

## Mapping Grey and White Matter Activity in the Human Brain with Isotropic ADC-fMRI

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### BACKGROUND

- BOLD-fMRI relies on neurovascular coupling. Therefore, spatial and temporal specificity is limited, and uncertainty surrounds the white matter BOLD signal [Grauskas et al., *Front Neurosci*, 2019].
- Apparent diffusion coefficient (ADC) offers an alternative fMRI contrast sensitive to cellular deformations during neural activity. However, the use of linear diffusion encoding introduces sensitivity to fibre directionality [Spees et al., *NeuroImage*, 2013].
- We introduce isotropic ADC-fMRI using spherical b-tensor encoding (Fig 1) to detect microstructure changes independent of fibre direction [Szczepankiewicz et al., *J Neurosci Methods*, 2021].

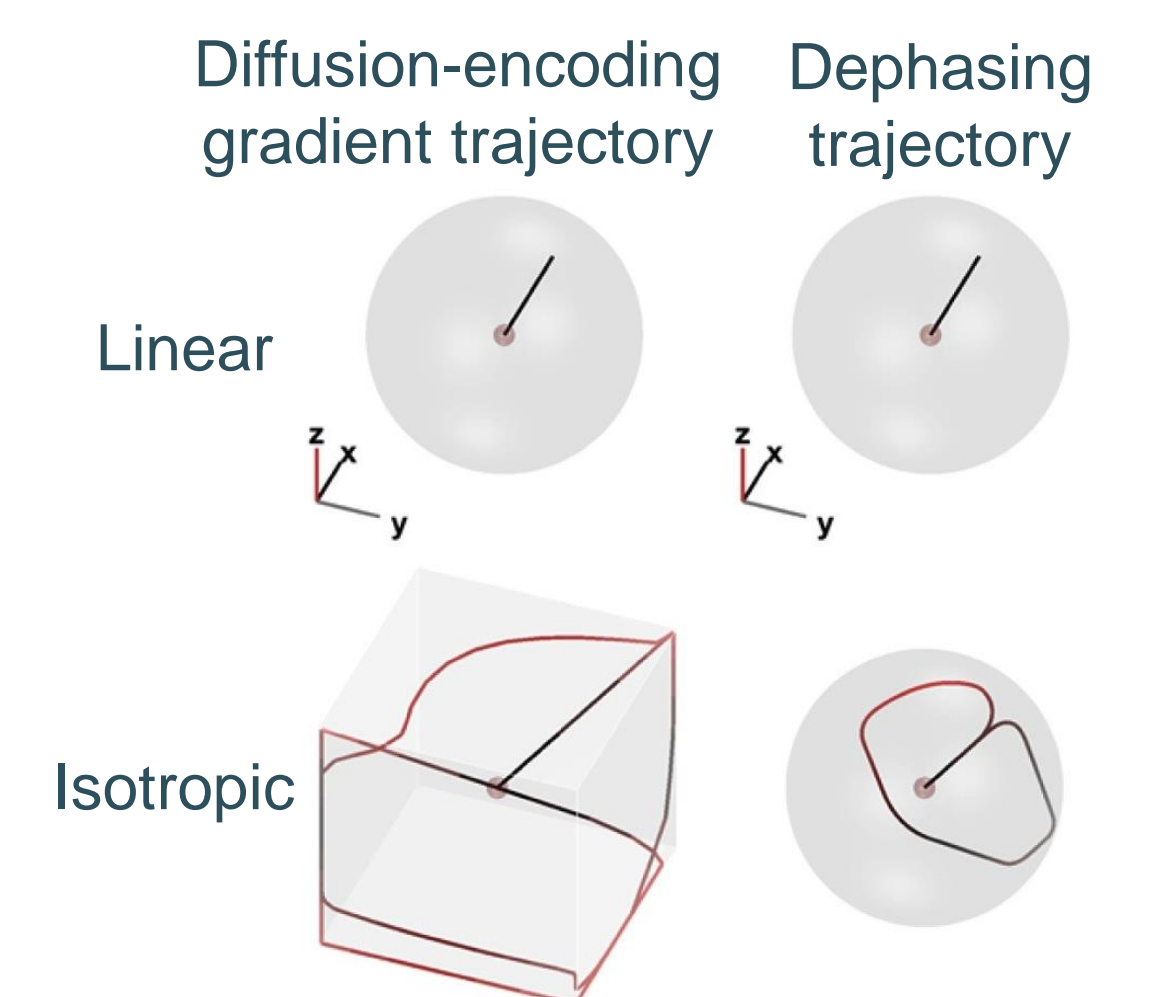


Figure 1: Linear vs isotropic diffusion encoding.

