Introduction to diffusion MRI

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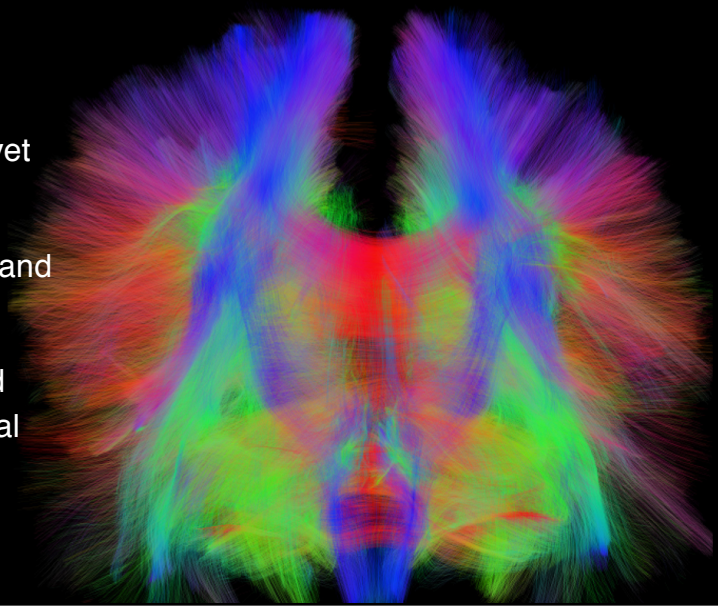
The role of white matter

- 50% of the brain, yet often ignored
- Consists of axons and myelin
- Impacts timing and integration of neural signals



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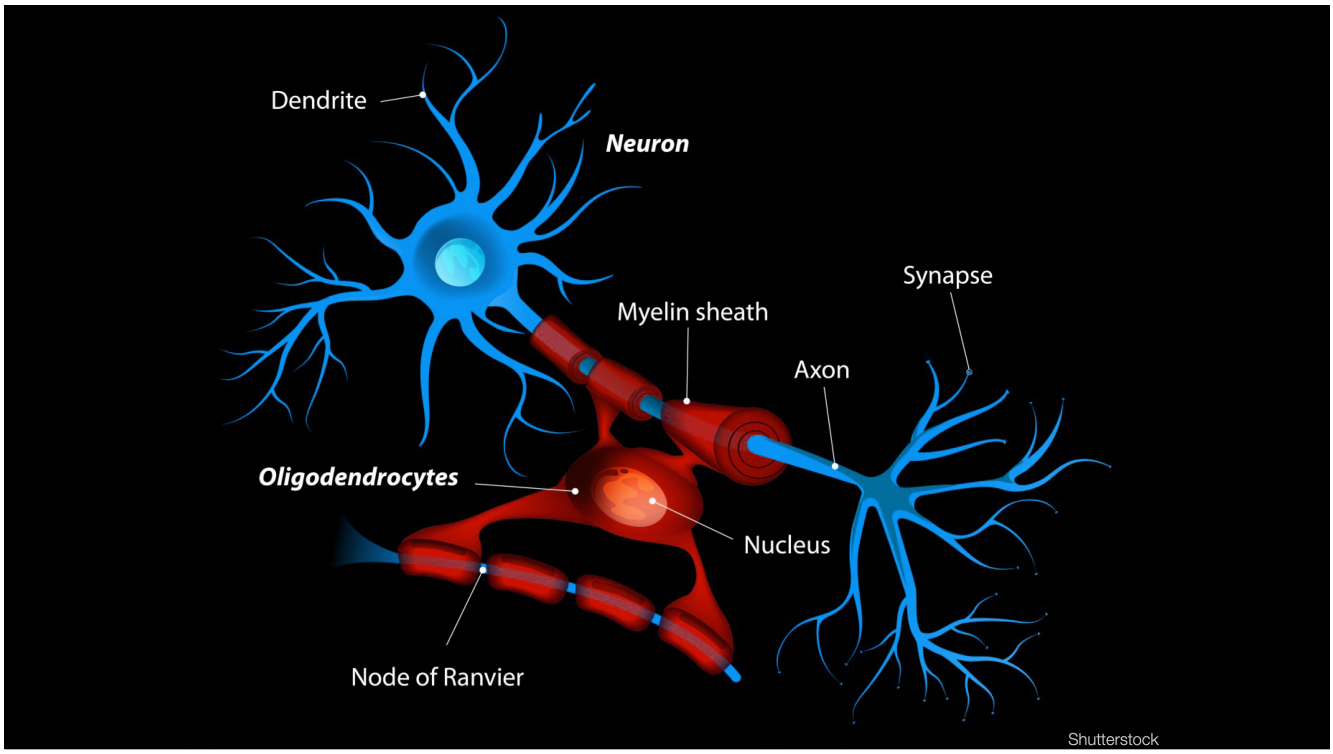

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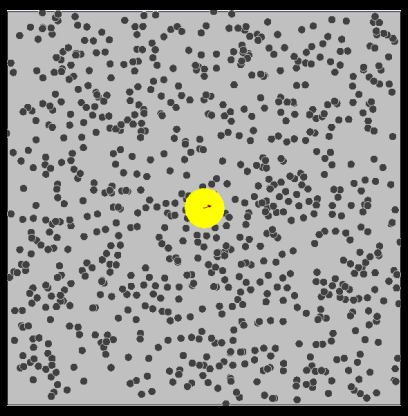
DTI: Diffusion Tensor Imaging

- In vivo measurement of white matter structure
- Uses conventional MRI scanner
- EPI sequence that measures Brownian motion of water



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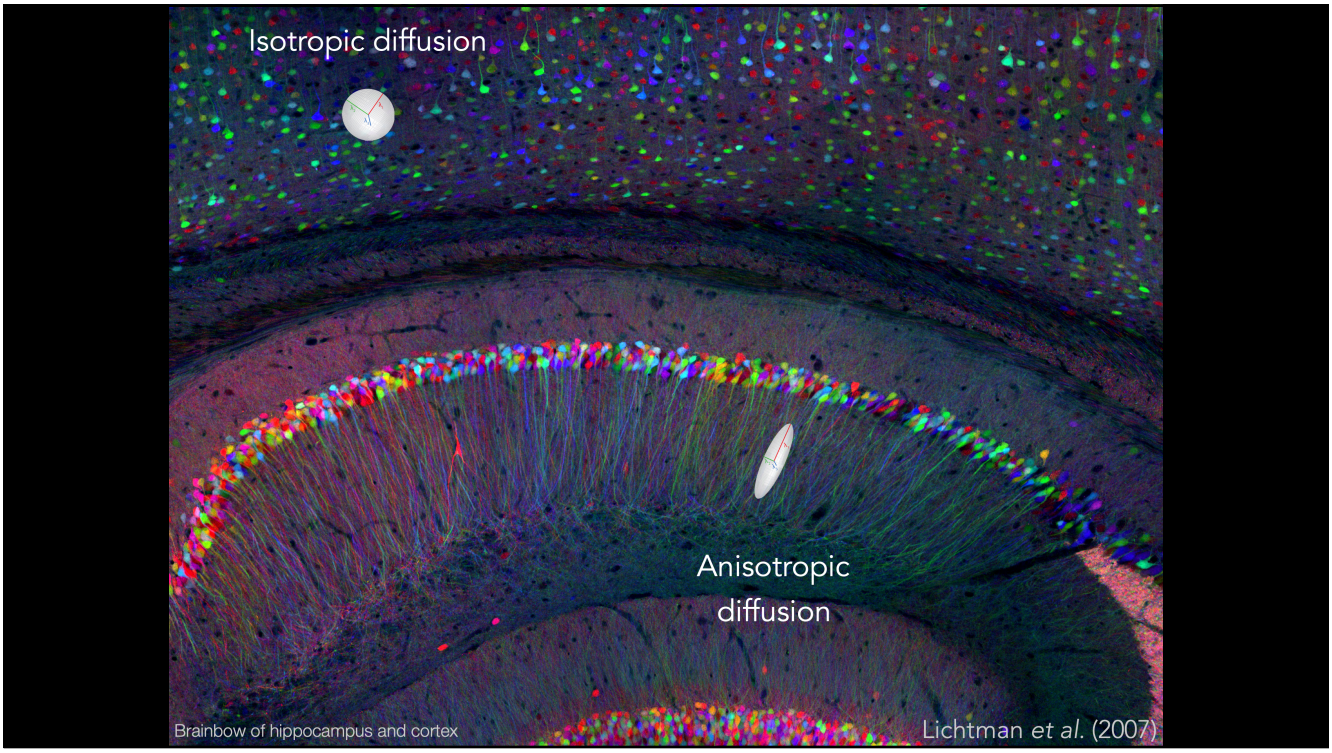
Isotropic diffusion
Anisotropic
diffusion
Brainbow of hippocampus and cortex
Lichtman *et al.* (2007)

