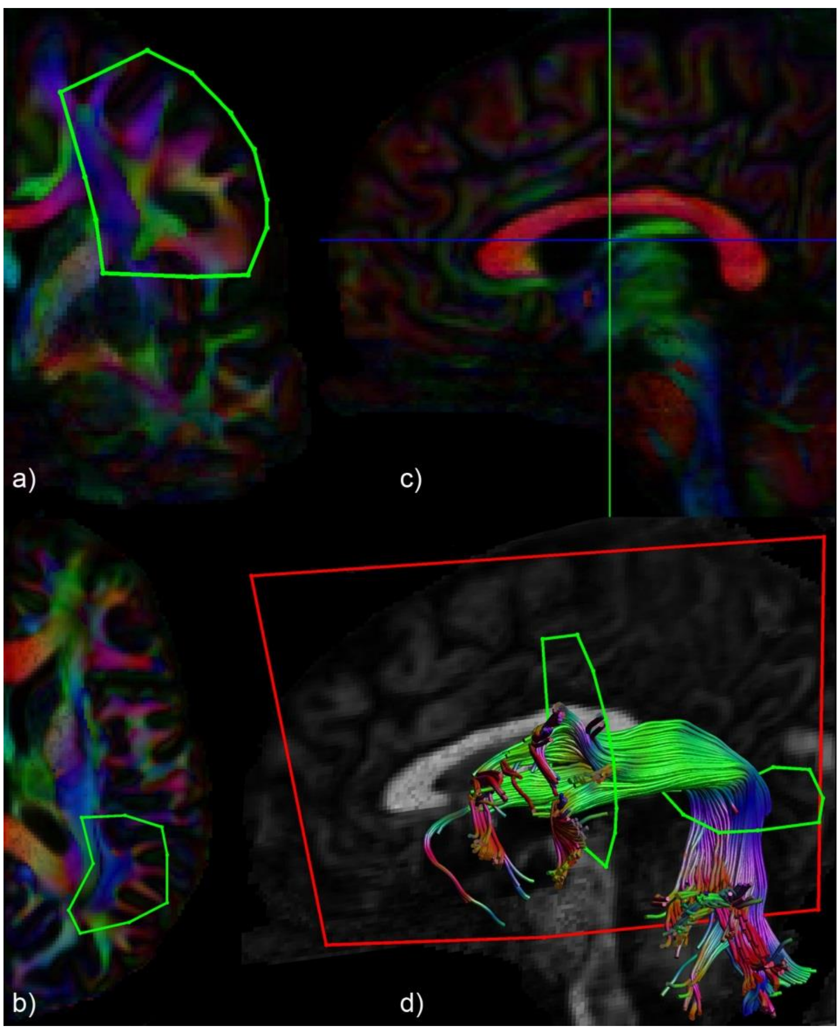
Supplementary material

Tract segmentation from whole-brain tractography

Arcuate fasciculus (AF)

The arcuate fasciculus was segmented by placing two inclusion masks and one exclusion mask.

