

Numerical Convex Optimization in diffusion MRI

Simona Schiavi

DICE LAB, Diffusion Imaging and Connectivity Estimation
Computer Science Department, University of Verona

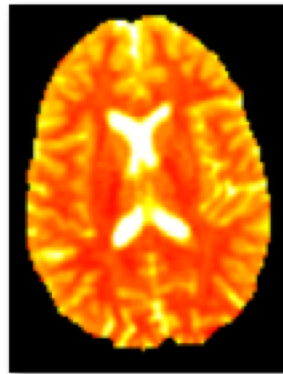
Course schedule

- May 31st, 8:30-10:30, alpha: Introduction to python
- June 07th, 8:30-10:30, alpha: How to obtain RM images and python lab (FFT)
- June 10th, 10:30-12:30, H: Bloch Torrey equation and homogenization techniques
- June 11th, 8:30-10:30, gamma: solution of Bloch Torrey equations in simple 2D geometry in FreeFem
- June 12th, 14:30-15:30, F: Numerical Convex Optimization applied to diffusion MRI

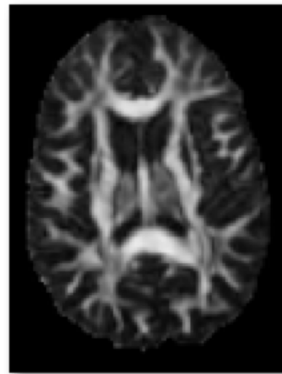
What kind of information can we extract from dMRI?

- **Intra-voxel tissue characterization**

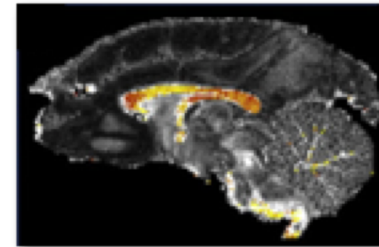
- Estimate *microstructural features* of the neuronal tissue



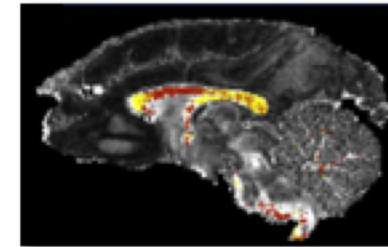
diffusion coefficient



diffusion anisotropy



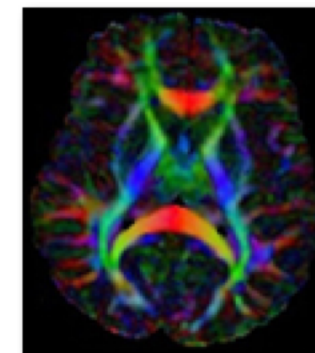
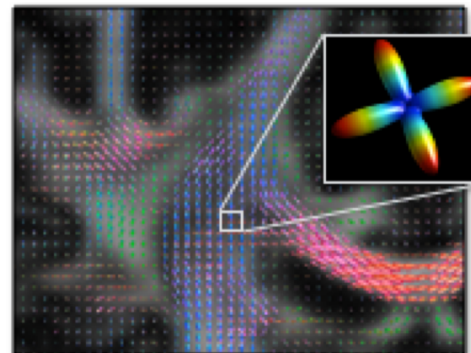
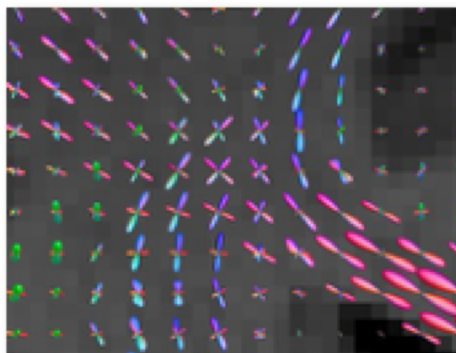
axonal diameter



axonal density

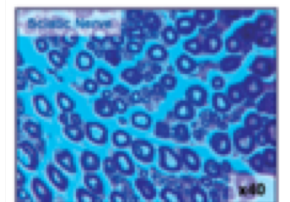
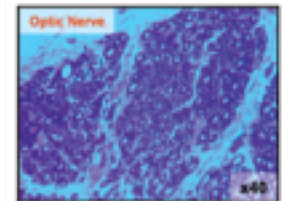
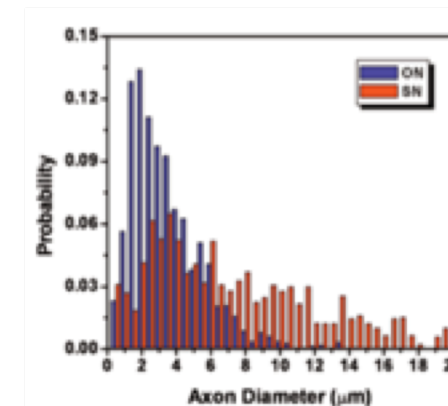
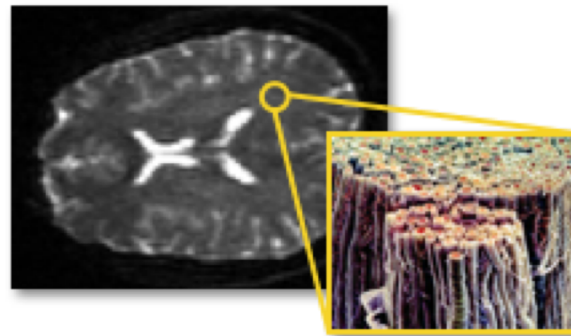
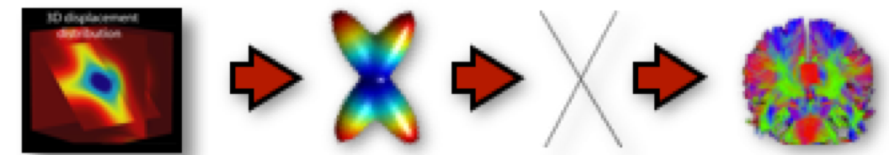
- **Intra-voxel white-matter structure —> fiber tracking**

- Estimate the *number and orientation of fiber populations* in each voxel



intra-voxel tissue characterization

- Algorithms whose aim is to **estimate microstructural features of the neural tissue** inside each voxel
- **Two main classes** of algorithms
 - Focus on **angular information** contained in the diffusion signal
 - Reconstruct the **geometry of the fiber bundles** inside a voxel
e.g. *number of fibers, their volume fraction, orientation...*
 - Tractography, connectivity estimation...
 - Acquire and use also the **radial component** of the signal
 - More advanced features of the **tissue microstructure**
e.g. *axonal diameter and density*



Low b-value approximation

- A way to model **anisotropic diffusion coefficients** is to use the **tensor formalism**
- **Assumption:** displacements of water molecules follow a *multivariate gaussian distribution*
 - Process fully characterized by its **covariance matrix**

diffusion
tensor

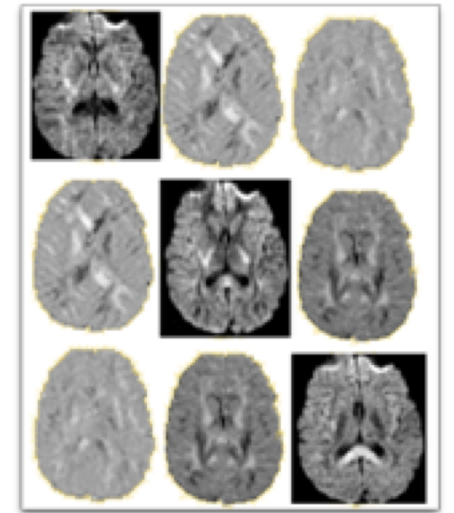
$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$

[Basser et al., 1994]

- \mathbf{D} is a 3×3 *positive-definite symmetric* matrix

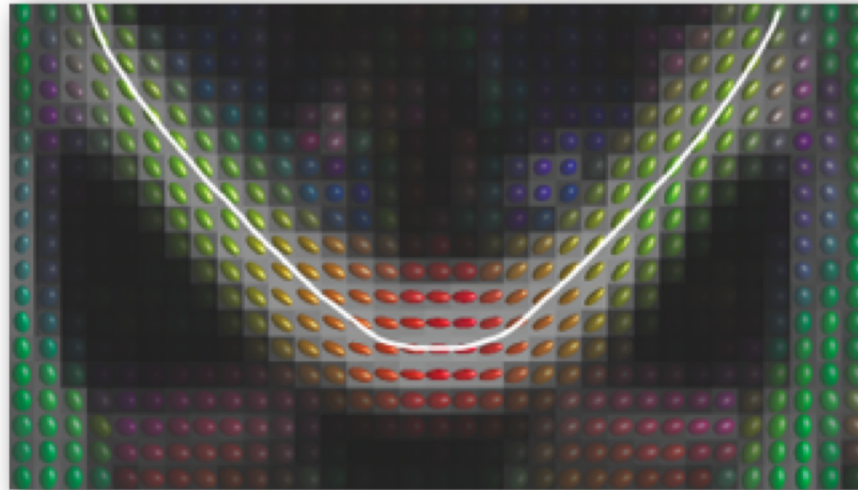
$$S(\mathbf{g}_k, b) = S_0 \exp(-b \mathbf{g}_k^T \mathbf{D} \mathbf{g}_k)$$

- **NOTE:** signal decay is **function of gradient direction**
 - is the orientation of the **diffusion gradient**



Application

- The *principal direction of \mathbf{D}* is assumed to be co-linear with the **dominant fiber orientation** within the voxel
 - Basic principle that is used in *tractography* (see later)



- **Advantages**
 - Fast acquisitions ($\approx 3-4$ min) clinically feasible
 - Does not require special hardware
 - Possibility to **extract useful information** about the neuronal tissue

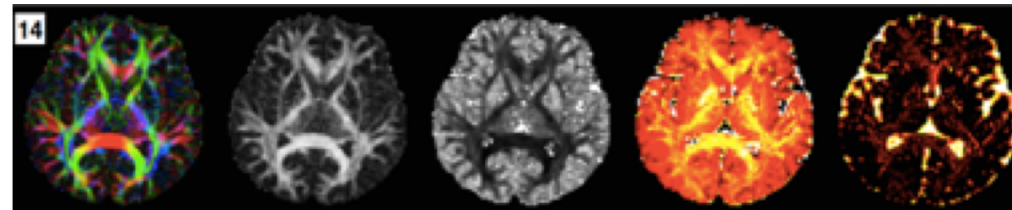
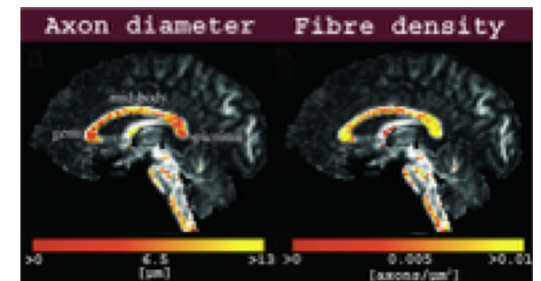
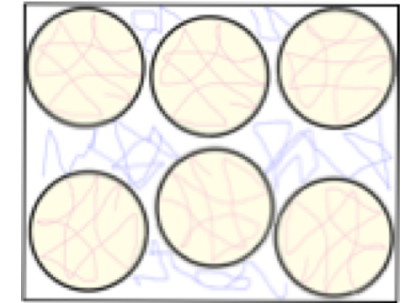
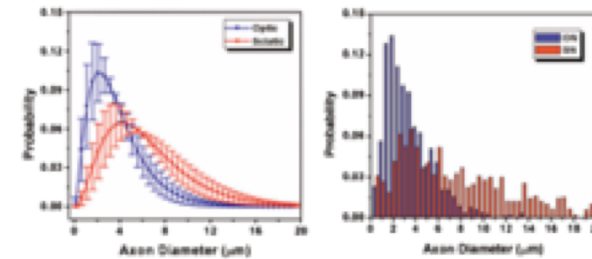
Accelerated Microstructure Imaging via Convex Optimization (AMICO) from diffusion MRI data

Daducci et al. 2015

Micro-structure imaging (modelling ADC)

- State-of-the-art techniques

- **Ball&stick** (*Behrens et al, 2003*)
 - no real link to micro-structure
- **CHARMED** (*Assaf et al, 2005*)
 - models separately *intra-axonal* and *extra-axonal* water pools
- **AxCaliber** (*Assaf et al, 2008*)
 - *distribution of axonal diameters*
 - fiber direction must be known
 - long acquisitions
- **ActiveAx*** (*Alexander et al, 2010*)
 - *orientationally invariant index of average axonal diameter*
 - strong gradients required
- **NODDI*** (*Zhang et al, 2012*)
 - discard axonal diameter estimation
 - focus on *intra and extra compartments*
 - feasible with clinical scans

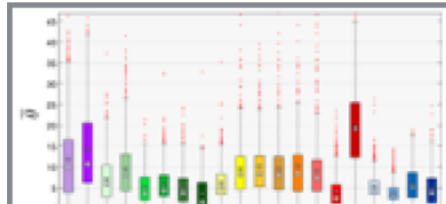


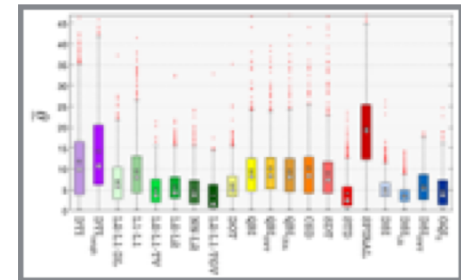
- **One common limitation:** computationally expensive!

