Diffusion MRI:
advanced tractography

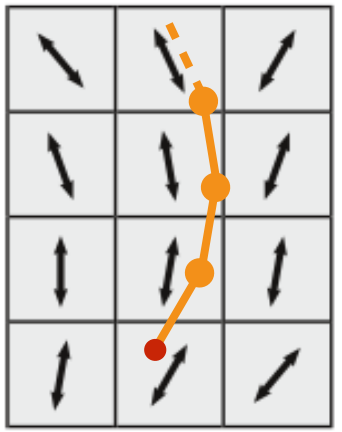
Outline

- **Line-propagation** tracking
  - Deterministic (previous lecture)
  - Probabilistic: extension to allow *uncertainty in the tracking*
- **Geodesic** tracking
  - Principle of *shortest path* between two ROIs
  - Fast marching, graph based
- **Global inverse problem**: bottom-up
  - Reconstruct all fibers at once by *fitting fiber models* to the data
  - GIBBS tracker
- **Global inverse problem**: top-down
  - First reconstruct a *superset of fibers* and then *filter* them
  - BlueMatter and SIFT/SIFT2

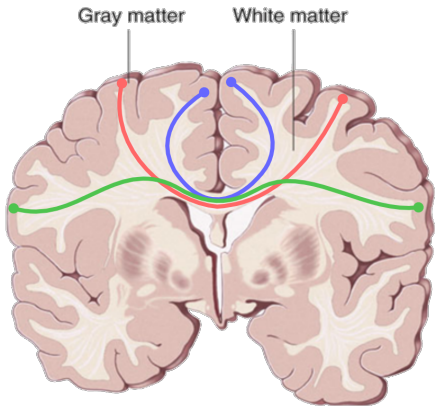
Line-propagation formulation (1/4)

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

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

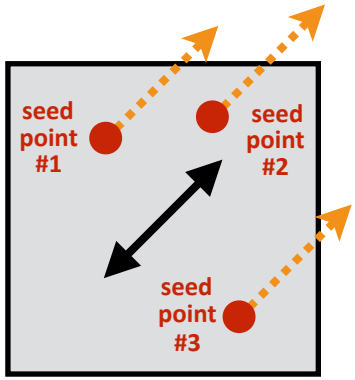


- $\mathbf{f}(\cdot)$: fiber trajectory (—)
- $\mathbf{d}(\cdot)$: main diffusion direction estimated in each voxel (⇕)
- $\mathbf{f}_0$: seed/starting point (●)
- t : step size

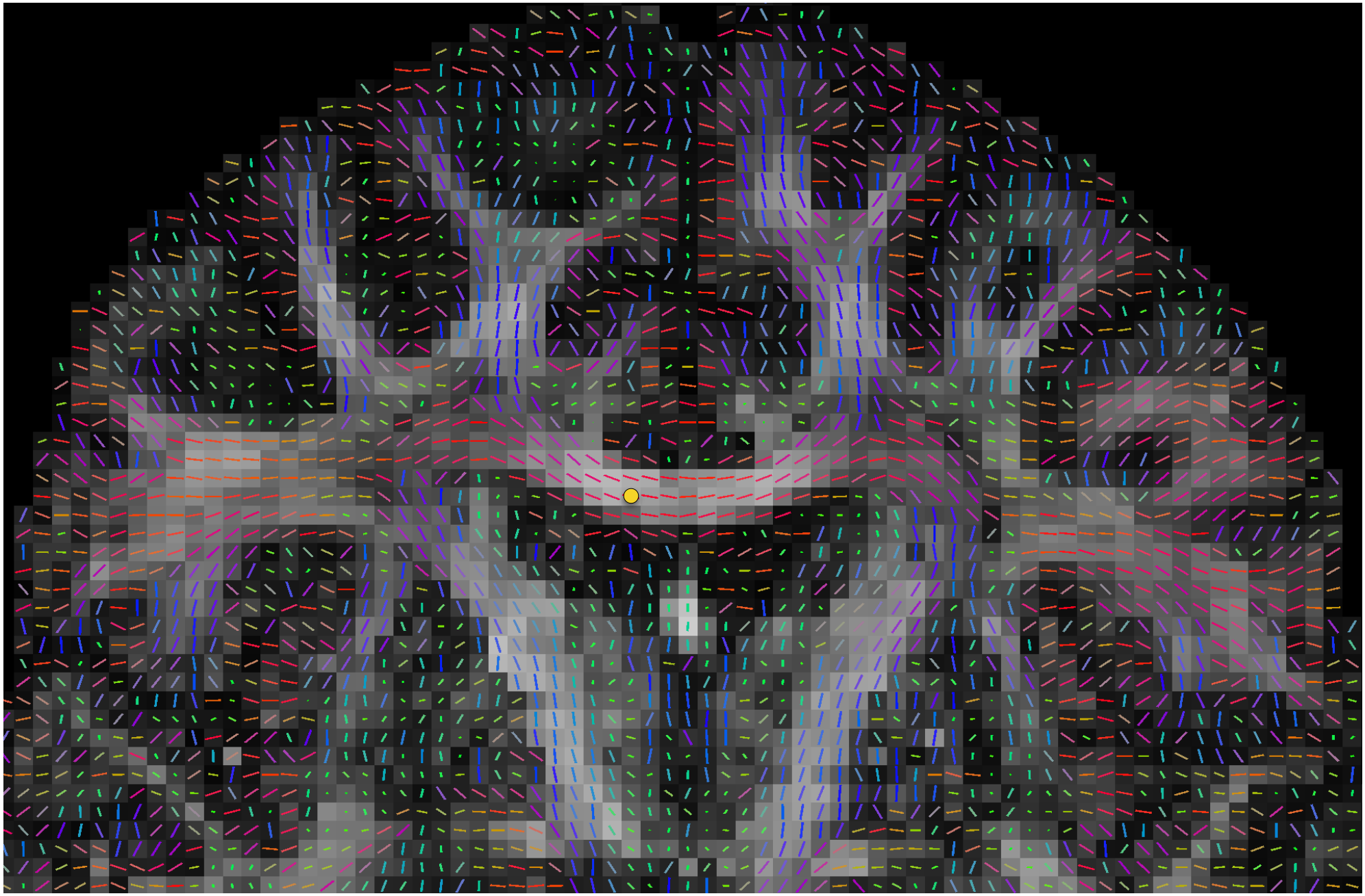


Notes

- ≃ few minutes/brain
- *Deterministic* = the **same trajectories** are reconstructed from same seed points
  - *Random seeding* is still considered deterministic



Line-propagation formulation (2/4)