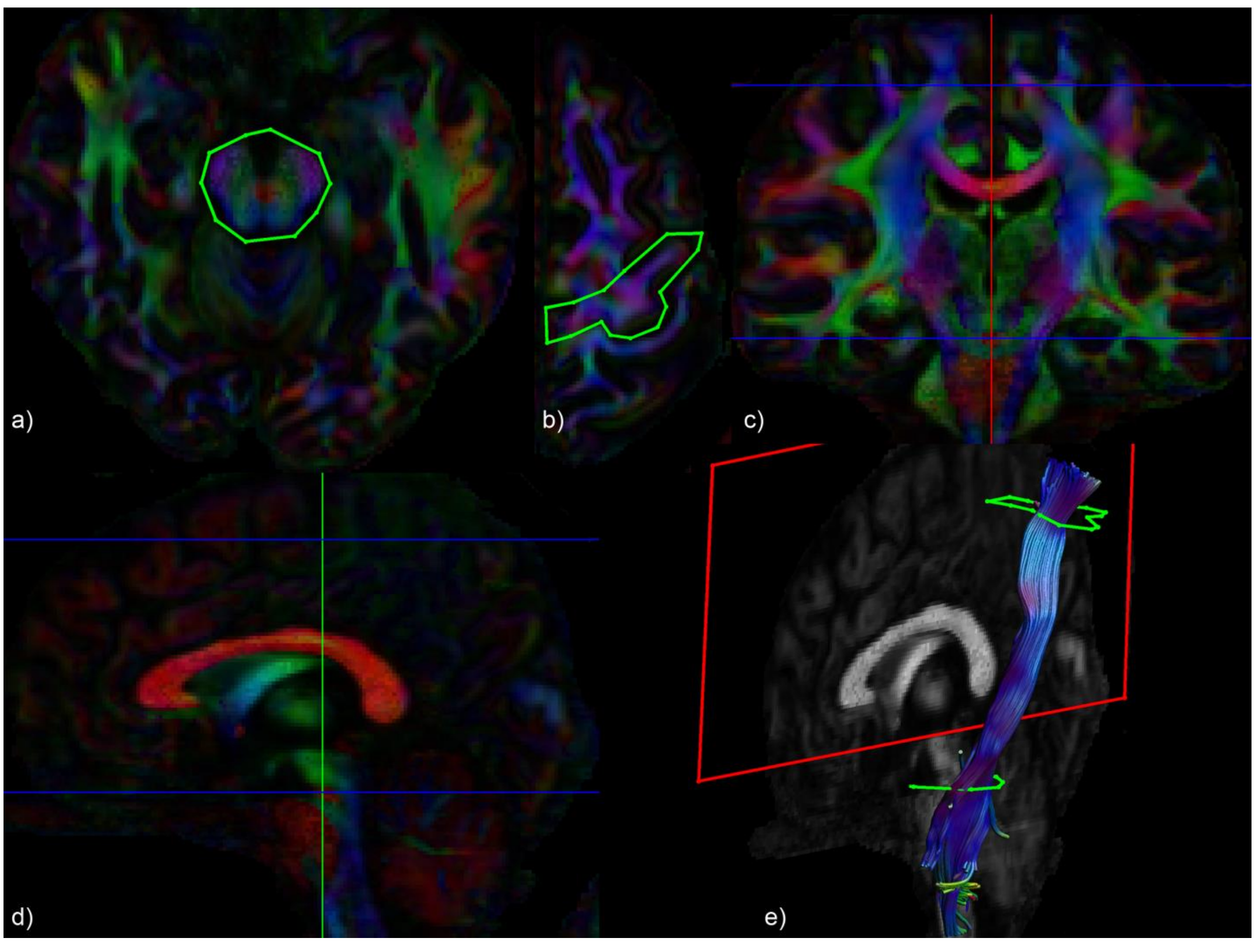
a) One inclusion mask was placed on a coronal slice midway between the genu and splenium of the corpus callosum, where the entire region around the arcuate fasciculus was included.
b) The other inclusion mask was placed on an axial slice around the inferior-superior going part of the fiber bundle
c) The green and blue lines indicate the location of the coronal and axial slices from a) and b), respectively.
d) The red exclusion region-of-interest (ROI) was placed on the mid-sagittal slice to prevent any possible spurious tracts from intersecting the mid-line. The resulting left arcuate fasciculus is shown for the 100_1.0 mm dataset reconstructed with L_{MAX}=8.



Corticospinal tracts (CST)

The CST was segmented with two inclusion masks and an exclusion mask.