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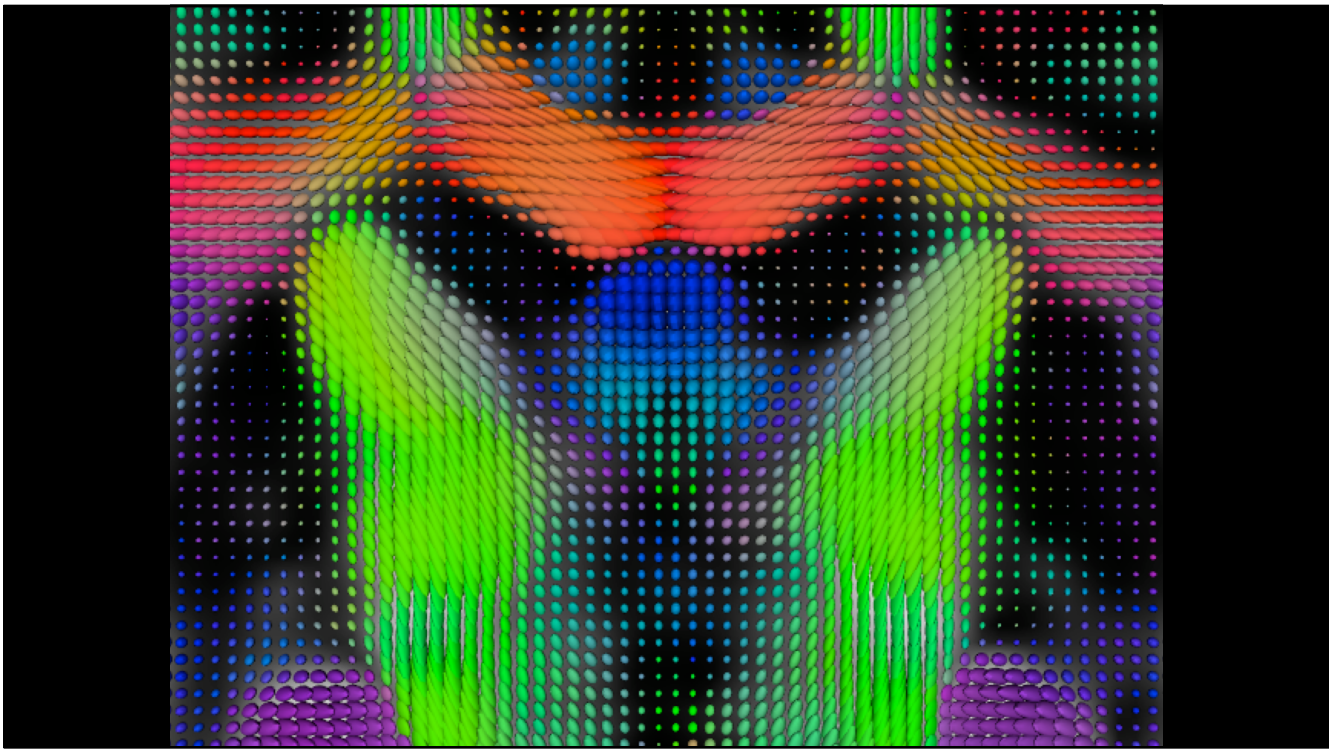

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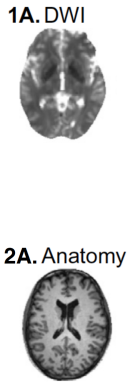
Identifying neural pathways



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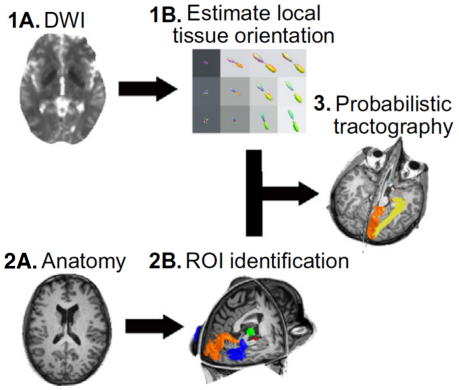

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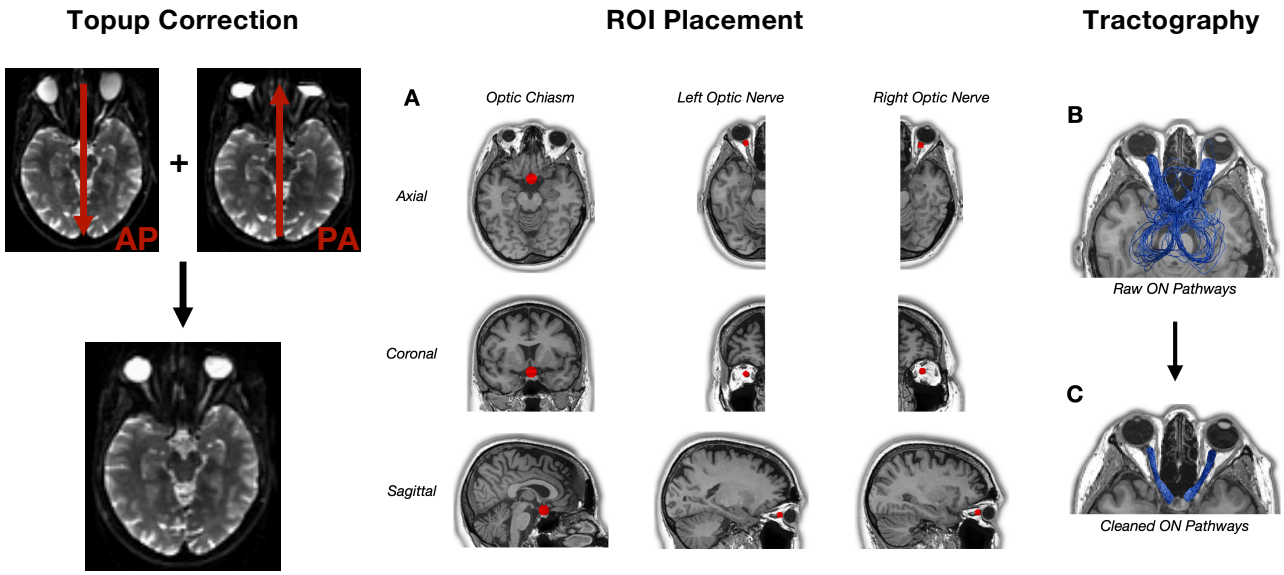
Tractography Pipeline