AMICO general idea

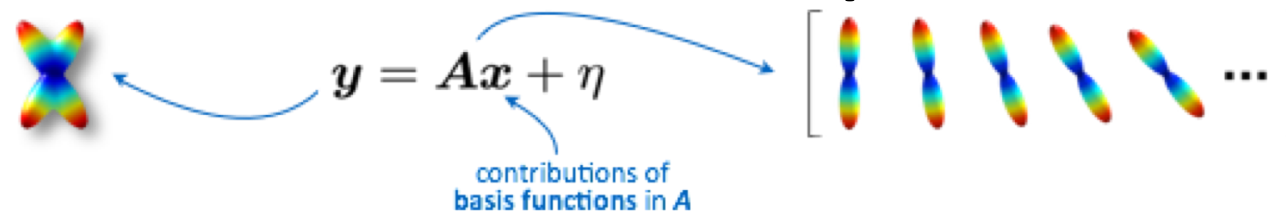
- **Fact 1**: based on a **generic multi-compartment model**

$$S(q) = \underbrace{f^{\text{IC}} R^{\text{IC}}(q)}_{\text{restricted}} + \underbrace{f^{\text{EC}} R^{\text{EC}}(q)}_{\text{hindered}} + \underbrace{f^{\text{ISO}} R^{\text{ISO}}(q)}_{\text{isotropic}}$$

- **Fact 2**: we can (linearly) fit these models as long as we **regularize the inverse problem**
 - **Fact 3**: dictionary-based reconstruction methods...
 - do not consider the micro-structure but...rcl
 - perform really well ($\approx 5^\circ$) for identifying the **main diffusion directions** (Daducci et al, 2013)
- 



- **Fact 4**: they can be formulated as **linear problems**



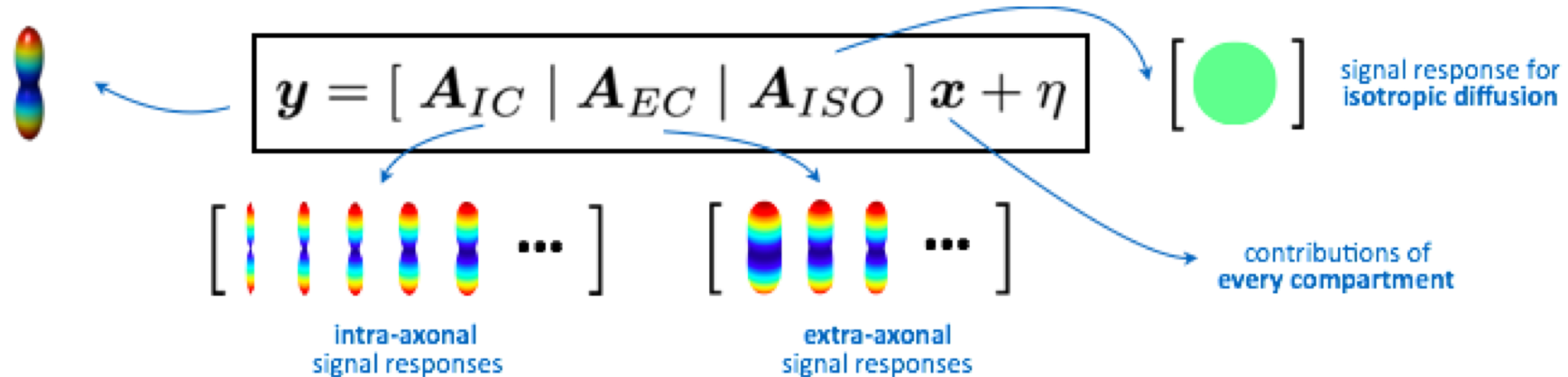
AMICO general idea

- Two-step procedure:

- identify in every voxel the **main diffusion direction** with classical algorithms



- construct a dictionary along this **fixed direction** and varying the signal responses to model **different possible micro-environments**

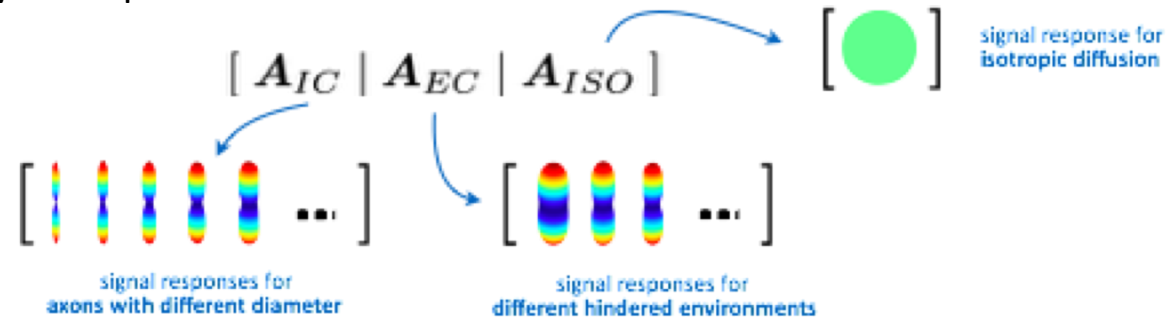


- **GOAL:** find the contribution of each compartment (inverse problem) using **convex optimization**

Linearization of ActiveAx

- **Dictionary construction:**

- \mathbf{A}_{IC} explicitly models axons having a different radii
- \mathbf{A}_{EC} explicitly models distinct hindered environments (e.g. packing)
- \mathbf{A}_{ISO} accounts for any isotropic contribution



- **Regularization:**

- Among all the possible regularizations the ***Tikhonov*** one was enough to improve condition number of \mathbf{A}

- **Formulation:**

$$\underset{\mathbf{x} \geq 0}{\operatorname{argmin}} \quad \underbrace{\frac{1}{2} \|\mathbf{Ax} - \mathbf{y}\|_2^2}_{\text{data fit}} + \underbrace{\frac{\lambda}{2} \|\mathbf{x}\|_2^2}_{\text{regularization}}$$

Linearization of ActiveAx

- Computation of microstructure indices:
 - Let's partition $\mathbf{x} = [\mathbf{x}^r \mid \mathbf{x}^h \mid \mathbf{x}^i]$ into the corresponding compartments (r=restricted, h= hindered, i=isotropic)
 - Let N_r, N_h, N_i be the number of atoms in $\mathbf{A}_{IC}, \mathbf{A}_{EC}, \mathbf{A}_{ISO}$
 - Let R_j be the radius of the axons corresponding to the j^{th} atom in \mathbf{A}_{IC}

intra-axonal
volume fraction

$$v' = \frac{\sum_{j=1}^{N_r} \mathbf{x}_j^r}{\sum_{j=1}^{N_r} \mathbf{x}_j^r + \sum_{j=1}^{N_h} \mathbf{x}_j^h}$$

mean
axonal diameter

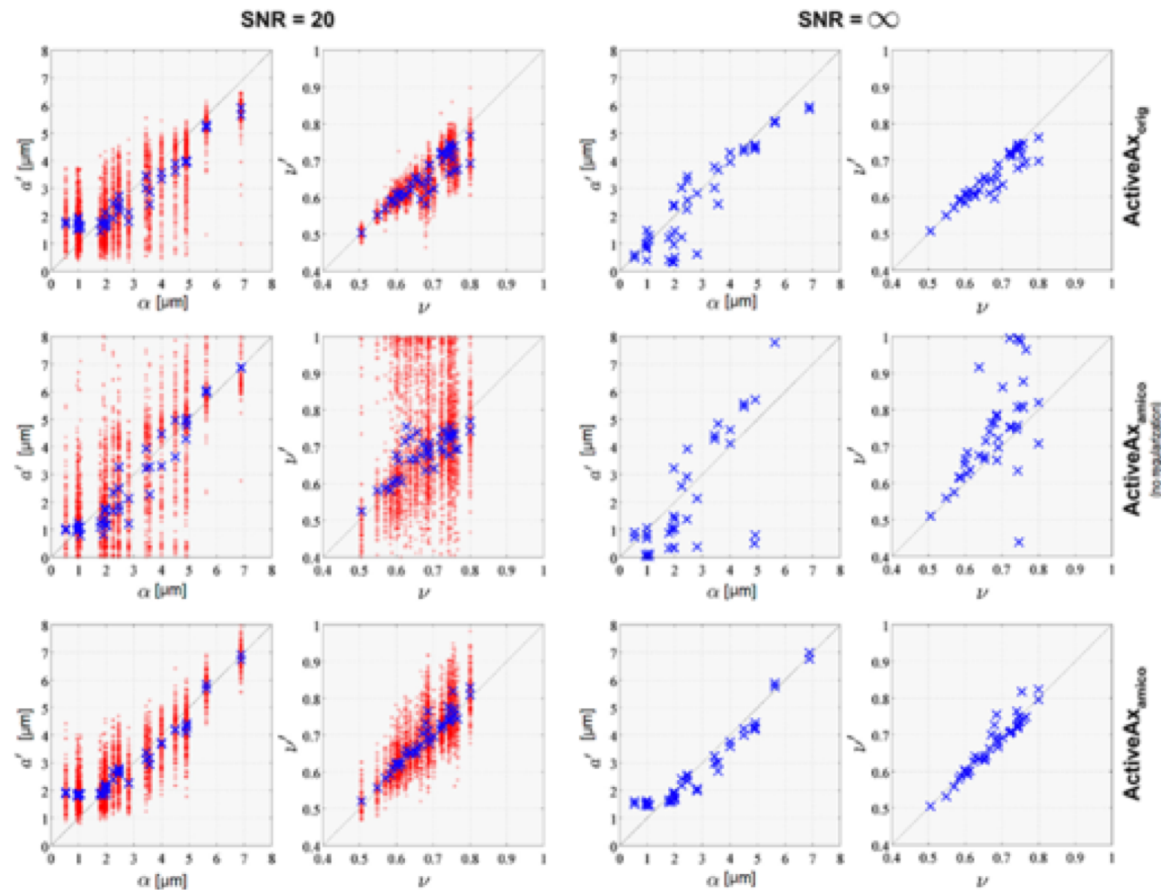
$$a' = \frac{\sum_{j=1}^{N_r} 2R_j \mathbf{x}_j^r}{\sum_{j=1}^{N_r} \mathbf{x}_j^r}$$

axonal density

$$\rho' = \frac{4v'}{\pi a'^2}$$

Numerical results

- Experimental setup
 - 44 different substrates used in (*Alexander et al, 2010*)
 - Compared to original ActiveAx implementation