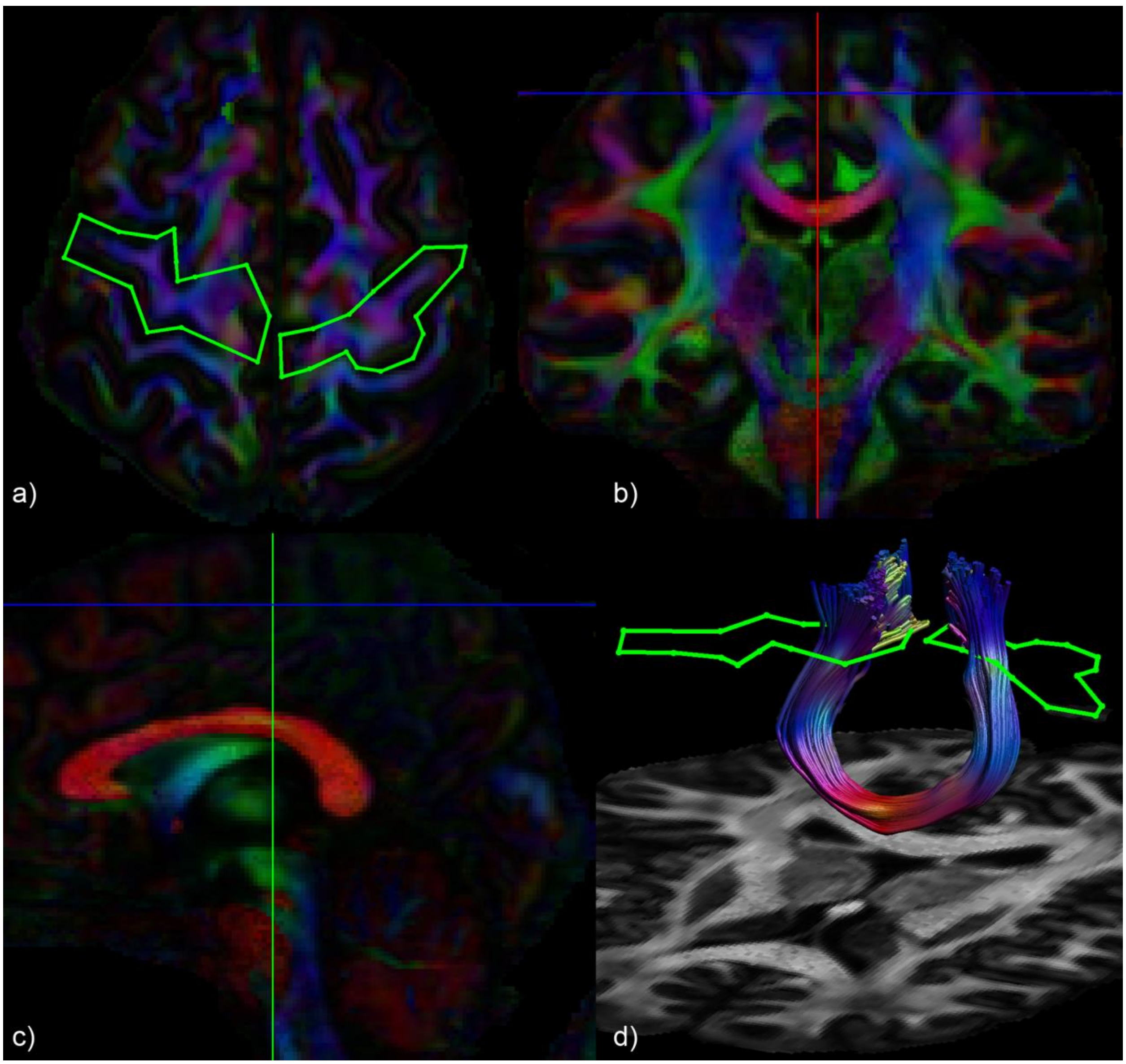
a) One axial inclusion mask on the level of the decussation of the cerebellar peduncles.
b) One axial inclusion mask selecting the primary motor area (M1), drawn on an axial slice 26 mm superior to the corpus callosum as seen on the mid-sagittal slice.
c) Coronal view indicating the locations of the two axial slices (blue lines) where the ROIs were drawn. The red line indicates the location of the sagittal slice shown in d).
d) Sagittal view indicating the locations of the two axial slices (blue lines) where the ROIs were drawn. The green line indicates the location of the coronal slice shown in c).
e) The exclusion mask (red) was placed on the mid-sagittal slice from the level of the external capsule extending to the top of the brain. The resulting left CST fasciculus is shown for the 100_1.0 mm dataset reconstructed with L_{MAX}=8.



Corpus callosum segment connecting M1—M1

Two inclusion masks were used to select the interhemispheric fiber bundle segment.

a) One axial inclusion mask selecting the primary motor area in each hemisphere, drawn on an axial slice 26 mm superior to the corpus callosum as seen on the mid-sagittal slice.
b) Coronal view indicating the locations of the two axial slices (blue lines) where the ROIs were drawn. The red line indicates the location of the sagittal slice shown in c).
c) Sagittal view indicating the locations of the two axial slices (blue lines) where the ROIs were drawn. The green line indicates the location of the coronal slice shown in b).
d) The resulting left CST fasciculus is shown for the 100_1.0 mm dataset reconstructed with L_{MAX}=8.



Investigating the trade-off in Human Connectome Project data

Using the 3D DWI dataset the investigated trade-off contained three degrees of freedom: spatial resolution, number of gradient directions, and the used Lmax value. This has already led to analyses and results with many facets. The preliminary analyses on an HCP dataset shown below add two degrees of freedom to this, given that HCP dataset has a different SNR per image to the 3D DWI, as well as multiple b-values.