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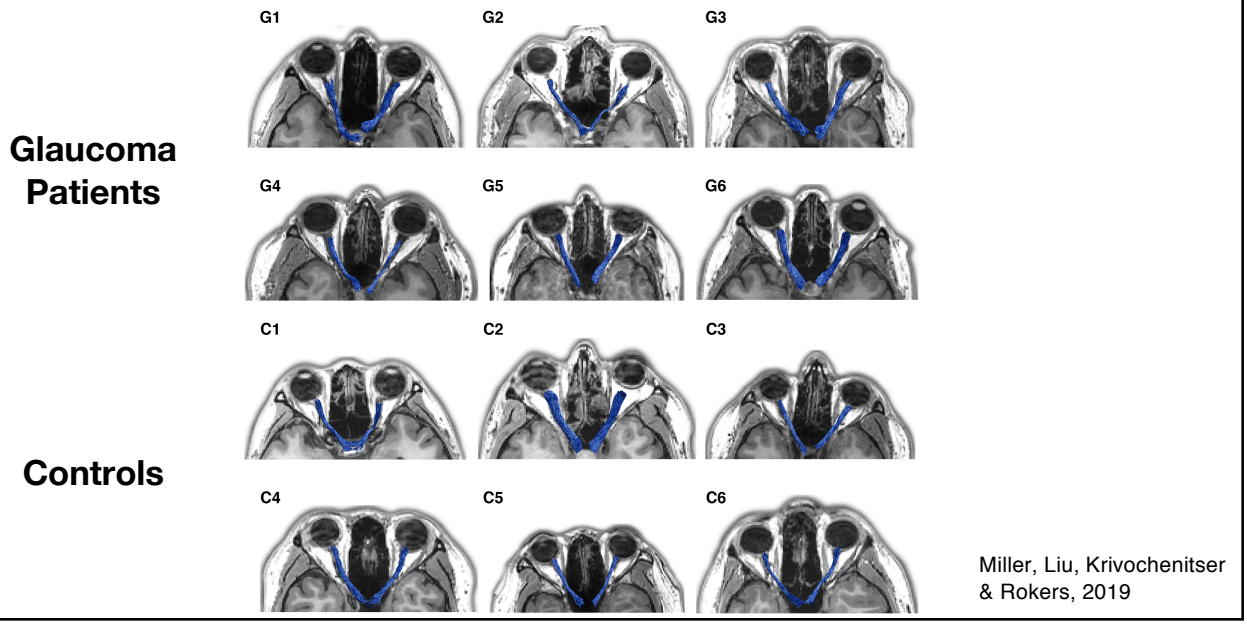
Optic Nerve Anatomical Variation



Miller, Liu, Krivochenitser & Rokers, 2019

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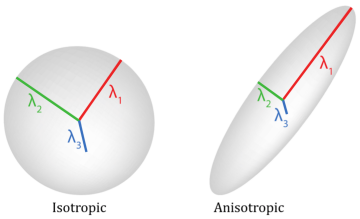
Quantifying diffusion



λ_1 = longitudinal (axial) diffusivity(AD)
$(\lambda_2 + \lambda_3)/2$ = radial diffusivity (RD)
$(\lambda_1 + \lambda_2 + \lambda_3)/3$ = mean diffusivity (MD)

$$\sqrt{\frac{1}{2}}\frac{\sqrt{(\lambda_1-\lambda_2)^2+(\lambda_1-\lambda_3)^2+(\lambda_2-\lambda_3)^2}}{\sqrt{(\lambda_1^2+\lambda_2^2+\lambda_3^2)}} = \text{fractional anisotropy (FA)}$$

diffusion-imaging.com

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Diffusion Properties

- Mean diffusivity (MD) - related to white-matter density and/or myelination
  - Component measures: radial diffusivity (RD) and axial diffusivity (AD)
- Fractional anisotropy (FA) - measure of diffusion directionality; indicative of general white matter integrity

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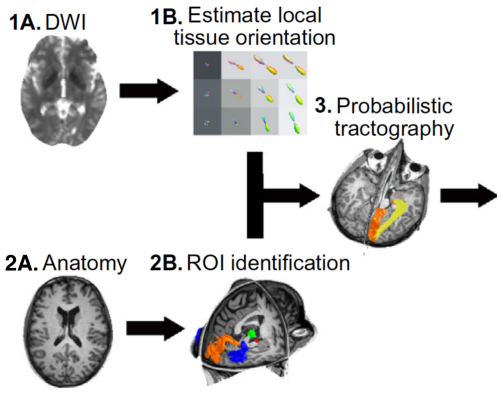
Identifying neural pathways



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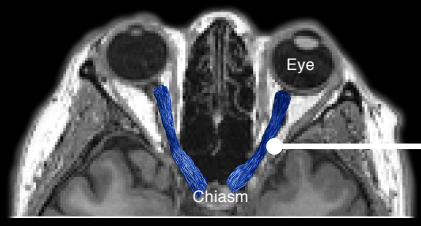
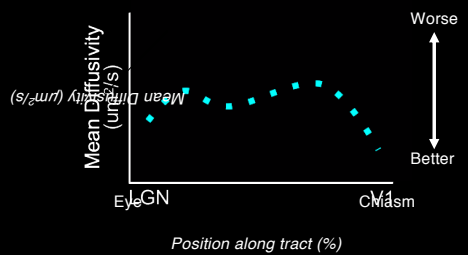
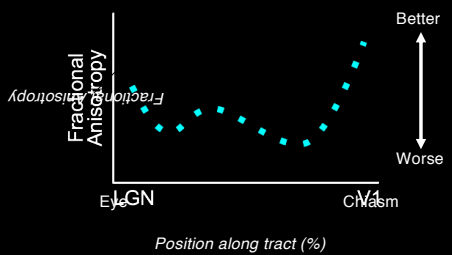
Measuring tract integrity







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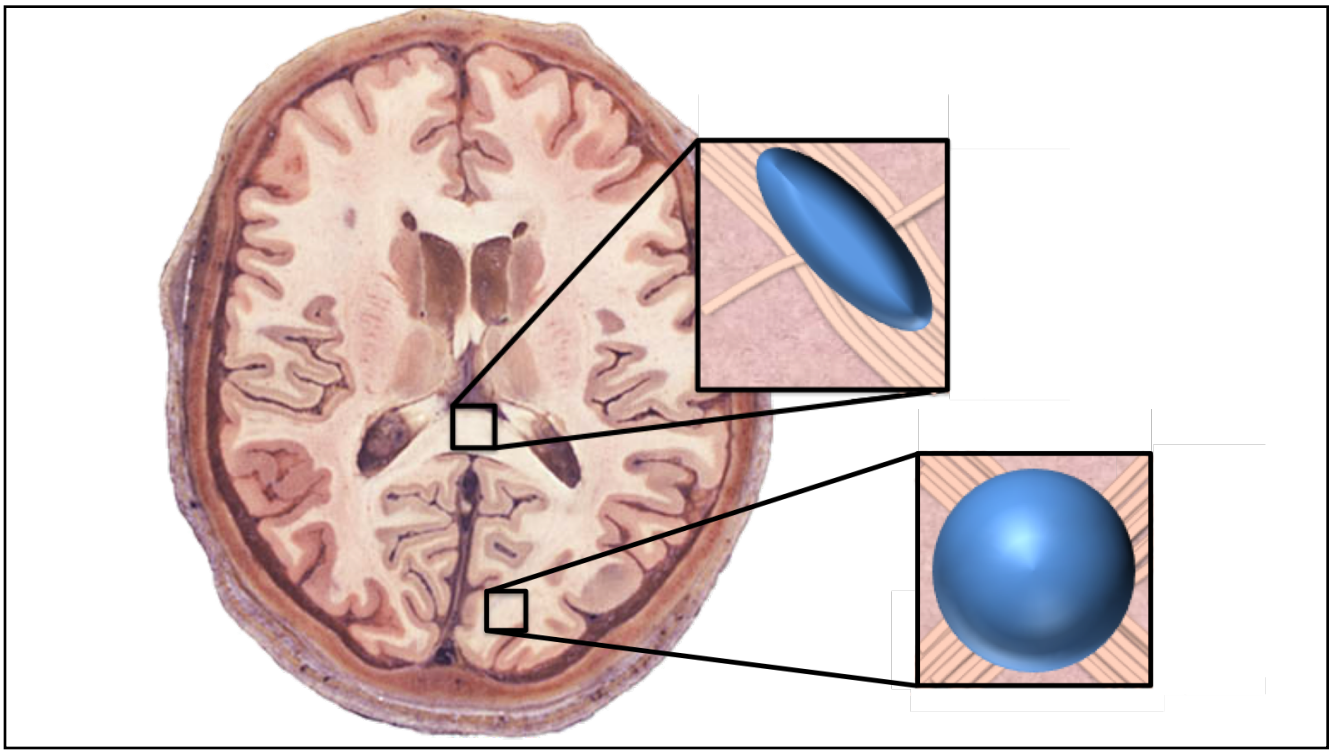

