

## BACKGROUND

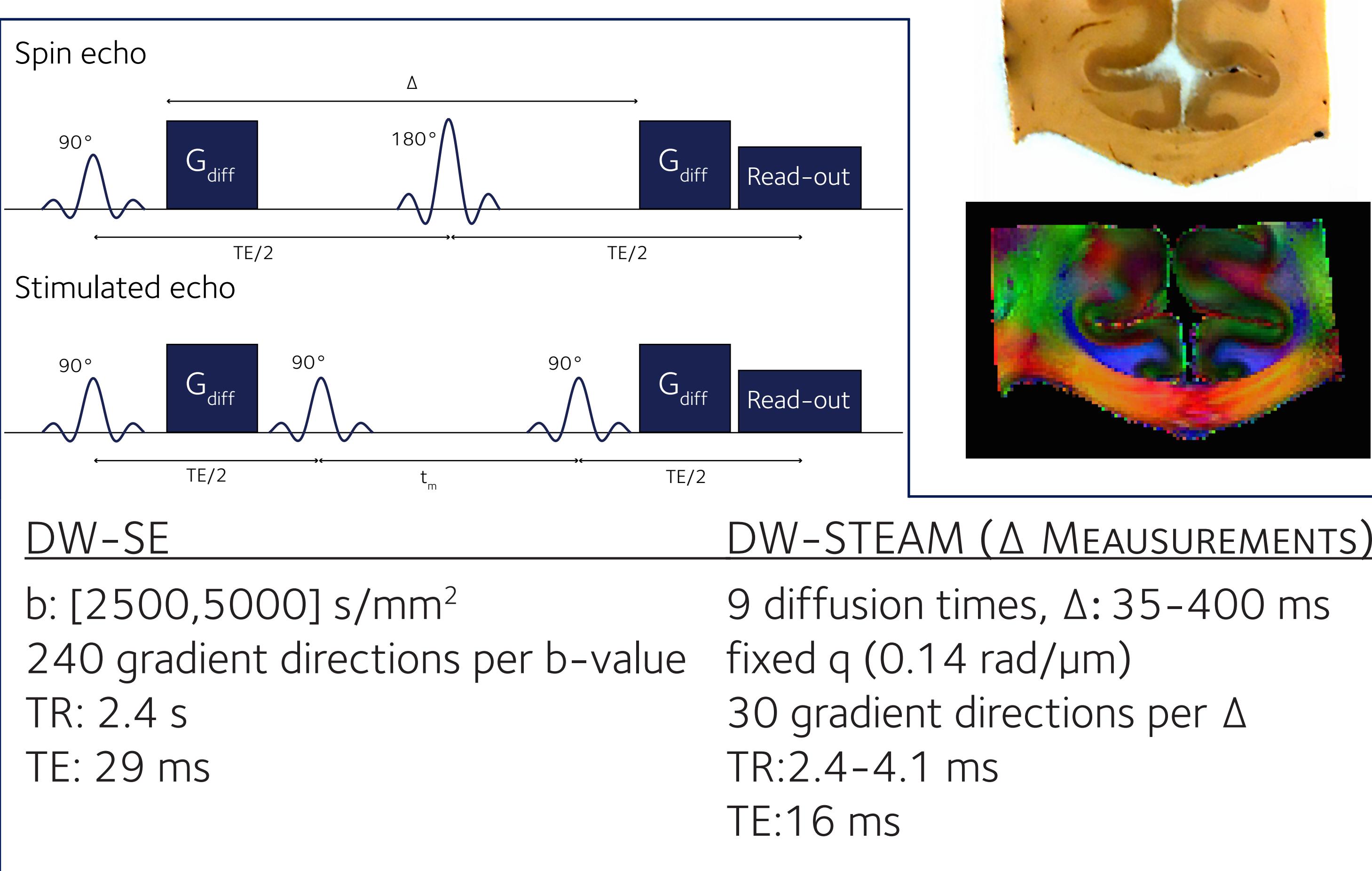
Microstructural imaging of the brain has gained an increasing amount of attention and development in recent years. Increasingly sophisticated models are being developed to describe underlying mechanism of diffusivity. Testing these models has been done with Monte Carlo simulations or in validation studies with reference data such as histology. A frequent test-bed for these models is the corpus callosum (CC) (Nilsson 2013). Here, axons are often assumed to be organized in parallel which may not always be appropriate suggested by recent studies (Mikula 2012, Budde 2013).