Tractography was performed on a single subject dataset from the Human Connectome Project. The 90 directions from each shell (b=1000, 2000, and 3000 s/mm^2) were taken and optimal angular subsets of 25, 50, and 75 directions were taken, all also subsampled from the acquired isotropic resolution of 1.25 mm to isotropic voxel grids of 1.50, 2.00, and 2.50 mm. Firstly, ten subsets of 89 directions were obtained, as in Section 2.7 and 3.3, with the results shown in Table S1. Values for the HCP b=1000 shell are somewhat lower than for the 3D b=1000 s/mm^2 data, with the HCP b=2000 and b=3000 s/mm^2 reproducibility overlap roughly similar to that of the 3D DWI data at b=1000 s/mm^2.

Table S1: Test-retest Dice overlap for left AF reconstructed from HCP data

	Mean [range]
b=1000 s/mm^2	0.81 [0.79 - 0.83]
b=2000 s/mm^2	0.84 [0.83 - 0.86]
b=3000 s/mm^2	0.85 [0.84 - 0.87]

Volumetric overlap

Comparing the angular and spatial subsets within each shell to the highest angular and spatial resolution dataset, the 90_1.25mm dataset (indicated R in Fig. S1), similar patterns are observed as in Fig. 5 for the left AF reconstructed from the 3D DWI data: the highest overlap was obtained for subsets closest to the reference, specifically the datasets with high spatial resolution (1.25 and 1.50 mm) and many directions (75 or 90), as long as Lmax values of 6 or 8 are used. Similar to Fig. 5, Lmax=4 seems to result in a pronounced drop in overlap compared to Lmax of 6 and 8. These patterns are consistent across the three b-values in the HCP data.

To compare all reconstructions to a single reference standard (Fig. S2), instead of per-shell, the 90_1.25mm dataset at b=3000 s/mm^2 is regarded as optimal as for CSD the highest b-value theoretically captures the diffusion signal the best (Tournier et al., 2013). This shows that overlap for virtually all combinations of spatio-angular resolution is lower at lower b-values compared to the b=3000 s/mm^2 reference. Still a definite drop in overlap is observed when choosing Lmax=4 over a higher Lmax – at all b-values. In all cases, a reduction in the number of directions from 75 to 50 causes a steep drop in overlap, mostly for Lmax=8 but also noticeably for Lmax=6. The biggest reduction in overlap as a function of spatial resolution seems to be from 1.50 mm to 2.00 mm, similar to the results in Fig. 5. This is in contrast with the corticospinal and interhemispheric M1—M1 tracts, where this happens from 2.00 to 2.50 mm.

Anatomical correspondence

Comparing the reconstructed fiber bundles visually (Figs. S3-S5), a similar trend is visible with a pronounced difference in reconstruction between the Lmax=4 and Lmax values of 6 and 8. At b=3000 s/mm^2, there is little improvement in using 90 over 75 directions at Lmax=8. With a b-value of 2000

s/mm², there is a clear benefit of using Lmax=8 over Lmax=6, allowing the reconstruction the most frontal projections that are absent at Lmax=6. At b=1000 s/mm², these most frontal projections are found with difficulty, mostly when the SNR is boosted by having a lower spatial resolution.
Interestingly, bundles reconstructed using only 50 directions showed best results using b=2000 s/mm² data. This is in contrast with the Dice overlap, which was higher for b=3000 s/mm² than b=2000 s/mm² for resolutions of 1.50 mm or lower. This could indicate that the higher angular contrast at b=3000 s/mm² requires more information to the described accurately than the b=2000 s/mm² data.
A detailed inspection shows that the reference dataset, 90_1.25mm at b=3000 s/mm² fails to reconstruct one of the more inferior and lateral temporal projections that datasets at lower spatial resolution do recover (Fig. S5). This imperfection in the reference dataset should be considered when interpreting the lower volumetric overlap, as it reveals that some of the decrease in overlap could be because of an improved reconstruction of the cortical projection. At the lowest spatial resolution, however, the larger partial voluming causes tractography to miss some frontal cortical projections.

