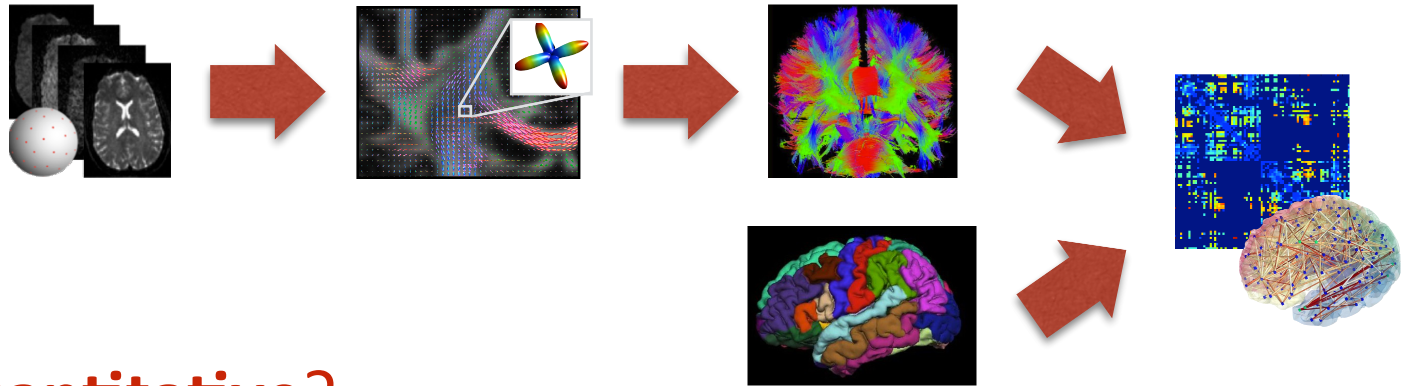
Diffusion MRI: quantifying structural connectivity

Connectivity mapping with diffusion MRI (1/2)

Typical pipeline



Is tractography **quantitative**?

One frustrating thing about tractography is that it takes a quantitative acquisition method (diffusion MRI) and makes it less quantitative. That is, less quantitative from the point of view of connectivity. Of course, diffusion MR is a quantitative method: it allows us to calculate the—albeit apparent—diffusion coefficient with great accuracy. Hence we can use

[Jbabdi et al., 2011]

Local reconstruction

Diffusion features

- Diffusion Tensor Imaging *(Basser et al, 1994)*
- Diffusion Spectrum Imaging *(Wedeen et al, 2000)*
- Spherical Deconvolution *(Tournier et al, 2004)*
- Diffusion Orientation Transform *(Ozarslan et al, 2006)*
- Q-BALL in Constant Solid Angle *(Aganj et al, 2010)*
- …

Microstructure features

- Ball-and-stick *(Behrens et al, 2003)*
- CHARMED *(Assaf et al, 2005)*
- AxCaliber *(Assaf et al, 2008)*
- MMWMD *(Alexander et al, 2010)*
- NODDI *(Zhang et al, 2012)*
- …

Tractography

Line-propagation

- FACT *(Mori et al, 1999)*
- RK4 *(Basser et al, 2000)*
- …

Probabilistic

- PICo *(Parker et al, 2003)*
- ProbTrackX *(Behrens et al, 2003)*
- …

Front-evolution

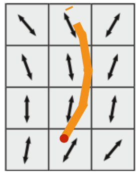
- Fast marching tractography *(Parker et al, 2002)*
- Anisotropic geodesic tractography *(Jbabdi et al, 2008)*
- …

Global energy-minimization

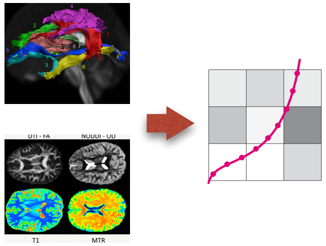
- GIBBS tracking *(Kreher et al, 2008)*
- Spin-glass tractography *(Fillard et al, 2009)*
- …

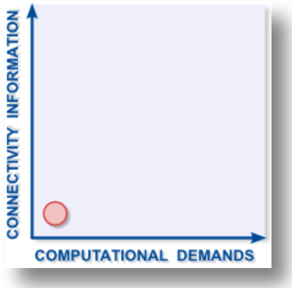
Connectivity mapping with diffusion MRI (2/2)

Line-propagation tracking

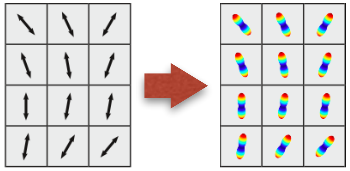


- ⬆ ≃ few minutes/brain, but…
- ⬇ …"fiber count" is not quantitative
- ⬆ Tractometry is (slightly) more quantitative, but…
- ⬇ …measures are indirect (superposition of effects)

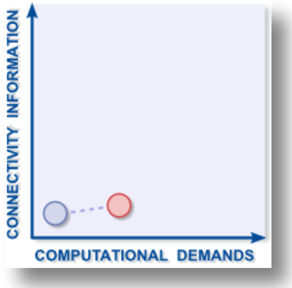




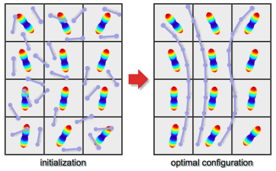
Probabilistic variant

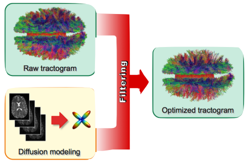


- ⬆ Slightly more informative (confidence), but…
- ⬇ …no significant benefits for connectivity