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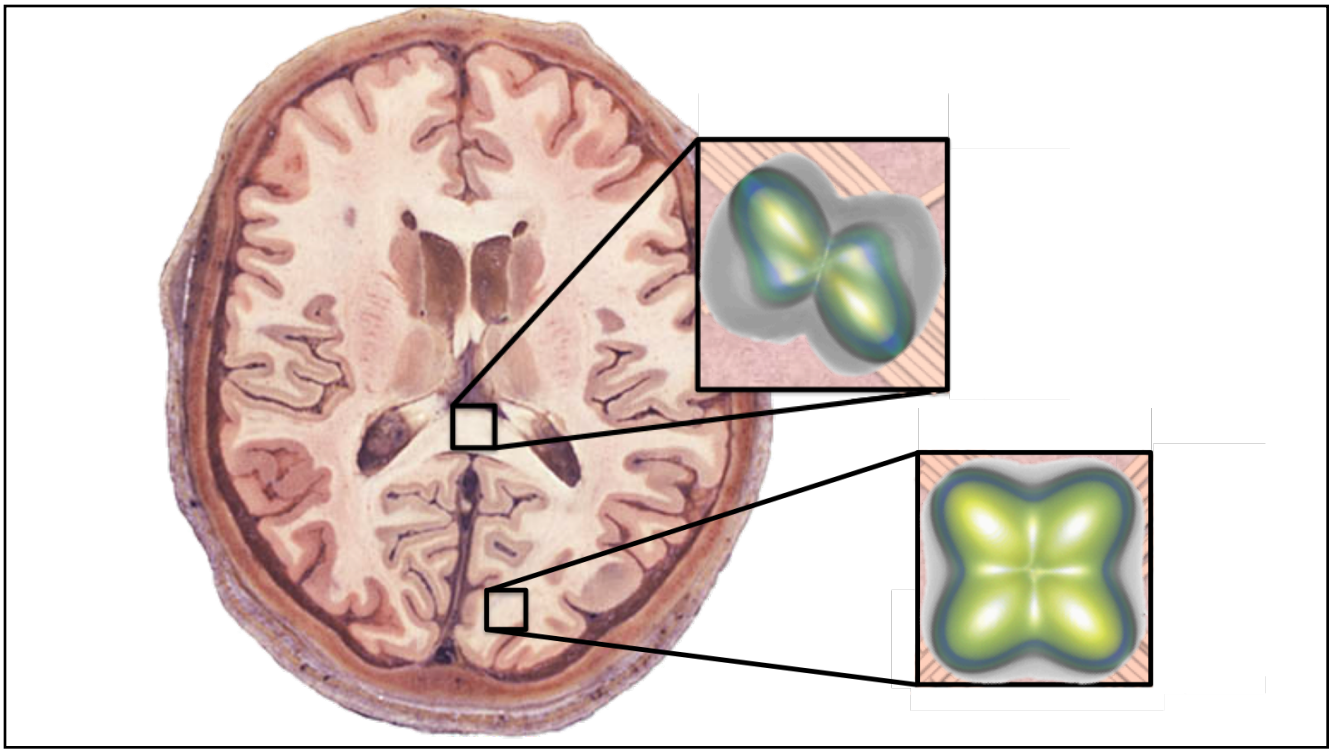

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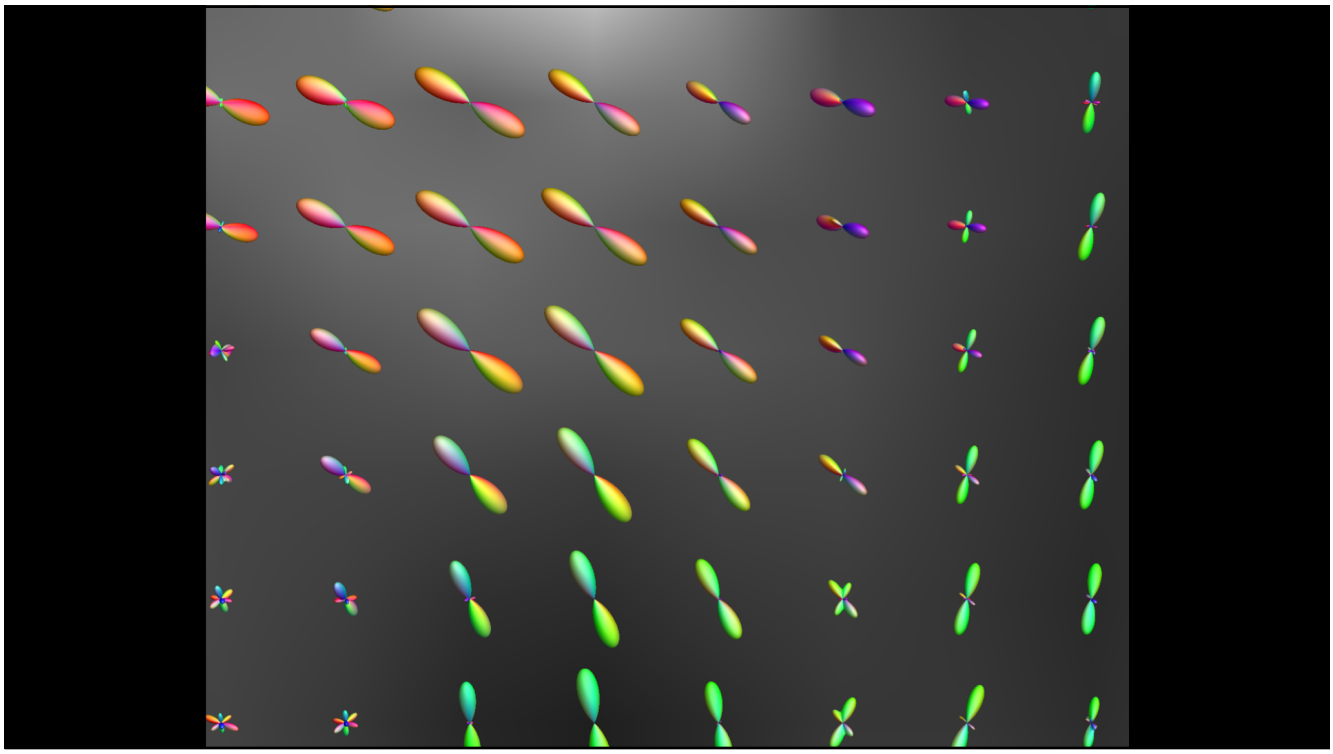

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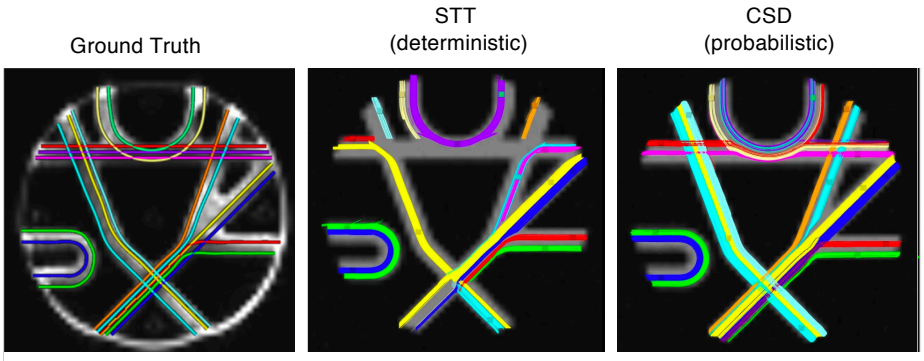
CSD: Constrained Spherical Deconvolution



from Wilkins, Lee & Singh, 2012

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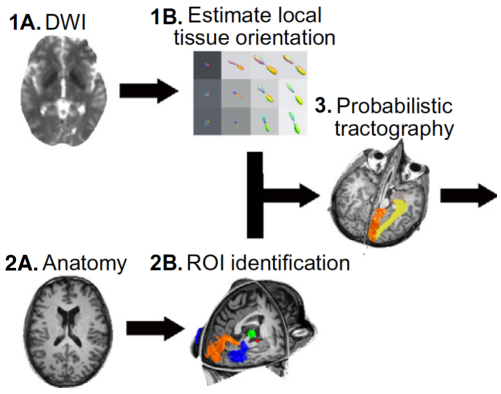
Identifying neural pathways