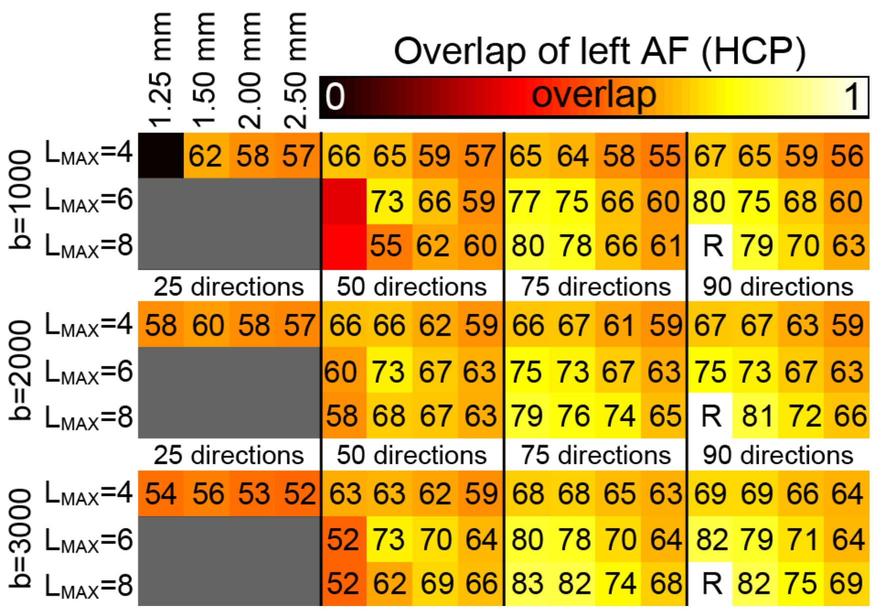


Fig. S1: Volumetric overlap values for the left arcuate fasciculus (AF) reconstructed using an HCP dataset. For each of the three panels, the different spatial resolutions and number of directions are along the horizontal axis with the rows indicating the used Lmax value. The top panel shows results of the data with a b-value of 1000 s/mm², the middle panel shows b=2000 s/mm², the bottom panel shows b=3000 s/mm². The overlap values are with respect to the 90_1.25mm tracts with Lmax=8 for each b-value separately. Overlap values (×100) are given in case of moderate overlap, i.e., ≥0.50.

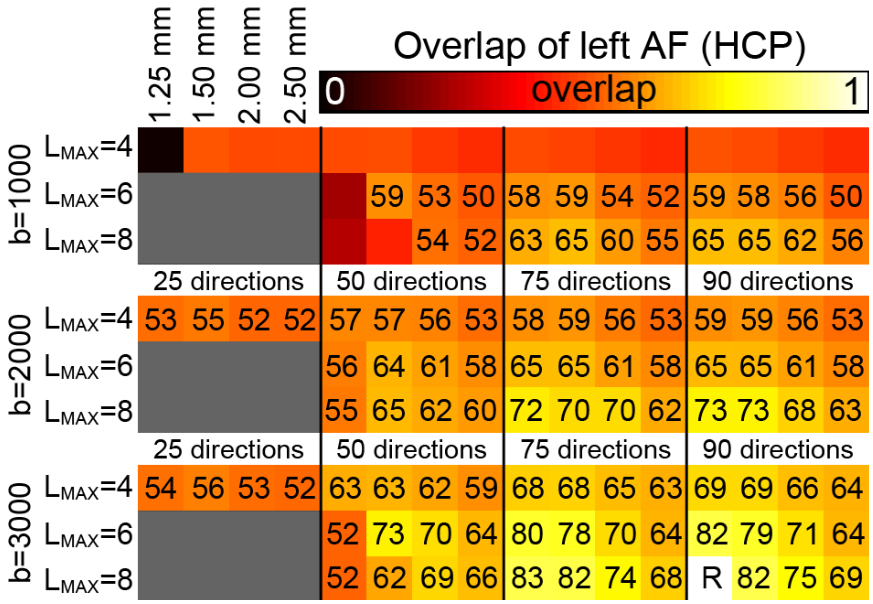


Fig. S2: Volumetric overlap values for the left arcuate fasciculus (AF) reconstructed using an HCP dataset. For each of the three panels, the different spatial resolutions and number of directions are along the horizontal axis with the rows indicating the used Lmax value. The top panel shows results of the data with a b-value of 1000 s/mm^2, the middle panel shows b=2000 s/mm^2, the bottom panel shows b=3000 s/mm^2. The overlap values are with respect to the 90_1.25mm tracts with Lmax=8 for b=3000 s/mm^2. Overlap values (×100) are given in case of moderate overlap, i.e., ≥0.50.