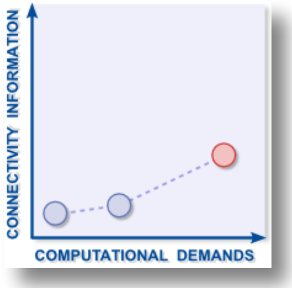


Global inverse problem

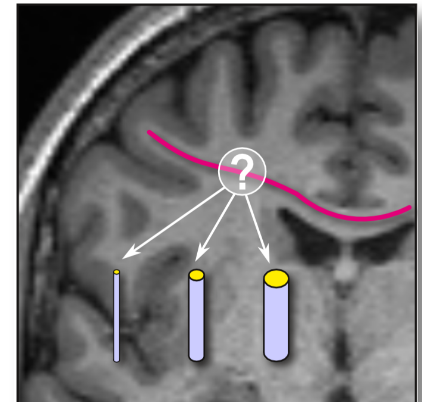




- ⬆ **Higher quality** of reconstructions, but…
- ⬇ …complexity leaves many **open-questions for connectivity**
- ⬆ Slightly more **quantitative** (fibers have contribution), but…
- ⬇ …forward-model based on **orientation information only**



Microstructure informed tractography



MicroTrack algorithm: [Sherbondy et al., 2010]

- Same filtering/top-down strategy of *BlueMatter*, but simultaneously estimates **fiber-specific features**, too
  i.e. <u>axon *density*</u> and <u>*mean diameter*</u>

- **Biophysical forward-model** [Alexander et al., 2010] :

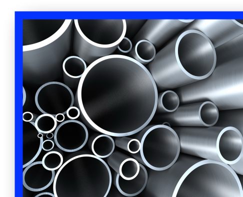
$$A(\mathbf{G},\Delta,\delta;\mathbf{n},r,f,d,d_p) = fA_r(\mathbf{G},\Delta,\delta;\mathbf{n},r,f,d) + (1-f)A_h(\mathbf{G},\Delta,\delta;\mathbf{n},d,d_p),$$

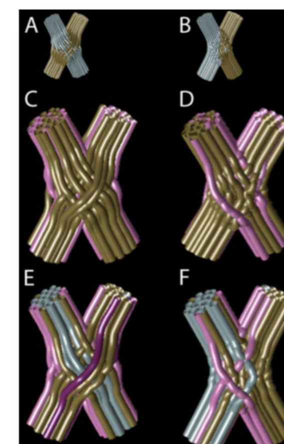
  - f, A_r : restricted water inside axons (cylinders)
  - $(1\text{-}f)$, A_h : hindered water between axons
  - G, δ, Δ : parameters of the acquisition sequence
  - $\mathbf{n}, r, d, d_p$: local parameters of a fiber tract

- Assumes **constant properties** along fibers

topology

morphology



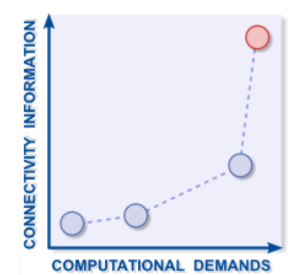


Notes:

- ⬆ Can <u>estimate directly</u> both:
  - Topology of the network, i.e. fibers *geometry* and *arrangement*
  - Morphology of the connections, e.g. their *average axon diameter*

- ⬆ Results showed that <u>common ambiguities can be solved</u> adding more information to tractography (**not only orientation!**)

- ⬇ ≃ ***21 days/brain***



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

measured signal

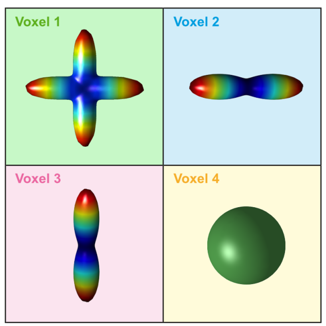
$$S = \mathbf{y}$$

predicted signal

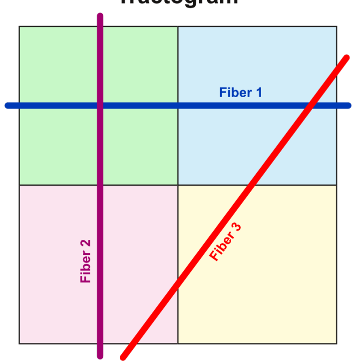
$$\hat{S}(\mathcal{F}) = \mathbf{Ax}$$

$$\underset{\mathbf{x}\geq 0}{\operatorname{argmin}} \|\mathbf{Ax} - \mathbf{y}\|_2^2$$

