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## **SANDI-AMICO: an open-source toolbox for fast Soma And Neurite Density Imaging (SANDI) with AMICO**

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# SANDI-AMICO: an open-source toolbox for fast Soma And Neurite Density Imaging (SANDI) with AMICO

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## Introduction:

Over the last decades, many techniques have been proposed to infer brain tissue microstructure from the diffusion-weighted MRI (dMRI) signal (1). Most of them assume geometrical configurations that are specific to white matter and are widely used also in clinical applications (2). Recently, the Soma And Neurite Density Imaging (SANDI) (3) has been proposed to estimate MR apparent neurite and soma density in grey matter. However, the estimation of these parameters from dMRI measurements is challenging (4) and time consuming when using conventional fitting methods based on non-linear least square (NLLS) minimization.

Here, we overcome these limitations by proposing SANDI-AMICO: a new implementation of SANDI inside the Accelerated Microstructure Imaging via Convex Optimization (AMICO) framework (5). We demonstrate the performance of SANDI-AMICO in simulations and in vivo data from mouse and human brains. The SANDI-AMICO toolbox is available at <https://github.com/daducci/AMICO>.

## Methods:

SANDI assumes that soma (cell bodies) and neurites can be approximated as two non-exchanging compartments, modeled as spheres of certain size and cylinders of zero radius ("sticks"), respectively. Under these assumptions, the normalized direction-averaged dMRI signal ( $S_{avg}$ ) is:

$$S_{avg}(b)/S(0) = f_n S_n(b, D_n) + f_s S_s(b, D_s, R_s) + (1 - f_n - f_s) S_e(b, D_e) \quad [1]$$

where  $f_n$  is the neurite signal fraction,  $D_n$  the intra-neurite diffusivity;  $f_s$  the soma signal fraction,  $R_s$  the apparent soma radius,  $D_s = 3 \mu\text{m}^2/\text{ms}$ , and  $D_e$  the extra-cellular diffusivity (3).  $S_n$ ,  $S_s$  and  $S_e$  are computed as in (3).

SANDI-AMICO rewrites eq.[1] as linear system  $Ax=y$ , where  $A$  is a matrix containing simulated signals of each compartment,  $y$  the vector of measured signals, and  $x$  the unknown contributions. To build  $A$ , we searched for the combination of sphere radii and diffusivities that produced sufficiently different signals according to the specific acquisition protocol. The elements of  $x$  are then estimated using a non-negative least square with Tikhonov regularization.

We used analytical simulations to compare the performance of AMICO and NLLS estimations under controlled conditions. We generated 2,500 different synthetic signals using random combinations of the SANDI model parameters and eq.[1], according to the mouse data protocol and adding Gaussian noise with  $\text{SNR}=100$ , similar to the data. We assessed the accuracy and precision of both AMICO and NLLS implementations by comparing the percent error and deviation of the estimated model parameters with the ground-truth values, known by design.

The in-vivo dMRI data from one healthy mouse brain was acquired with a PGSE-EPI sequence at 9.4T (Bruker/Biospec) with:  $\text{TE/TR} = 36.8/4000$  ms;  $\delta/\Delta = 5.5/20$  ms;  $b = 0, 1, 2.5, 4, 5.5, 7, 8.5, 10, 12.5$   $\text{ms}/\mu\text{m}^2$ ; 40 gradient directions each, resolution  $0.12 \times 0.12 \times 0.4$   $\text{mm}^3$ .