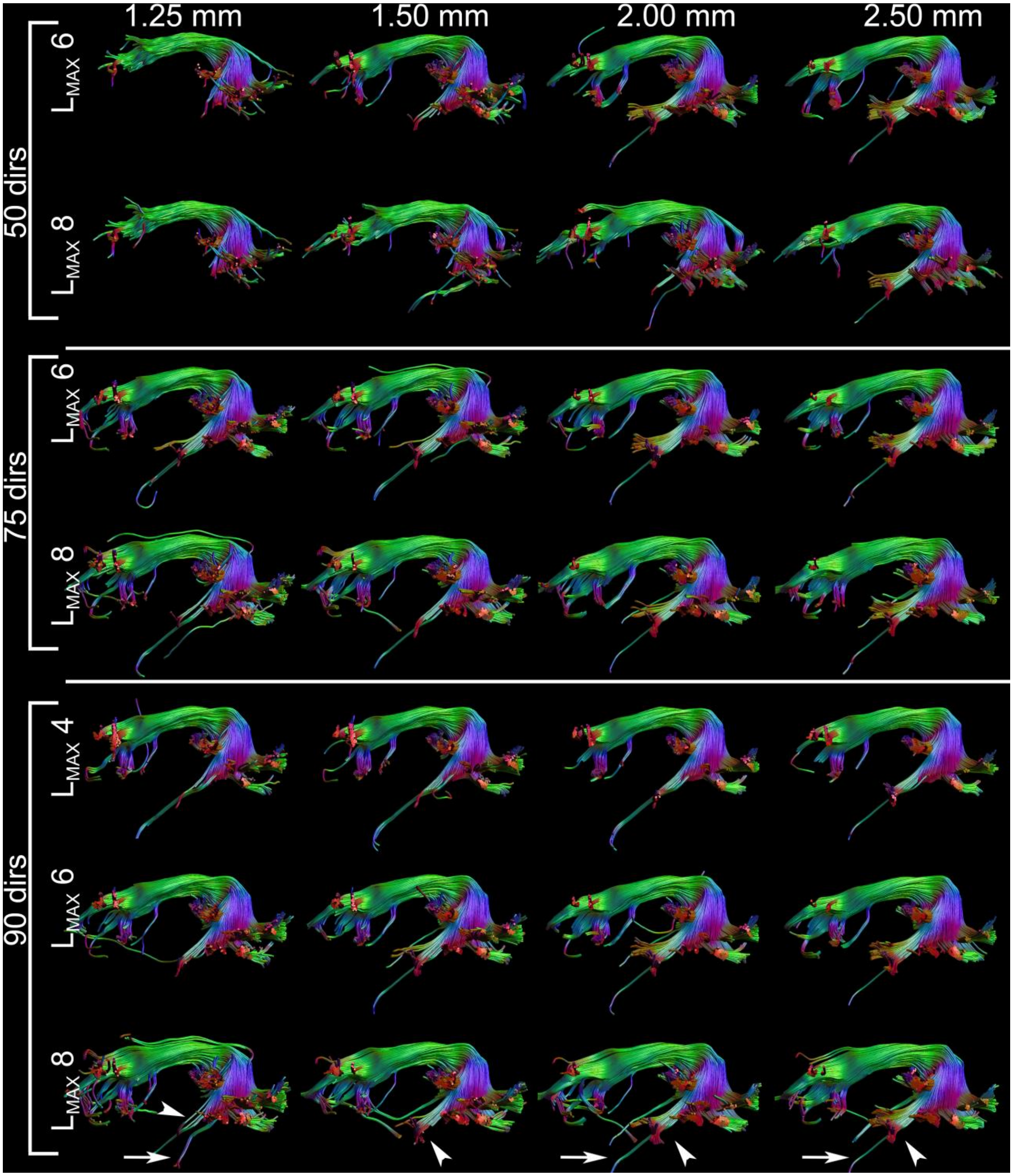


Fig. S3: Tractography results of the left arcuate fasciculus for datasets with 50, 75, and 90 directions at all Lmax values for all spatial resolutions using an HCP dataset with b=3000 s/mm^2. The 90_1.25mm at Lmax=8, bottom left corner, is taken as the reference. This reference dataset misses a most lateral temporal projection that is reconstructed in datasets with lower spatial resolution (arrowhead). The tracts to the temporal pole (arrow) most likely belong to the inferior longitudinal fasciculus, and should thus be regarded as erroneous. Datasets with more directions and higher Lmax found more temporal and frontal projections (similar to Fig. 10), although there is relatively little difference between the 75 and 90 datasets when Lmax and spatial resolutions are matched. Datasets with only 50 directions are only acceptable at low spatial resolution, but those still demonstrate cortical projections that are less well-defined. Compared to the bundles reconstructed using Lmax=6 and 8, the Lmax=4 bundles shown - using 90 directions – all seem to lack the most frontal projections of the AF. Tracts reconstructed with Lmax=4 were only shown for the datasets with 90 directions. At lower angular resolution the tracts were identical in what they were missing as the Lmax=4 at 90 directions – or worse.