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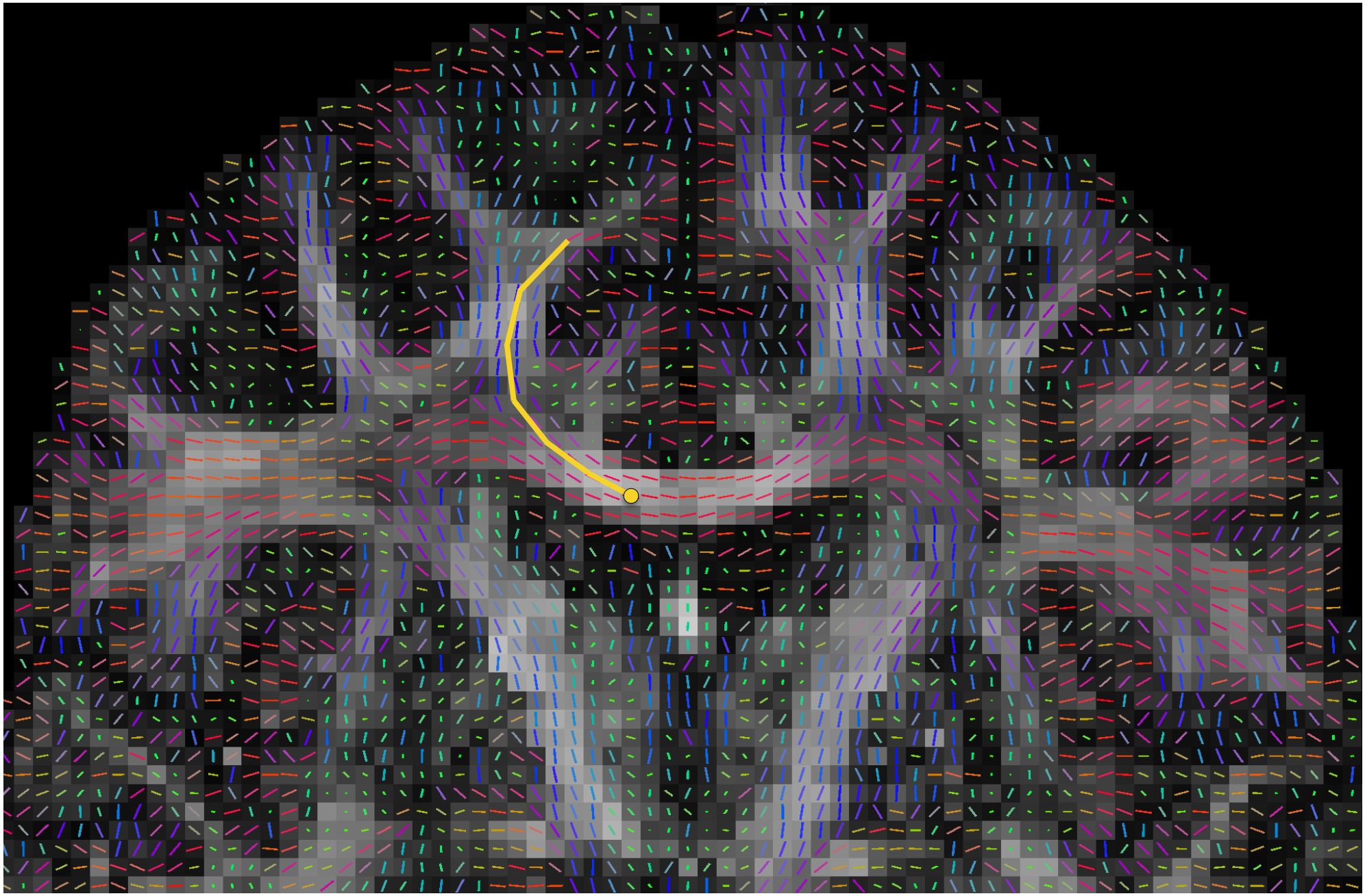
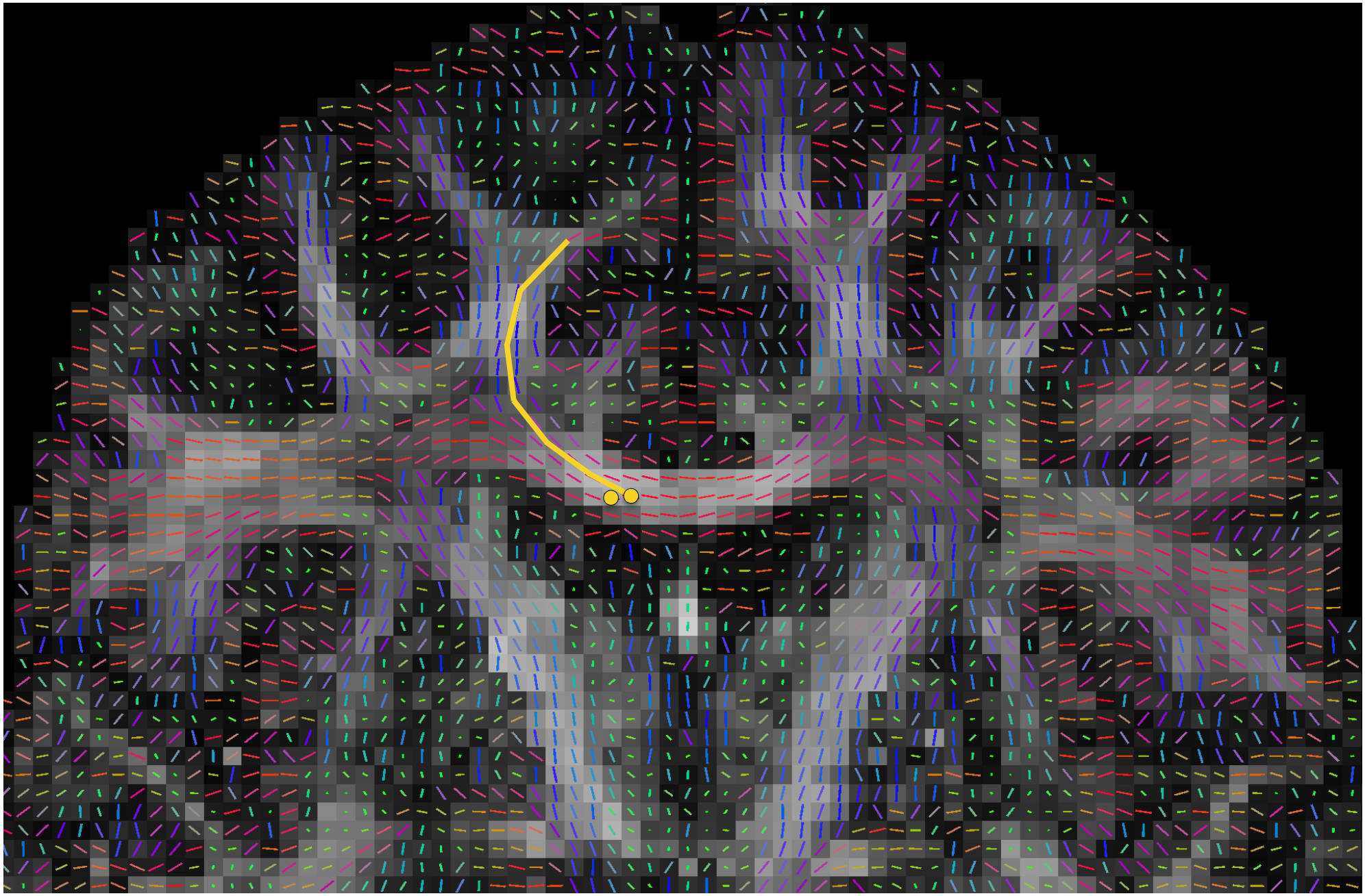
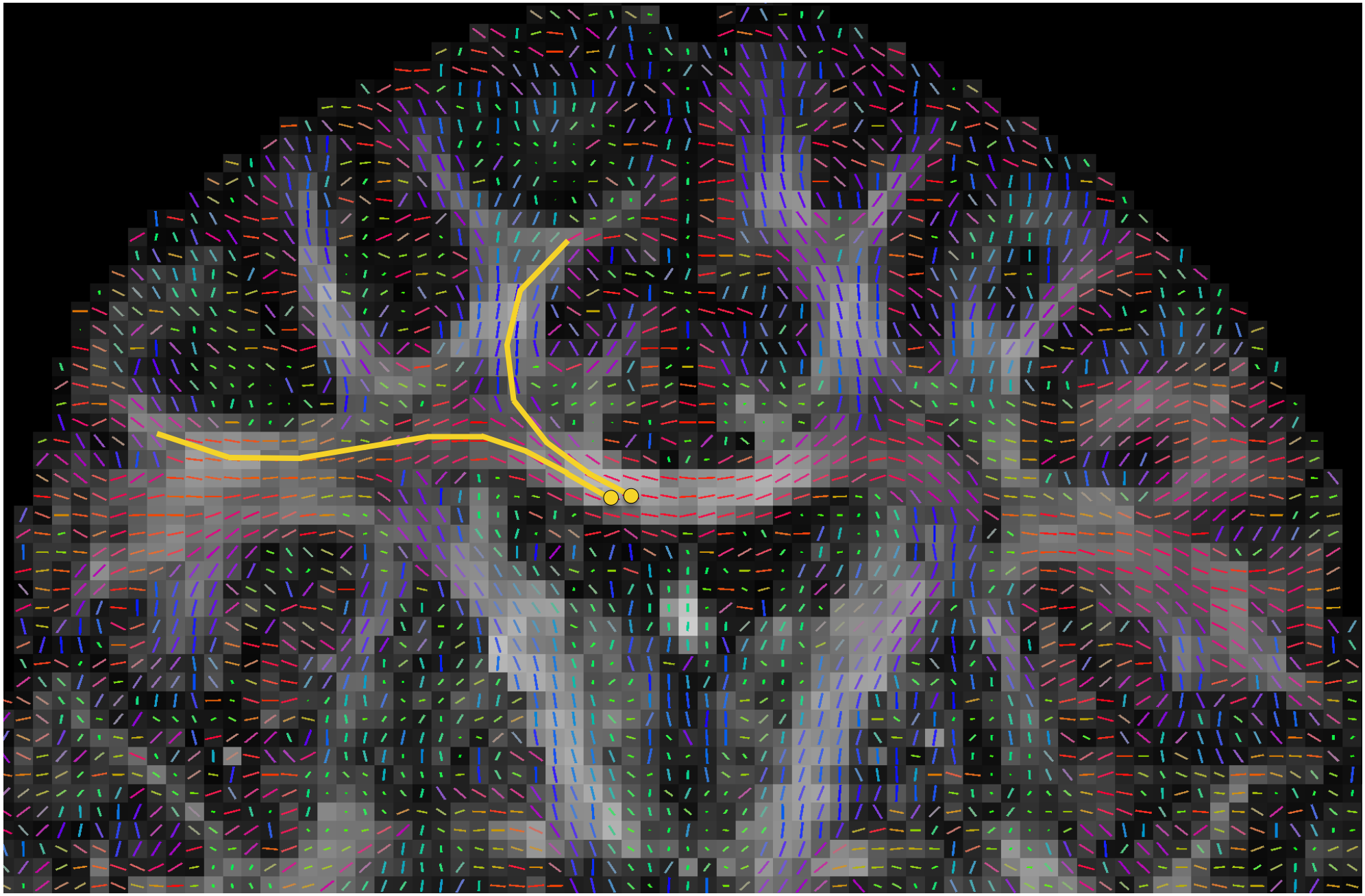


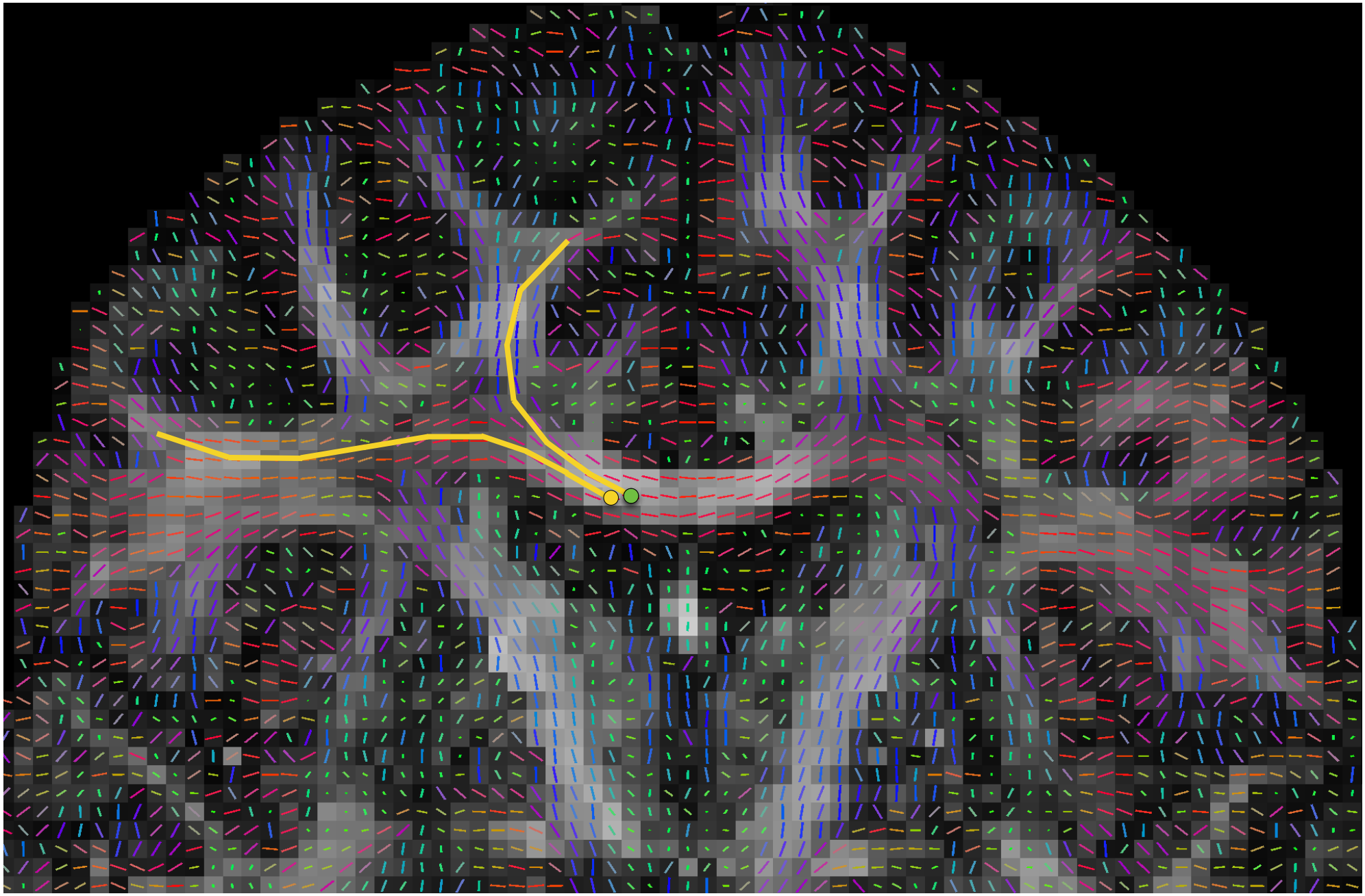
Line-propagation formulation (2/4)