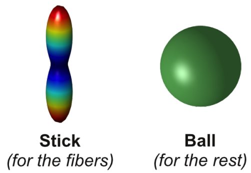
Acquired DWI image

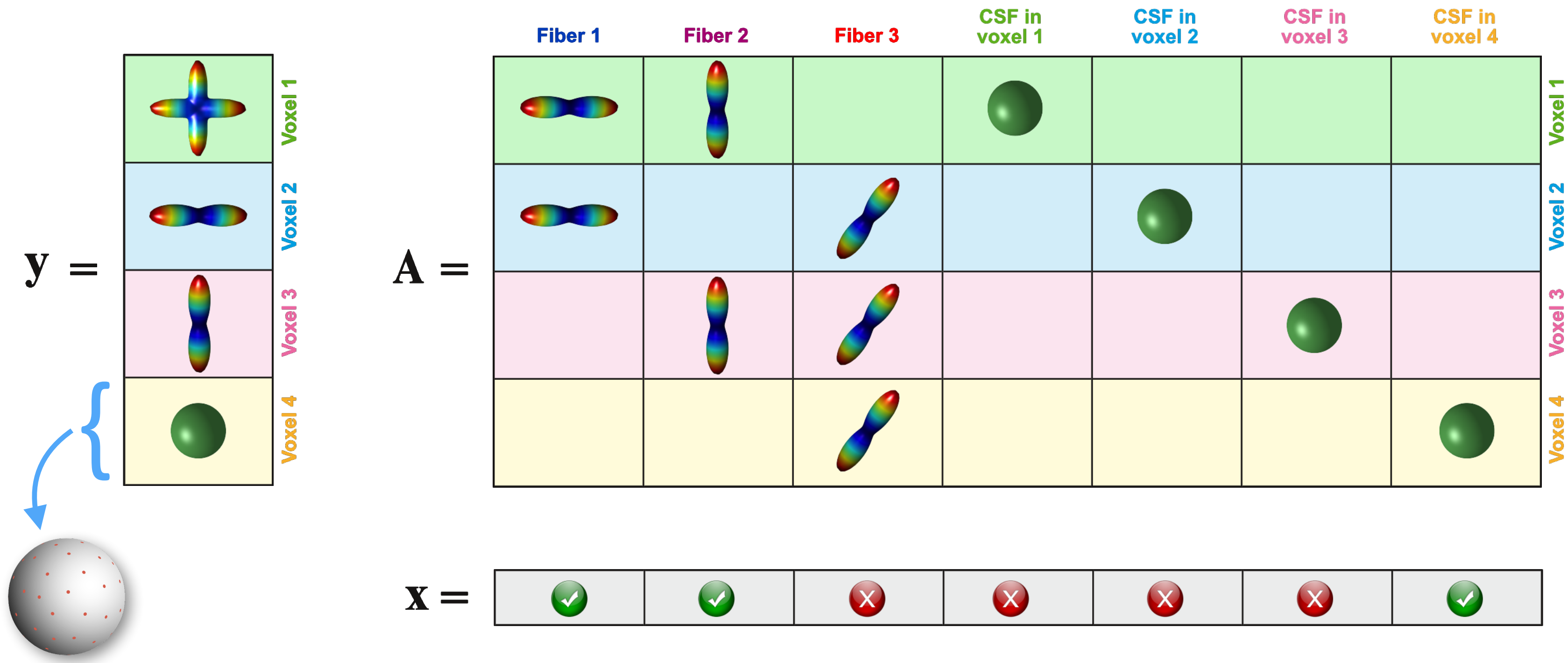


Tractogram



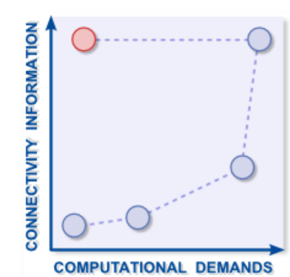
Forward model





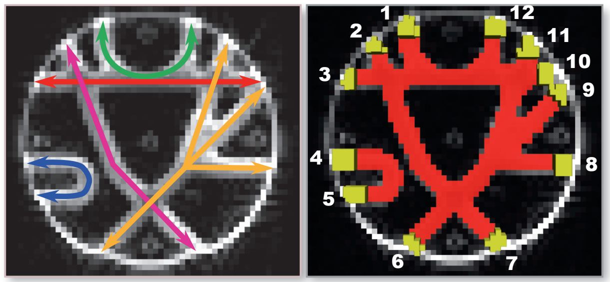
NOTES

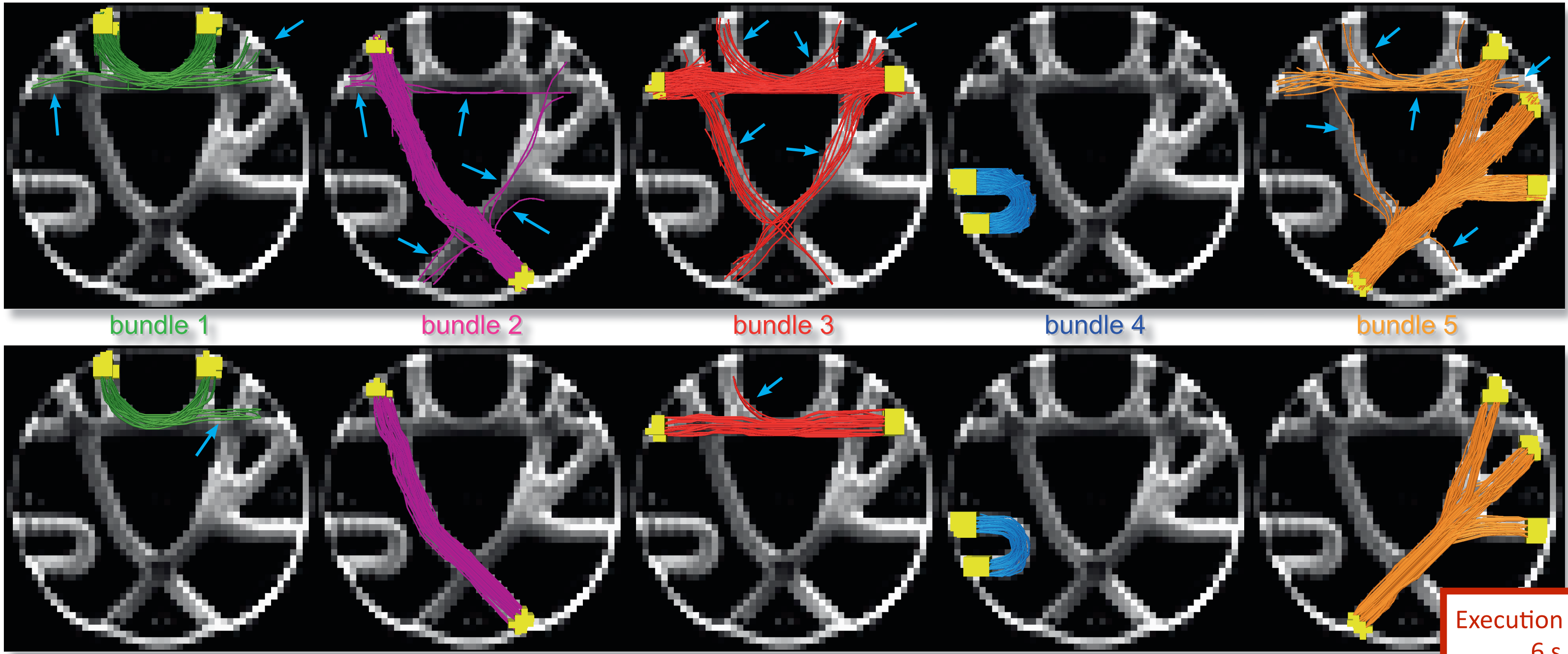
- *Any forward-model* can be used
- Not restricted to *diffusion MRI, e.g. myelin, T1, T2 etc*