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dMRI as a measure of neural impairment

- Demyelinating diseases such as multiple sclerosis lead to cell death
- Conversely, cell death leads to reduced myelin density
- Potential method for early diagnosis

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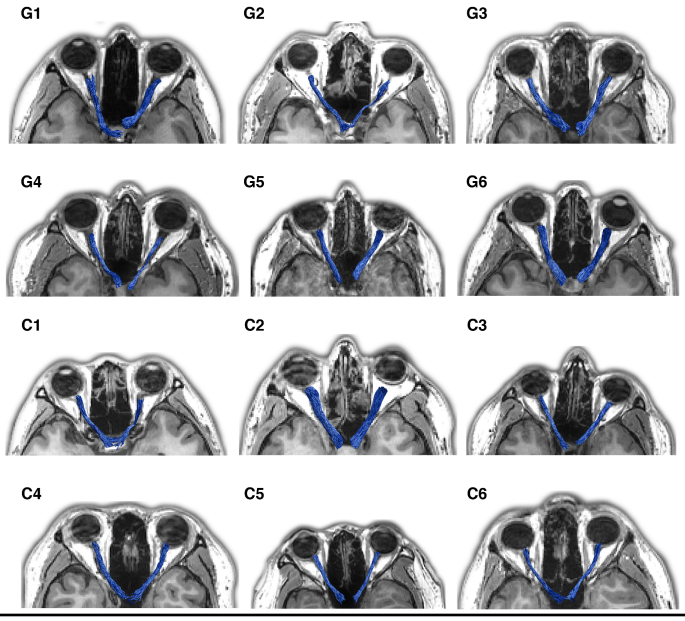
Optic Nerve Anatomical Variation

Glaucoma Patients

Controls



Miller, Liu, Krivochenitser & Rokers, 2019

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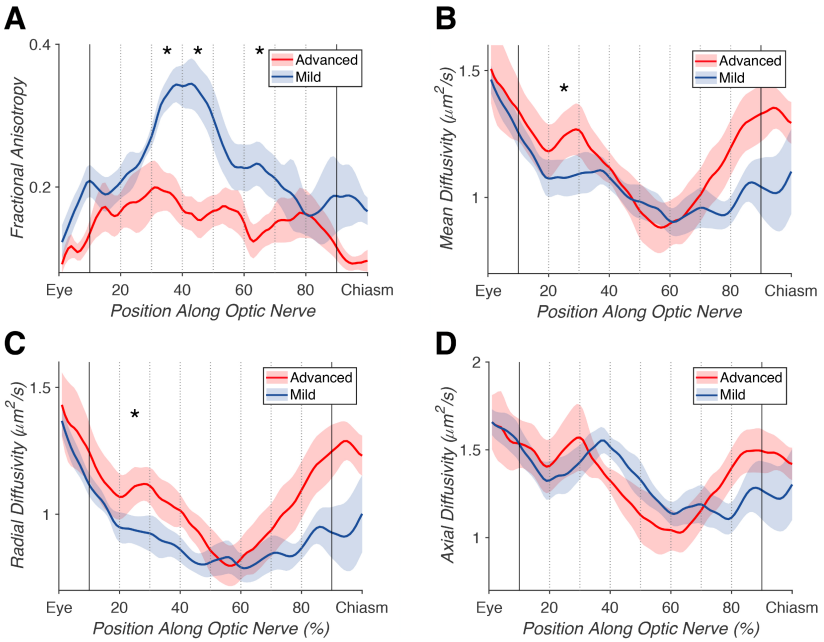
Structural Changes in Glaucomatous Optic Nerves



* FDR < 0.05

Miller, Liu, Krivochenitser & Rokers, 2019

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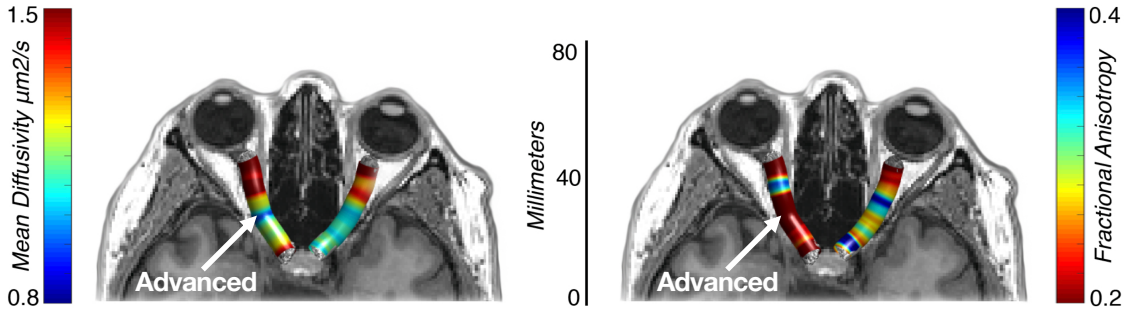
Reduced FA & Increased MD in Advanced ONs



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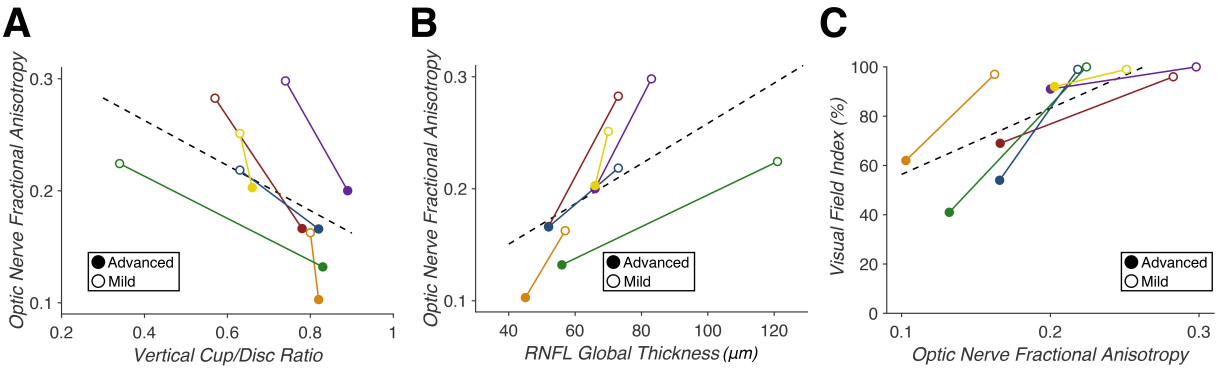
Correlation with Clinical Measures

Retina → Brain

Retina → Brain

Brain → Behavior



All p < 0.01

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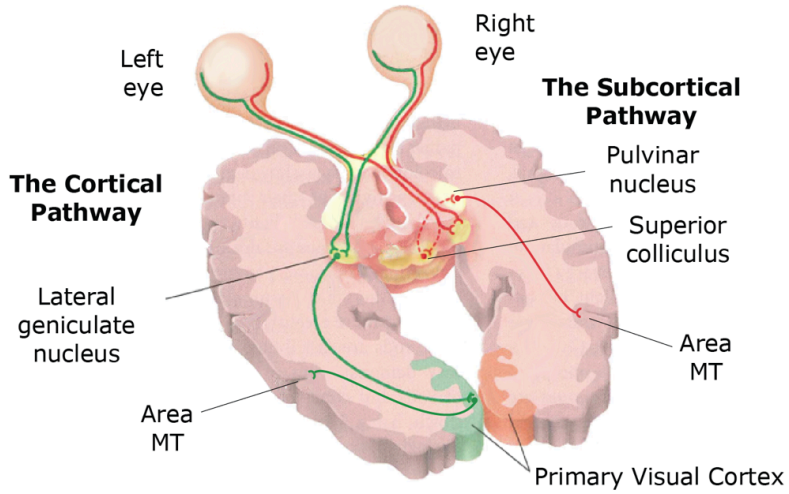
Beyond the optic nerve