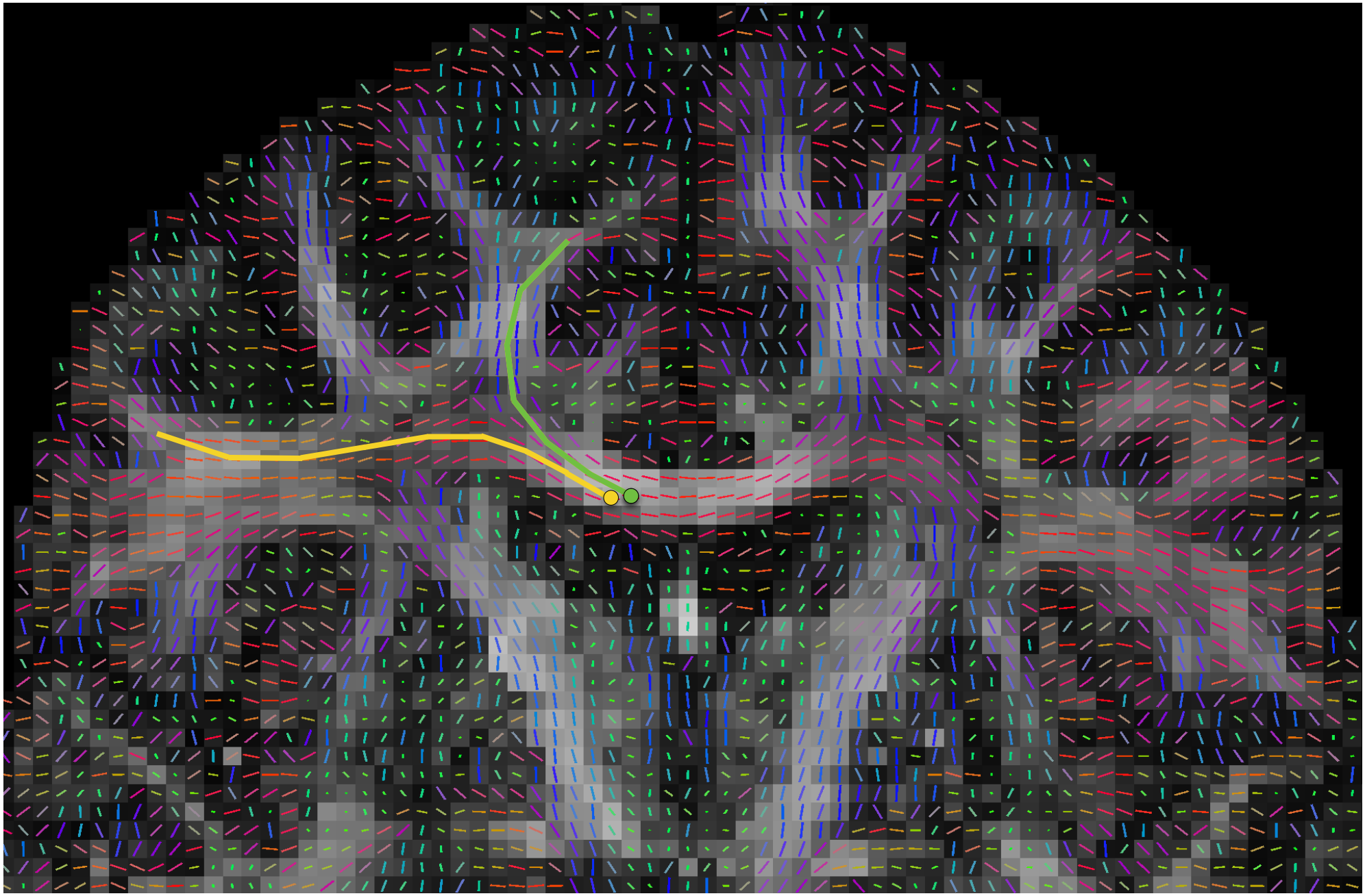
Line-propagation formulation (2/4)



Line-propagation formulation (2/4)



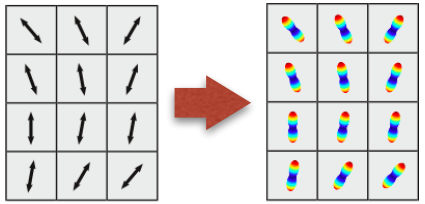
Line-propagation formulation (2/4)



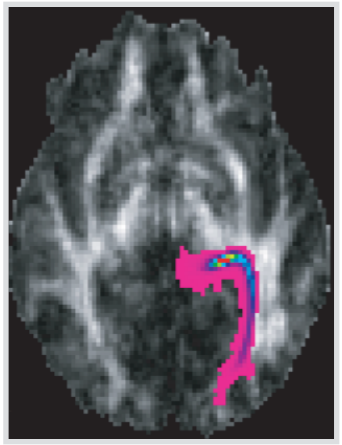
Line-propagation formulation (3/4)

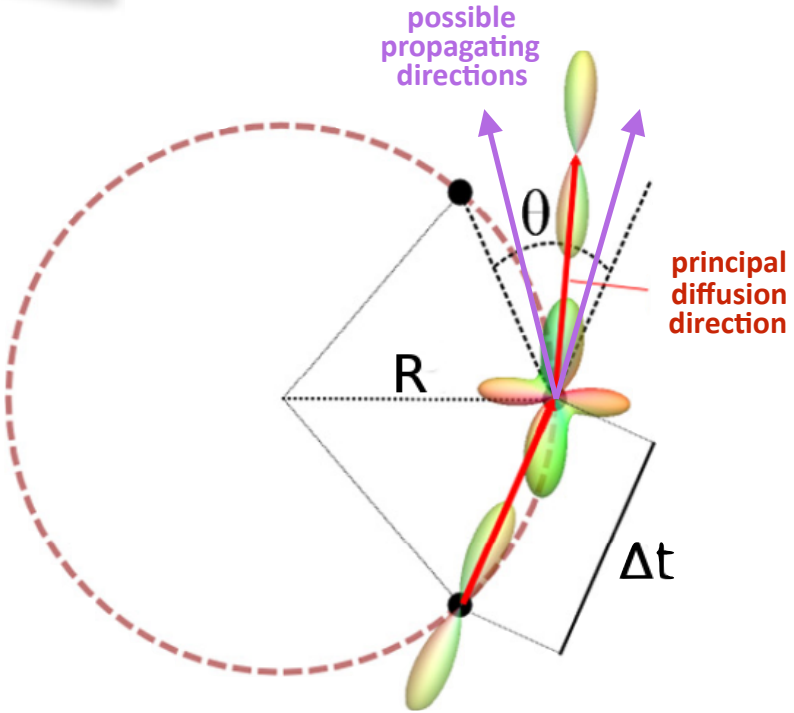
Probabilistic tracking [Parker et al., 2003; Behrens et al., 2003; …]

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



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

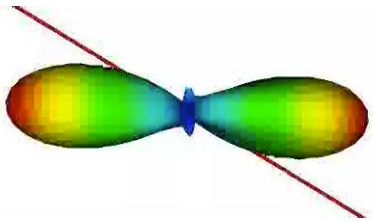




Notes

- ≃ *1 day/brain*
- Adds **confidence levels** to tracts
- Probabilities maps are **difficult to interpret**