EXAMPLE 1: false positives identification

- False positives are a **major problem in tractography**:
  - *Sensitivity vs specificity* trade-off [Thomas et al., 2014; Descoteaux et al., 2016]
  - False positives are <u>critical for connectivity</u> [Zalesky et al., 2016]
- *Experimental setup:*
  - *FiberCup* dataset : 64@b=1500 s/mm^2, 3x3x3 mm
  - ***Stick-Ball*** model

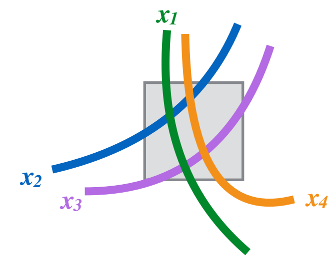


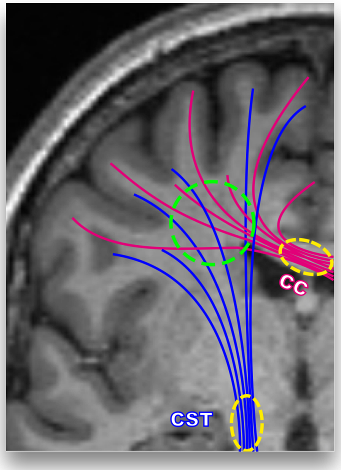


Execution time: 6 s

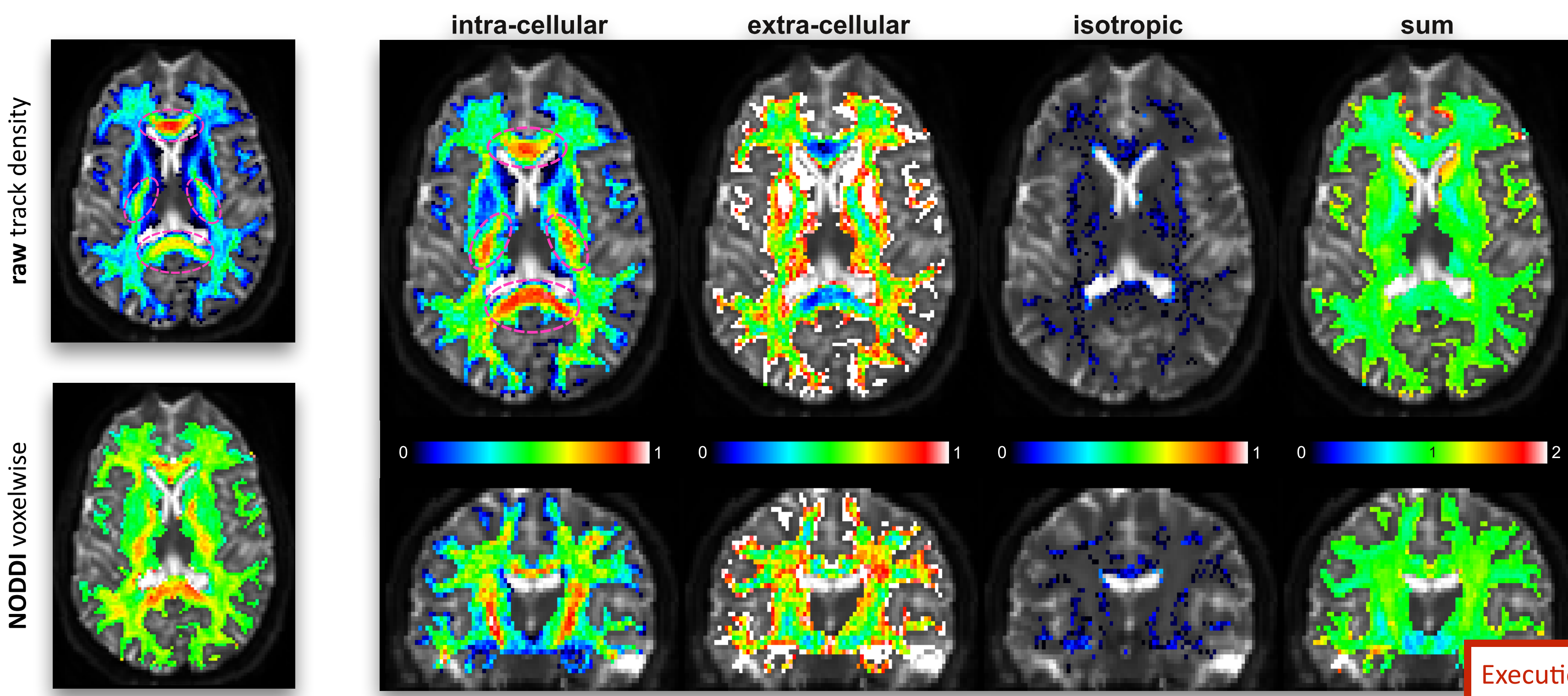
EXAMPLE 2: biological plausibility

- Project weights x of fibers to each voxel and **compare to previous studies**





- *Experimental setup:*
  - *Clinical* dataset : 24@b=700 s/mm^2 and 48@2000 s/mm^2, G=40 mT/m