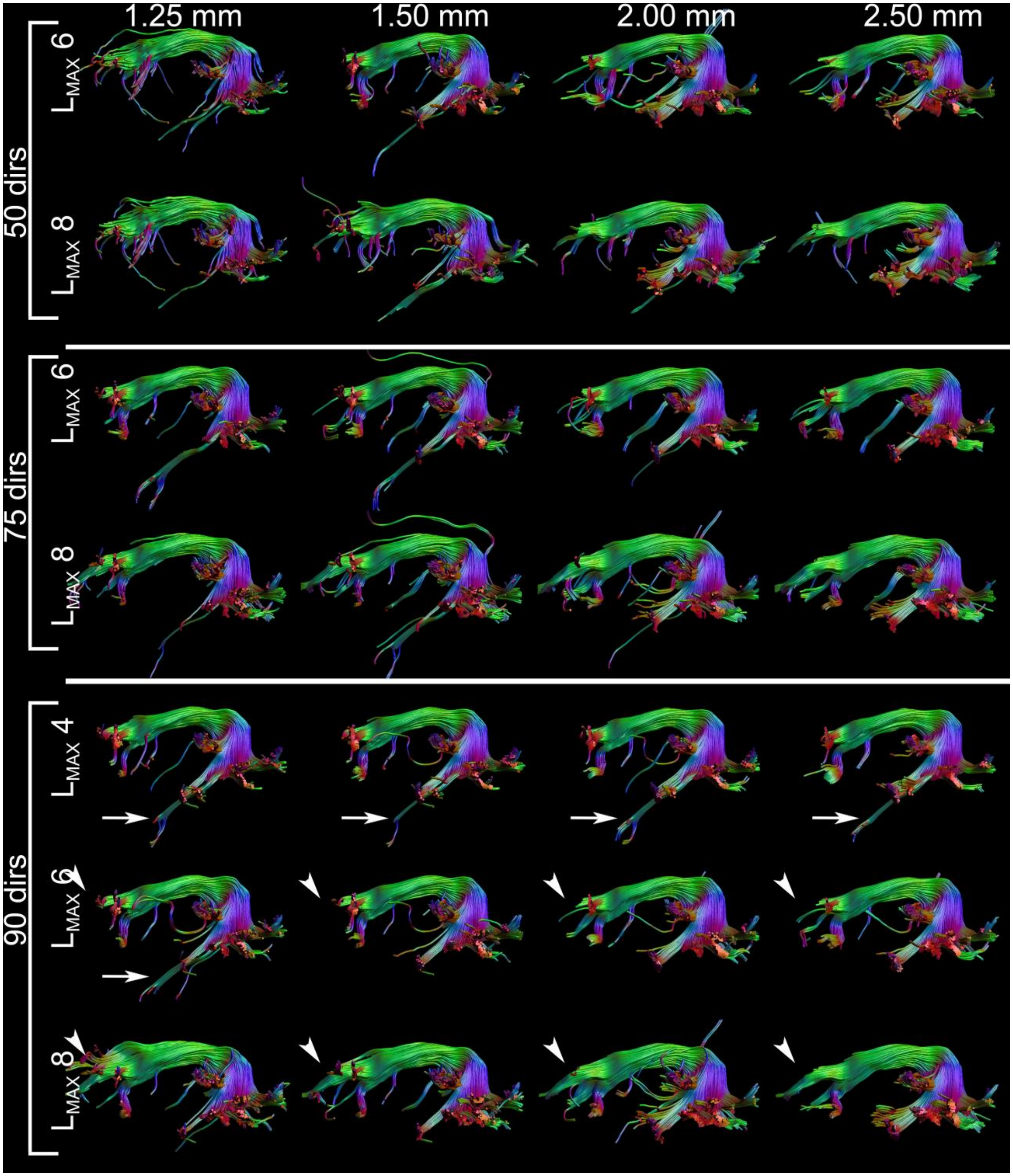


Fig. S4: Tractography results of the left arcuate fasciculus for datasets with 50, 75, and 90 directions at all Lmax values for all spatial resolutions using an HCP dataset with b=2000 s/mm^2. The 90_1.25mm at Lmax=8, bottom left corner, is taken as the reference. The variation in tract reconstructions at different spatial and angular resolutions is similar to that in Fig. S3, with the notable difference that at b=2000 s/mm^2 there seems to be a strong benefit of using Lmax=8 over Lmax=6, especially in the most frontal parts of the bundle, and a larger benefit of 90 over 75 directions than in the b=3000 s/mm^2 data (e.g., no erroneous tracts to the temporal pole, arrows).