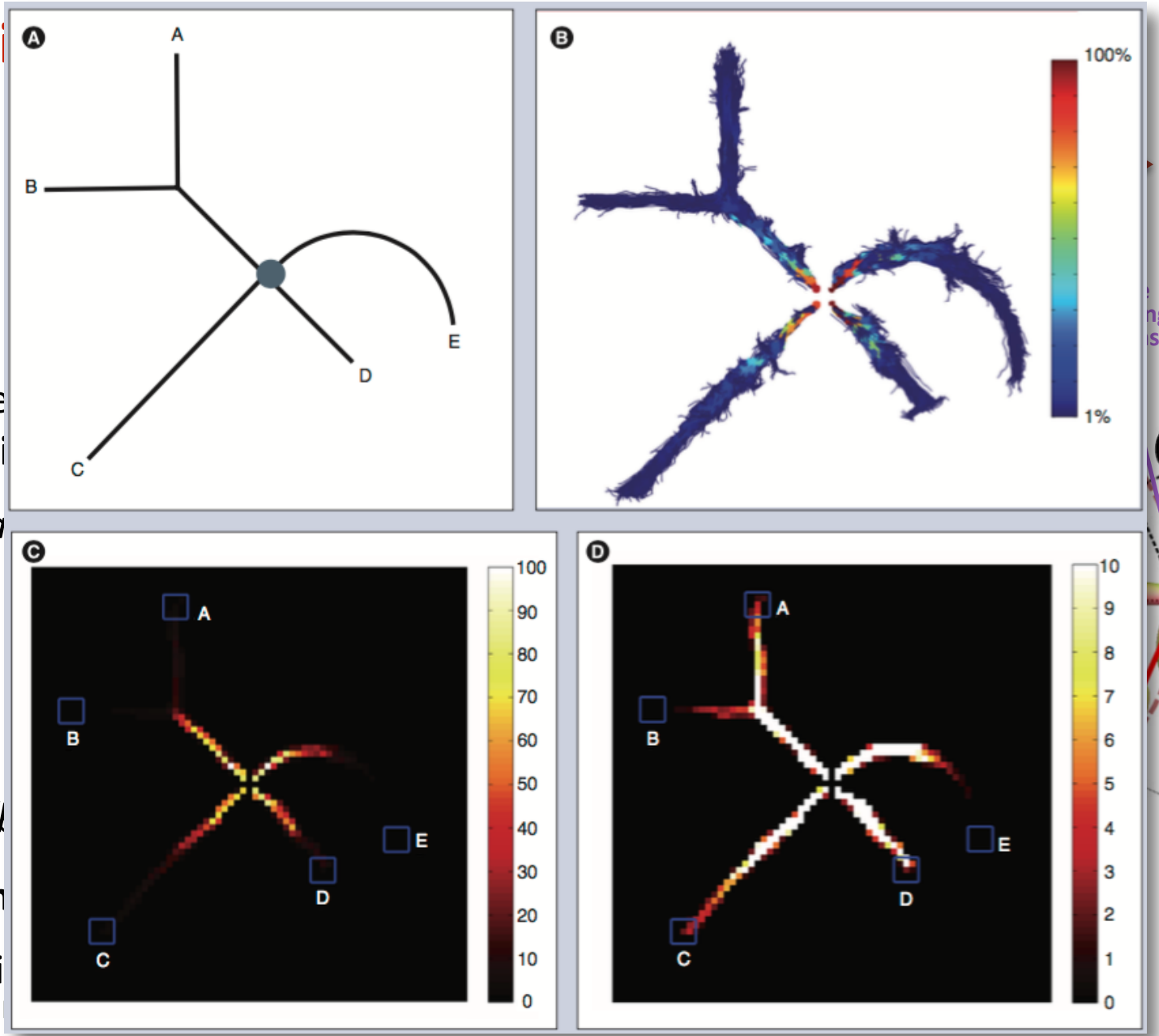
[Jones, 2010; Jbabdi et al., 2011; Jones et al., 2013]

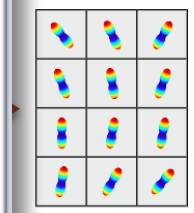


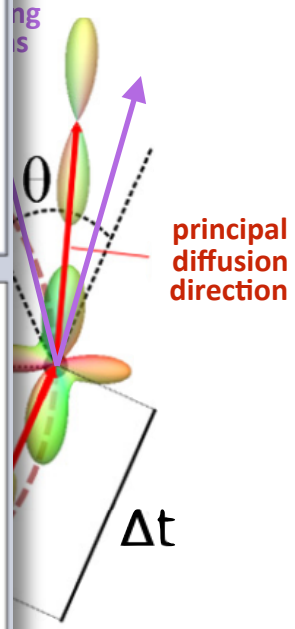
Line-propagation formulation (3/4)