Diffusion imaging at long diffusion times ( $\Delta$ ), informs on microstructural tissue features up to  $\sim 100 \mu\text{m}$  scales. Here we employ diffusion time measurements in a post-mortem CC to study diffusion time dependence on the apparent diffusion coefficient (ADC). In addition, its fibre architecture was studied with dispersion models using Diffusion MRI and Polarized Light Imaging (Aixer 2011) to support forward simulations.

## METHODS

### POST-MORTEM MR IMAGING

Human corpus callosum formalin fixed specimen at the level of the anterior commissure (30x20x5 mm). Soaked in PBS and scanned in fluorinert on a Varian 9.4 T preclinical system. The voxel size is 0.4 mm isotropic.



### POLARIZED LIGHT IMAGING

Polarized Light Imaging utilizes polarized light to estimate birefringence in the myelin sheath. A variety of parameters can be extracted from thin brain specimens from which fibre orientation is the primary target.

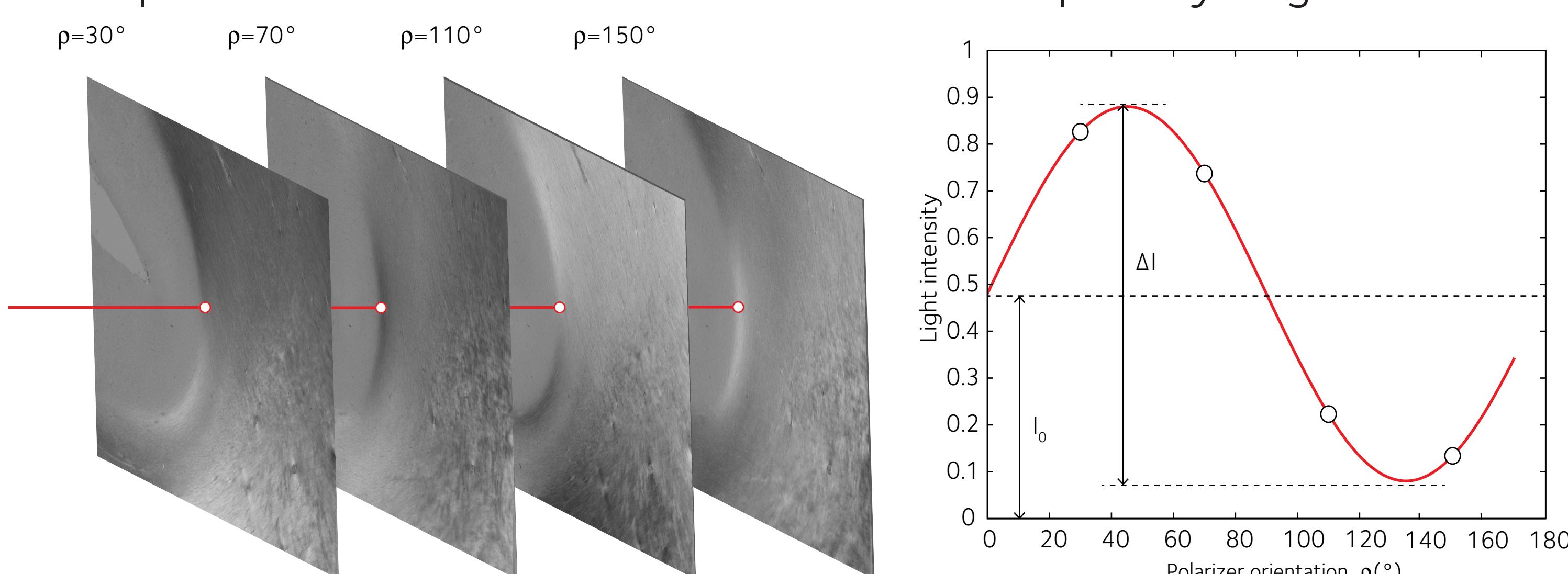