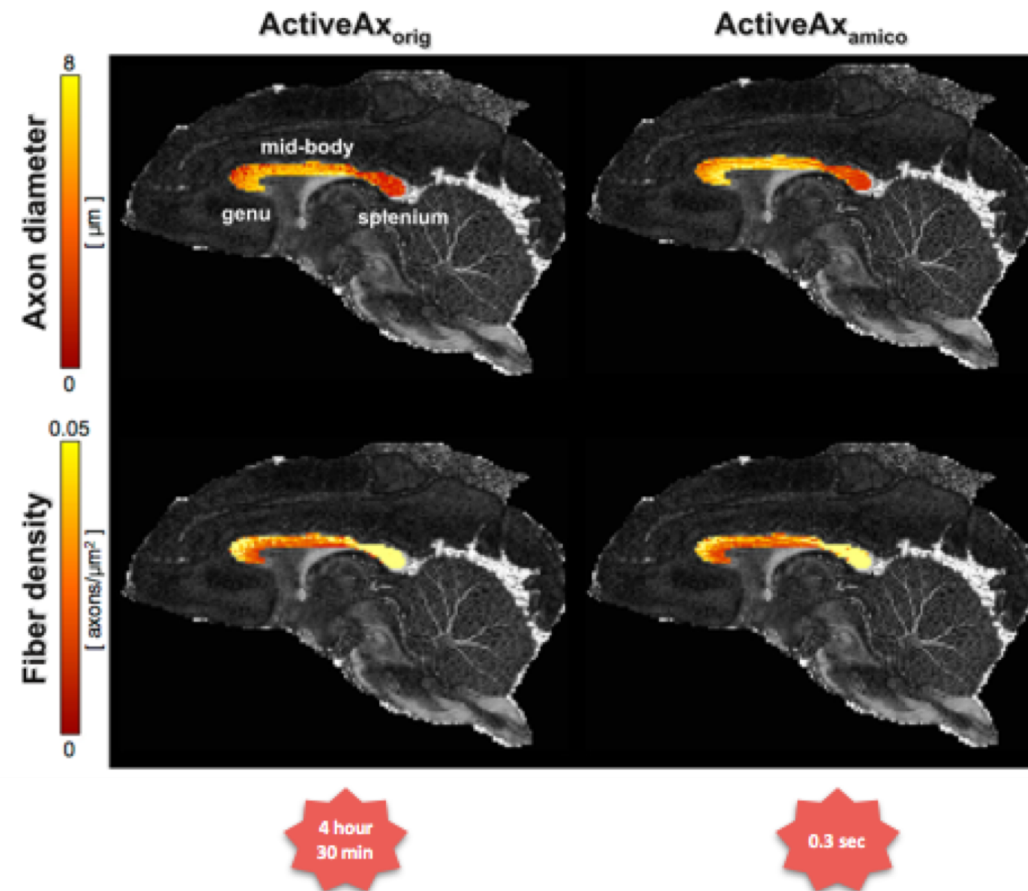
11 days
14 hours
40 min

18 sec

18 sec

In-vivo results

- Experimental setup
 - Dataset used in *(Alexander et al, 2010)*
 - Fixed monkey brain acquired with $G_{\max} = 140$ mT/m



Summary

- AMICO is a **convex formulation** for microstructure imaging



- **Advantages**

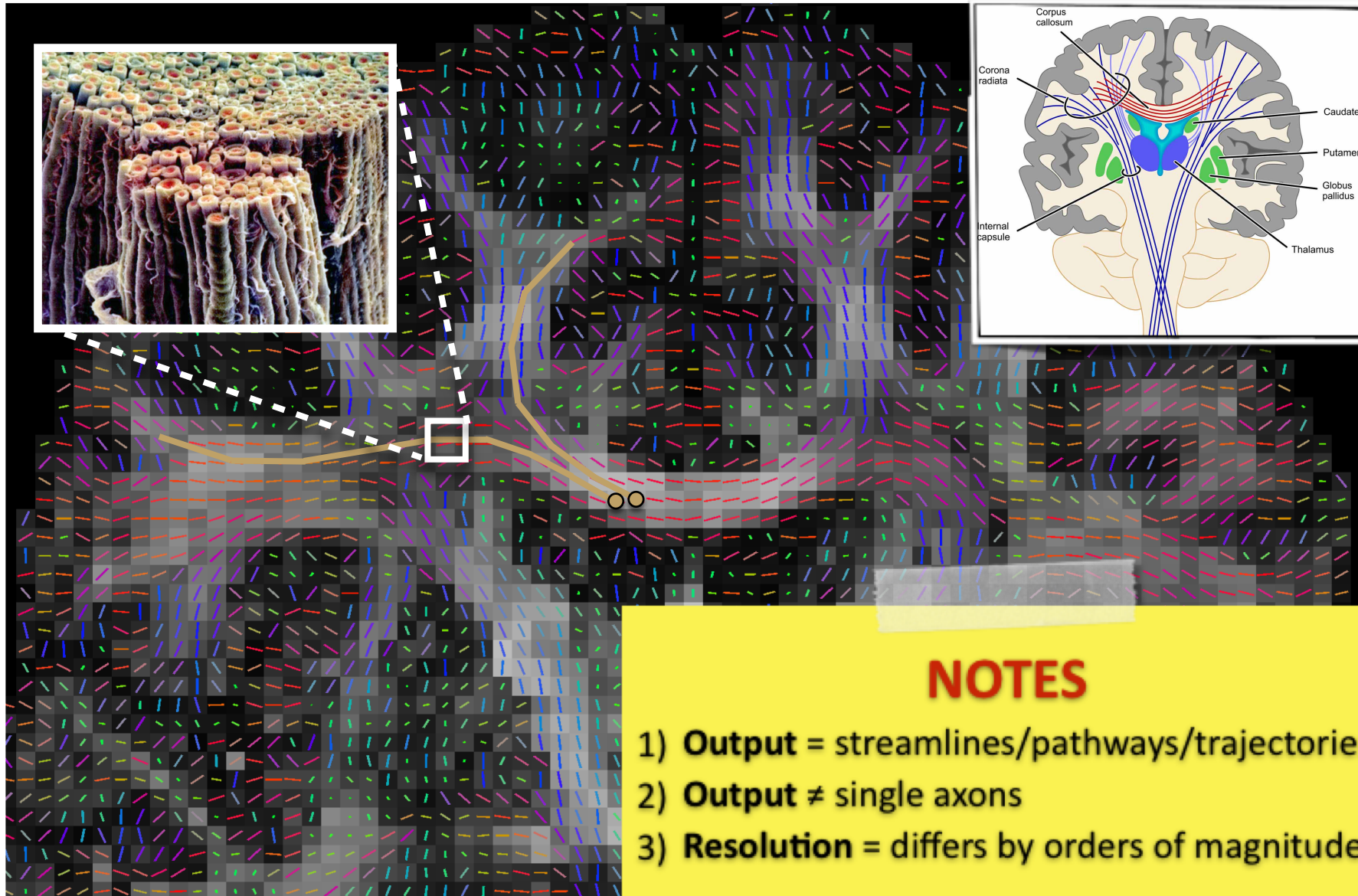
- It is **much faster** than original formulations
- Can provide higher quality reconstructions (avoid local minima)
- It is **very flexible** and **easily extendable**

- **Ongoing work/future research**

- Linearization of **other models**
- Extension to **multiple fiber populations**
- Addition **spatial regularization**
- Avoid the **two-step** procedure
- Investigate **data under-sampling** for microstructure imaging
- Inclusion of the correct **noise model** (low SNR regimes)

Tractography

What is tractography?

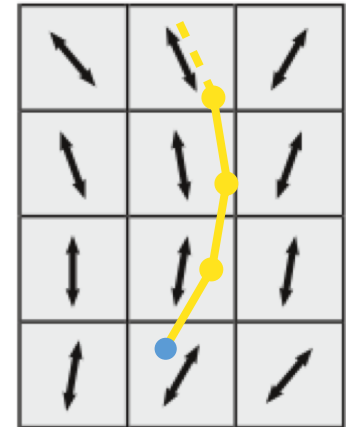
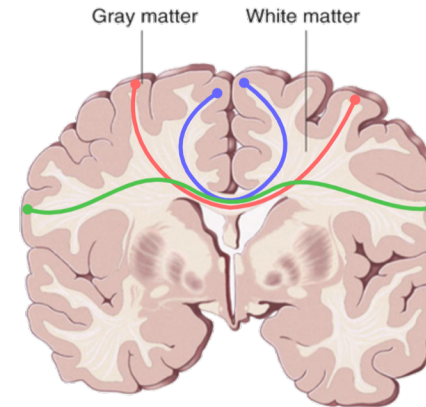


Main idea and standard algorithms

- **Deterministic tracking** [Conturo et al., 1999; Mori et al., 1999; ...]

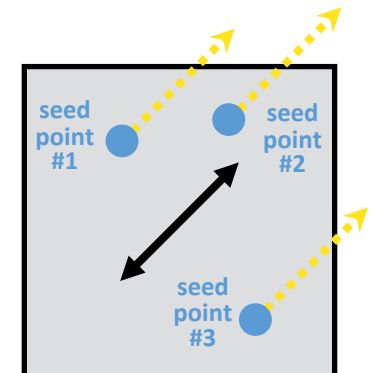
$$\frac{df(t)}{dt} = \mathbf{d}(f(t)) \quad \text{with} \quad \begin{cases} 0 \leq t \leq 1 \\ \mathbf{f}(0) = \mathbf{f}_0 \end{cases}$$

- $\mathbf{f}(\cdot)$: fiber trajectory (—)
- $\mathbf{d}(\cdot)$: main diffusion direction estimated in each voxel (\nwarrow)
- \mathbf{f}_0 : seed/starting point (●)
- t : step size

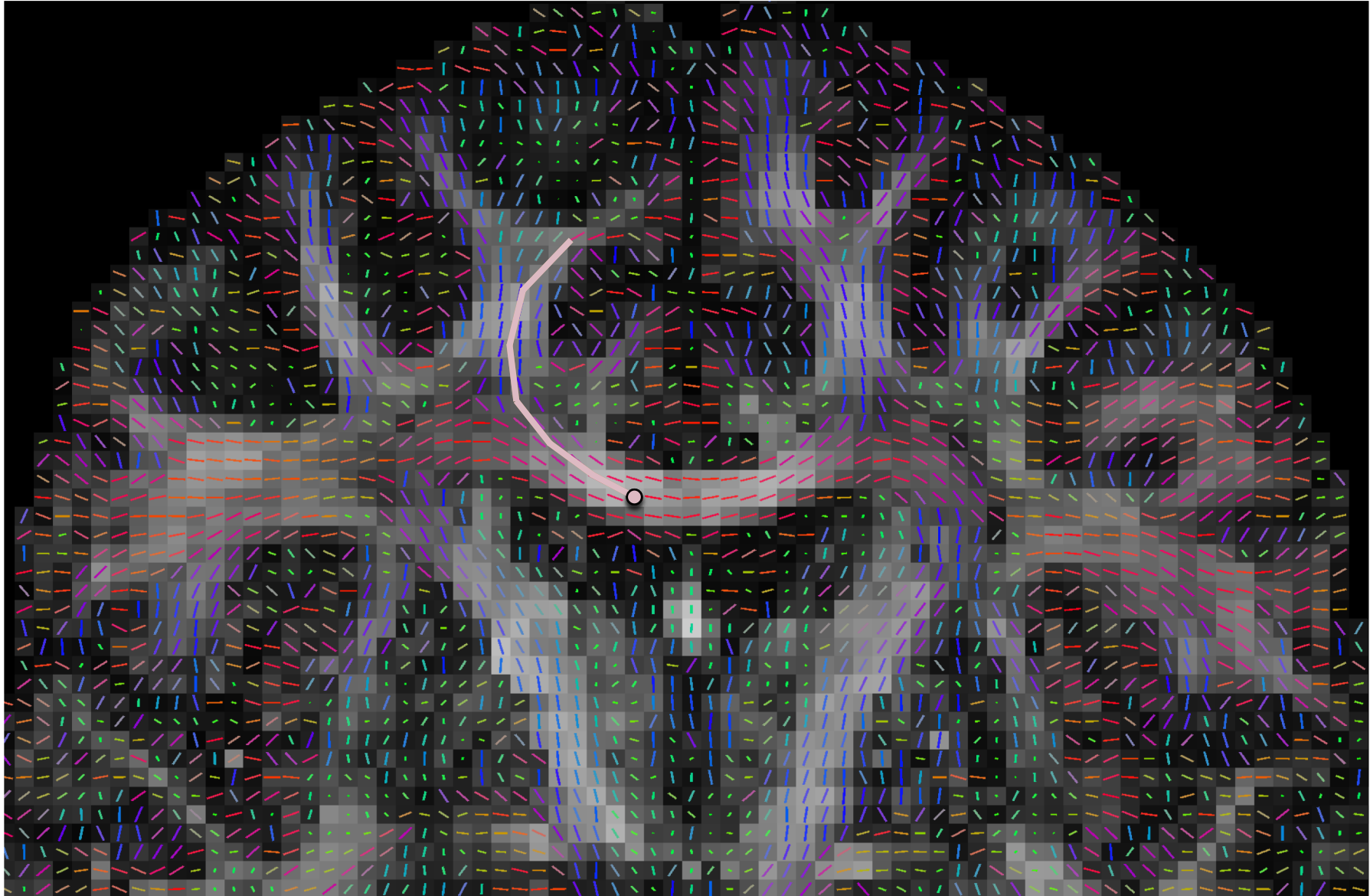


- **Notes**

- \simeq few minutes/brain (real-time)
- *Deterministic* = the **same trajectories** are reconstructed from same seed points
- Suffers from **false negatives** (*low sensitivity*)





Example of deterministic tracking

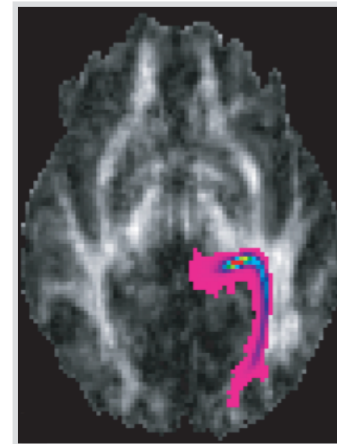


Main idea and standard algorithms

- **Probabilistic tracking** [Parker et al., 2003; Behrens et al., 2003; ...]