Probabili

- $\mathbf{d}(\cdot)$:
- Next dire
  (**uncertai**
- Seed a *la*
  (**probabi**





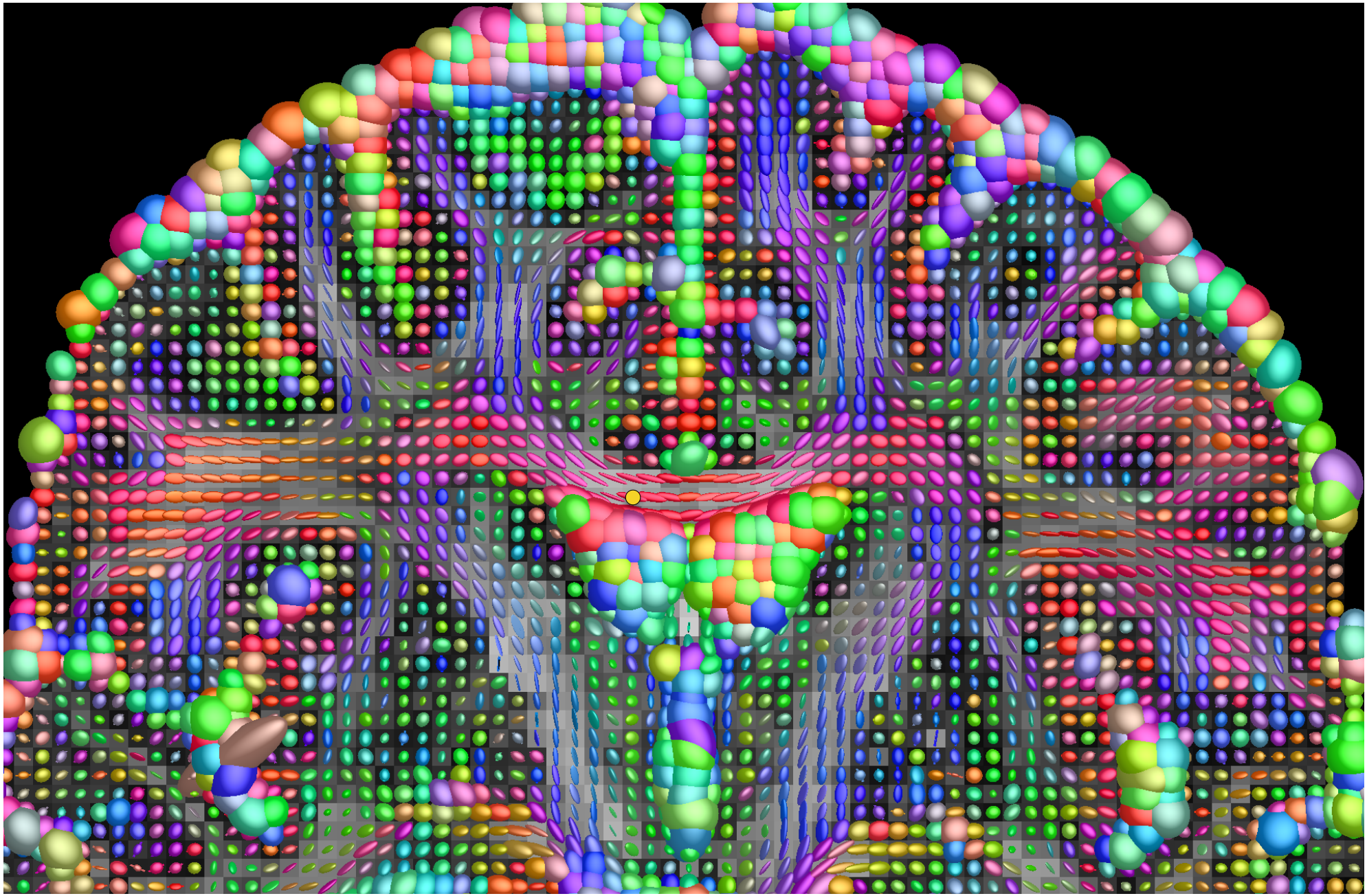


Notes

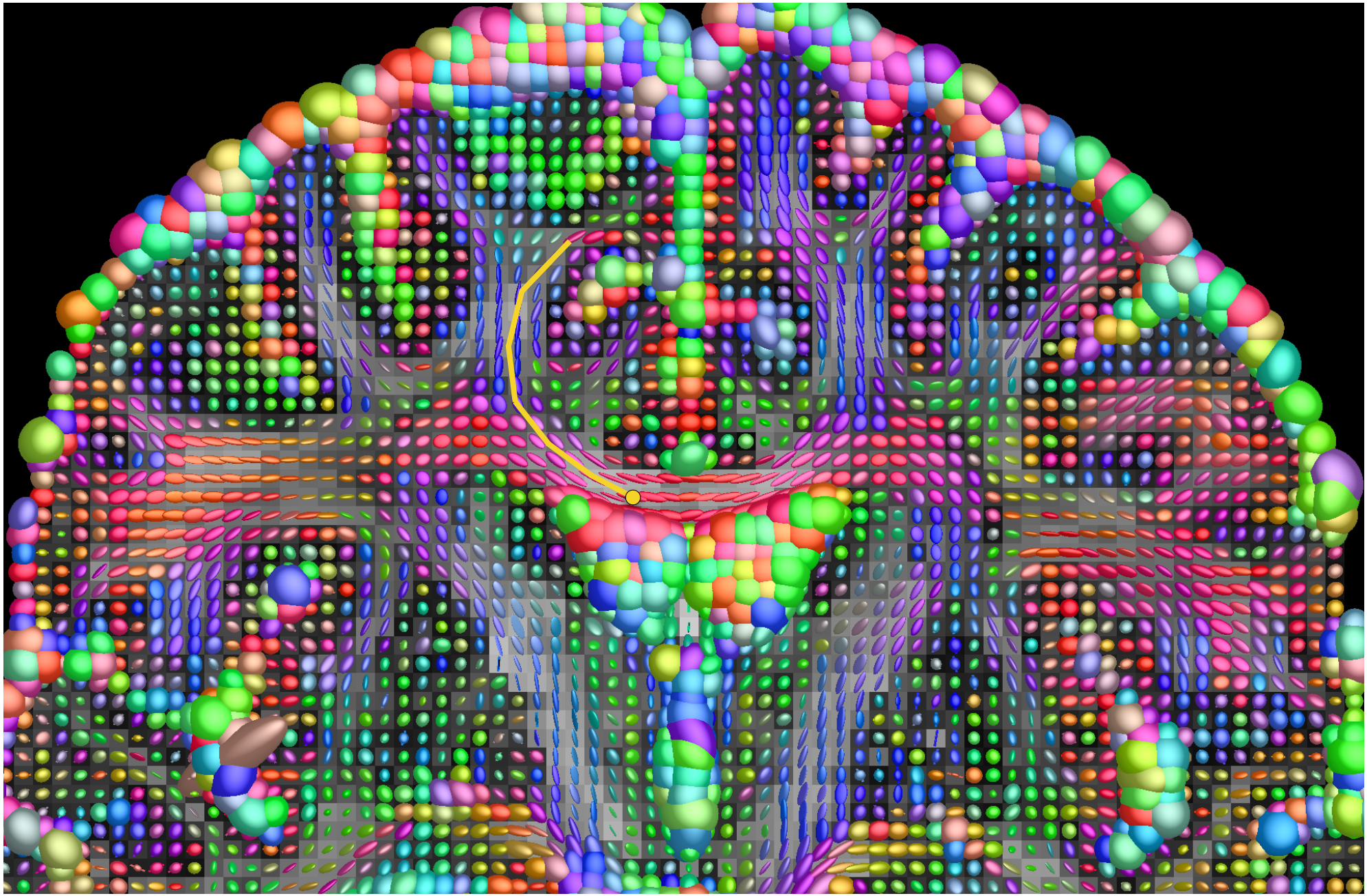
- ≃ *1 day/*
- Adds **con**
- Probabili

[Jones, 2010; J

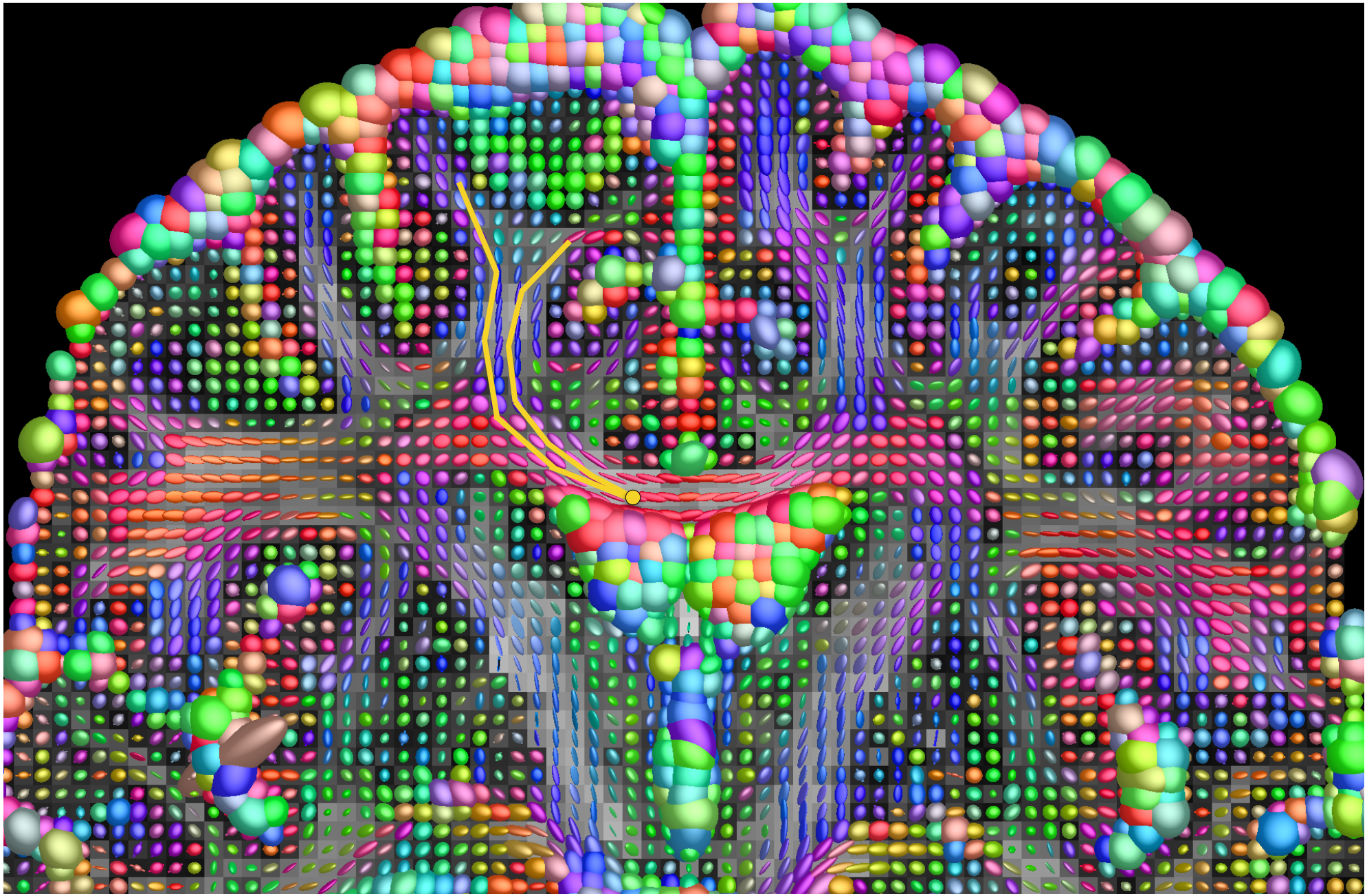
Line-propagation formulation (4/4)



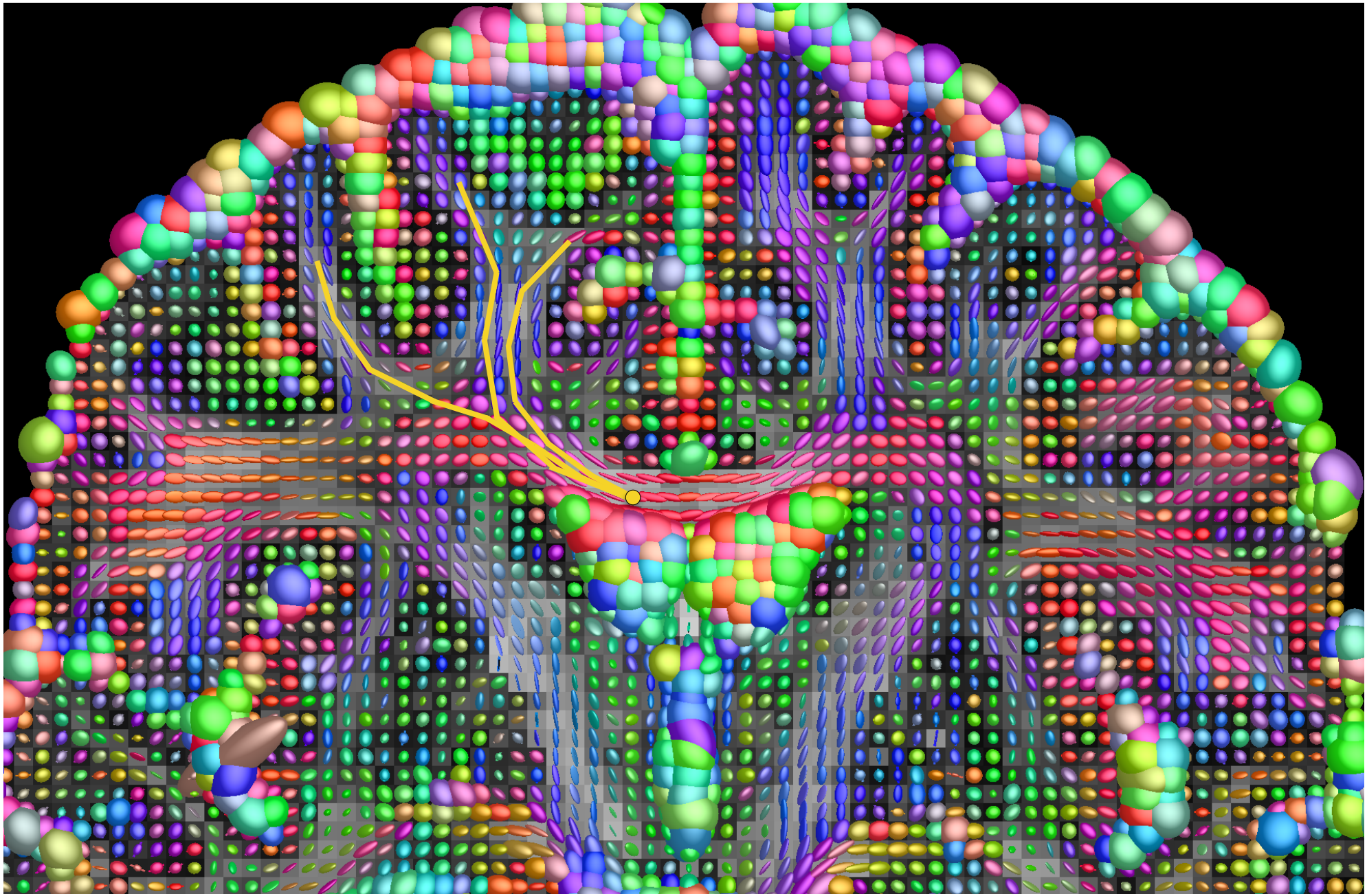
Line-propagation formulation (4/4)