  - ***Stick-Zeppelin-Ball*** model

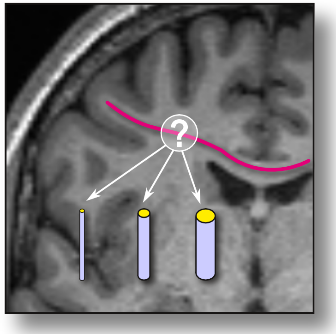


Execution time:
5 min

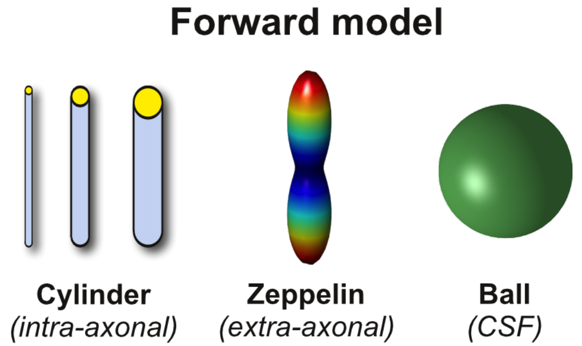
Microstructure informed tractography (5/5)

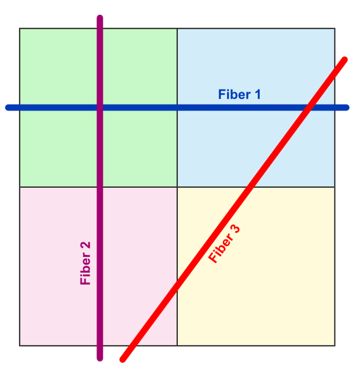
EXAMPLE 3: towards quantitative connectivity mapping

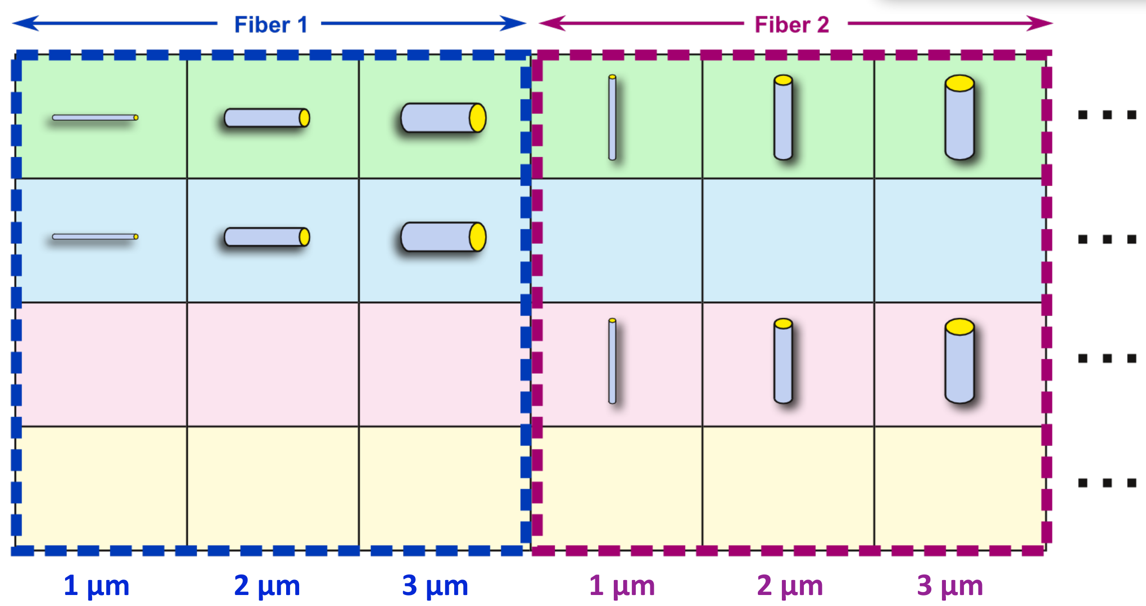
- Microstructure imaging only possible **voxel-wise** [Assaf et al., 2008; Alexander et al., 2010; …] and our aim was to estimate properties specific to the tracts



- *Experimental setup:*
  - *Ex-vivo* monkey dataset : G={300,220,300} mT/m, Δ={12,20,17} ms, δ={6,7,10} ms
  - ***Cylinder-Zeppelin-Ball*** model







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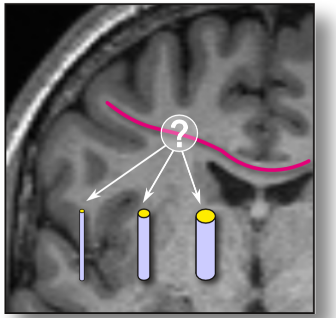