Figure 1. Raw PLI images are acquired by varying the polarizing filter inside the microscopy set-up. A sinusoidal behaviour is observed within a white matter pixel from which fibre orientation is derived as the phase of the signal.

## CONCLUSION

Fibre orientation dispersion in the corpus callosum cannot be neglected as was demonstrated with Polarized Light Imaging. The effect of the diffusion time dependence of the ADC along tract direction however could not be fully explained by dispersion. Currently, no model was found to describe the observed diffusion signal with realistic parameters or biophysical meaning. Monte Carlo simulations in axonal geometries will further support the understanding of diffusion hindrance along tracts and the development of appropriate models.

## RESULTS

### FIBRE ARCHITECTURE IN THE CORPUS CALLOSUM

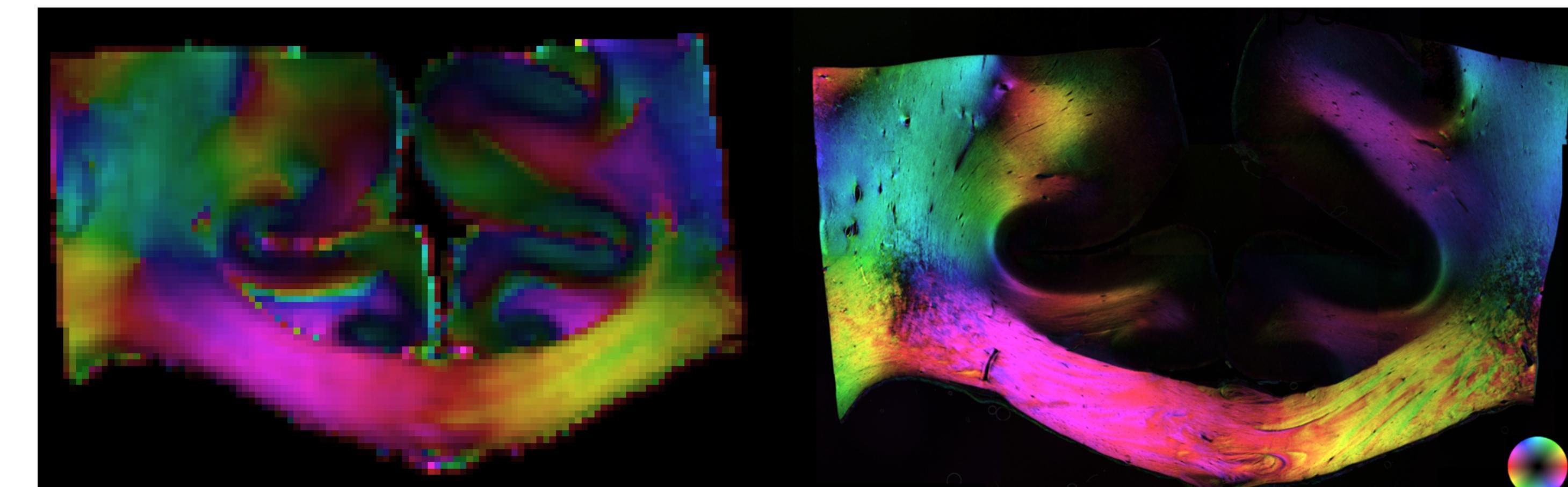


Figure 2. HSV colormap for principal diffusion direction and in-plane fibre orientation according to DTI and PLI, respectively. Hue channel codes for the angular orientation with intensity modulated for either FA or birefringence.

