

Fast multi-compartment microstructure fingerprinting using deep neural networks

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Synopsis

We estimate microstructural features of crossing fascicles in the white matter by using a fast multi-compartment fingerprinting, an extension of MR fingerprinting to diffusion MRI. The acceleration uses efficient sparse optimization and a dedicated feed-forward neural network to circumvent the inherent combinatorial complexity of the fingerprinting estimation. The accuracy of the results and the speedup factors obtained on *in vivo* brain data suggest the potential of our method for a fast quantitative estimation of microstructural features in complex white matter configurations.

Purpose

In previous work, we extended the MR Fingerprinting (MRF) framework¹ to multi-compartment fingerprinting and applied it to multi-fascicle microstructure estimation of the white matter (WM) from diffusion MRI (dMRI)². That approach allowed us to use a biophysically-realistic Monte Carlo simulator to represent the dMRI signal, similarly to the way a Bloch simulator models the MR signal in traditional “single-compartment” MRF. However, its multi-compartment nature negatively affects the inference runtime complexity as dictionary size increases. In this work, we leverage efficient sparse optimization and a dedicated feed-forward neural network, inspired in part by developments in MRF^{3,4,5} and in WM microstructure estimation^{6,7,8,9,10}, and propose a 2-stage method for fast inference. We validate its efficiency and accuracy on data from the MGH Human Connectome Project (HCP).

Methods

Signal model

We assume the dMRI signal in a WM voxel with intersecting populations of axons to result from the independent contribution of each population, weighted by its voxel occupancy fraction ν . Each axon population is modeled by randomly-packed, straight, parallel cylinders with fixed intra-axonal diffusivity $D_{in} = 2.0\mu m^2/ms$ and fixed diameter distribution. Alongside the volume fractions ν_k , the free parameters to estimate in each population k are the fiber volume fraction fvf_k and extra-axonal diffusivity $D_{ex,k}$. We restricted our analysis to 2-way population crossings.

Microstructure Fingerprinting

Figure 1 (a) summarizes the mathematical operations involved. In a precomputing phase, Monte Carlo simulations of the dMRI signal were performed in a single axon population for all combinations of 38 values of fvf and 10 values of D_{ex} , leading to $N = 380$ fingerprints $A_j (1 \leq j \leq N)$ stored in a canonical dictionary $C_0 = [A_1 \dots A_N] \in \mathbb{R}^{M \times N}$. At runtime in each WM voxel, given measurements $\mathbf{y}$, a matrix is formed by concatenating C_1 and C_2 obtained from rotating C_0 along the orientation of each population, detected using an external routine (here, constrained spherical deconvolution¹¹). An exact solution is obtained by solving a large number N^2 of small non-negative linear least squares (NNLS) problems of 2 variables each, ensuring that only one fingerprint per compartment (i.e., axon population) contributes to the reconstructed signal. This $\mathcal{O}(N^2)$ complexity prevents the use of large dictionaries (large N) in practice.

Microstructure Fingerprinting

$$\begin{aligned}
 \begin{bmatrix} y_1 \\ \vdots \\ y_M \end{bmatrix} &\rightarrow \hat{\mathbf{w}} = \underset{\mathbf{w} \geq 0}{\operatorname{argmin}} \left\| \mathbf{y} - [\mathbf{C}_1 \mathbf{C}_2] \cdot \begin{bmatrix} \mathbf{w}_1 \\ \mathbf{w}_2 \end{bmatrix} \right\|_2^2 \text{ subject to } |\mathbf{w}_1|_0 = 1, |\mathbf{w}_2|_0 = 1 \rightarrow \\
 &\Leftrightarrow (\hat{j}_1, \hat{j}_2) = \underset{1 \leq j_1, j_2 \leq N}{\operatorname{argmin}} \min_{w_1, w_2 \geq 0} \left\| \mathbf{y} - [\mathbf{A}_{j_1}^1 \mathbf{A}_{j_2}^2] \cdot \begin{bmatrix} w_1 \\ w_2 \end{bmatrix} \right\|_2^2 \\
 (a) & \quad \nu_1 = \frac{w_1}{(w_1 + w_2)} \\
 & \quad fvf_1 = fvf_{\hat{j}_1} \\
 & \quad D_{ex,1} = D_{ex,\hat{j}_1} \\
 & \quad \nu_2 = \frac{w_2}{(w_1 + w_2)} \\
 & \quad fvf_2 = fvf_{\hat{j}_2} \\
 & \quad D_{ex,2} = D_{ex,\hat{j}_2}
 \end{aligned}$$