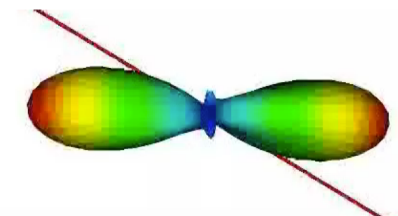
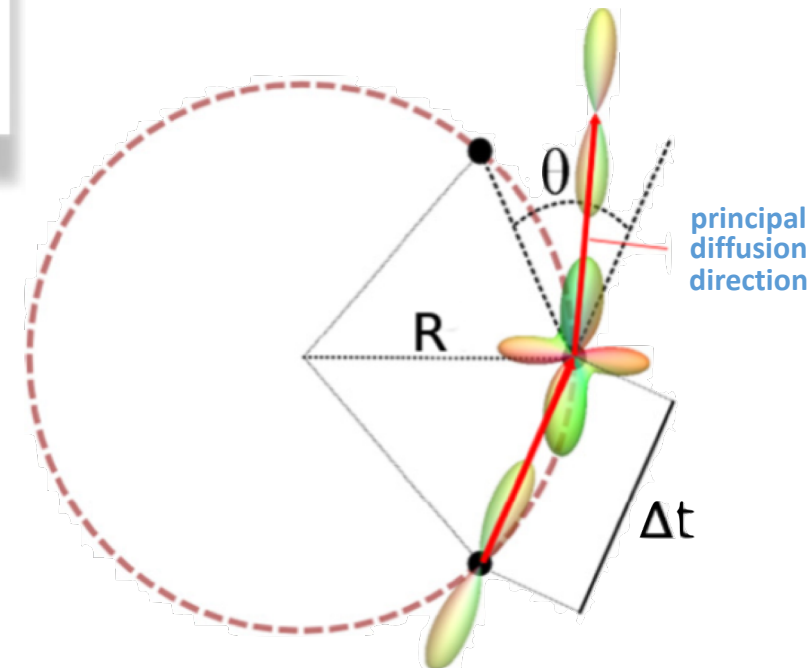
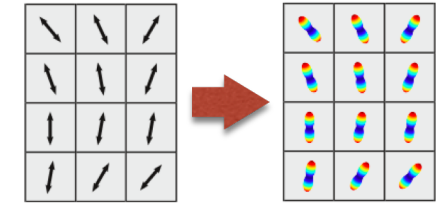
$$\frac{d\mathbf{f}(t)}{dt} = \mathbf{d}(\mathbf{f}(t)) \quad \text{with} \quad \begin{cases} 0 \leq t \leq 1 \\ \mathbf{f}(0) = \mathbf{f}_0 \end{cases}$$

- $\mathbf{d}(\cdot)$:  replaced by 
- Next direction drawn from distribution (**uncertainty** in the tracking)
- Seed a *large number of fibers* (**probability of connection**)

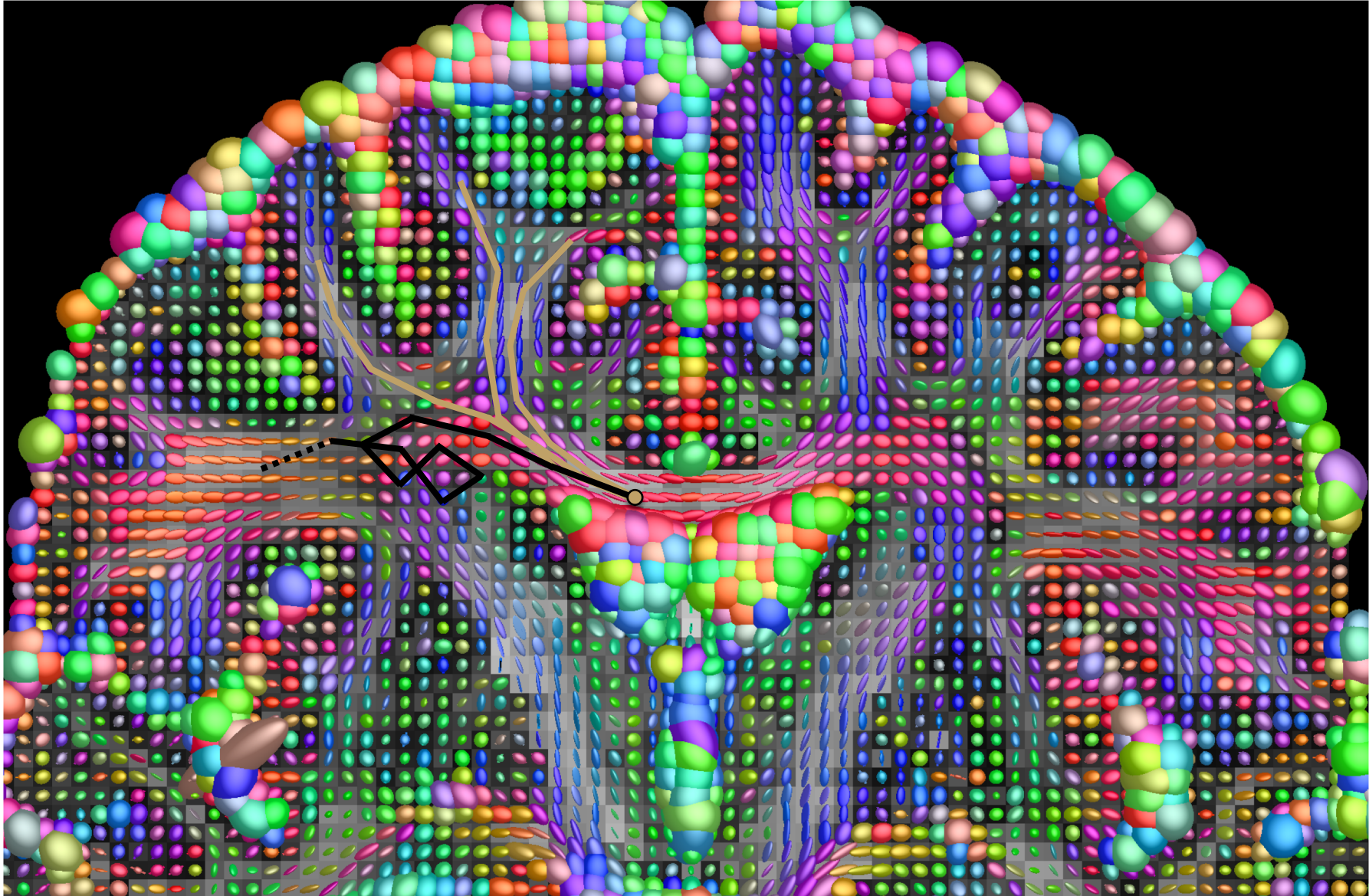


- **Notes**

- $\simeq 1$ day/brain
- Adds **confidence levels** to tracts (probabilities maps are *difficult to interpret*) [Jones et al. 2010;2013; Jbabdi et al., 2011]
- Suffers from **false positives** (*low specificity*)



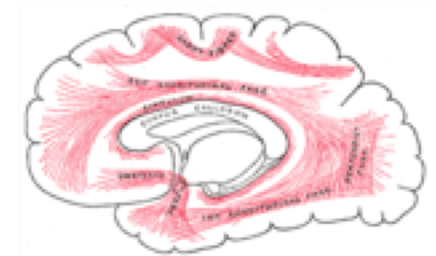
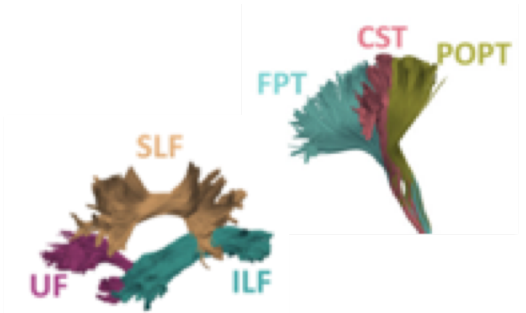
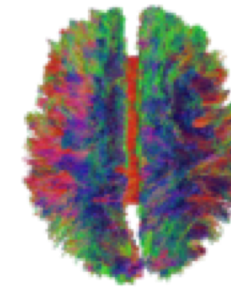
Example of probabilistic tracking



From tractography to structural brain connectivity

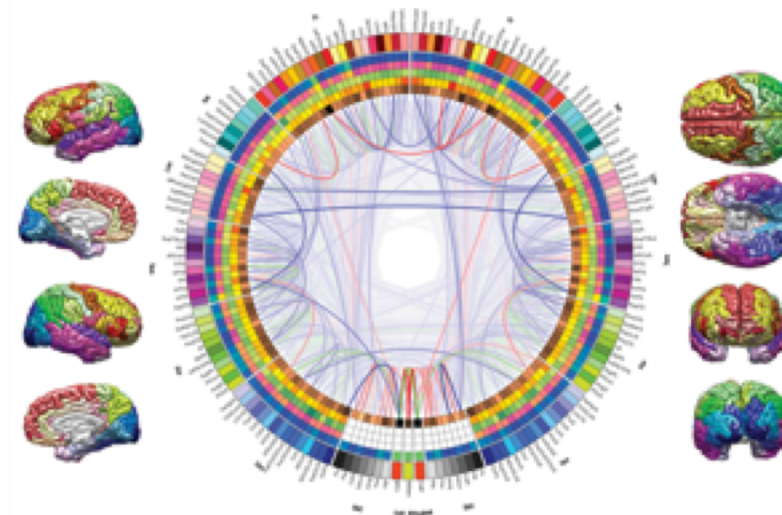
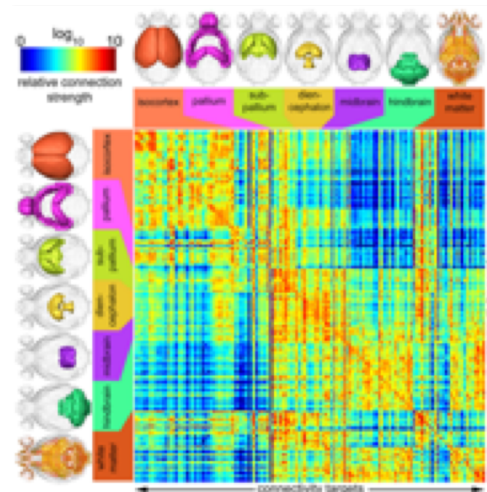
- **Connectivity analysis** of the brain with dMRI

- Consider **all reconstructed fibers as a whole**
- **Subdivide them in bundles**
(e.g. connecting different *gray matter* nuclei)
- Analyze their **properties and organization**
(e.g. to monitor progression of disease)



