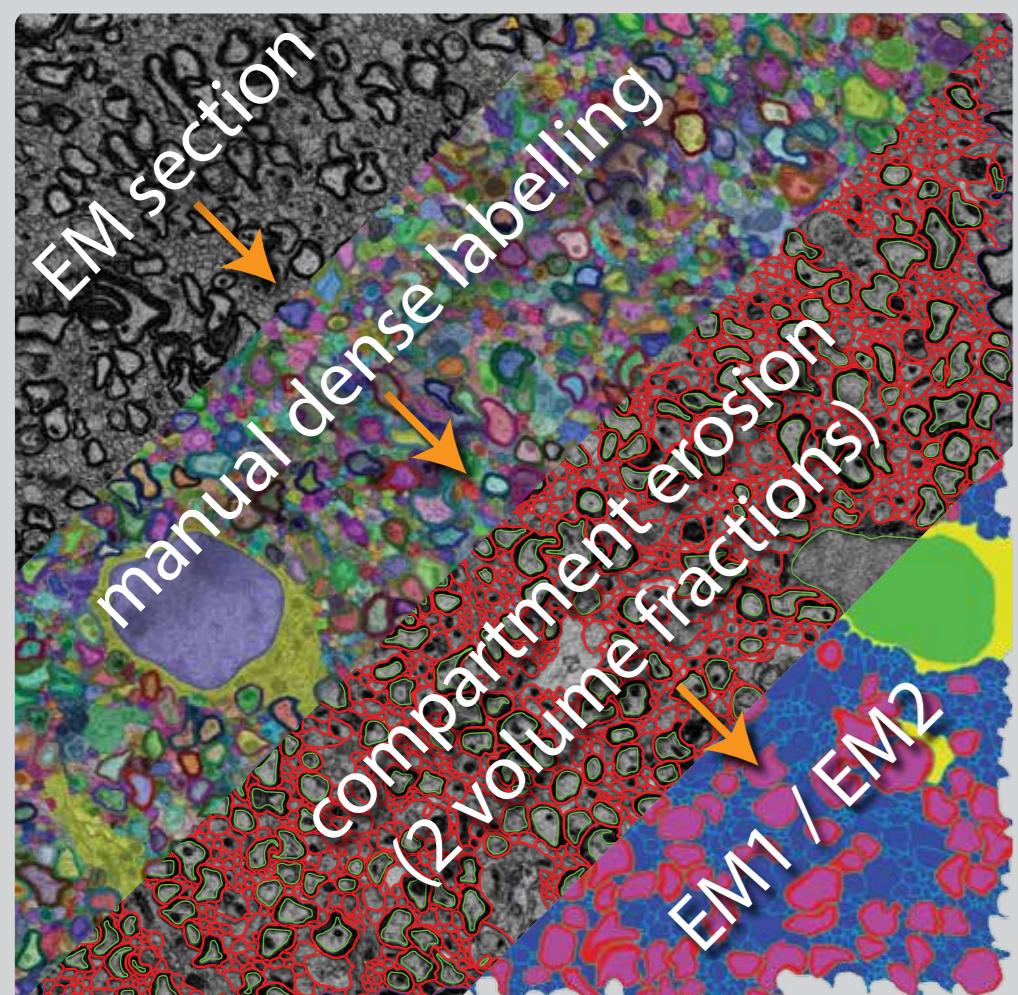
This work explores more realistic geometry derived from electron microscopy (EM) and aims to showcase how the influence of shape and compartments on the diffusion signal can be investigated.

REALISTIC GEOMETRY FROM ELECTRON MICROSCOPY

- serial blockface scanning EM (Zeiss SEM+Gatan 3View)
- matrix: 4000x4000x469; FOV: 29.2x29.2x23.5 μm
- mouse corpus callosum (genu)