Fast Approach

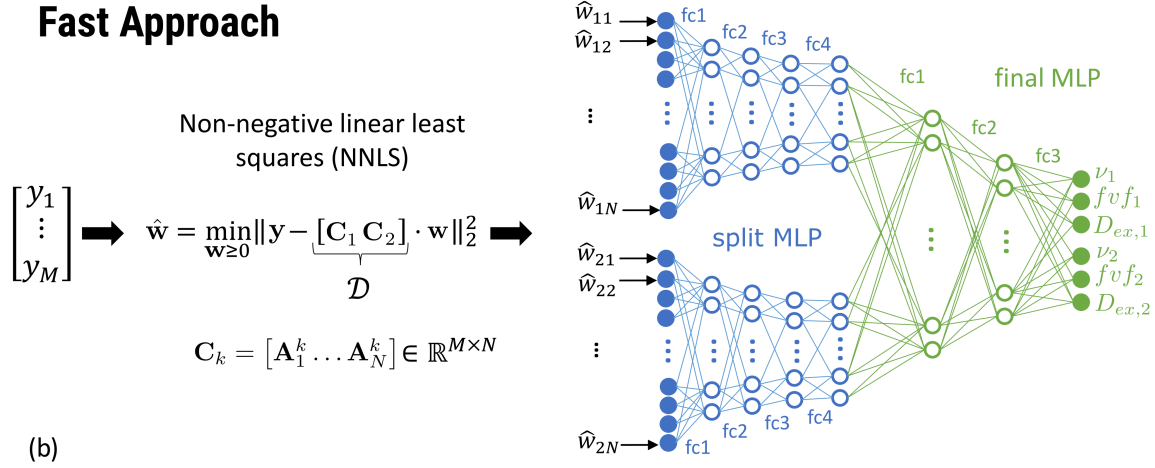


Figure 1: **Reference Microstructure Fingerprinting vs Fast Approach.** In microstructure fingerprinting, a large number of small NNLS problems must be solved leading to long computation times as N increases. In the fast approach, the execution time is dominated by the first stage in which one single NNLS problem is solved. Final inference is performed by a split-MLP neural network.

Fast method

In the first stage (Fig. 1 (b)), the same matrix $[\mathbf{C}_1 \mathbf{C}_2]$ is assembled. However, one single NNLS problem of $2N$ variables is solved without any knowledge about that 2-compartment structure and without any sparsity constraint on the weight vector $\mathbf{w}$. This effectively projects the measurements $\mathbf{y}$ in the space of dictionary fingerprints. NNLS is known to naturally enforce sparsity^{12,13} and has an empirical runtime proportional to the number of matrix columns (here, $2N$), making it much more efficient than the exhaustive fingerprinting described above.

The second stage consists in passing the NNLS weight vector through a feed-forward neural network. The network initially has split arms independently processing the weights (unknowingly) attributed to each compartment by NNLS before merging into a common multi-layer-perceptron (MLP) for final parameter inference. The advantage of this architecture is to reduce the number of free parameters and facilitate training. The network was trained on synthetic dMRI data corrupted with Rician noise (SNR in 30-100).

Table 1 summarizes the characteristics of both methods.

Experiments

To assess efficiency and accuracy, the reference and the fast method were applied to the 34 healthy young adults of the MGH HCP dataset¹⁴. The parameter maps were projected into the XTRACT HCP probabilistic atlas¹⁵. The mean absolute error (MAE) for each WM property (ν , fvf , D_{ex}) were averaged across WM regions and reported for each subject.

Results

Performance

As predicted by theory, the fast method was 1-2 orders of magnitude faster than the reference method (Table 1), with inference time dominated by the 1st stage NNLS problem.