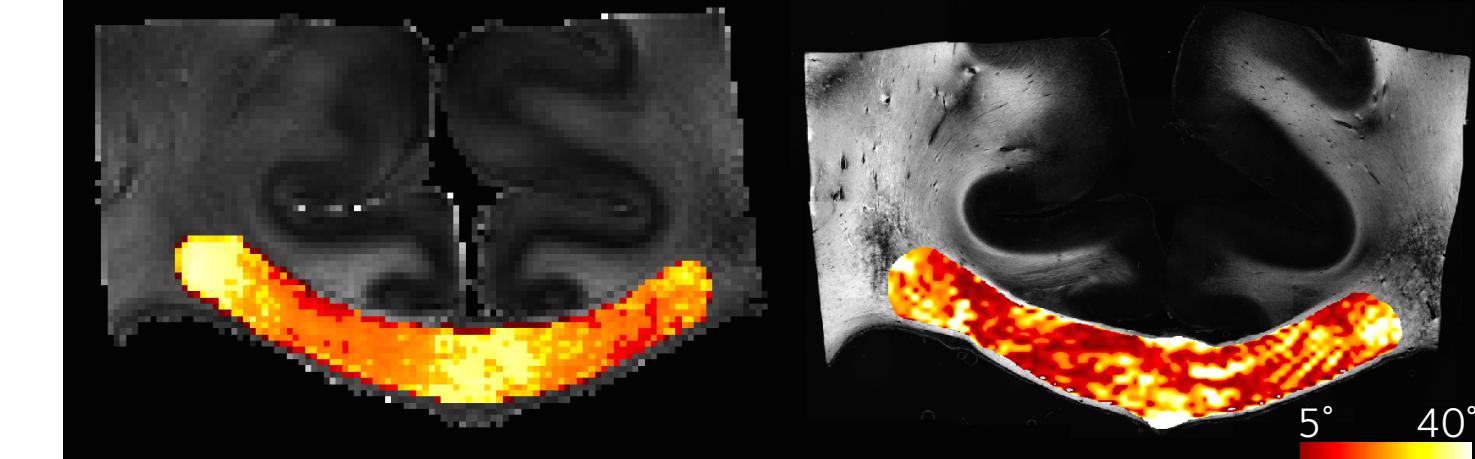


Figure 3. Fibre orientation dispersion was estimated in the corpus callosum with the Ball and Rackets model (Sotropoulos, 2012) applied to the DWI data and with fibre orientation distribution analysis on the PLI data.

- Great correspondence of the macropic fibre orientation in PLI and DWI.
- Fibre orientation dispersion in the CC is considerable.
- On average PLI agrees with the Ball and Rackets model, i.e. higher dispersion in the medial CC compared to its lateral aspects. Voxelwise comparison between both modalities however shows some discrepancy.