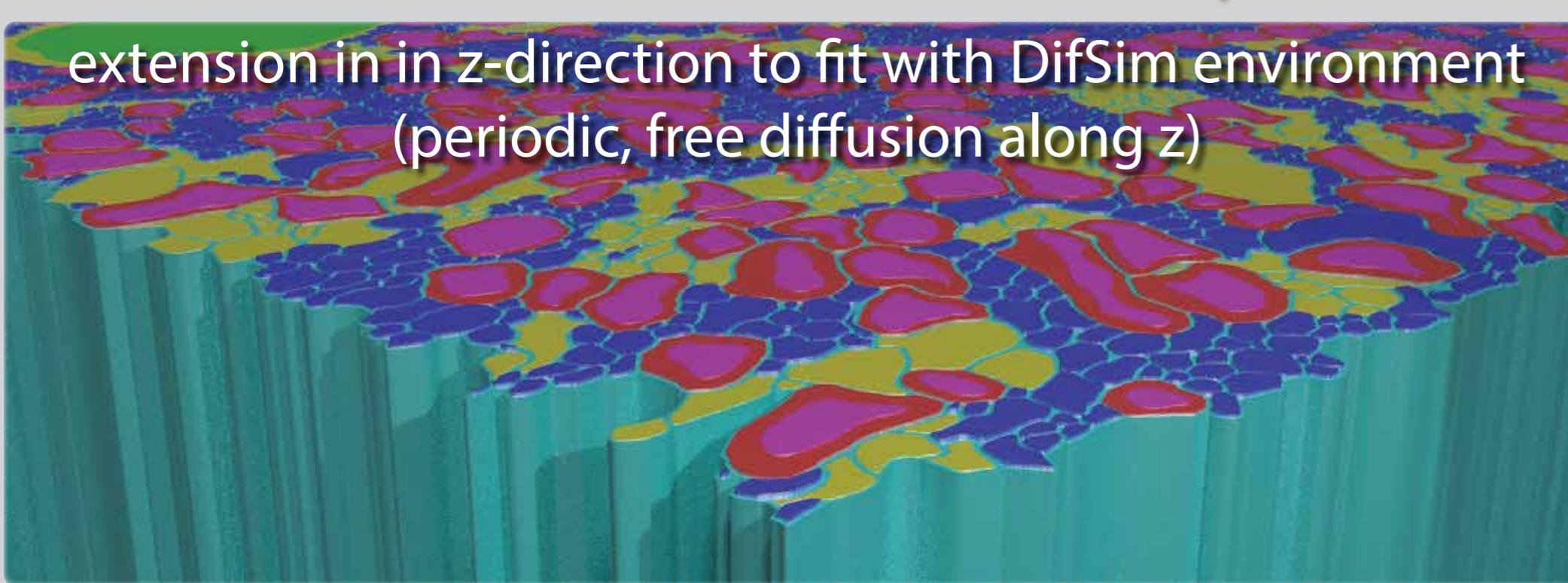


Generating geometries for Monte Carlo simulation



compartments overview:

geometries overview:



SIMULATION PARAMETERS

- Particle trajectories from MCcell³:
 - $dt = 1 \mu\text{s}$
 - for ECS, ICS, MM: $D = [2.0; 0.75; 0.03] \mu\text{m}^2/\text{ms}$
 - $N = 35 * [0.95; 0.88; 0.50]^4 \mu\text{m}^{-3}$
- dMRI signals from DifSim⁵:
 - PGSE parameter sweep
 - $\Delta = [2 - 160] \text{ ms}$
 - b -values: $100 - 32000 \text{ ms}/\mu\text{m}^2$
 - 30 diffusion gradient directions (perpendicular semicircle)

INVESTIGATIONS

AXON SHAPE:

- EM1, EM2, CT1, CT2, CM1 and CM2
- impermeable membranes

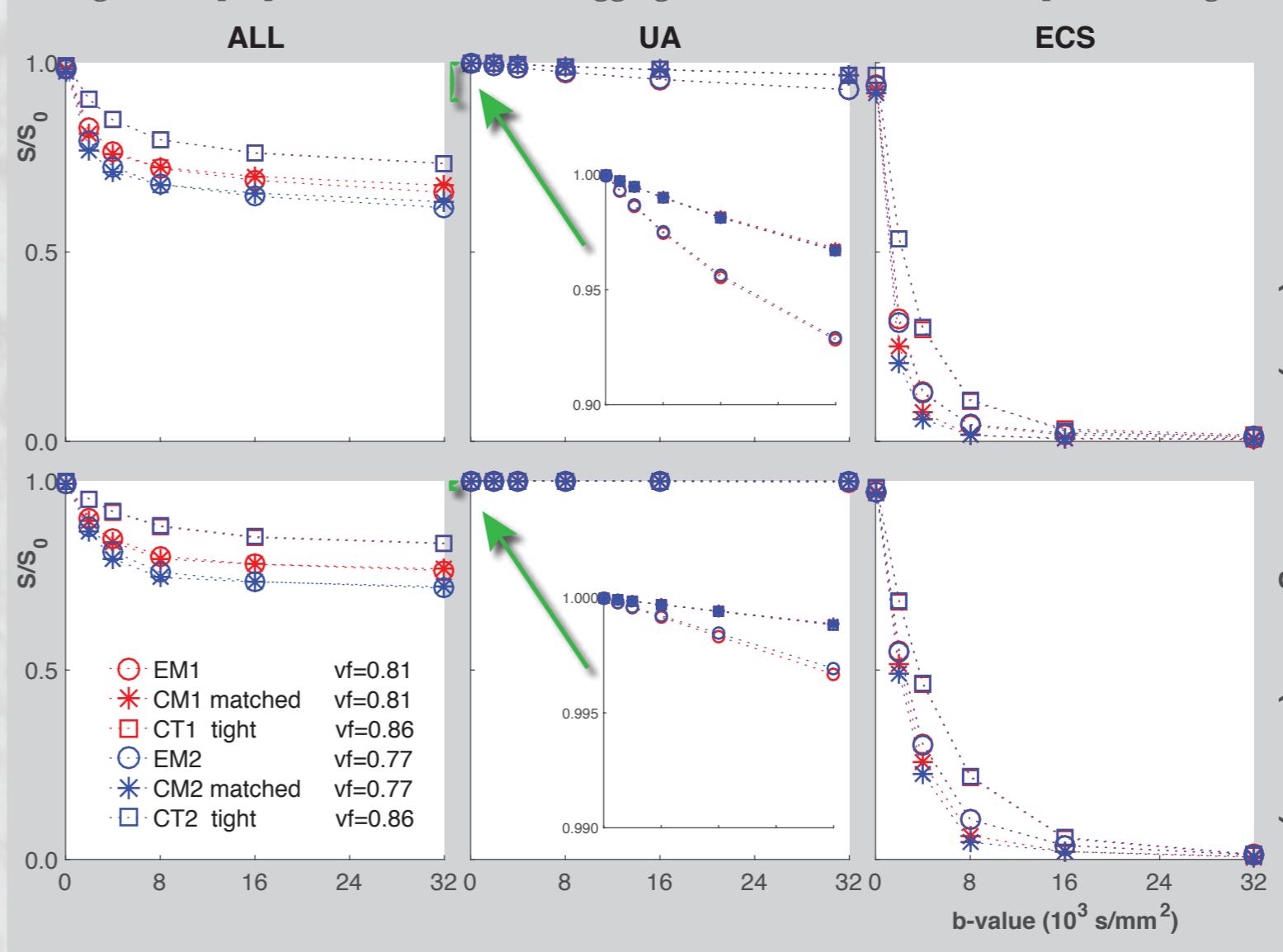
MYELINATION:

- EM1 vs. NM1 (with / without myelin)
- three permeabilities: low-mod-high
 - transition probabilities $[10^{-3}; 10^{-4}; 10^{-5}]$ for UA to ECS, others adapted accordingly
 - exchange into myelin sheath MM two orders of magnitude lower than into ICS

RESULTS

AXON SHAPE:

Simulated signal vs. b-value for EM-derived^o and cylindrical^{*□} geometries averaged over perpendicular directions. Aggregate (ALL) and UA/ECS compartment signals are shown for long and short Delta.