Adapted from Gazzaniga et al., 2002

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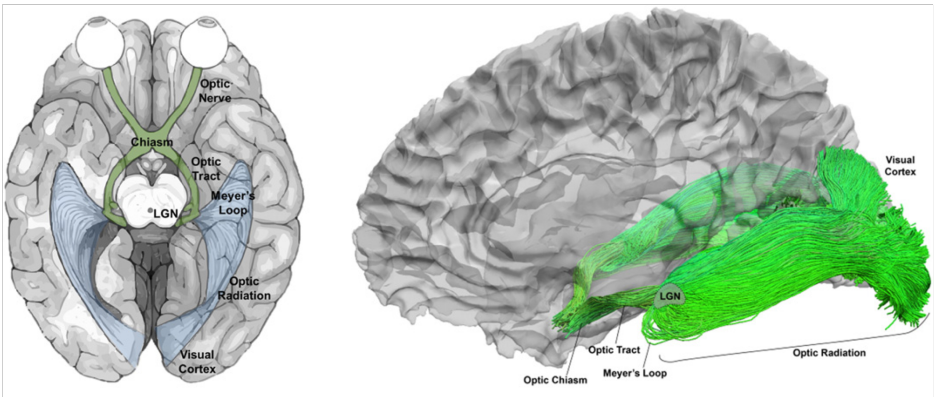
The Challenge



Kammen et al., 2016

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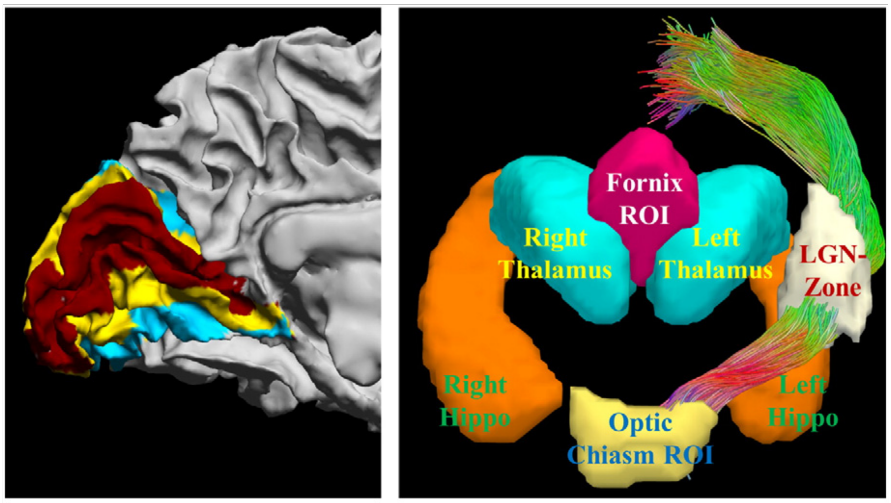
V1 and LGN estimation



Kammen et al., 2016

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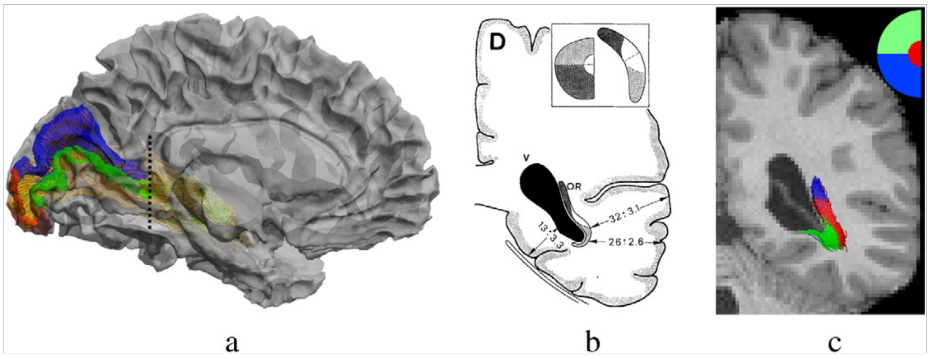
Retinotopic organization of OR



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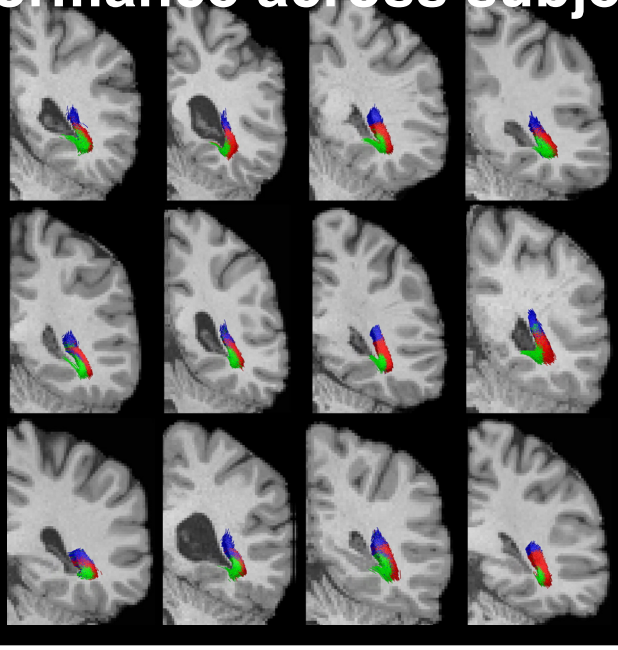
Performance across subjects



Kammen et al., 2016

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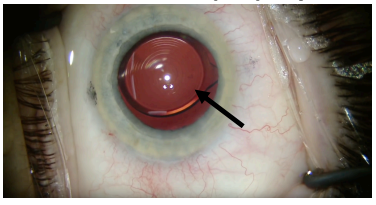
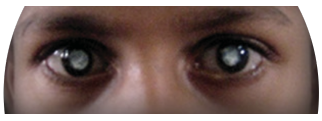
Project Prakash: dMRI over time

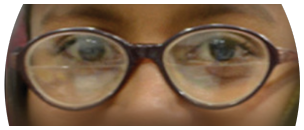
- Children living in rural India receive surgery for congenital cataracts (after putative critical period)
- After surgery, patients show perceptual improvements in:
  - Acuity (Gandhi, Singh, et al., 2017)
  - Contrast sensitivity (Ganesh, Arora, et al., 2014)
  - Face recognition (Kalia, Lesmes, et al., 2014)

Intraocular Lens (IOL) Implant



Pre-Op





Post-Op

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What is the neural impact of sight-recovery?

Does sight-recovery induce white matter plasticity?