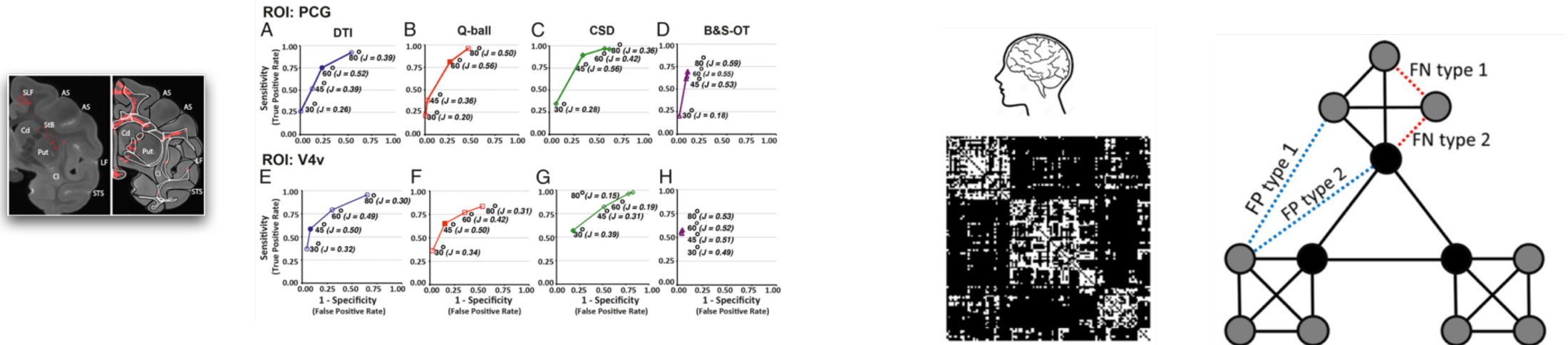
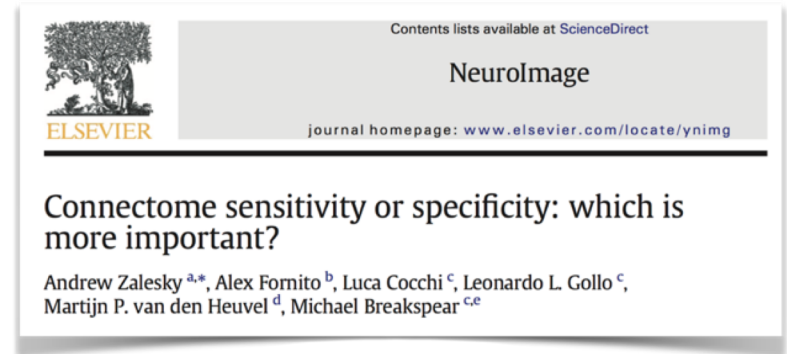
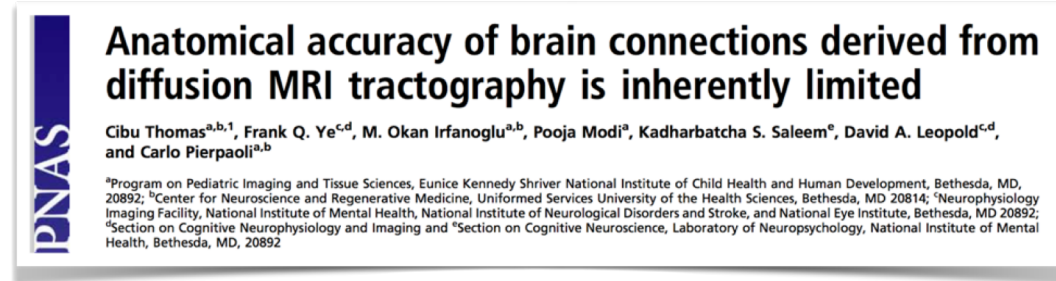
- **Connectomics**

- **Connectomics**: production and study of *connectomes*
- **Connectome**: comprehensive *map of connections* in the nervous system



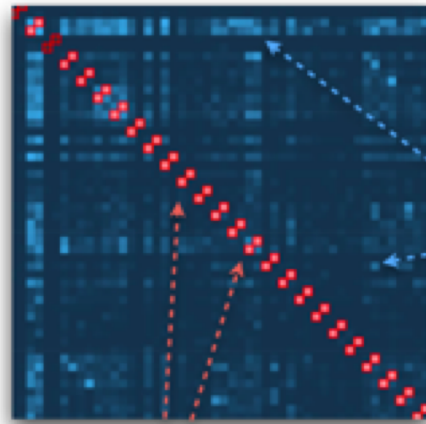
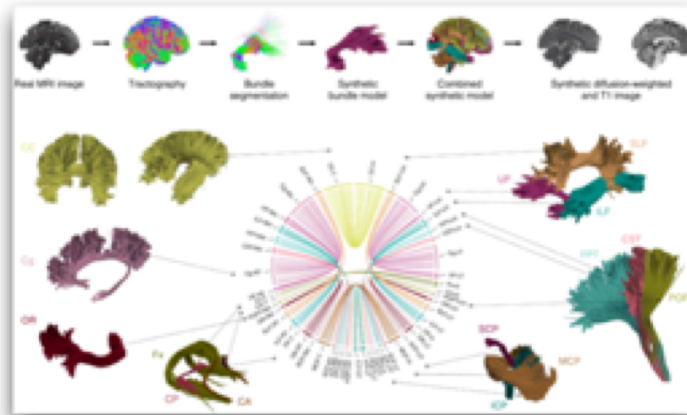
Unfortunately tractography is limited..

❖ **False positive connections** are a major problem in tractography

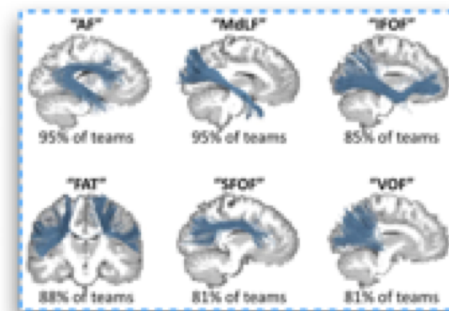


Unfortunately tractography is limited..

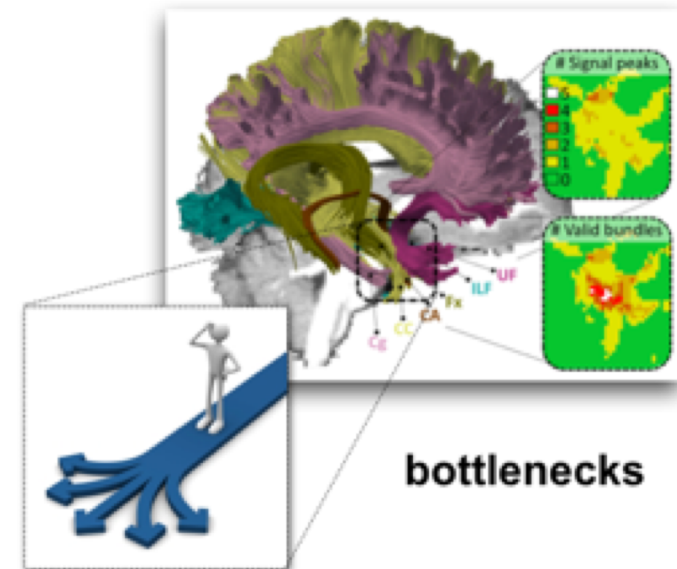
ISMRM 2015
challenge



True Positives (TP)
23/25 found on average



False Positives (FP)
88 found on average...
...but not in the ground-truth!



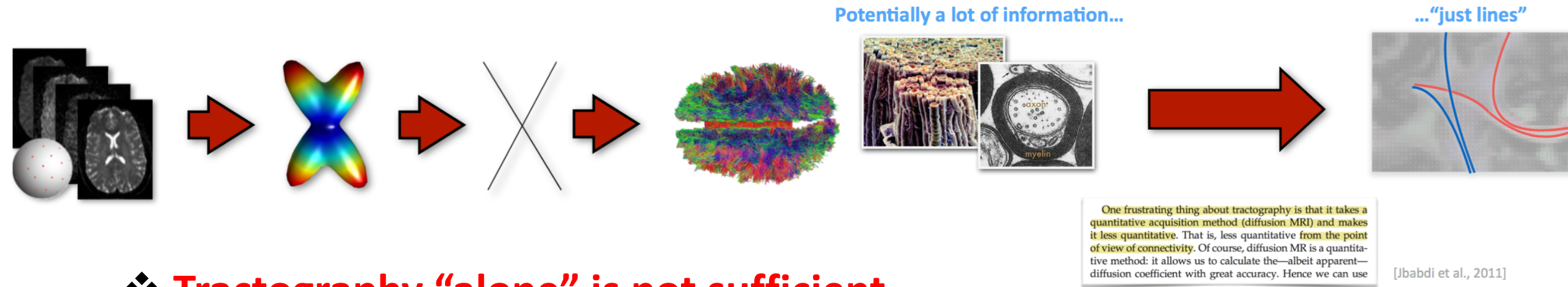
Can we help?

COMMIT: Convex Optimization
Modeling for Microstructure
Informed Tractography

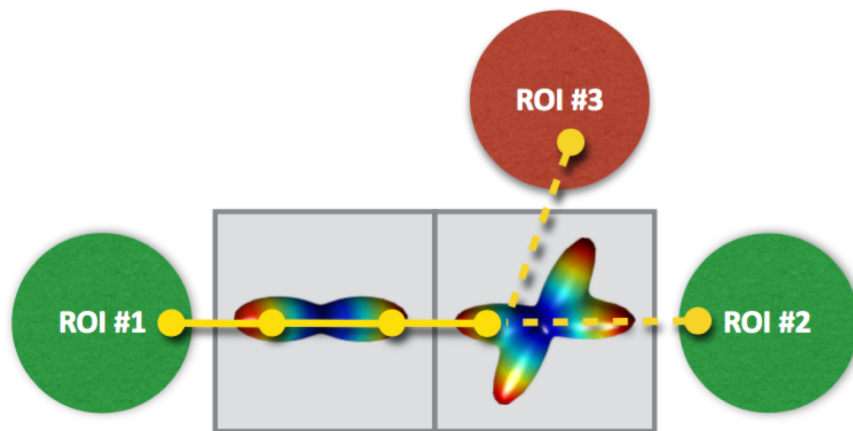
Daducci et al. 2014

Idea

❖ **A lot of information is lost on the way**

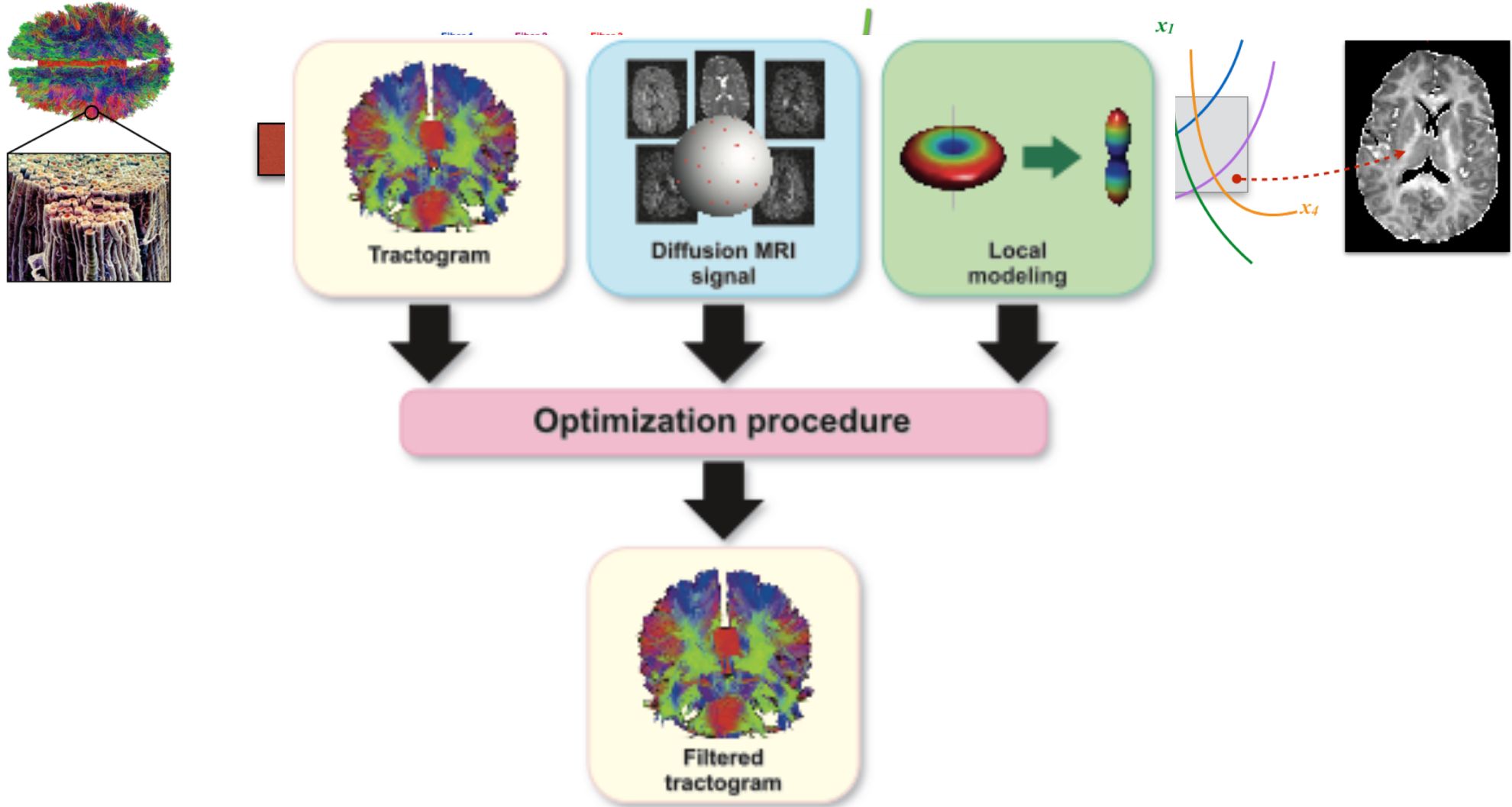


❖ **Tractography “alone” is not sufficient**



Streamlines hold also other properties...