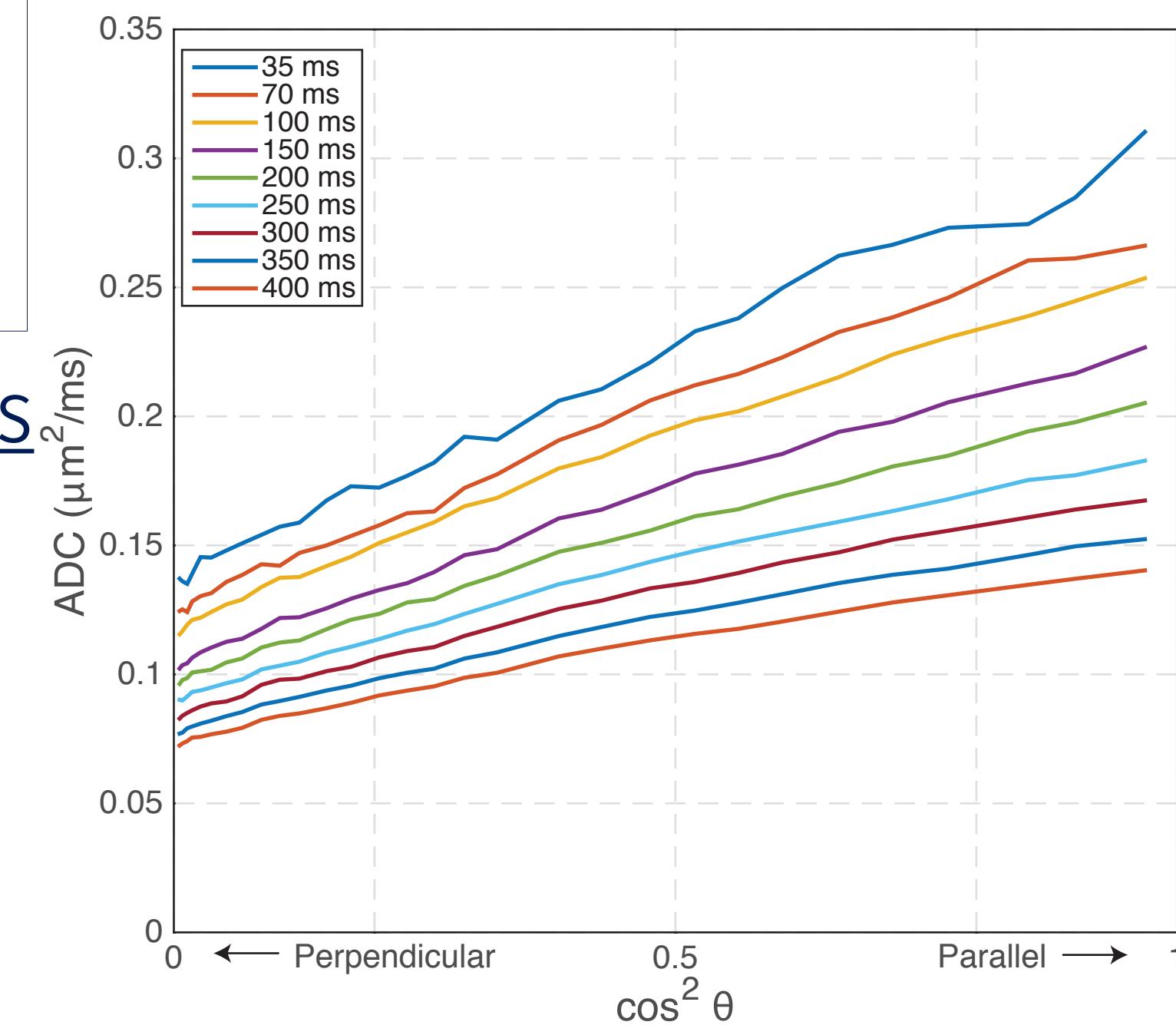


Figure 4. Plots of the ADC as a function  $\cos^2 \theta$ , where  $\theta$  is the angle between the diffusion gradient direction and the principal diffusion direction. Each line represents a different diffusion time.

### DIFFUSION TIME MEASUREMENTS

- The ADC in the corpus callosum decreases with  $\Delta$  across and along the tract.
- This implicates hindrance not only perpendicular to tract but also in parallel direction.
- Is fibre orientation dispersion the underlying mechanism of hindrance along the tract direction?

### FORWARD SIMULATIONS

Though dispersion partially drives the diffusion signal, it is not completely explaining hindrance along tract directions. Even in the presence of a restricted spherical compartment, the amount of dispersion observed in PLI cannot replicate the STEAM data.