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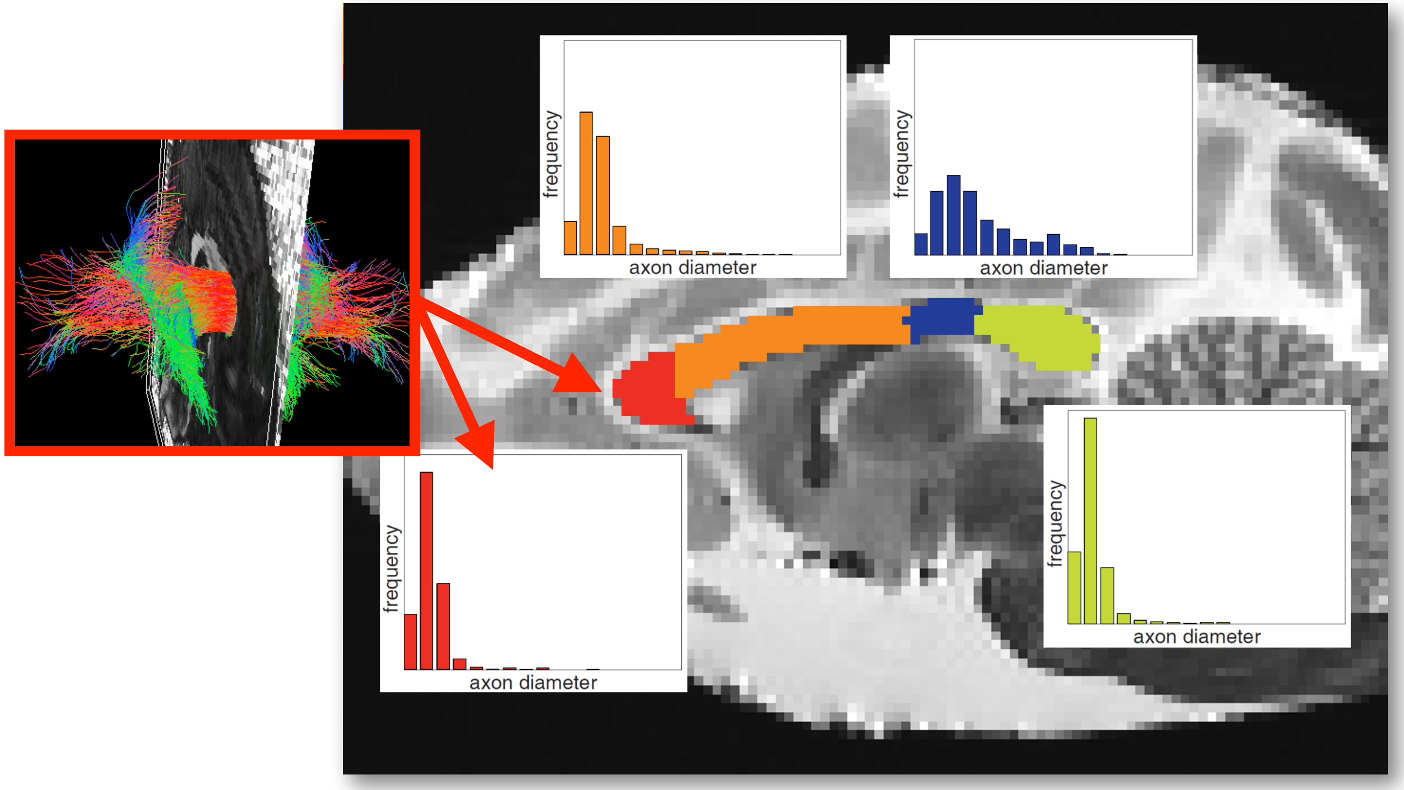

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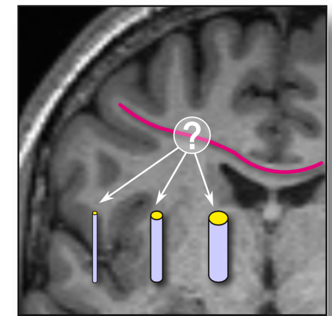