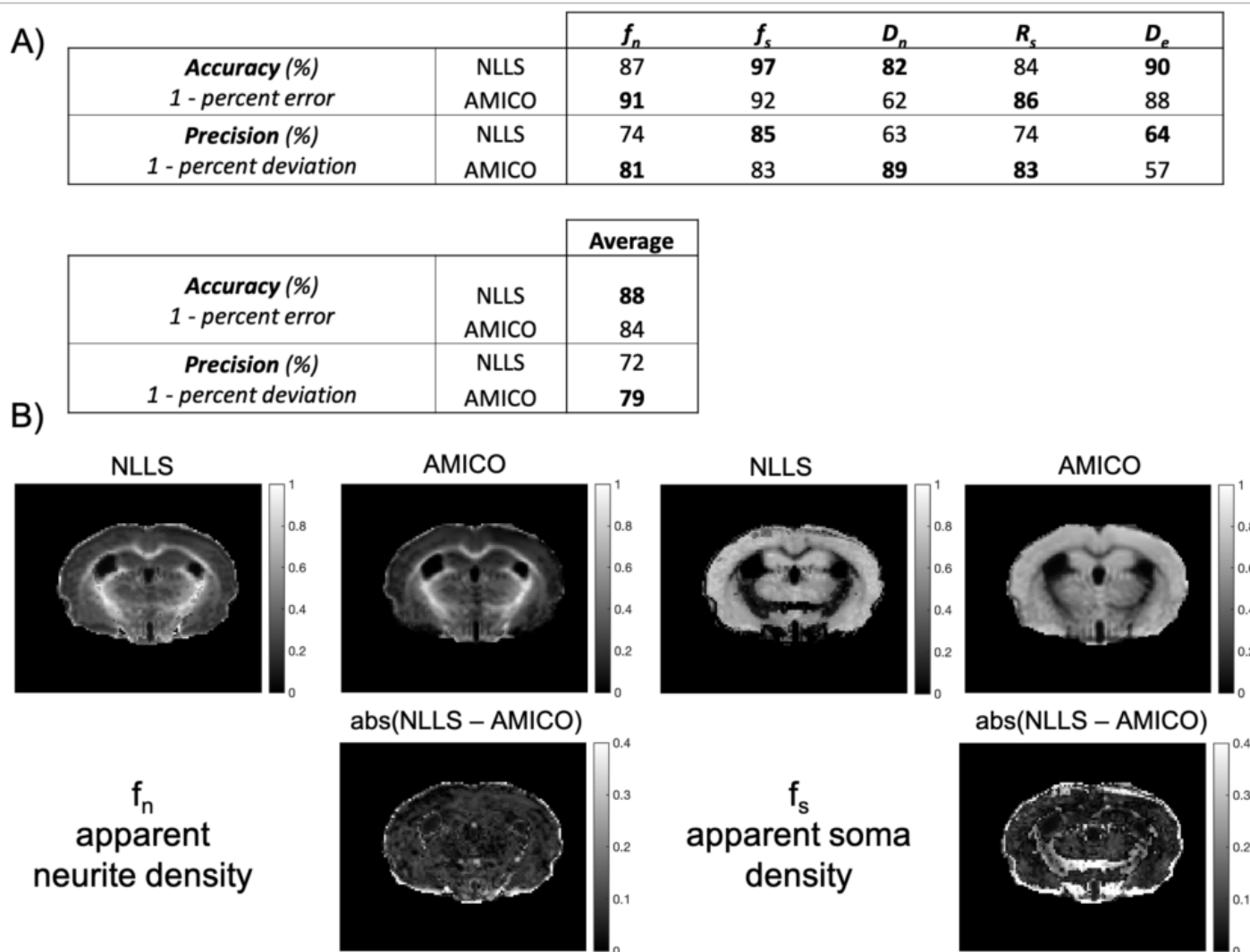
We tested the quality of the fitting also using one human subject from the MICRA dataset, acquired at 3T (Siemens/Connectom). Acquisition details can be found in (6). We used Freesurfer (7) to project the SANDI-AMICO  $f_s$  map onto the midpoint cortical surface.

## Results:

From the simulation study, we found that AMICO outperformed NLLS in terms of precision (~10% higher), showing higher robustness to noise with only minimal loss in accuracy (<5%) (Fig.1A).

On the mouse data, the AMICO fit was much faster than NLLS (23 s vs 943 s) and the estimated parametric maps of much higher quality (Fig.2B). In particular,  $f_n$  and  $f_s$  mirrored well the known myelo- and cyto-architecture of the mouse brain (Fig.1B).