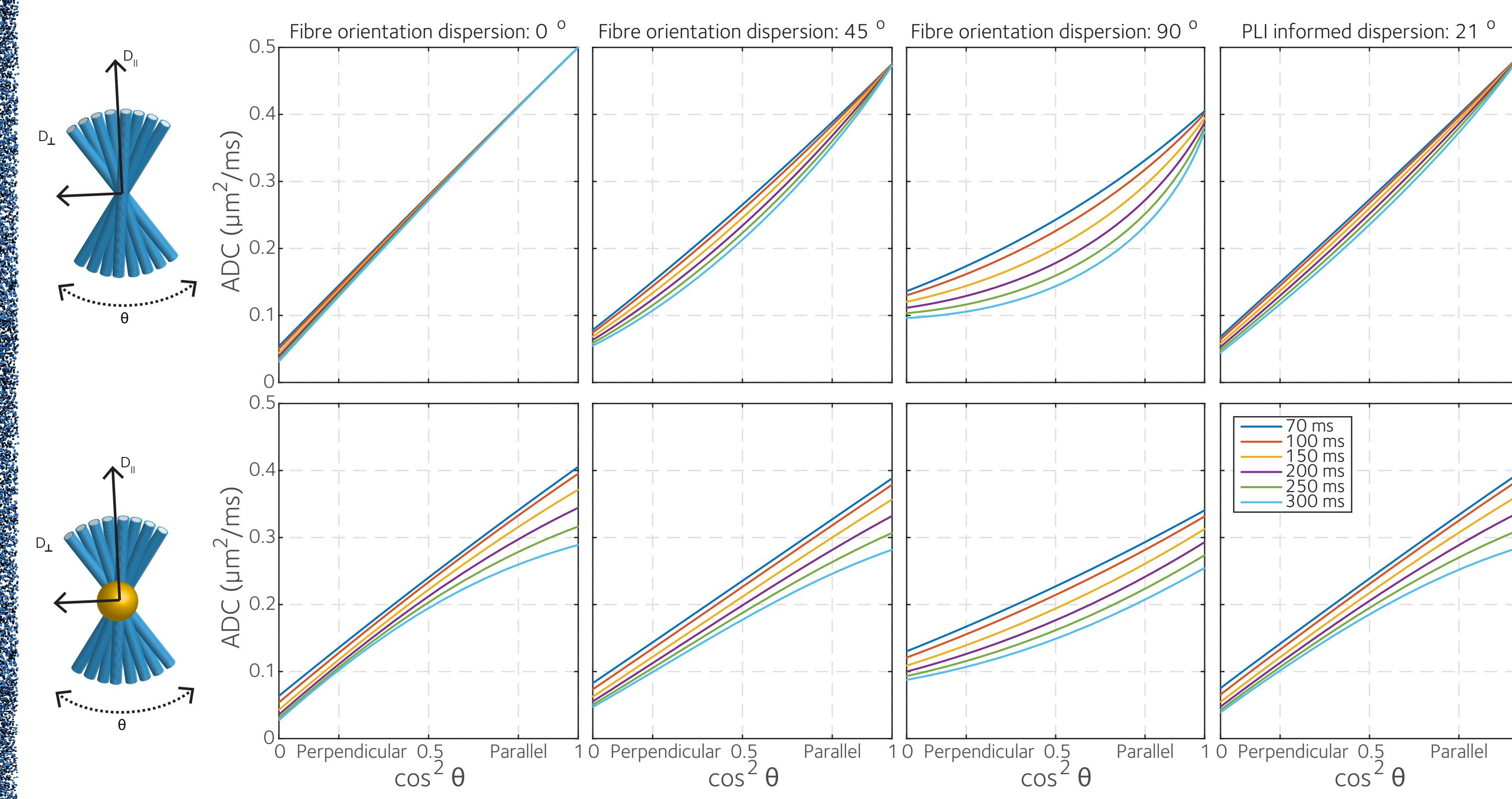


Figure 5. See figure 4 for plot description. Forward simulations of diffusion signal in tissue compartment models exhibiting various amounts of dispersion. The rows represent different compartment models as illustrated by the animations on the left.