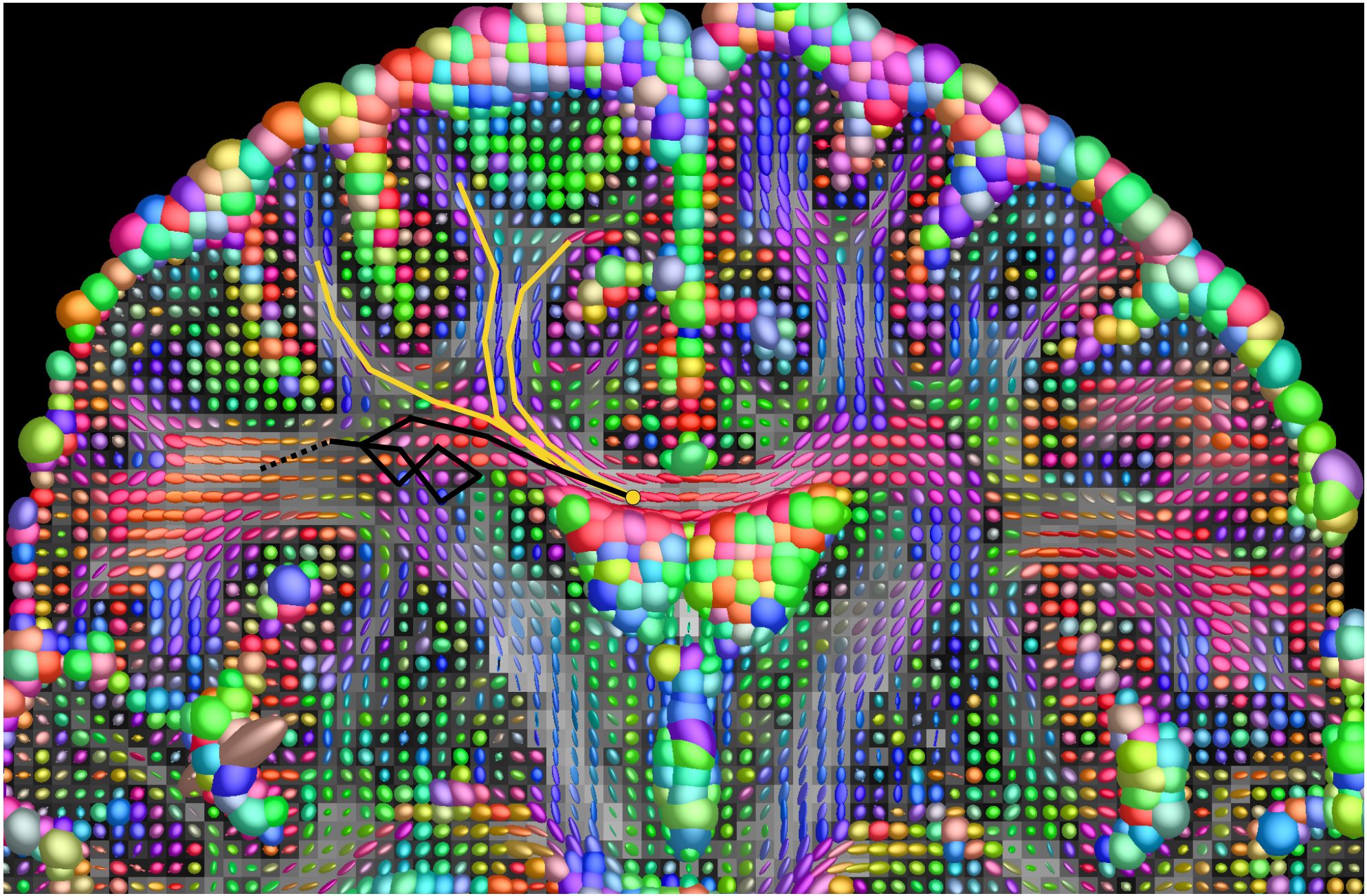
Line-propagation formulation (4/4)



Line-propagation formulation (4/4)



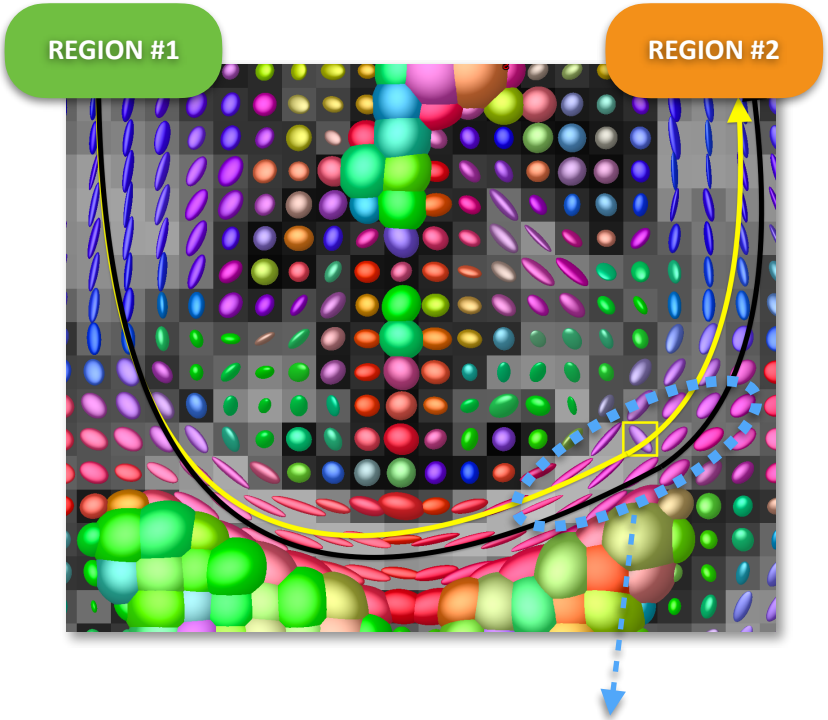
Line-propagation formulation (4/4)



Geodesic tracking (1/3)

Intrinsic issues of previous **local formulations**

- *Line-propagation* **suffers from <u>local</u> inaccuracies** along the path
  - e.g. wrong fODF estimated due to high noise
- While tracking, **algorithm has no information** about the region it will end up in



Possible improvement

- **Optimize a <u>global</u> criterion** while reconstructing
- *Global* = information not only from the voxel

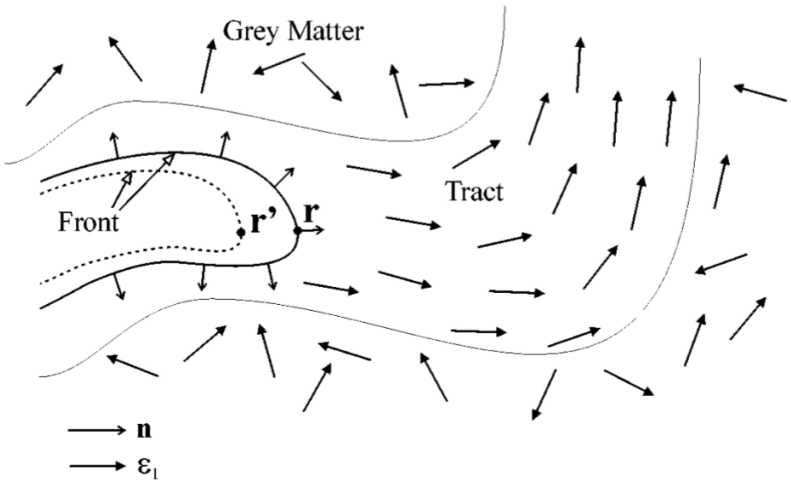
Basic hypothesis used in geodesic tracking

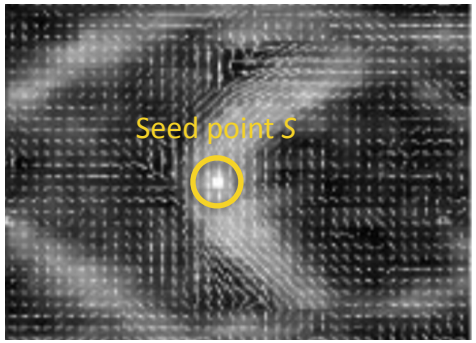
- Fiber tracts *between two gray-matter regions* can be interpreted as **minimal distance paths** (geodesics) **for a metric** derived from dMRI data
- **NB**: the *shortest path* is <u>intended with respect to a given metric</u>

Geodesic tracking (2/3)

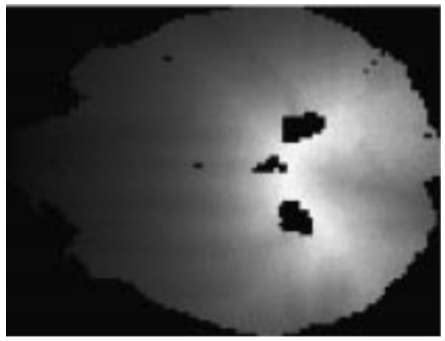
Front-evolution algorithms [Parker et al., 2002; Jbabdi et al., 2008]

- Model the **evolution over time of an interface** (or front) from a seed point
- *Local diffusion profiles* (e.g. tensors) are the **speed function** controlling the propagation
  - different variants proposed in the literature
  - *e.g.* coherence between front *normals* ($\mathbf{n}$) and the *field* ($\boldsymbol{\varepsilon}_1$)
- As front propagates, different regions will be reached with a **different arrival time**
- *Path with minimal arrival time* between two regions interpreted as the **globally optimal fiber tract**
  - using *gradient descent* through time-of-arrival map

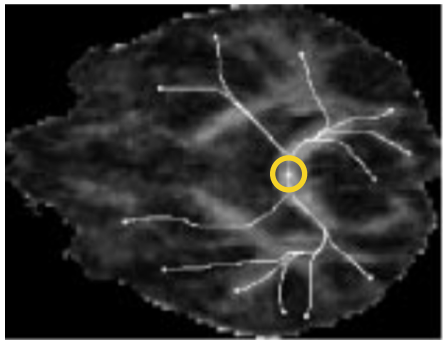




Local **diffusion information**



Time-of-arrival map

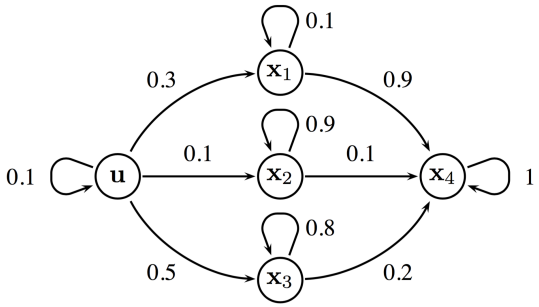


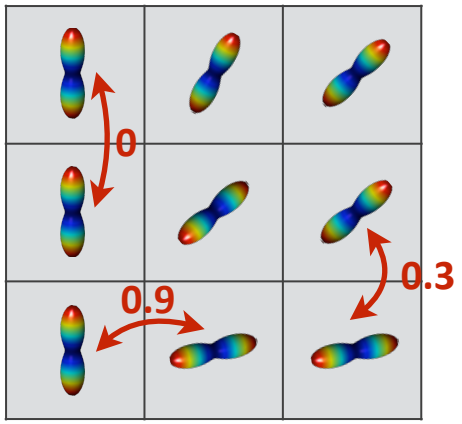
Optimal paths from *S*

Geodesic tracking (3/3)

Graph-based algorithms [Zalesky et al., 2008]

- Pose tractography as computing **minimal paths in a weighted graph**
  - Vertices: center of the *voxels*
  - Edges: *cost of transition* from one voxel to its neighbor
- Lower costs are assigned to edges that are **aligned with fiber trajectories** in their close proximity
- Shortest paths between regions can be found using **classical algorithms**, e.g. *Dijkstra*
- **NB**: the terms *shortest path* or *minimal cost path* are always intended w.r.t a given metric