- ❖ Streamlines are not “**just lines**”, they have a **volume**!

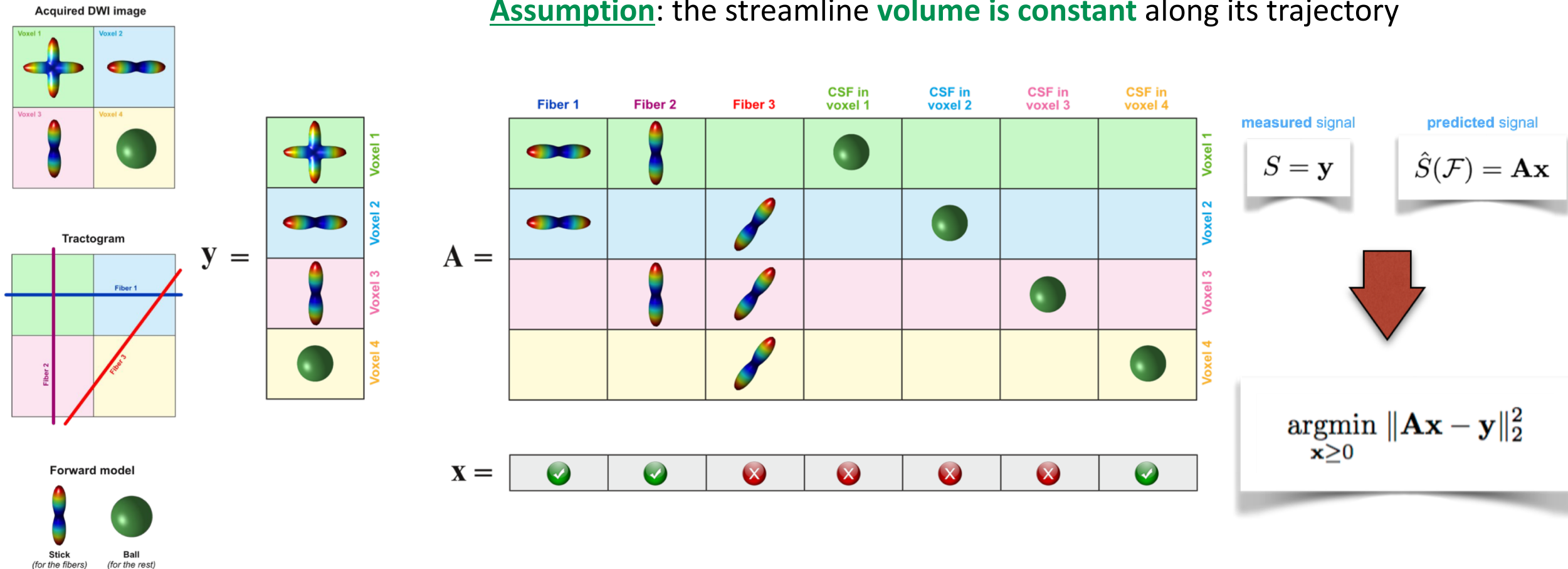


Microstructure Informed Tractography

❖ **COMMIT**: Convex Optimization Modelling for Microstructure Informed Tractography [Daducci et al., 2013; 2014]

➤ streamlines are not “**just lines**”, they have a **volume**

Assumption: the streamline **volume is constant** along its trajectory

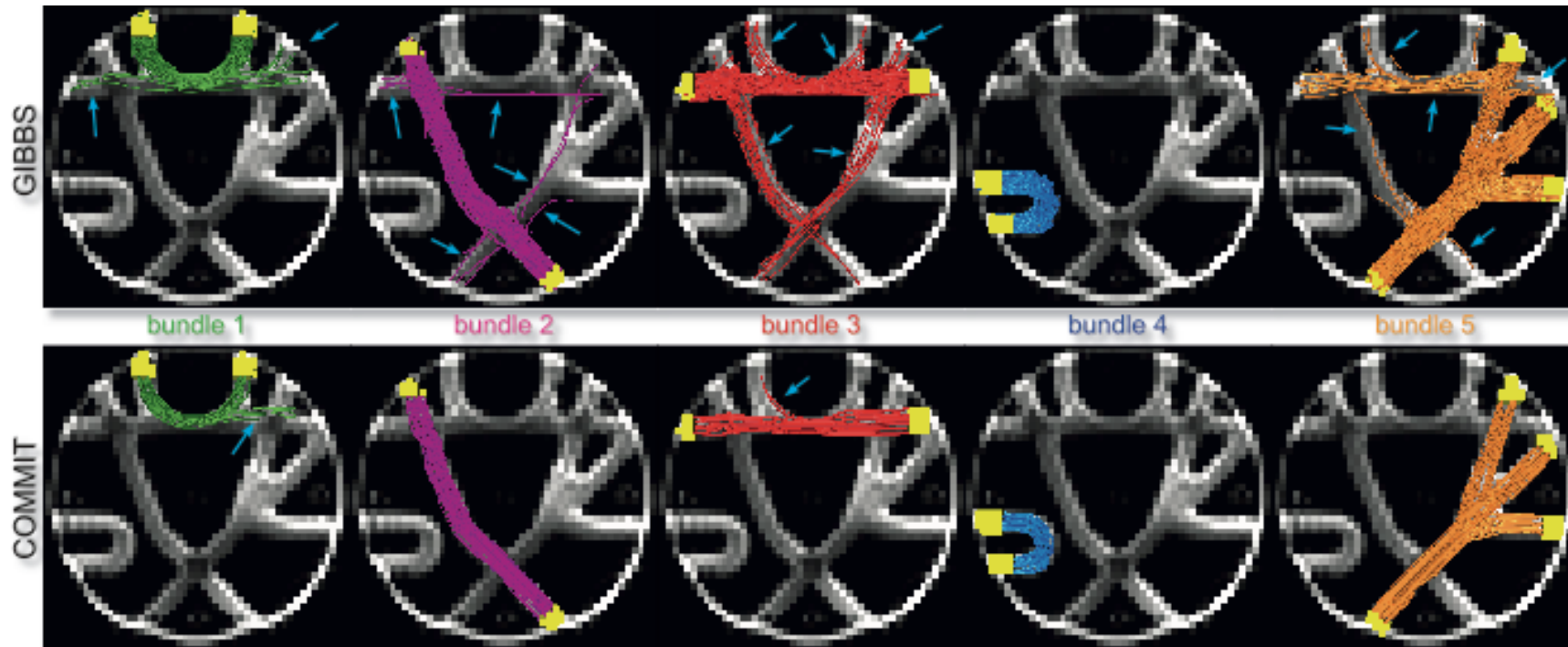
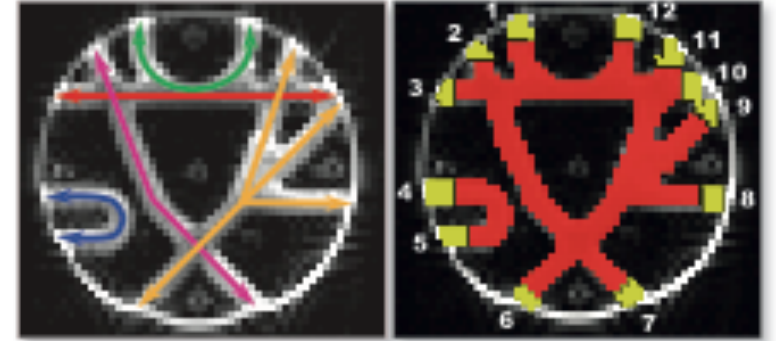


Synthetic data results

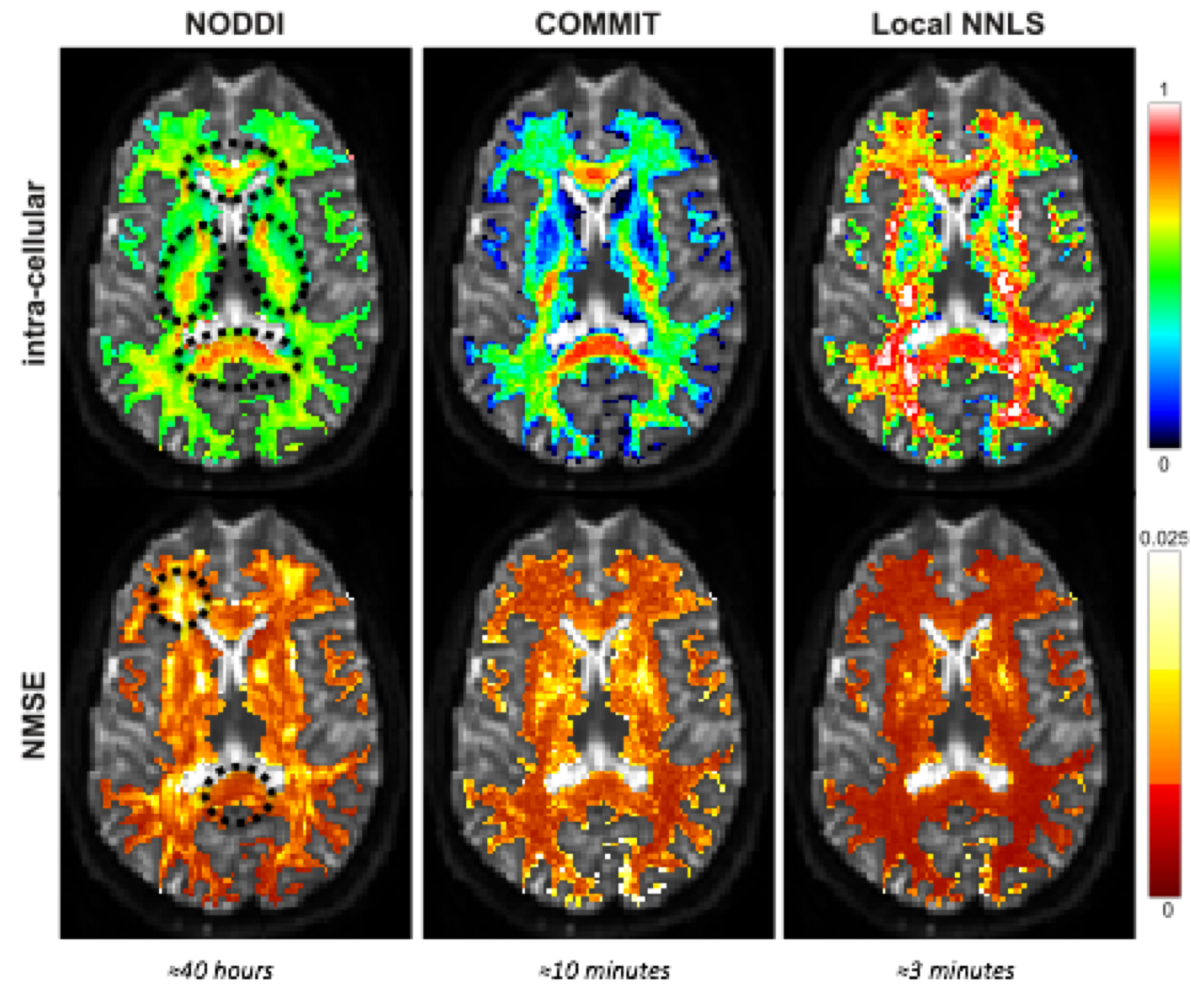
- Experimental setup
 - Dataset used for the *FiberCup* challenge
 - 1 shell (64 b=1500 s/mm²), 64x64x3 voxels, 3x3x3 mm

| Tractometer scores (Côté et al, 2013) | VB | IB | NC (%) | VC (%) | IC (%) | TIME (min) |
|--|----|----------|-----------|-------------|------------|---------------|
| GIBBS | 7 | 12.5 | 76.5 | 19.8 | 3.7 | 43.6 |
| COMMIT | 7 | 1 | 0 | 97.9 | 2.1 | 0.4 |

data) for the fibers + **1 isotropic** in each voxel



In-vivo results



Summary

- COMMIT is a novel **convex formulation** for tractography

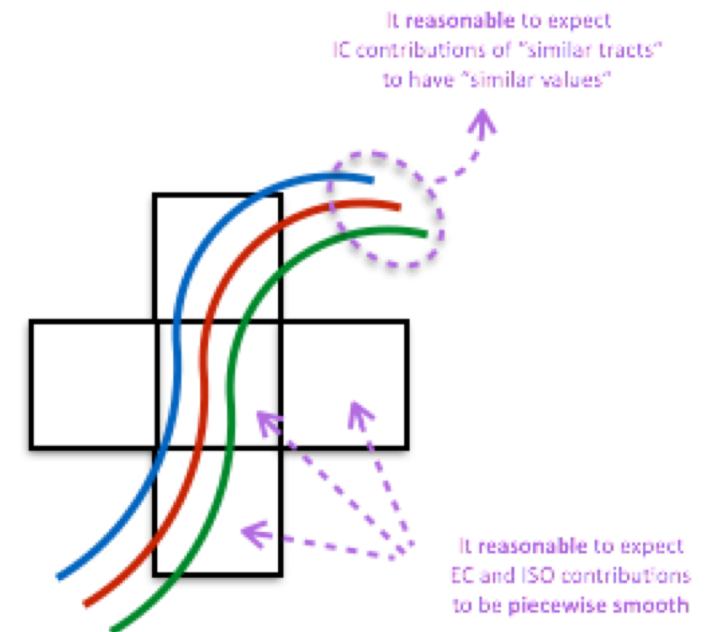


- **Advantages**

- It is truly **global**
- It is **quantitative**
- It is **fast, flexible** and guarantees **convergence**