### METHODS

- Flashing checkerboard visual stimulation task (16 epochs)
- ADC-fMRI with alternating b-values (200 & 1000 s mm<sup>-2</sup>) with two sequences:
  - isotropic ADC-fMRI (n = 12)
  - linear ADC-fMRI (n = 10)
- Multi-echo gradient echo BOLD-fMRI (n = 7)
- Denosing (NORDIC); Gibbs correction; Topup; motion correction; calculate ADC for each b-value pair

$$S(b, t) = S_0 e^{-\frac{T_E}{T_2(t)} - b \text{ADC}(t)} \quad \text{ADC} = \frac{1}{b_1 - b_2} \ln \frac{S_2}{S_1}$$

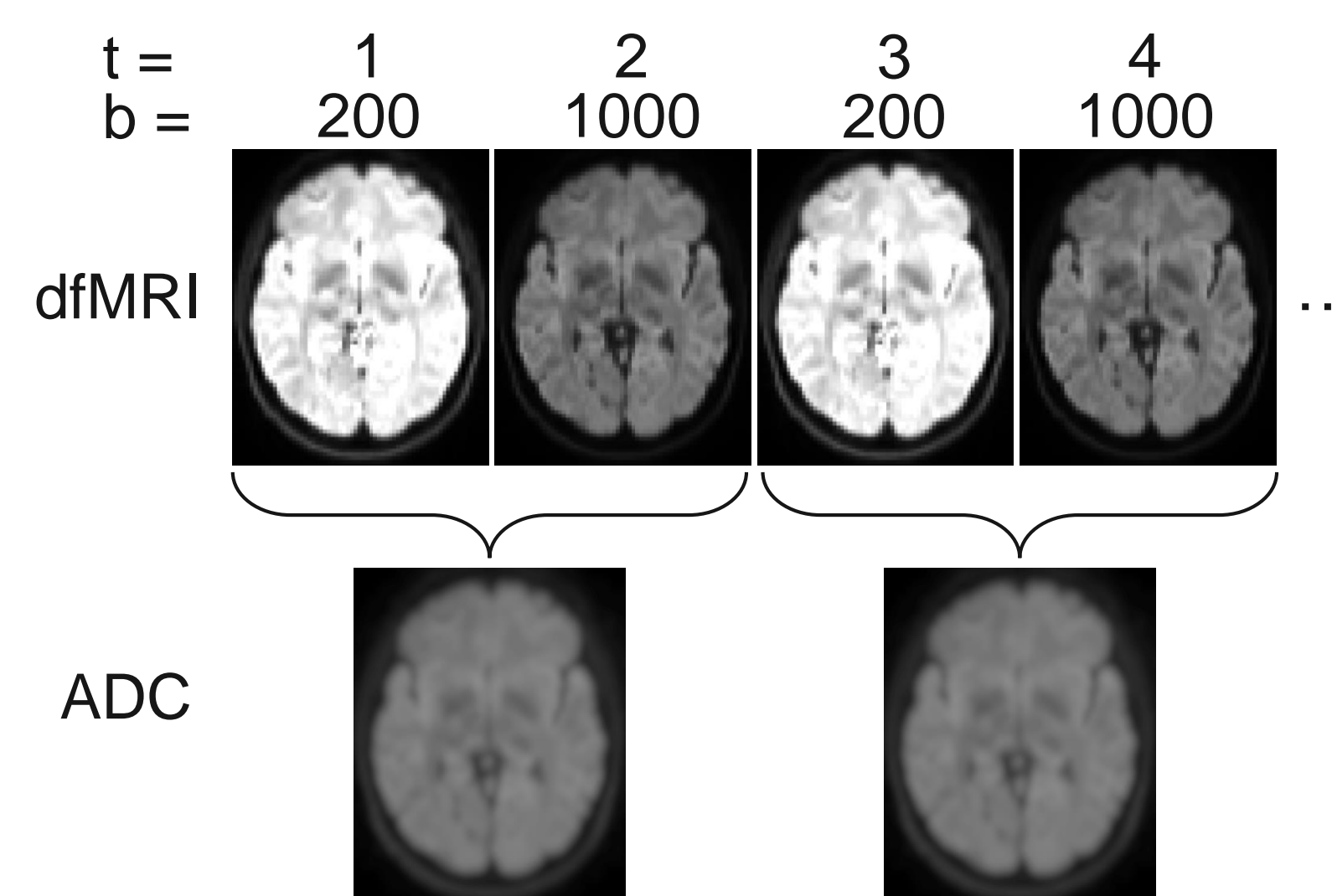


Figure 2: ADC-fMRI was calculated from a series of interleaved dfMRI volumes acquired at b = 200 and 1000 s mm<sup>-2</sup>.

Resolution	2.5x2.5x2.5 mm <sup>3</sup>
Slice gap	50%
TR	1000 ms
TE	82/72 ms (iso/dir)
Flip angle	90°
Number of slices	16
GRAPPA	2
Multiband factor	2
Partial Fourier	0.75

Table 1: Acquisition parameters.