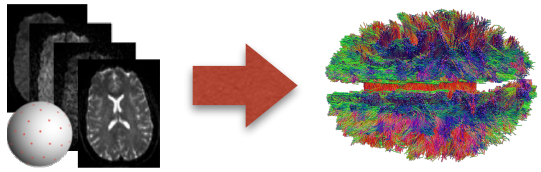


NB: this approach is similar to previous one

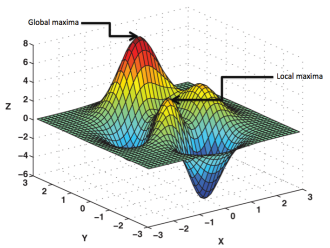
- It uses a direct formulation of the **problem as a graph**
- **More intuitive** but also usually **more efficient**

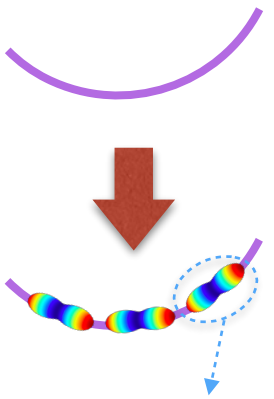
Global inverse problem

Basic ideas



1. Tractography is an **inverse problem**
2. Use **forward-models** to associate a **contribution** to each fiber
3. **Fit to the data** to estimate these contributions





General formulation

$$\mathcal{F} = \operatorname{argmax}\ \mathcal{E}\left(S, \hat{S}(\mathcal{F})\right)$$

- $\mathcal{F}$: *fiber tracts* to be estimated
- S and $\hat{S}(\mathcal{F})$: *acquired* and *predicted* diffusion data
- $\mathcal{E}(\cdot,\cdot)$: *similarity function* to drive optimization
- All fibers *simultaneously estimated*

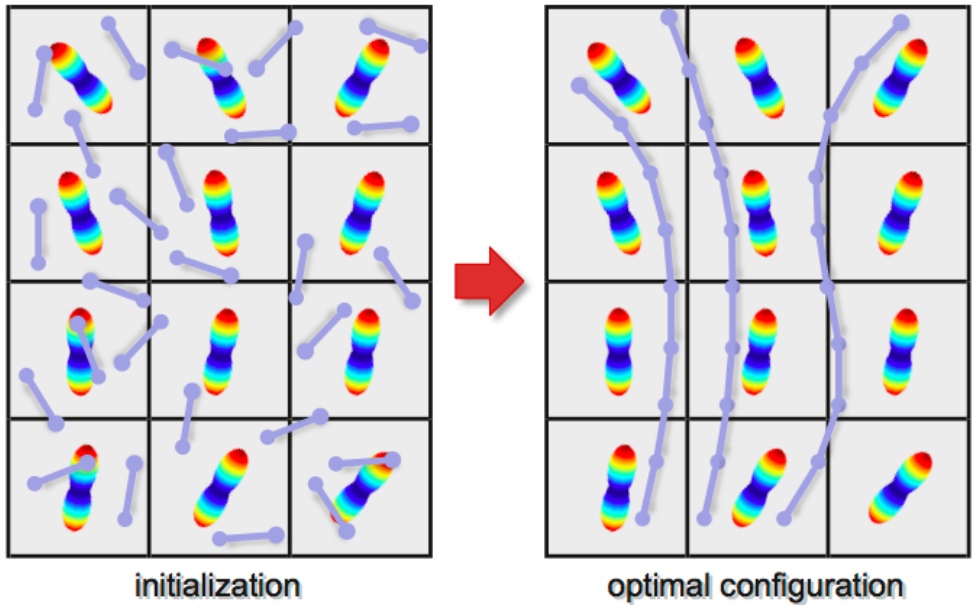
Two major strategies: *"bottom-up"* and *"top-down"*

Global inverse problem: bottom-up (1/5)

Bottom-up strategy [Kreher et al., 2008; Fillard et al., 2009]

$$\mathcal{F} = \text{argmax } \mathcal{E}\left(S, \hat{S}(\mathcal{F})\right)$$

- Fiber trajectories $\mathcal{F}$ parametrized as **collection of segments**
  - Defined by *position*, *orientation* and *length*
  - *Contribute to the dMRI signal* in corresponding voxels according to a *given model*
- $\mathcal{E}(\cdot,\cdot)$ consists of **two terms**:
  - *data fitting*, e.g. $||S - \hat{S}(\mathcal{F})||_2$
  - *regularization*, e.g. segments should join and form long chains



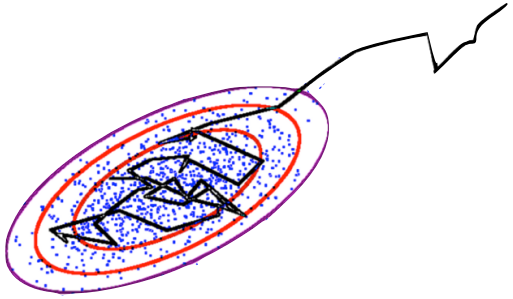
Different reconstruction paradigm from before

- Fiber tracts are **not** **"tracked one-by-one"**, e.g. following local diffusion directions
- They are "**built piece-by-piece" all together**
- **Driven by** how well a configuration of segments explain the measured dMRI data

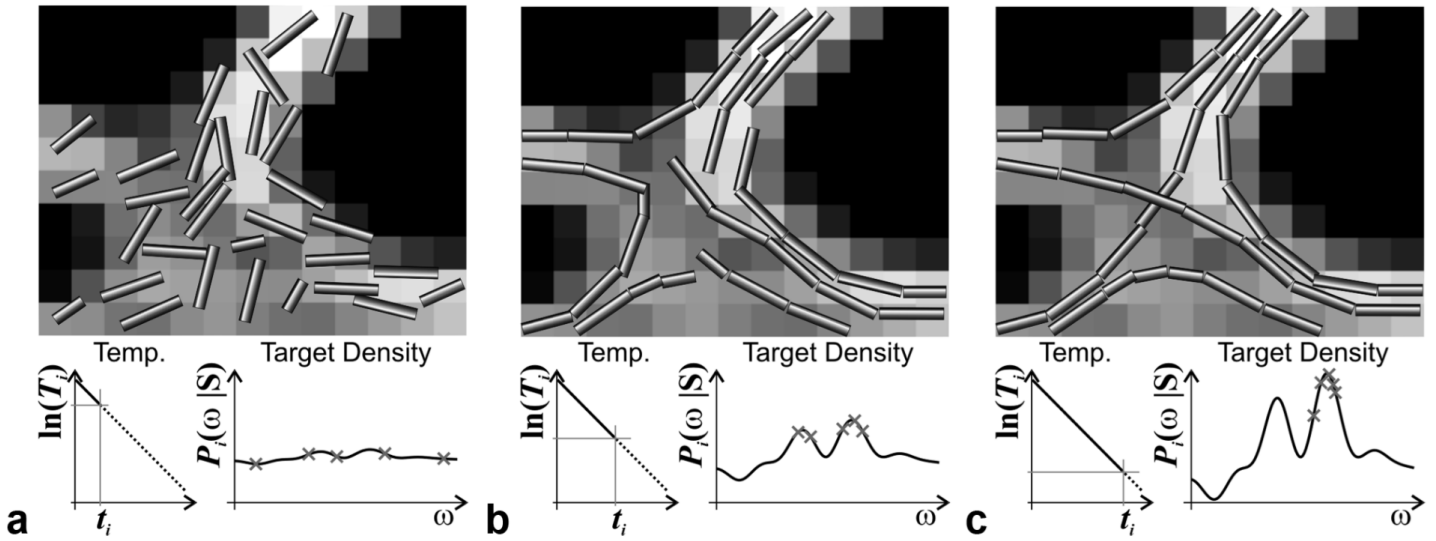
Global inverse problem: bottom-up (2/5)

GIBBS Tracker algorithm [Kreher et al., 2008]

- **Basic principle**:
  1. Creation of an *initial configuration of segments*
  2. Calculation of the *corresponding dMRI signal*
  3. *Adjustment* of the segments to explain better the measured dMRI data



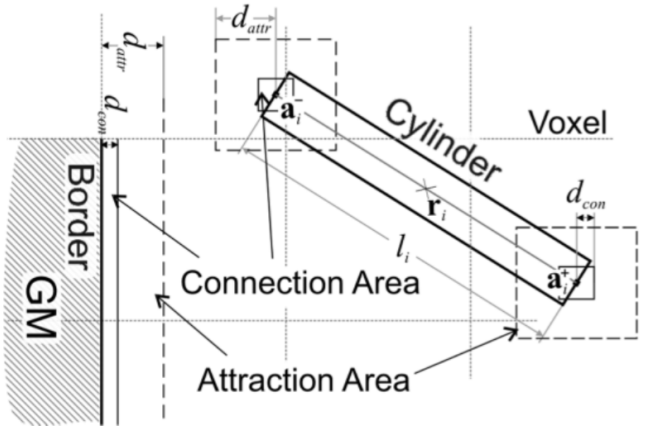
- **Segments are modified** using a combination of:
  - Monte Carlo Markov Chain (MCMC) sampler
    - *Randomly changes* the current configuration of segments
    - A proposal can be either *accepted* or *rejected*
  - Simulated Annealing (SA) ➜ to make small changes while converging



Global inverse problem: bottom-up (3/5)