modest effect of shape
 $EM1 \approx CM1^*$

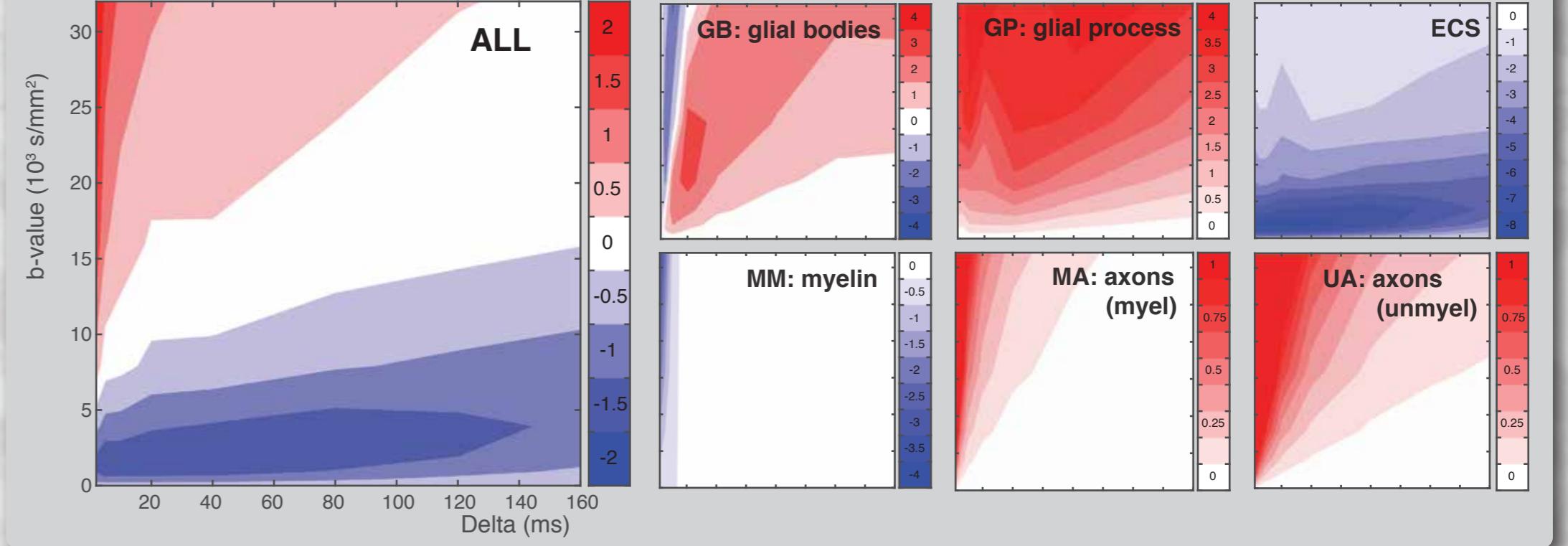
substantial effect of volume fraction
 $EM1 > EM2$, while
 $CT1 \approx CT2$

- two regimes where shape might be relevant (ALL)
- i) short Δ , high b (MA/UA)
 - ii) low b , across Δ 's (ECS)

Percent difference between EM/matched cylinder models

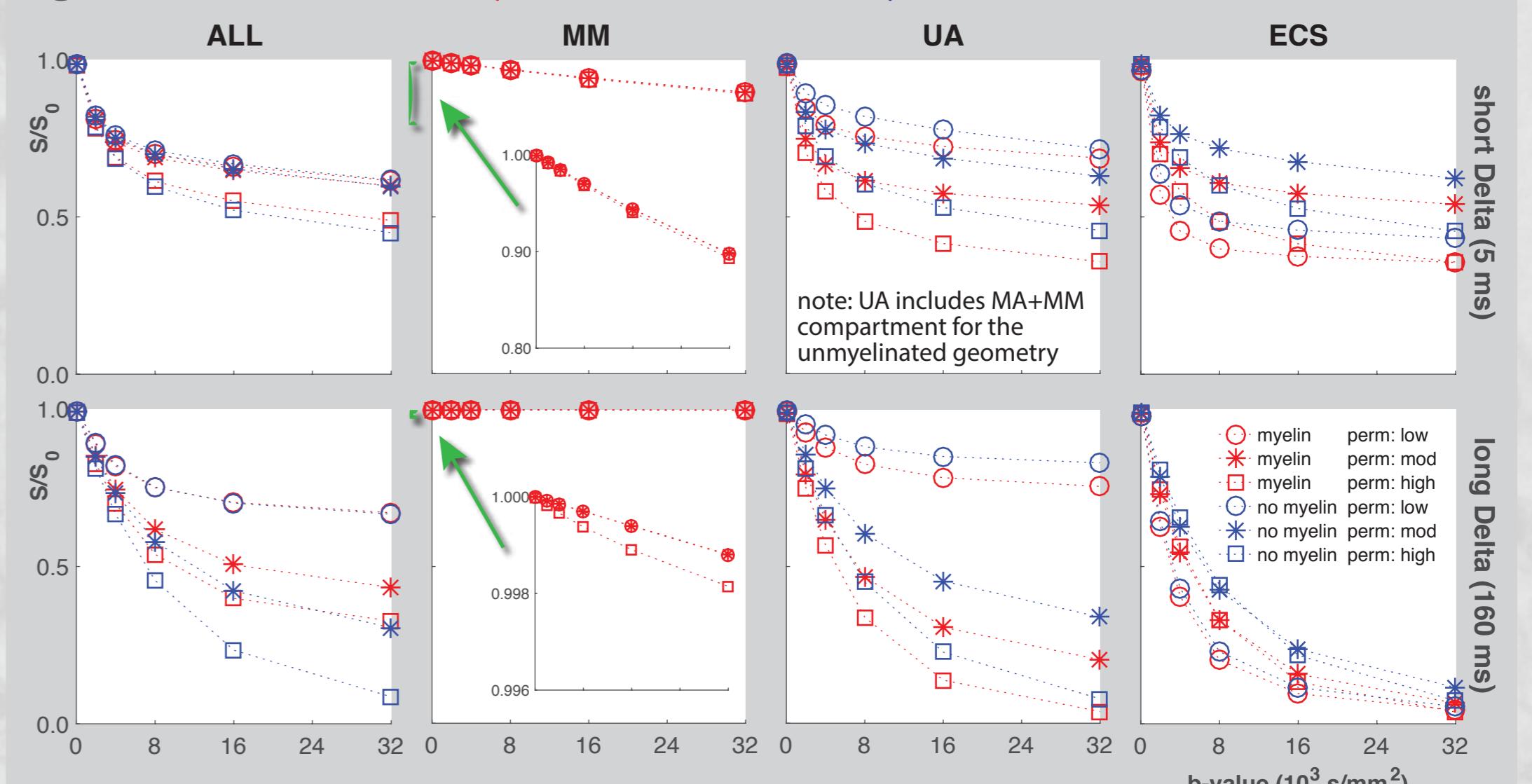
for the (direction-averaged) aggregate signal and the signal from the six compartments.