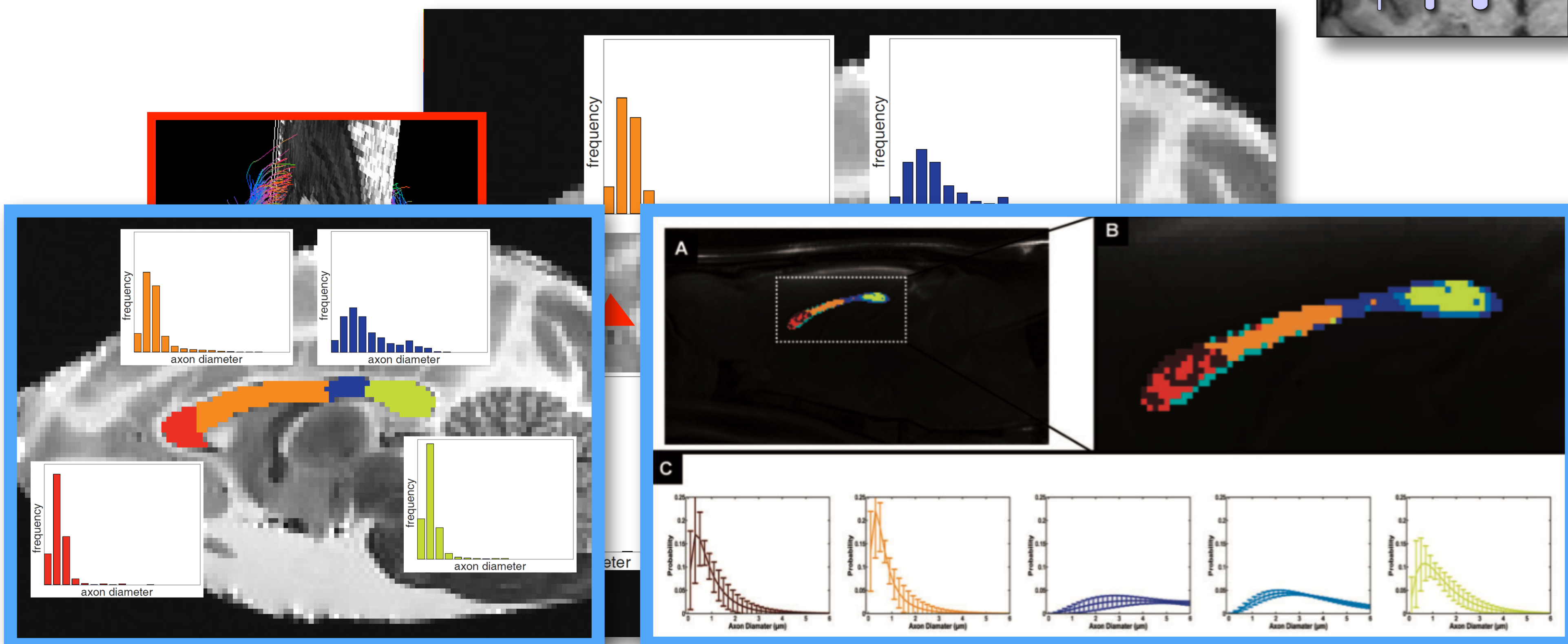

bundle-specific

voxel-wise [Barazany et al., 2009]

EXAMPLE 3: towards quantitative connectivity mapping

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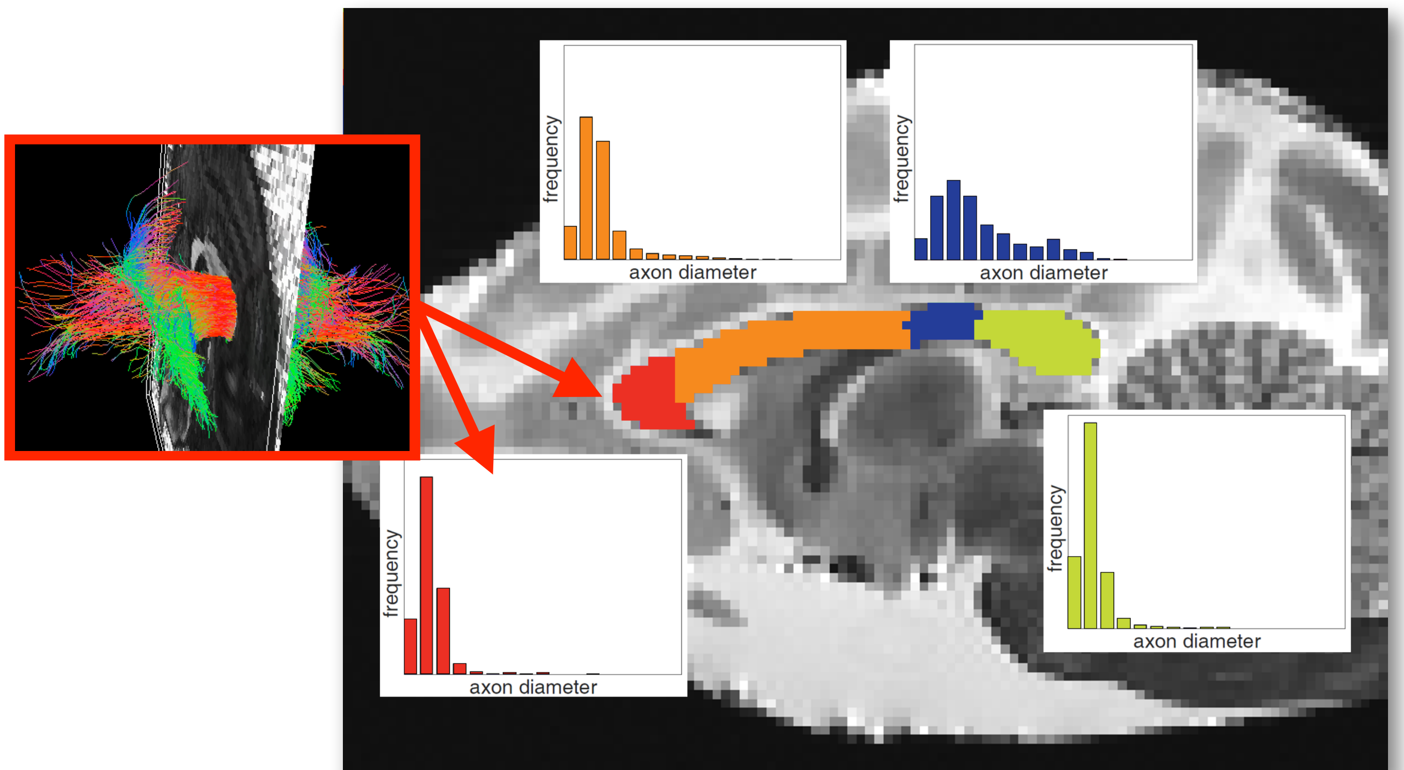
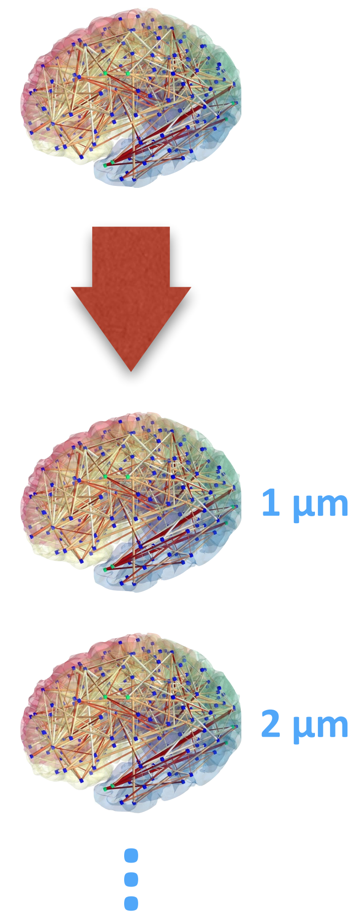