### RESULTS

- ADC-fMRI has earlier onset than BOLD-fMRI (Fig 3).
- ADC-fMRI detects activity in a higher proportion of white matter voxels than b200-dfMRI, b1000-dfMRI and BOLD (Fig 4).
- In white matter, linear ADC-fMRI is biased towards detecting activity in voxels with fibres more perpendicular to the diffusion encoding gradient, whereas isotropic ADC-fMRI is independent of fibre angle (Fig 5A & B).
- This is replicated *in silico* using the CATERPillar numerical phantom (Fig 5C & D) [Nguyen-Duc et al., *ISMRM*, 2024].

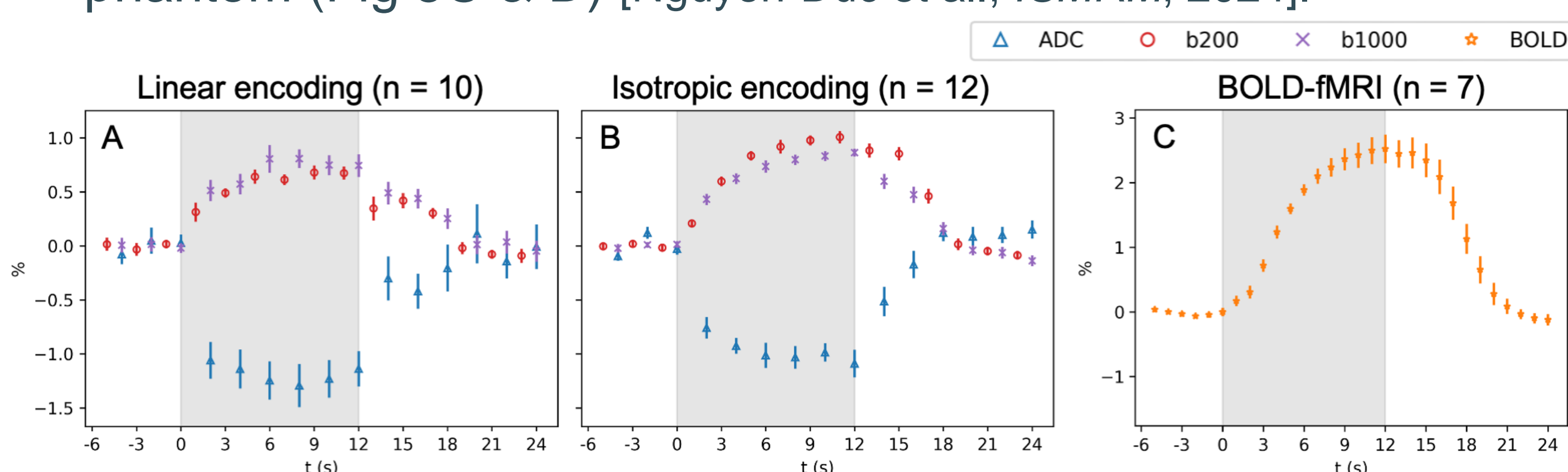


Figure 3: Visual task response for linear and isotropic ADC-fMRI, b200-dfMRI, b1000-dfMRI and BOLD-fMRI. In each subject, timeseries were averaged across voxels significantly associated with the task (cluster-corrected  $z > 1.5$ ,  $p < 0.05$ ) and across task epochs. Plots show the mean and standard error across subjects.