	MICROSTRUCTURE FINGERPRINTING	FAST APPROACH
MINIBATCH SIZE	$\times$	5000
DROPOUT RATE	$\times$	0.1
LEARNING RATE	$\times$	1×10^{-4}
TRAINING SAMPLES	$\times$	1.2×10^6
HIDDEN UNITS	$\times$	2820
PARAMETERS	$\times$	3×10^6
PRECOMPUTATION TIME	≈ 2 d	≈ 2 d
DICTIONARY ROTATION TIME/VOXEL	8.10×10^{-3} s	8.10×10^{-3} s
EXHAUSTIVE FINGERPRINTING TIME/VOXEL	9.09×10^{-1} s	$\times$
FIRST STAGE: SOLVING NNLS TIME/VOXEL	$\times$	1.47×10^{-2} s
SECOND STAGE: NN FORWARD PASS TIME/VOXEL	$\times$	4.24×10^{-5} s
TOTAL INFERENCE TIME/VOXEL	9.18×10^{-1} s	2.36×10^{-2} s
ACCELERATION FACTOR	1	38.9
INFERENCE COMPLEXITY	$\mathcal{O}(N^K K)$	$\mathcal{O}(NK)$

Table 1: Meta parameters and efficiency of the two methods when performing inference on all 34 subjects from the MGH Adult Diffusion data release.

Accuracy

Overall, the estimates of WM properties obtained with the fast method were very close to those of the exhaustive microstructure fingerprinting across all 34 subjects and all brain regions (Figure 2). In the worst region of the worst subject, the error for D_{ex} represented 7% of the possible range in the dictionary (around 2.5% for most other regions); for fvf this was less than 2%. The errors were higher for the volume fractions ν around 0.06. Figure 3 suggests that the error on fvf was kept under control even at the voxel level across the cohort. Figure 4 shows consistent fiber volume fraction maps for a representative subject.

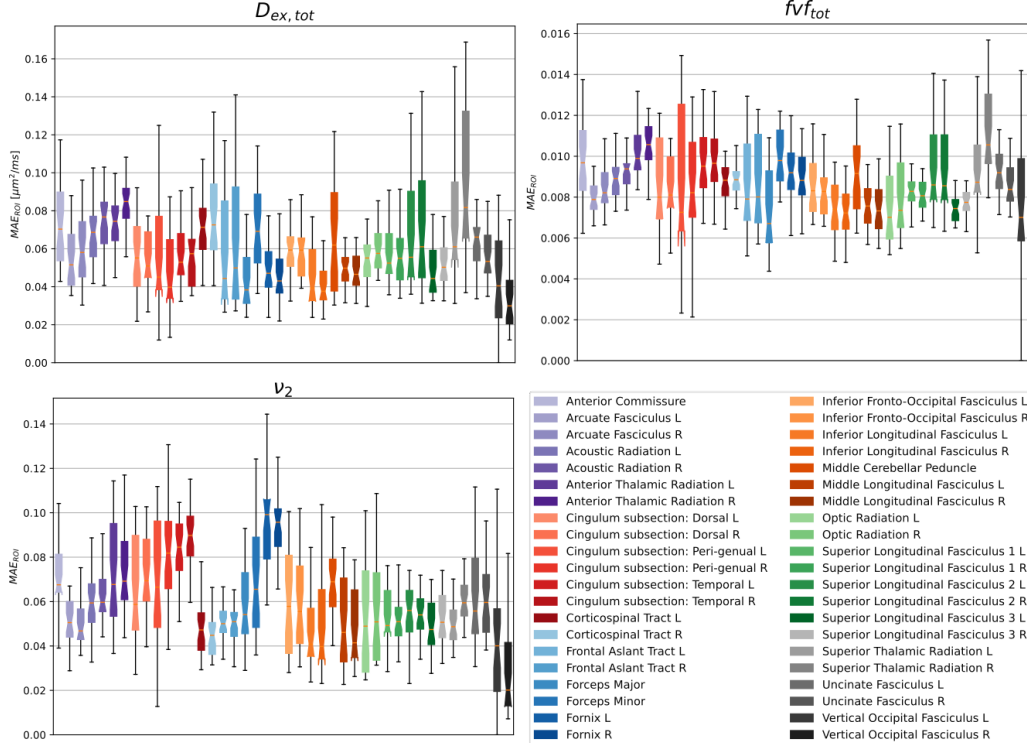


Figure 2: **Region-wise accuracy.** Mean absolute error (MAE) between the reference and the fast method for each microstructural metric, averaged across WM regions of interest (XTRACT HCP probabilistic atlas). Boxplots over all 34 subjects of the MGH Adult Diffusion dataset. The errors are very low for the extraaxonal diffusivity D_{ex} (mostly in $[0.04, 0.10]$ while max value in precomputed dictionary was $2.4 \mu m^2/ms$) and fiber volume fraction fvf (mostly in $[0.006, 0.012]$ with max dictionary value 0.80) and slightly larger for the volume fraction.