$CM1 > EM1$; $EM1 > CM1$



MYELINATION:

Signal behaviour with myelin and without myelin for three permeabilities^{○□}



signal loss in unmyelinated vs myelinated geometry at high permeability
less restriction due to larger MA compartment
more diffusion due to exchange

CONCLUSIONS

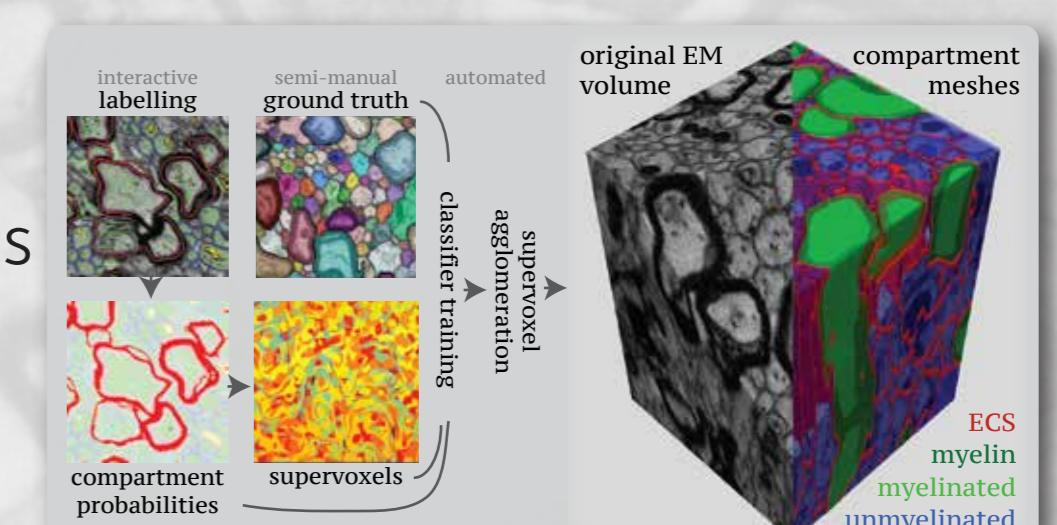
The EM-based geometry and simulation environment was developed as a flexible tool for investigating tissue features. Our two examples:

AXON SHAPE: The circular model seems a fair approximation for bundled axons in cross-section.

MYELINATION: At low permeability, myelin accounts for little variation.

OUTLOOK

- microstructure parameter estimates
- further compartmentalisation
- using EM data in full 3D



METHODS

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