- **Ongoing work/future research**

- **Model** development
 - improve/add more regularization terms to exploit all the redundancy
 - develop a strategy to construct “good” dictionaries
- Investigate **data-undersampling**
- **GPU** implementation
- Embed COMMIT into an “**active**” tractography algorithm
- “Quantitative” structural connectivity functional connectivity

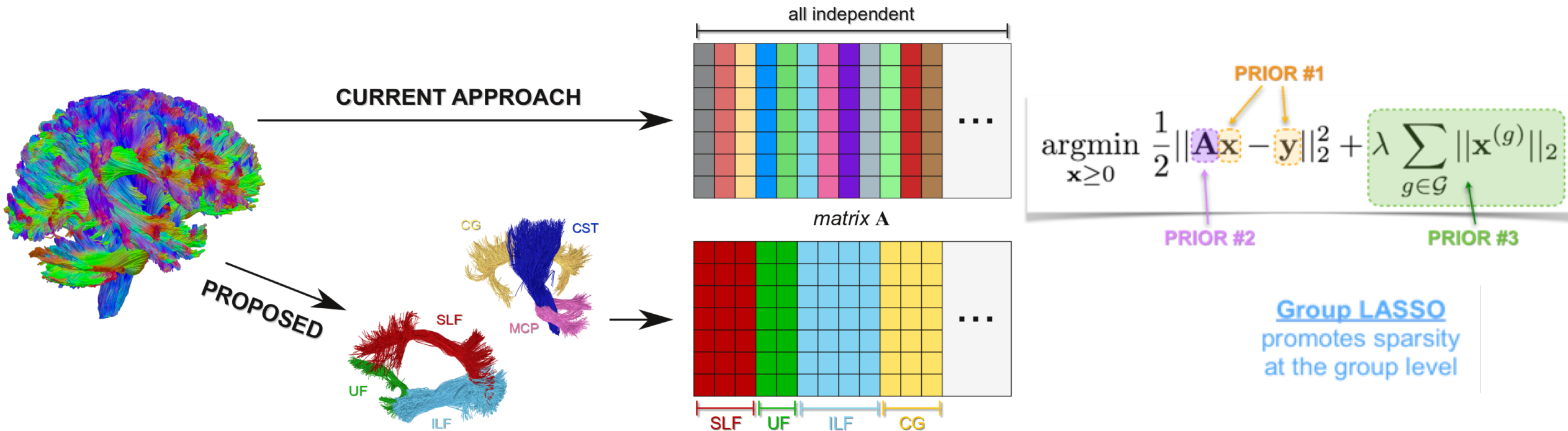


Can we do better?

Axons in the CNS are naturally organized in bundles

COMMIT2 allows grouping streamlines together and injecting priors on them.

[Daducci et al., 2018; Schiavi et al., 2019]

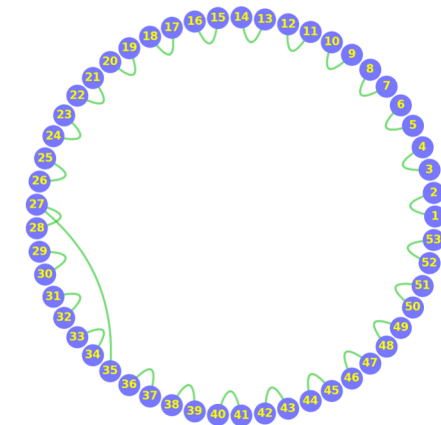
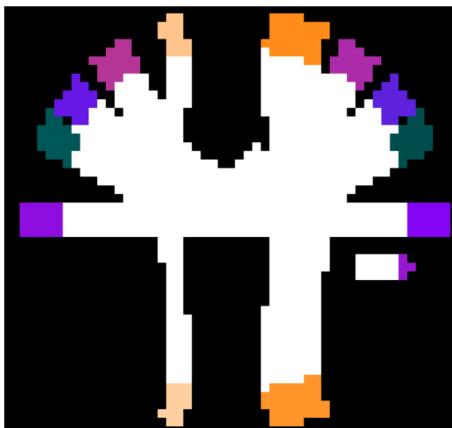
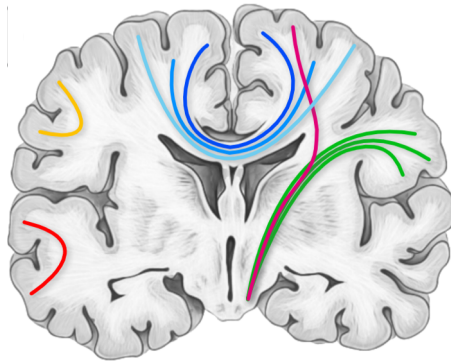
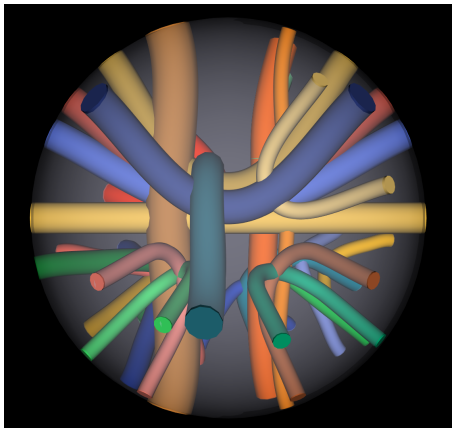


The **groups are arbitrary** and can be defined using anatomy information, atlases, other imaging modalities, ...

Synthetic data results

Schiavi et al., biorxiv 2019

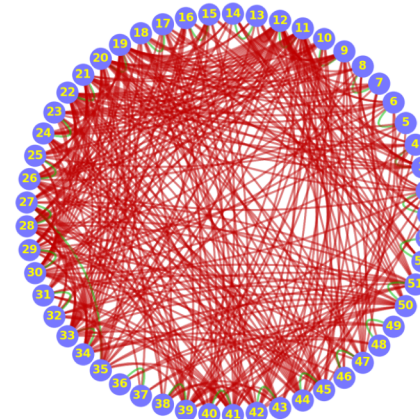
Ground Truth



probabilistic

Raw tractogram

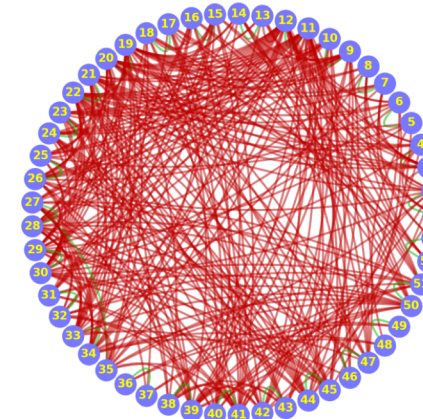
*no microstructure information
no anatomical priors*



VB = 27 (sensitivity=100.0%)
IB = 393 (specificity= 14.9%)

After COMMIT

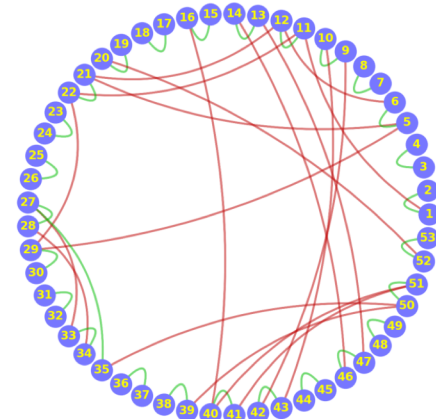
*with microstructure information
no anatomical priors*



VB = 27 (sensitivity=100.0%)
IB = 374 (specificity= 19.0%)

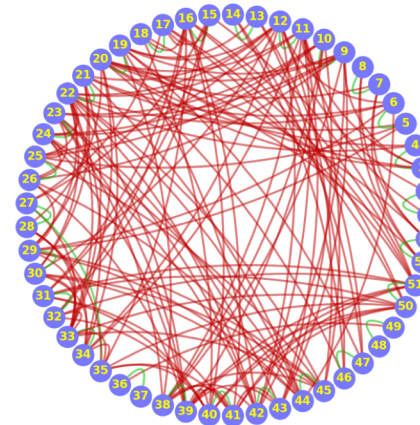
After COMMIT2

*with microstructure information
with anatomical priors*

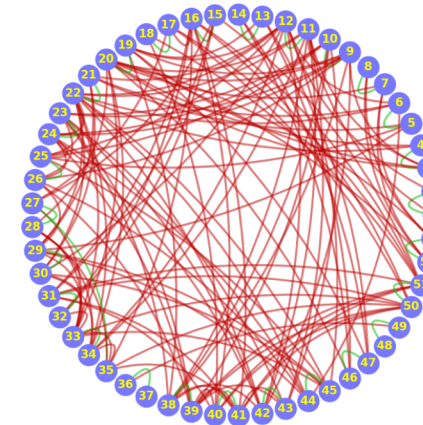


VB = 27 (sensitivity=100.0%)
IB = 20 (specificity= 95.7%)

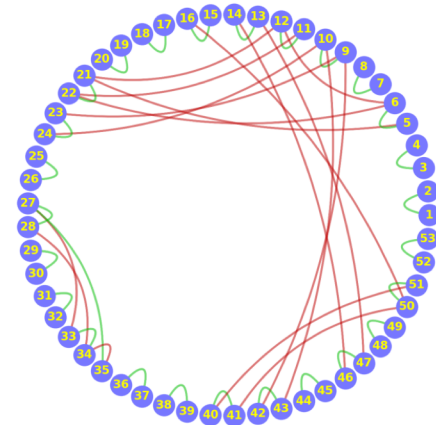
deterministic



VB = 27 (sensitivity=100.0%)
IB = 204 (specificity= 55.8%)