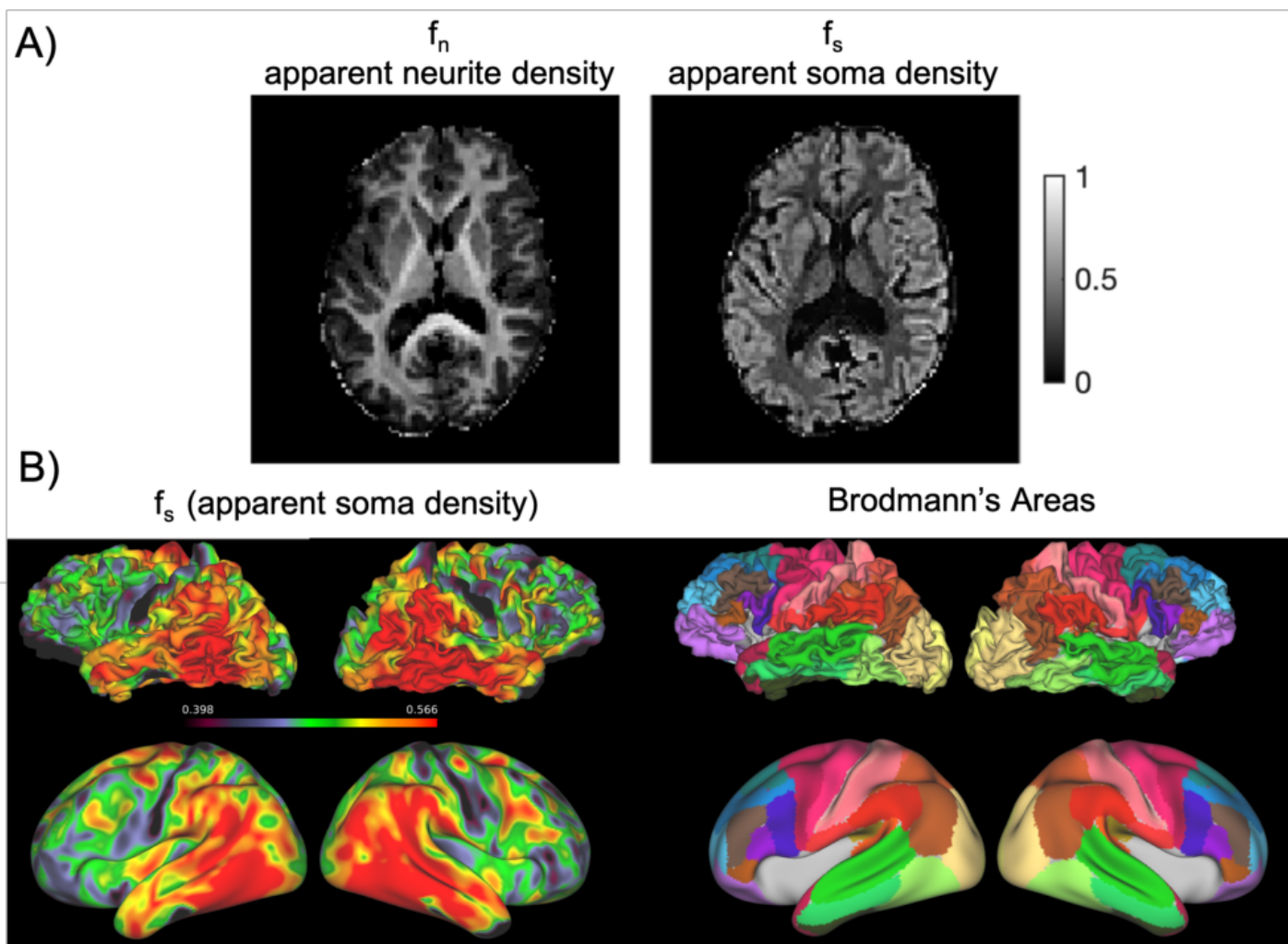
The SANDI-AMICO  $f_n$  and  $f_s$  maps from the human data showed a remarkable contrast, matching the expected myelo- and cyto-architecture of the human brain (Fig.2A). Furthermore, the variations of  $f_s$  values over the midpoint cortical surface followed the expected cyto-architectonics of several Brodmann's areas (Fig.2B), confirming previous observations (3).



**Figure 1:** Comparison between AMICO and the standard NLLS fitting of SANDI model in simulations (A) and in-vivo mouse data (B). In the tables (A), we report the accuracy and precision of both methods on synthetic data with SNR=100. Overall, our AMICO implementation results ~10% higher in precision while losing only <5% in accuracy. In panel (B) we show the MR apparent neurite (left) and soma (right) densities recovered by both methods and the absolute difference between them. AMICO is ~50 times faster than NLLS and the recovered maps appears smoother.

([https://files.aievolution.com/prd/hbm2101/abstracts/abs\\_2028/Figure1\\_v5.png](https://files.aievolution.com/prd/hbm2101/abstracts/abs_2028/Figure1_v5.png))

·Figure 1



**Figure 2:** Results on one subject of the MICRA dataset. In panel (A) we show an axial view of the apparent neurite and soma densities obtained with SANDI-AMICO. In panel (B) we compare the projection on the midpoint cortex of the MR apparent soma density with the parcellations in Brodmann's areas.

([https://files.aievolution.com/prd/hbm2101/abstracts/abs\\_2028/Figure2\\_v3.png](https://files.aievolution.com/prd/hbm2101/abstracts/abs_2028/Figure2_v3.png))

·Figure 2

## Conclusions:

We presented SANDI-AMICO: an open-source toolbox for the fast and robust fitting of the SANDI model.

## Modeling and Analysis Methods:

Diffusion MRI Modeling and Analysis <sup>1</sup>

Neuroanatomy, Physiology, Metabolism and Neurotransmission:

Cortical Anatomy and Brain Mapping

Cortical Cyto- and Myeloarchitecture <sup>2</sup>

## Novel Imaging Acquisition Methods:

Diffusion MRI

## Keywords:

Computational Neuroscience  
Cortex  
Informatics  
Modeling  
MRI  
Open-Source Code  
Structures  
WHITE MATTER IMAGING - DTI, HARDI, DSI, ETC  
Other - Grey Matter, SANDI, AMICO

<sup>1|2</sup>Indicates the priority used for review

My abstract is being submitted as a Software Demonstration.

Yes

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Yes

Please indicate which methods were used in your research:

Diffusion MRI  
Computational modeling

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL  
Free Surfer

## Provide references using author date format

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