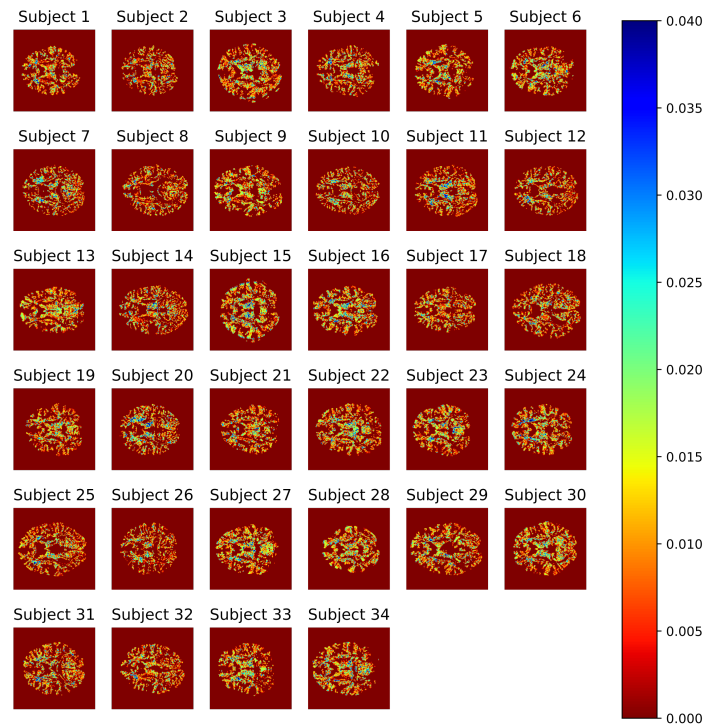


Figure 3: **Voxel-wise accuracy.** Voxel-wise difference in fiber volume fraction (fvf, average of the two populations in each voxel) between the reference and the fast method, for the entire HCP MGH cohort.

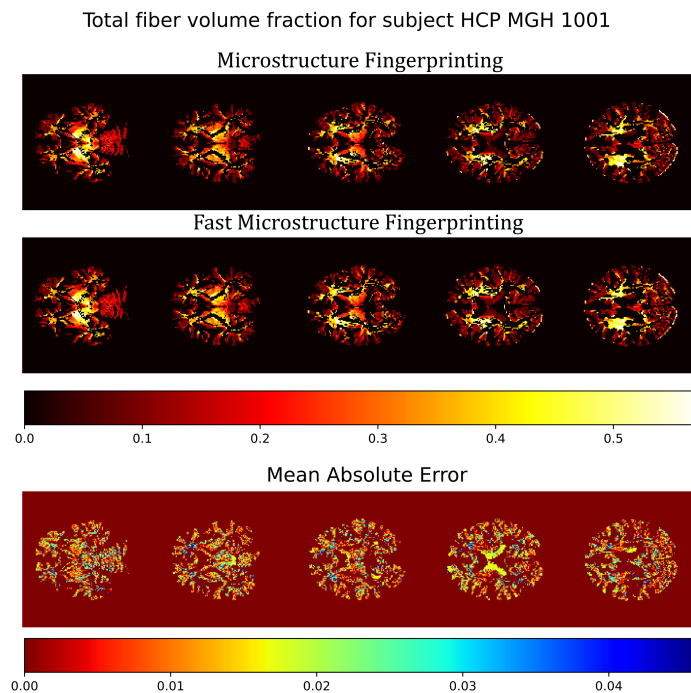


Figure 4: **Voxel-wise accuracy.** Detailed visualization on subject MGH 1001. Voxel-wise maps of the differences in fiber volume fraction (fvf, average of the two populations in each voxel) between the reference and the fast method.

Discussion and Conclusion

A neural network coupled with an optimization routine was used to estimate microstructural properties of crossing axon populations in an *in vivo* dataset. While the accelerated method was 1-2 orders of magnitude faster than the reference method, speedup factors are expected to be even larger with larger dictionaries as

execution time of the fast method grows linearly rather than quadratically with dictionary size. *In vivo* results suggested the ability of our framework to extract accurate microstructural properties when dealing with crossing fascicles. This suggests the potential to deal with larger dictionaries and consequently use more complex models to represent populations of axons in the WM, all the while leveraging the superior modeling capabilities of Monte Carlo simulations.