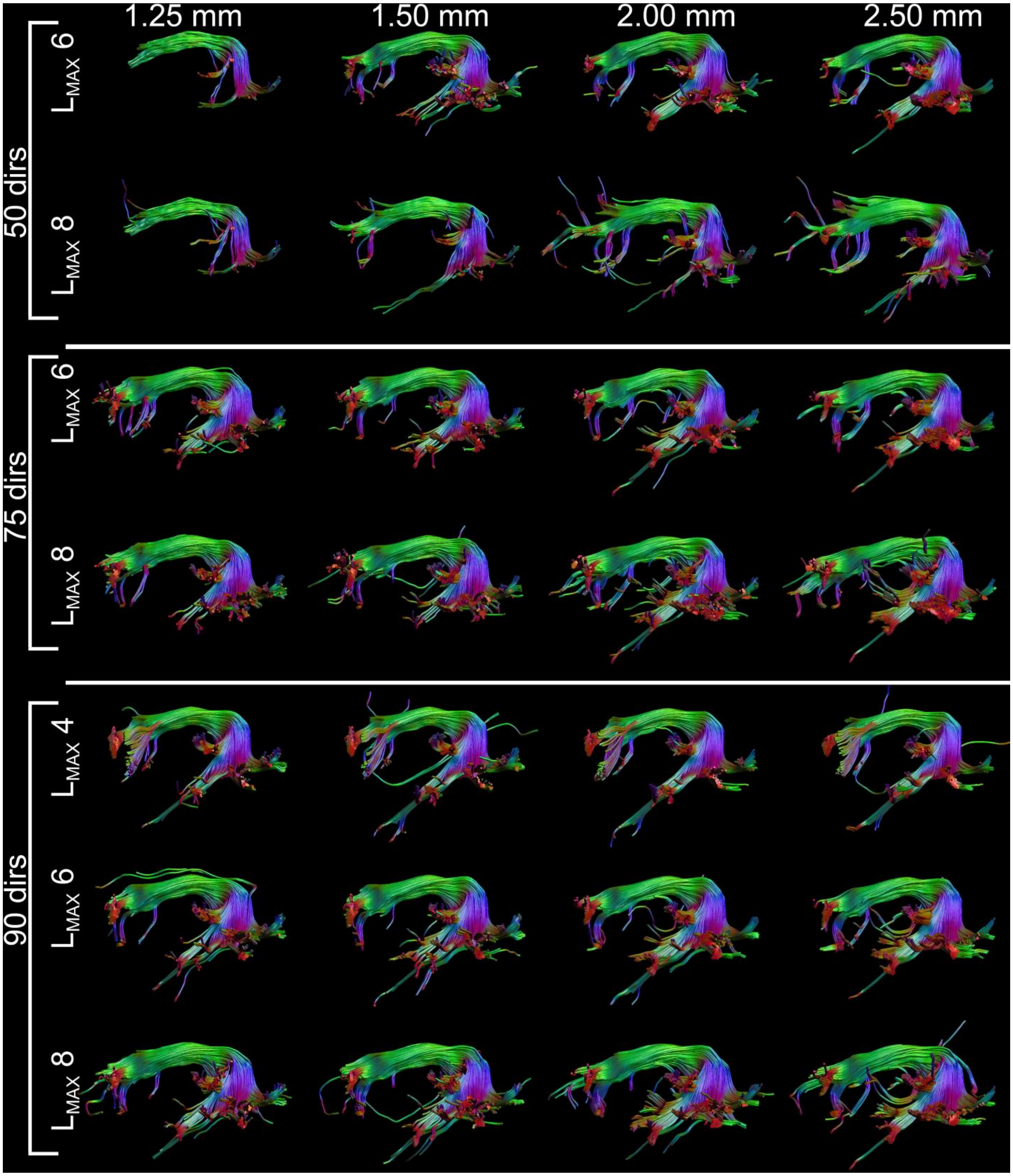


Fig. S5: Tractography results of the left arcuate fasciculus for datasets with 50, 75, and 90 directions at all Lmax values for all spatial resolutions using an HCP dataset with b=1000 s/mm^2. The 90_1.25mm at Lmax=8, bottom left corner, is taken as the reference. The variation in tract reconstructions at different spatial and angular resolutions is similar to that in Figs. S3, with the notable difference that at b=1000 s/mm^2 the most frontal parts of the bundle are reconstructed with difficulty. Additionally, with the inherent lower angular resolution of data with b=1000 s/mm^2 compared to b=3000 s/mm^2, there is a larger benefit of having 90 instead of 75 directions.