If so, is that plasticity:

1. *pathway-specific?*
2. *age-dependent?*

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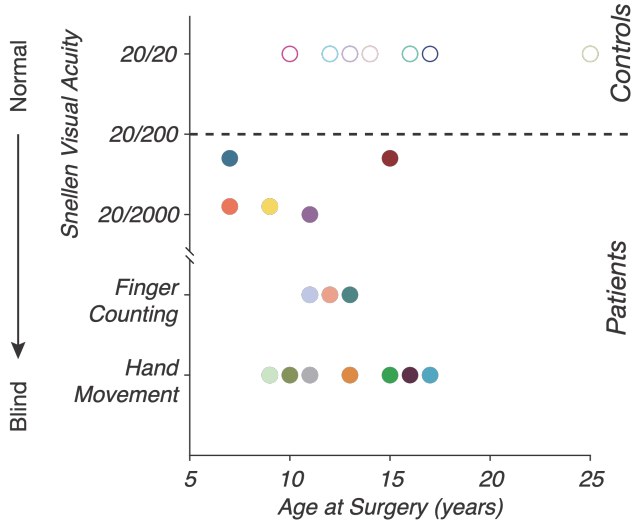
Participants



- 15 cataract patients (4 female)
  - 7-17 years (mean 11.7 ± 3.1 years)
  - Severe bilateral cataracts
- 7 control subjects (2 female)
  - 10-25 years (mean 15.3 ± 4.9 years)
  - Normally-sighted

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Methods

- Longitudinal dMRI scans acquired for each patient
  - 1-6 scans collected over a range of weeks to years
  - 44 total scans included in analysis (patients & controls)
- Scanning parameters
  - 3T GE Scanner
  - T1 anatomical scans
  - Diffusion sequence: 40-directions, AP* phase-encoding, b=1000 s/mm^2

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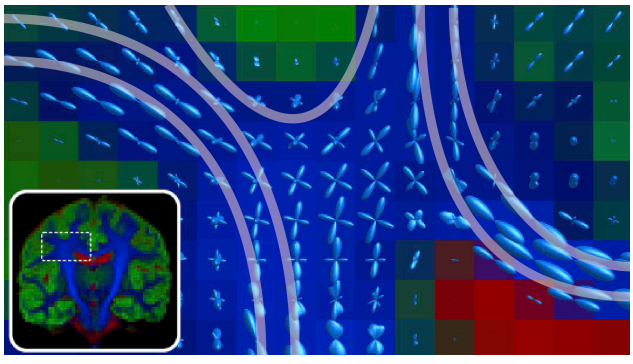
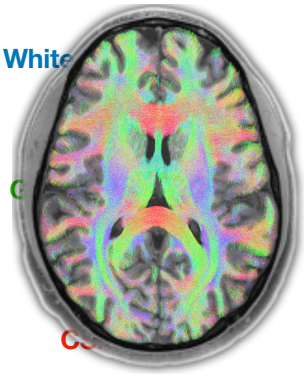
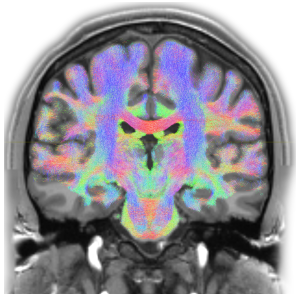
dMRI Tractography

- Probabilistic MRTrix2 tractography with constrained spherical deconvolution (Tournier, et al., 2004; Tournier, et al., 2007)







(Tournier, et al., 2019)

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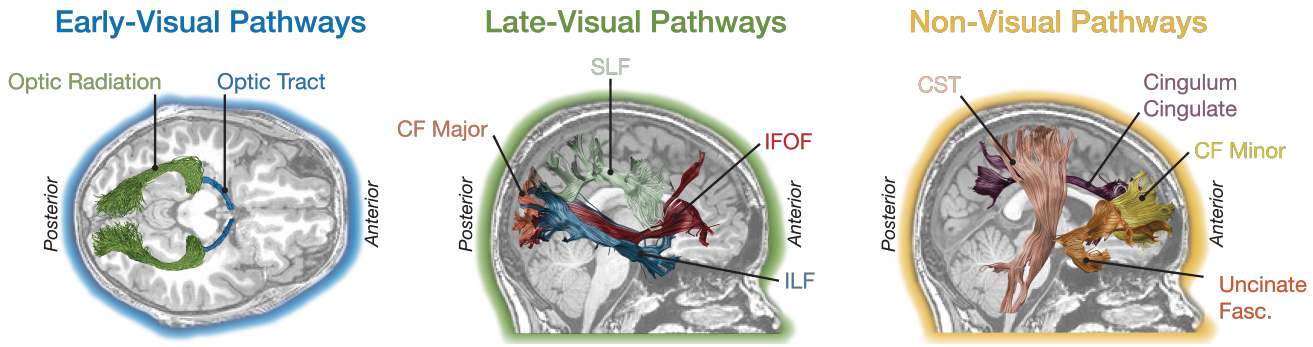
White Matter Pathways

- 10 major white matter pathways assessed
  - Identified using manual and probabilistic methods (Allen, et al., 2018; Yeatman, et al., 2016)



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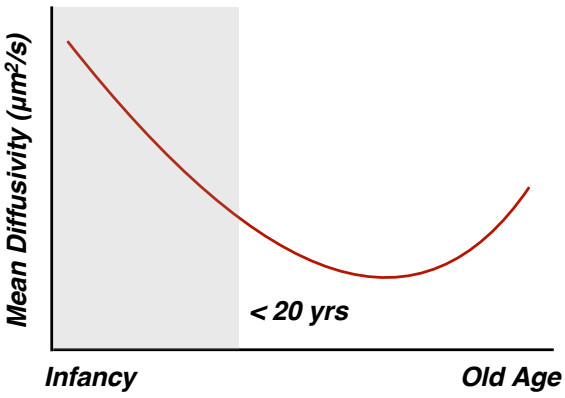
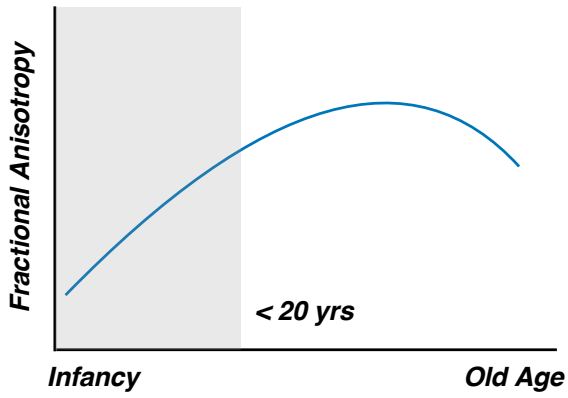
General White-Matter Development Trends





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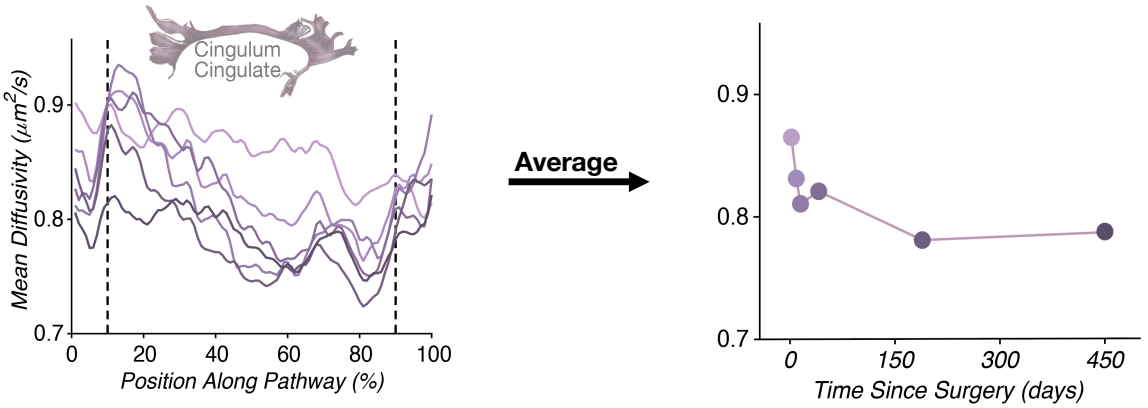
Longitudinal Data Analysis



- Linear mixed effects (LME) model:
  - Pathway MD/FA ~ 1 + DaysSinceSurgery * Age + Cataracts + (1 | Subject)
  - Correct for multiple comparisons using false discovery rate testing