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References

- ¹ Ma, D., Gulani, V., Seiberlich, N., Liu, K., Sunshine, J.L., Duerk, J.L. and Griswold, M.A., 2013. Magnetic resonance fingerprinting. *Nature*, 495(7440), pp.187-192.
- ² Rensonnet, G., Scherrer, B., Girard, G., Jankovski, A., Warfield, S.K., Macq, B., Thiran, J.P. and Taquet, M., 2019. Towards microstructure fingerprinting: estimation of tissue properties from a dictionary of Monte Carlo diffusion MRI simulations. *NeuroImage*, 184, pp.964-980.
- ³ Cohen, O., Zhu, B. and Rosen, M.S., 2018. MR fingerprinting deep reconstruction network (DRONE). *Magnetic resonance in medicine*, 80(3), pp.885-894.
- ⁴ Fang, Z., Chen, Y., Liu, M., Xiang, L., Zhang, Q., Wang, Q., Lin, W. and Shen, D., 2019. Deep learning for fast and spatially constrained tissue quantification from highly accelerated data in magnetic resonance fingerprinting. *IEEE transactions on medical imaging*, 38(10), pp.2364-2374.
- ⁵ Lundervold, A.S. and Lundervold, A., 2019. An overview of deep learning in medical imaging focusing on MRI. *Zeitschrift für Medizinische Physik*, 29(2), pp.102-127.
- ⁶ Ye, C., 2017. Tissue microstructure estimation using a deep network inspired by a dictionary-based framework. *Medical image analysis*, 42, pp.288-299.
- ⁷ Gibbons, E.K., Hodgson, K.K., Chaudhari, A.S., Richards, L.G., Majersik, J.J., Adluru, G. and DiBella, E.V., 2019. Simultaneous NODDI and GFA parameter map generation from subsampled q-space imaging using deep learning. *Magnetic resonance in medicine*, 81(4), pp.2399-2411.
- ⁸ Ye, C., Li, X. and Chen, J., 2019. A deep network for tissue microstructure estimation using modified LSTM units. *Medical image analysis*, 55, pp.49-64.
- ⁹ Ye, C., Li, Y. and Zeng, X., 2020. An improved deep network for tissue microstructure estimation with uncertainty quantification. *Medical image analysis*, 61, p.101650.
- ¹⁰ de Almeida Martins, J.P., Nilsson, M., Lampinen, B., Palombo, M., While, P.T., Westin, C.F. and Szczepankiewicz, F., 2021. Neural Networks for parameter estimation in microstructural MRI: a study with a high-dimensional diffusion-relaxation model of white matter microstructure. *bioRxiv*.
- ¹¹ Tournier, J.D., Calamante, F. and Connelly, A., 2007. Robust determination of the fibre orientation distribution in diffusion MRI: non-negativity constrained super-resolved spherical deconvolution. *Neuroimage*, 35(4), pp.1459-1472.
- ¹² Lawson, C.L. and Hanson, R.J., 1995. Solving least squares problems. Society for Industrial and Applied Mathematics.
- ¹³ Canales-Rodríguez, E.J., Legarreta, J.H., Pizzolato, M., Rensonnet, G., Girard, G., Rafael-Patino, J., Barakovic, M., Romascano, D., Alemán-Gómez, Y., Radua, J. and Pomarol-Clotet, E., 2019. Sparse wars: A survey and comparative study of spherical deconvolution algorithms for diffusion MRI. *NeuroImage*, 184, pp.140-160.
- ¹⁴ Setsompop, K., Kimmlingen, R., Eberlein, E., Witzel, T., Cohen-Adad, J., McNab, J.A., Keil, B., Tisdall, M.D., Hoeft, P., Dietz, P. and Cauley, S.F., 2013. Pushing the limits of in vivo diffusion MRI for the Human Connectome Project. *Neuroimage*, 80, pp.220-233.
- ¹⁵ Warrington, S., Bryant, K.L., Khrapitchev, A.A., Sallet, J., Charquero-Ballester, M., Douaud, G., Jbabdi, S., Mars, R.B. and Sotiropoulos, S.N., 2020. XTRACT-Standardised protocols for automated tractography in the human and macaque brain. *Neuroimage*, 217, p.116923.