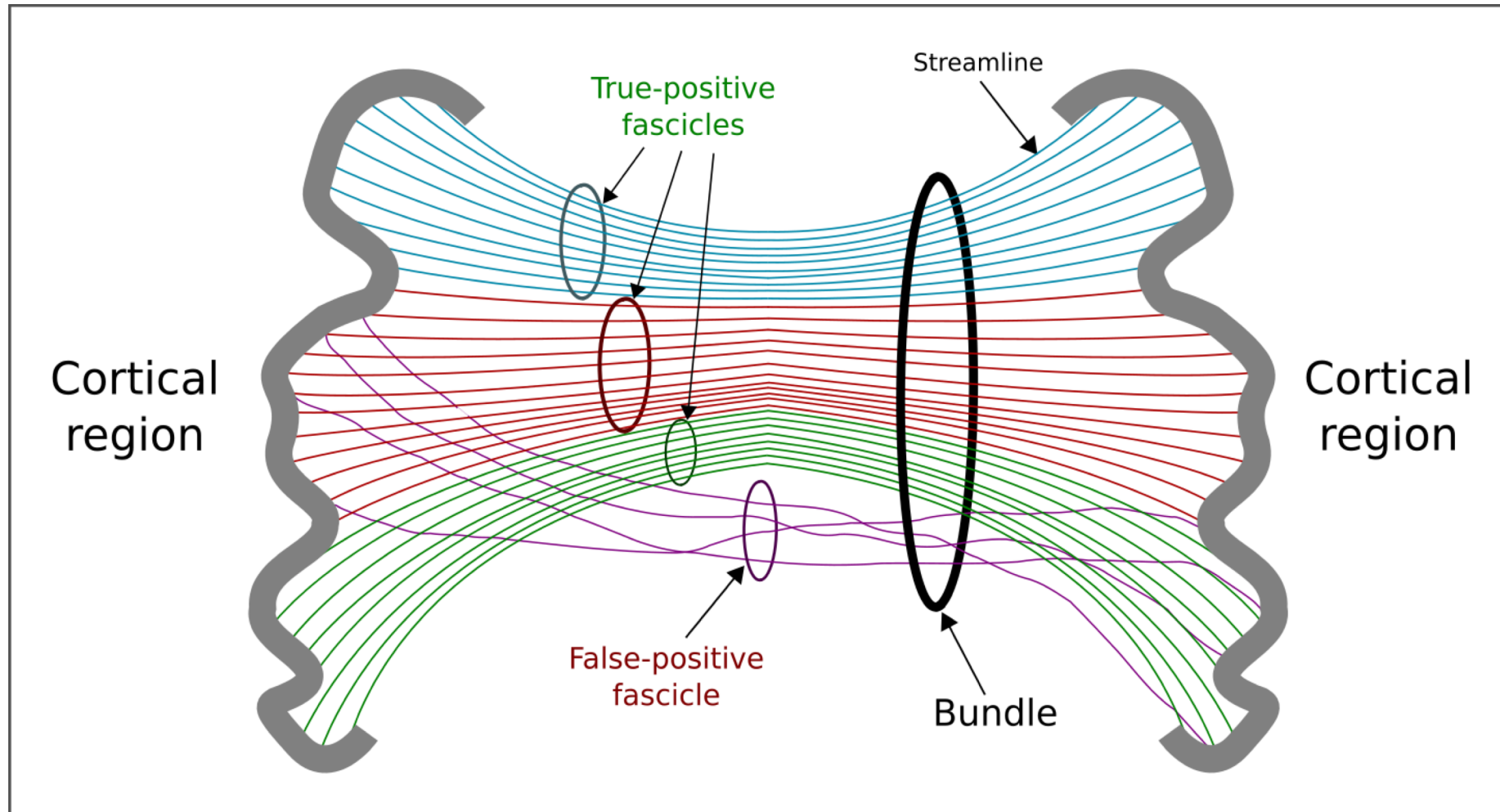


VB = 27 (sensitivity=100.0%)
IB = 190 (specificity= 58.9%)



VB = 27 (sensitivity=100.0%)
IB = 17 (specificity= 96.3%)

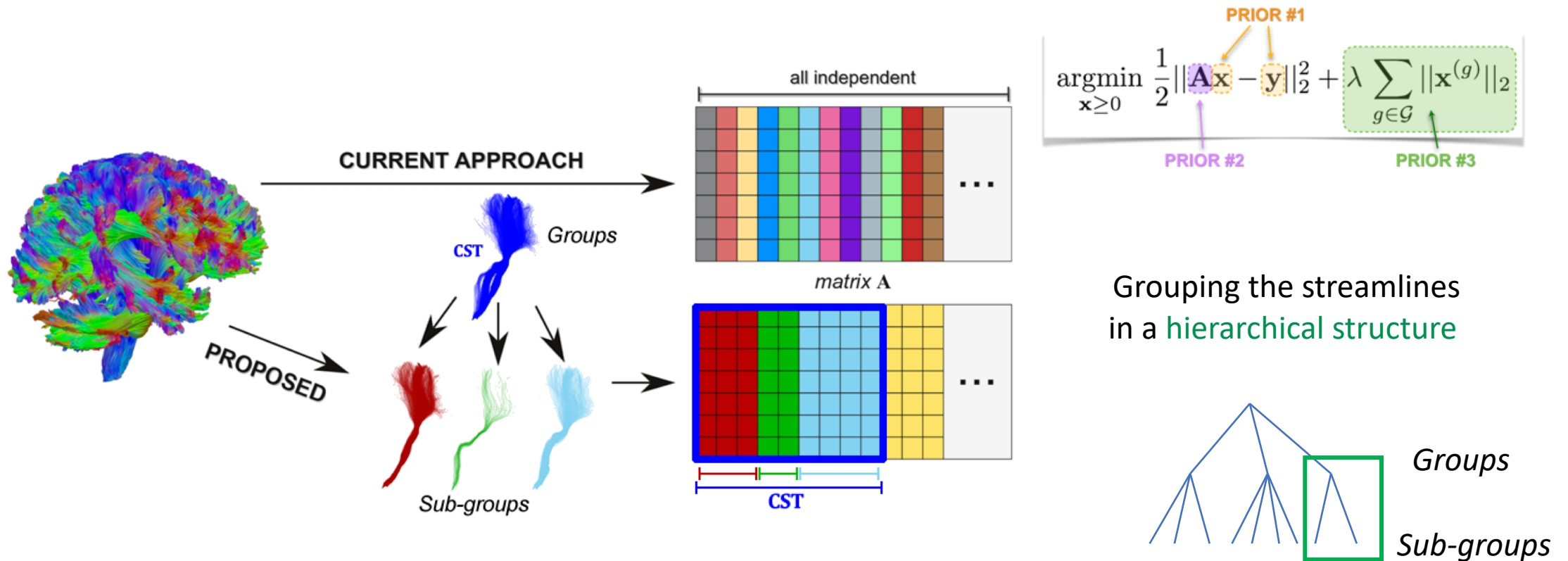
Bundles are composed by fascicles



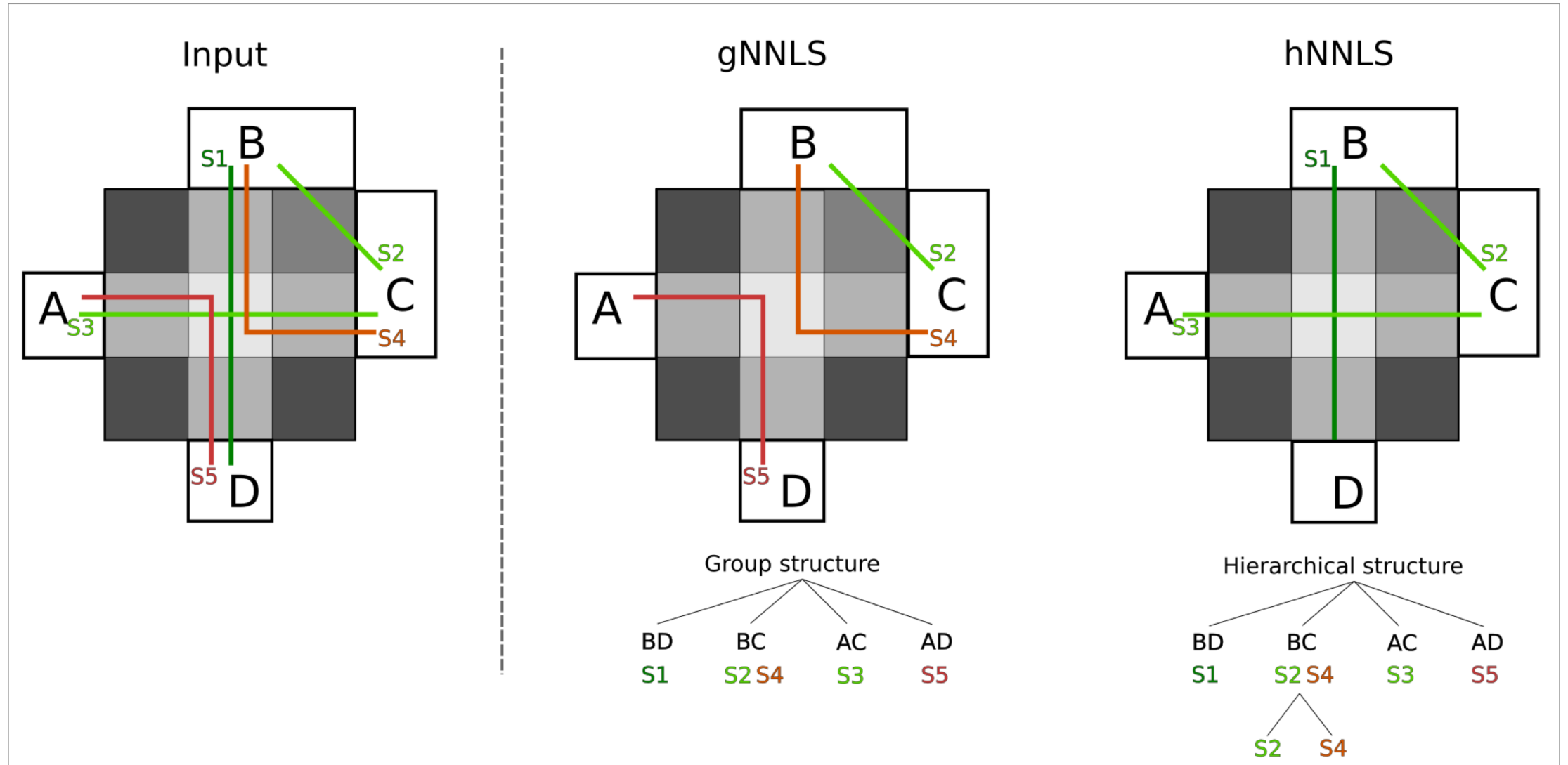
Ocampo-Pineda ISMRM 2019

Modified COMMIT2 allows injecting hierarchical priors

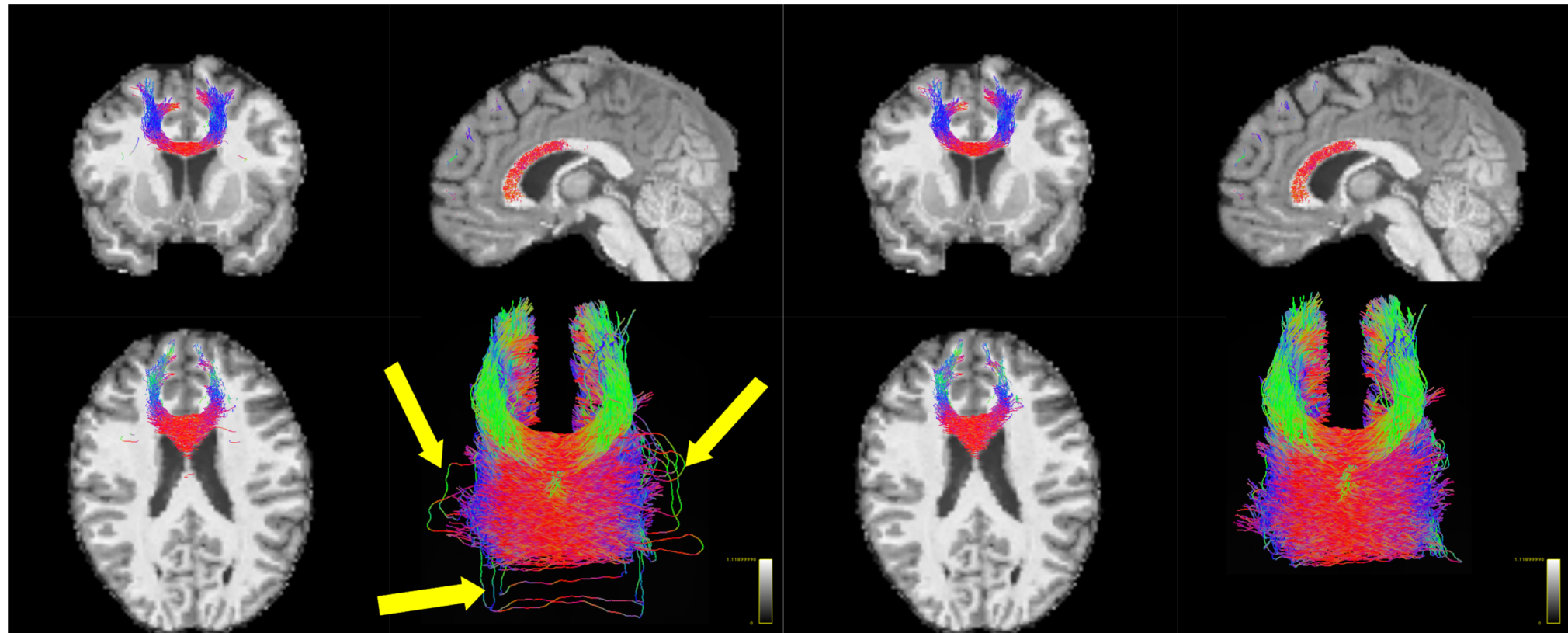
Streamlines are organized in bundles, and can be organized in a **hierarchical structure** e.g. using cortical regions to define the groups and clustering the streamlines in sub-groups



Synthetic results



In-vivo results



After COMMIT2
Group structure

After COMMIT2
Hierarchical structure

Questions?