Multi-scale connectivity analysis



Critical issue: interpretation of outcomes

- **Interpretation** is challenging:
  - Tractography reconstructions are *huge*
  - These global techniques are *new* and *very complex*

- *COMMIT* provides a **convenient analogy** to easily **highlight potential dangers** in connectivity mapping

$$\underset{\mathbf{x}\geq 0}{\operatorname{argmin}} \; \underbrace{\|\mathbf{A}\mathbf{x}-\mathbf{y}\|_2^2}_{\text{data fitting}} + \underbrace{\lambda\,\Phi(\mathbf{x})}_{\text{regularization}}$$

Local reconstruction

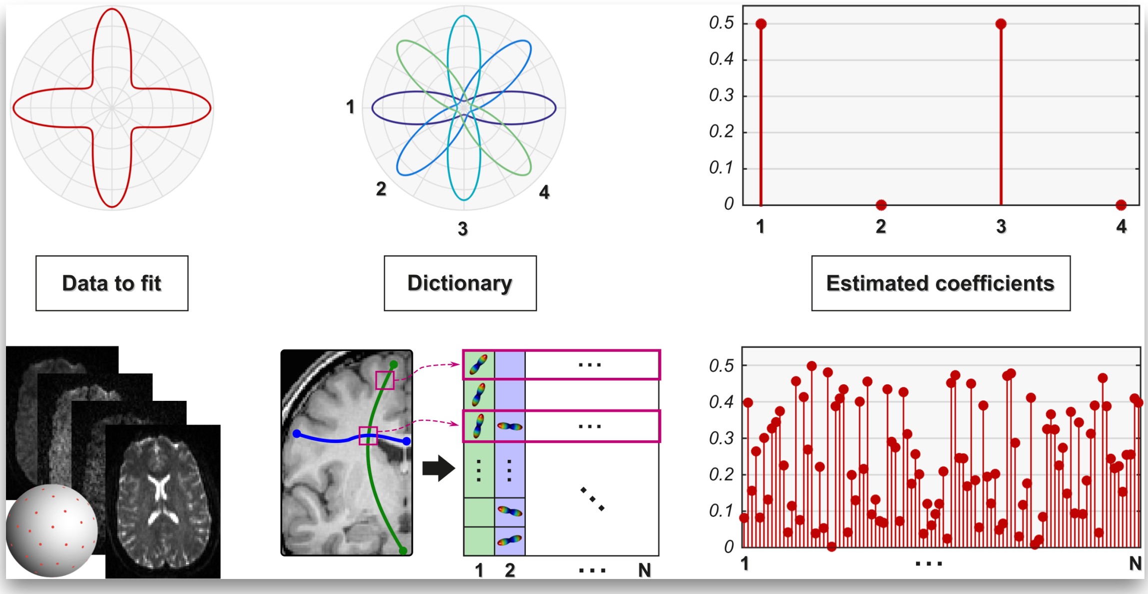
e.g. [Tournier et al., 2007]

$$f_{i+1} = \arg\min\{\|\mathbf{A}f_i - b\|^2 + \lambda^2\|\mathbf{L}f_i\|^2\}$$

Global reconstruction

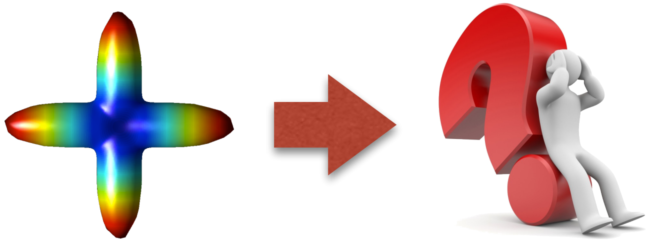
e.g. [Daducci et al., 2014]

$$\underset{\mathbf{x}\geq 0}{\operatorname{argmin}} \|\mathbf{A}\mathbf{x}-\mathbf{y}\|_2^2$$



Summary

- Tractography alone is **not quantitative**
  - *Orientation information* only is not enough



- *Microstructure informed tractography* seems a promising avenue to **improve connectivity quantification**…
  - *Flexible*: allows combining tractography with any microstructure model
  - *Tractable:* fast and efficient

- …but there's **still work to do**!
  - *Interpretation* of outcomes is non-trivial
  - Many *open questions* still remain
  - Many *issues* still need to be solved

Microstructure Informed Tractography: Pitfalls and Open Challenges

frontiers in Neuroscience

TECHNOLOGY REPORT
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To give it a **try** or **contribute**: https://github.com/daducci/COMMIT