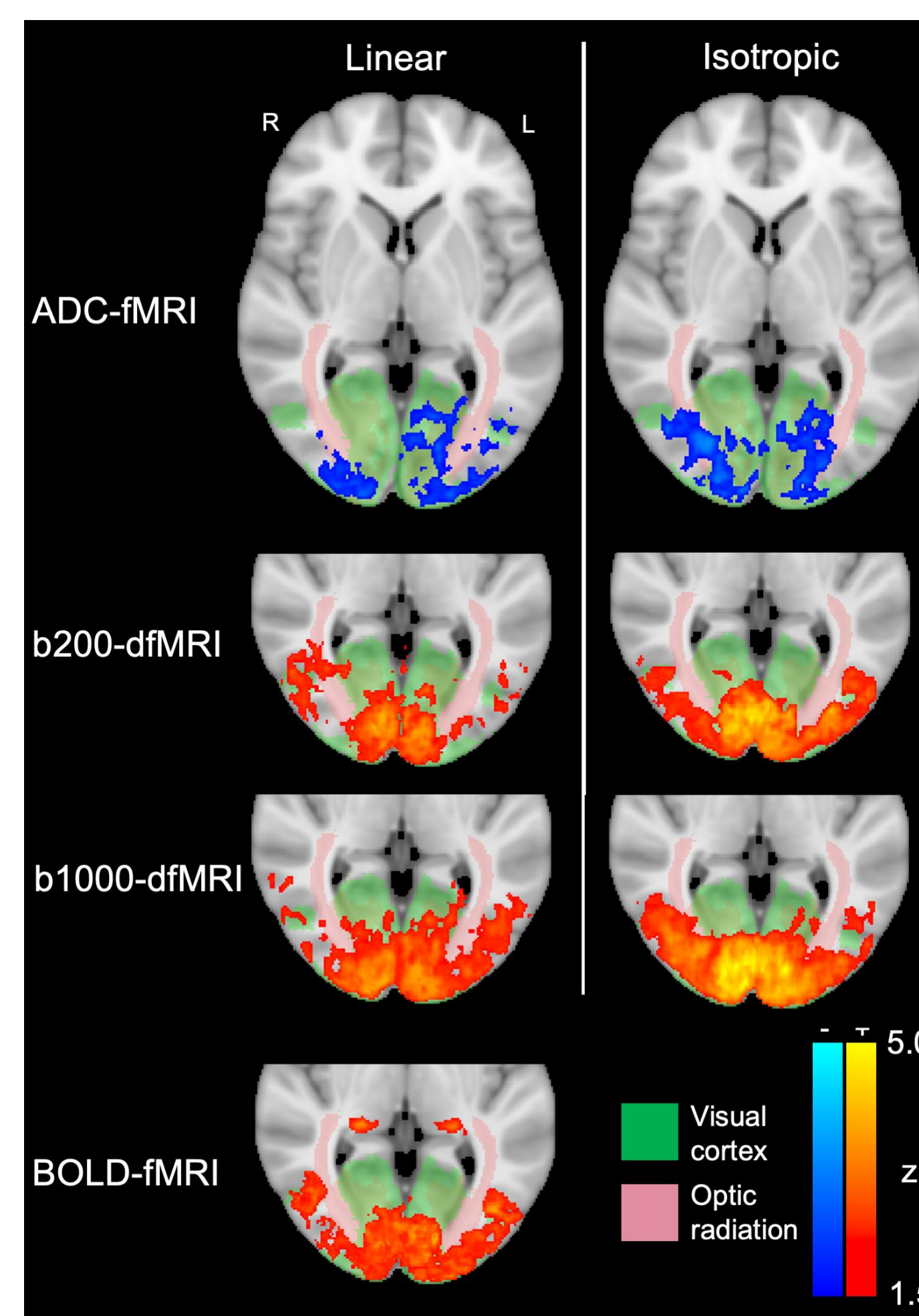


Figure 4: Group-level spatial activation in response to visual stimulation, following group-level cluster correction ( $z > 2.3$ ,  $p < 0.05$ ).