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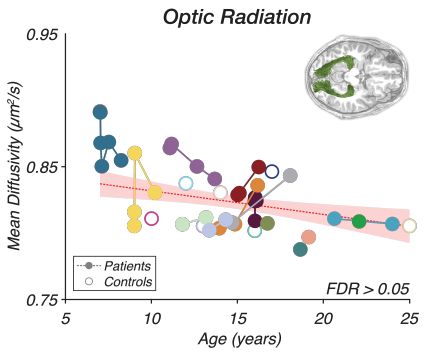
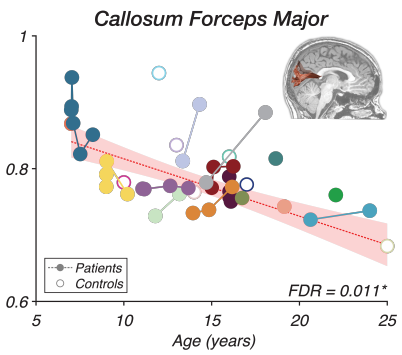
Maturational White Matter Changes

Early-Visual Pathways



All pathways FDR > 0.05

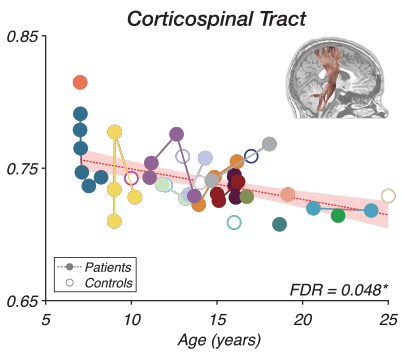
Late-Visual Pathways



CF Major (FA; FDR = 0.033)

All other pathways FDR > 0.05

Non-Visual Pathways



Cingulum (FA; FDR = 0.011)
Uncinate (FA; FDR = 0.022)

All other pathways FDR > 0.05

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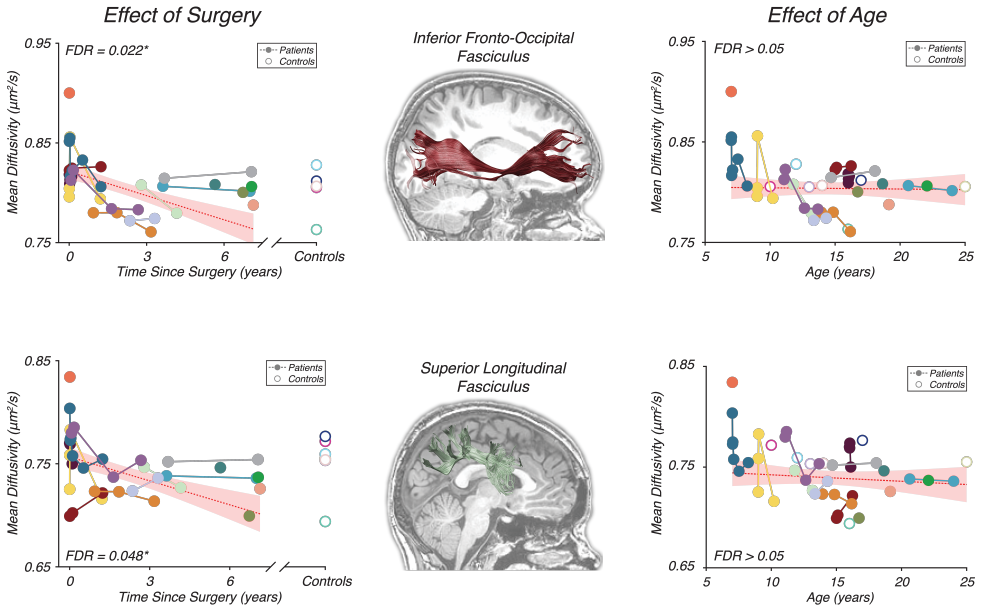
Plasticity in Late-Visual Pathways



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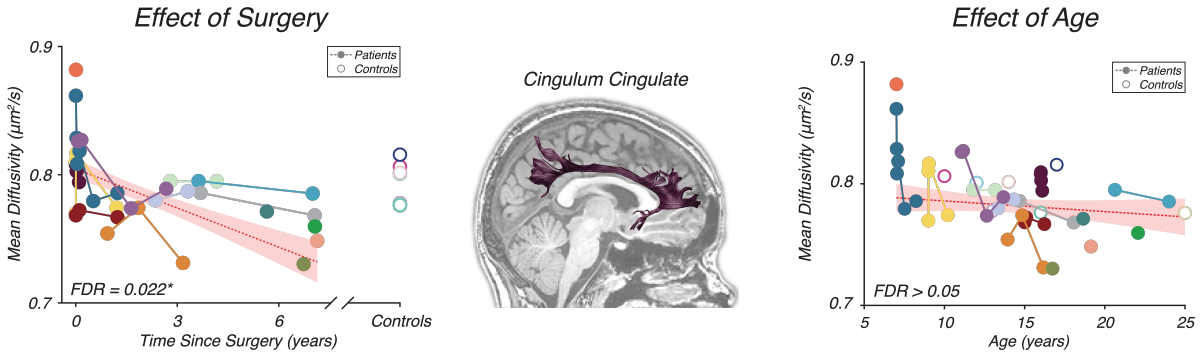
Plasticity in Non-Visual Pathways



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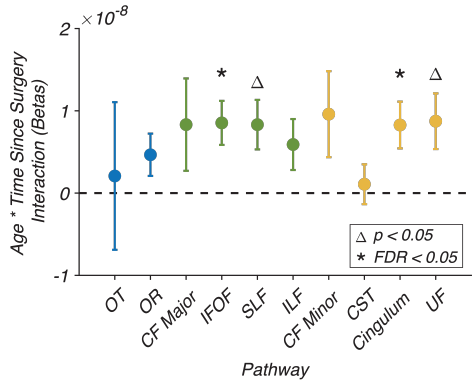
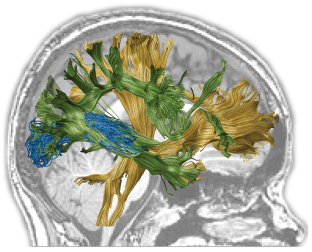
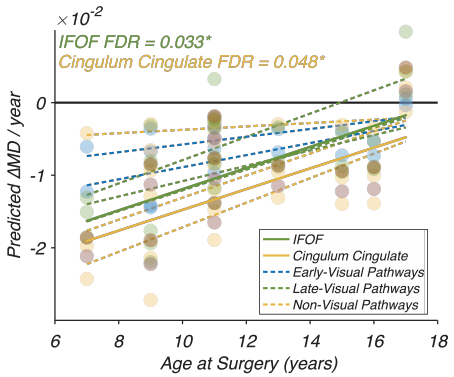
Plasticity Depends on Age at Treatment





Early-Visual
Late-Visual
Non-Visual



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Conclusions

- Evidence for long-term white matter plasticity in late-visual and non-visual pathways (IFOF, SLF, Cingulum Cingulate)
  - Extent of plasticity depended on age in IFOF and Cingulum Cingulate – earlier intervention is more impactful
- No evidence for plasticity in early-visual system (optic tract, optic radiation)
  - Consistent with critical period closure and limited improvements in low-level perception
- Results reveal potential neural basis for behavioral improvement following sight-recovery

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Where to go from here

- Do changes in white matter structure predict behavioral improvements?
  - Quantifying the relationship between structural changes in certain pathways and behavioral recovery in different domains
    - Acuity, contrast sensitivity (no expected relationship)
    - Face recognition?
    - Other behaviors?

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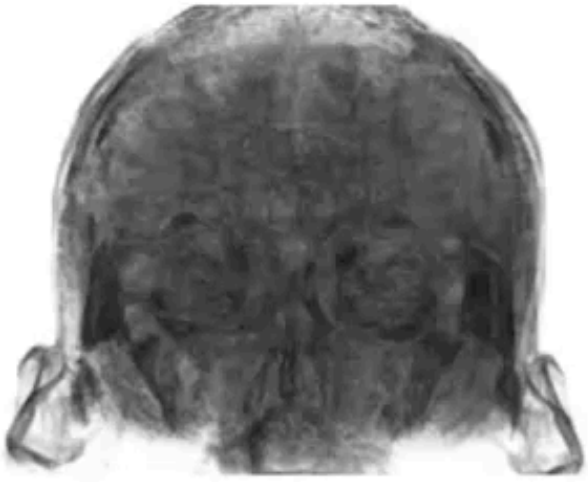

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