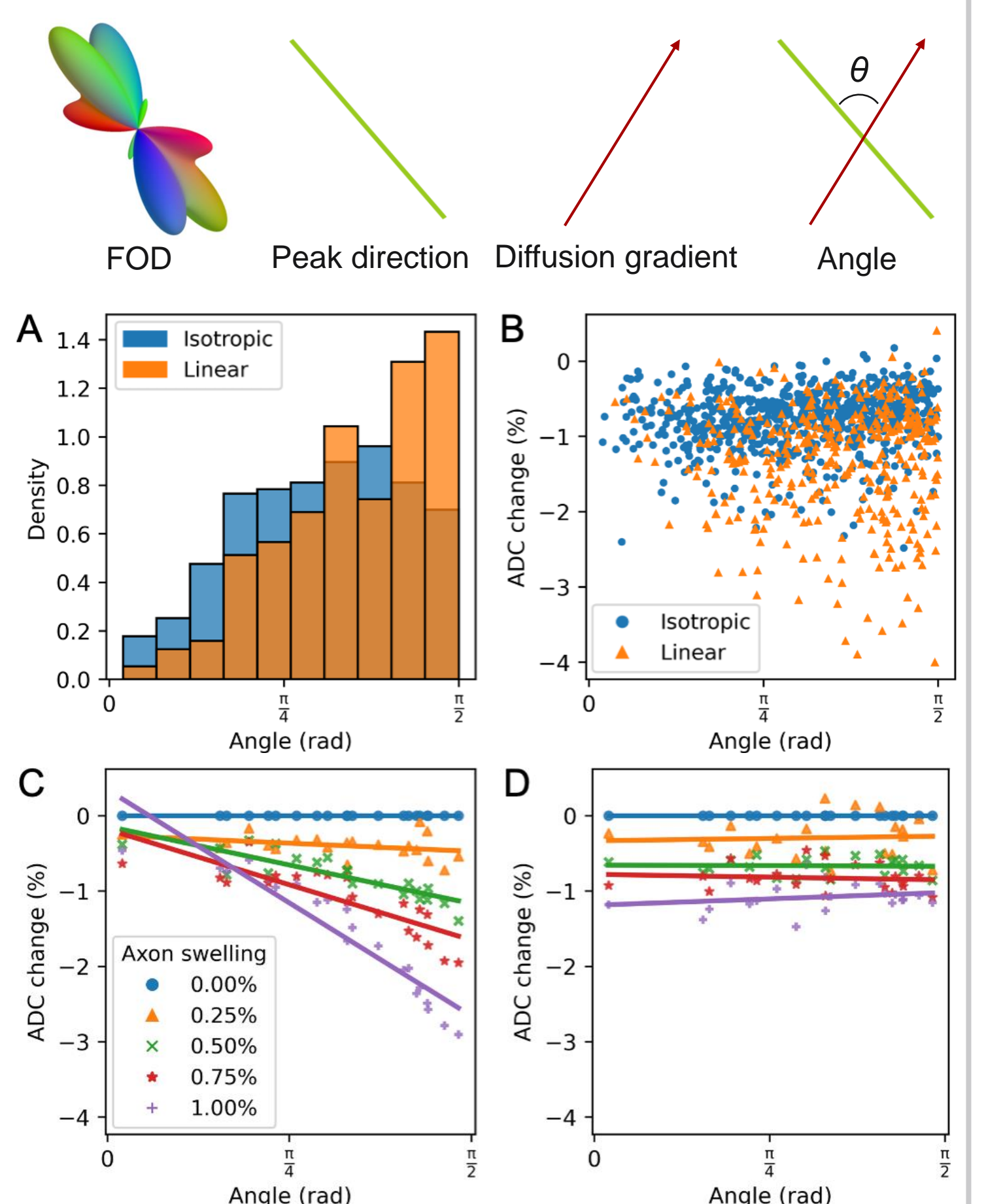


Figure 5: The angle between the largest FOD peak and the diffusion gradient direction was measured in voxels significantly associated with the task. A) Histogram of fibre angles. B) ADC change vs fibre angle. C) Simulated ADC change vs fibre angle for linear encoding and D) isotropic encoding.

### CONCLUSION

- Isotropic ADC-fMRI is more temporally specific and offers better mapping of white matter activity than BOLD-fMRI.
- Isotropic ADC-fMRI detects white matter activity independently of fibre direction, while linear ADC-fMRI preferentially detects activity in voxels containing fibres perpendicular to the diffusion encoding direction.
- This opens opportunities for whole-brain grey and white matter functional connectivity analysis.

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