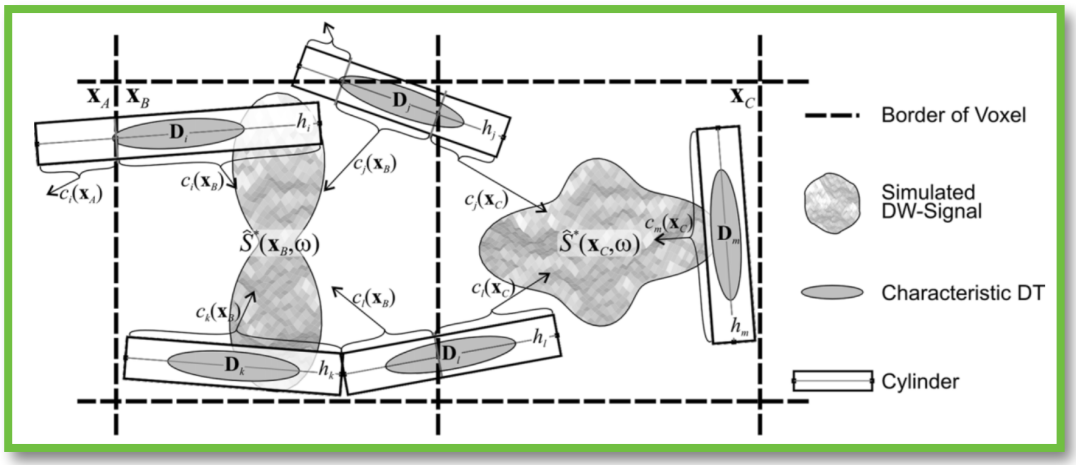
Main elements

- **Segments** (cylinders with *position*, *orientation*, *length*…)
- *Attraction* and *connection* **areas**
- Elementary **random proposals**
  - Create new segment (birth) or remove an existing one (death)
  - Move/rotate segment
  - Connect two close segments

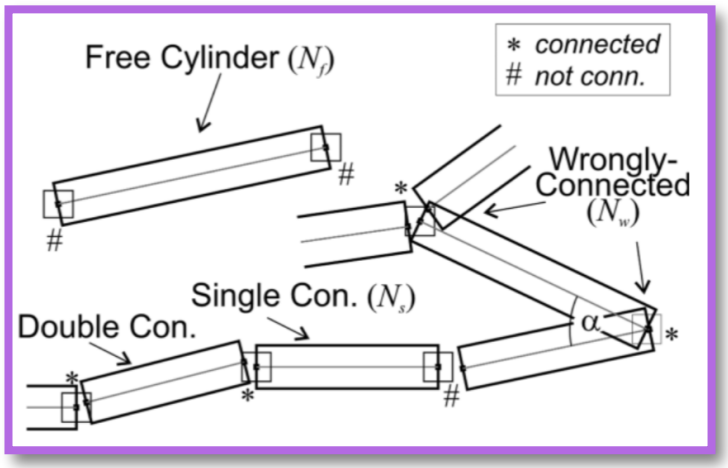


Objective function

- data energy
- interaction energy



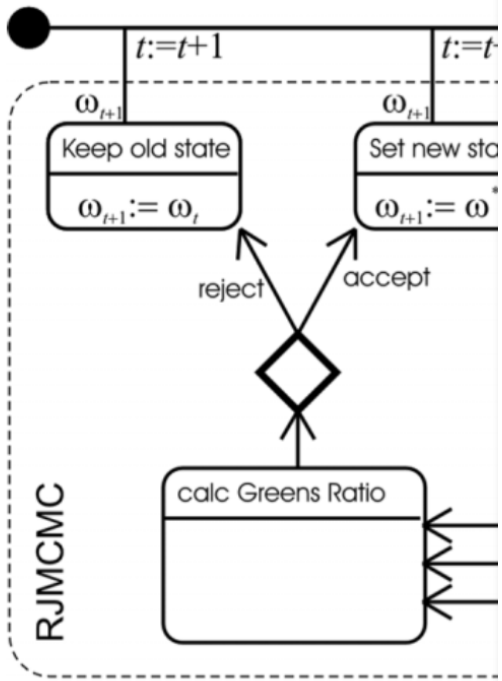
How well the current configuration explains the measured dMRI data

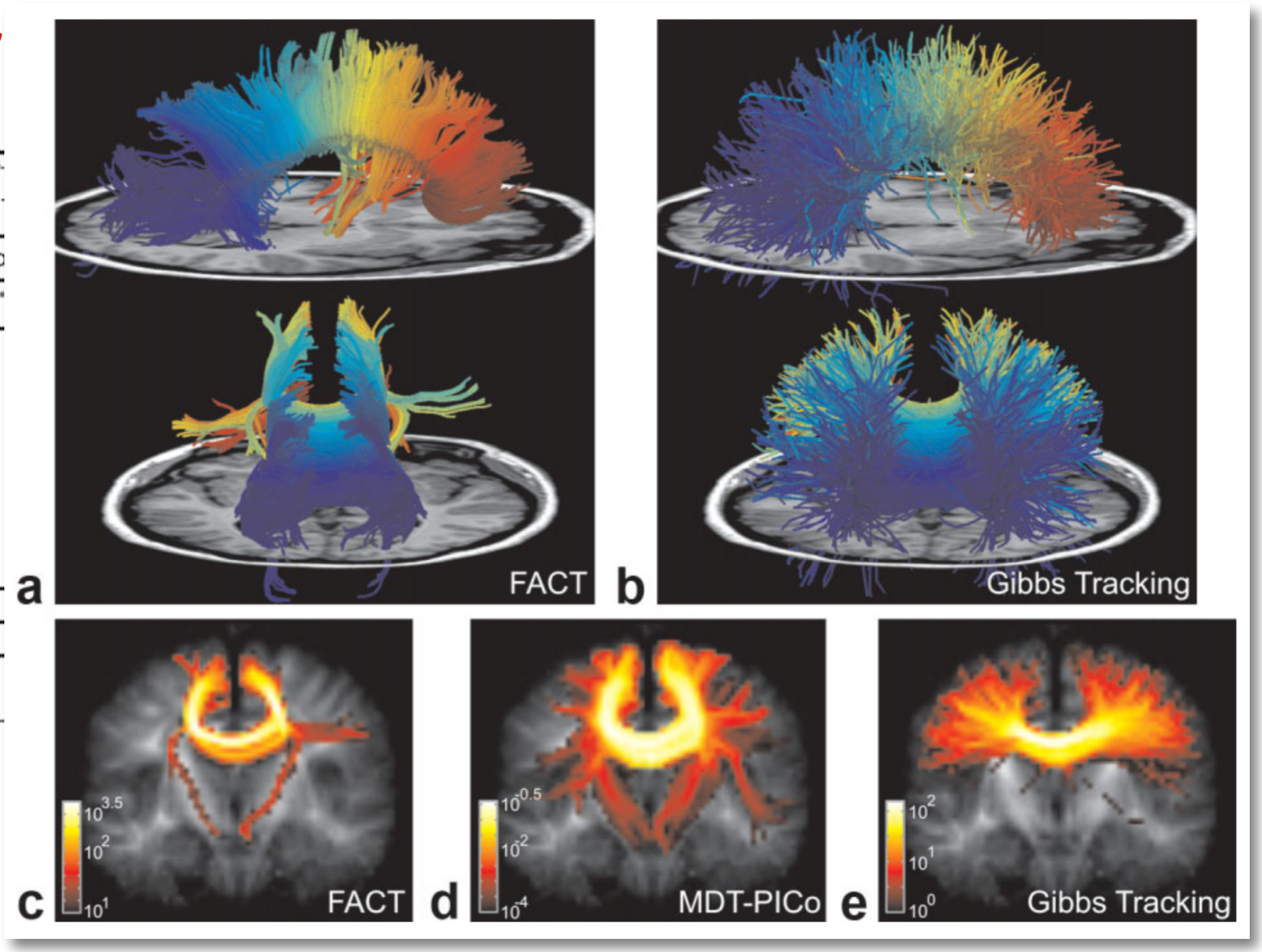


Favors the formation of the cylinders into chains

Global inverse problem: bottom-up (4/5)

Algorithm overv





Notes

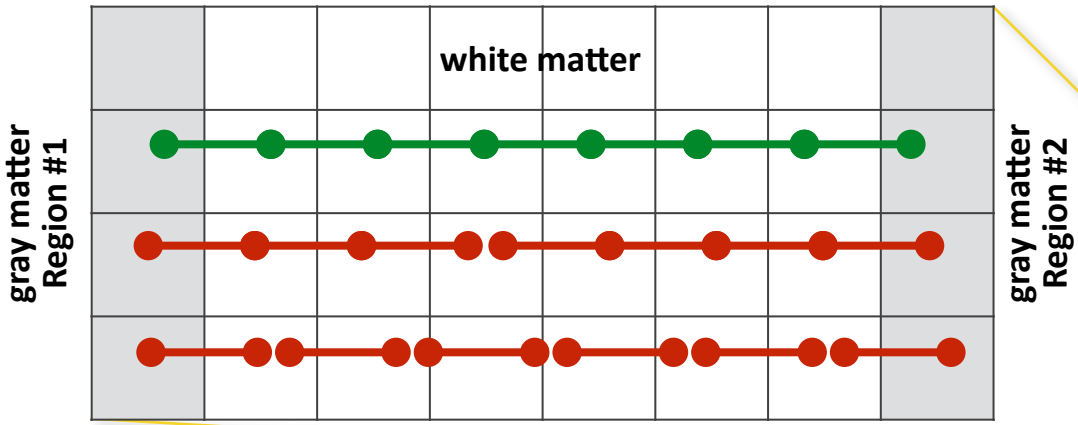
- ≃ *1 month/brain*
- **Higher quality** of reconstructions, but…
- …**huge complexity** leaves many open problems

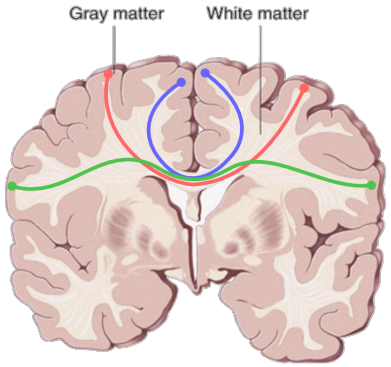
Billions of segments
For each: position, orientation, length etc…
Constraints for joining them and form chains

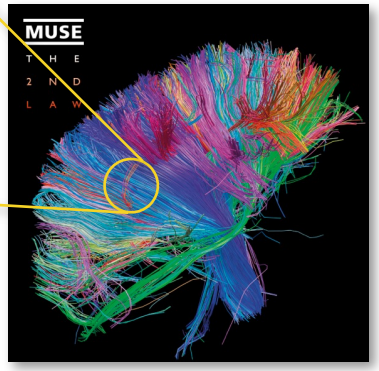
Global inverse problem: bottom-up (5/5)

- **Example**: problems for connectivity estimation

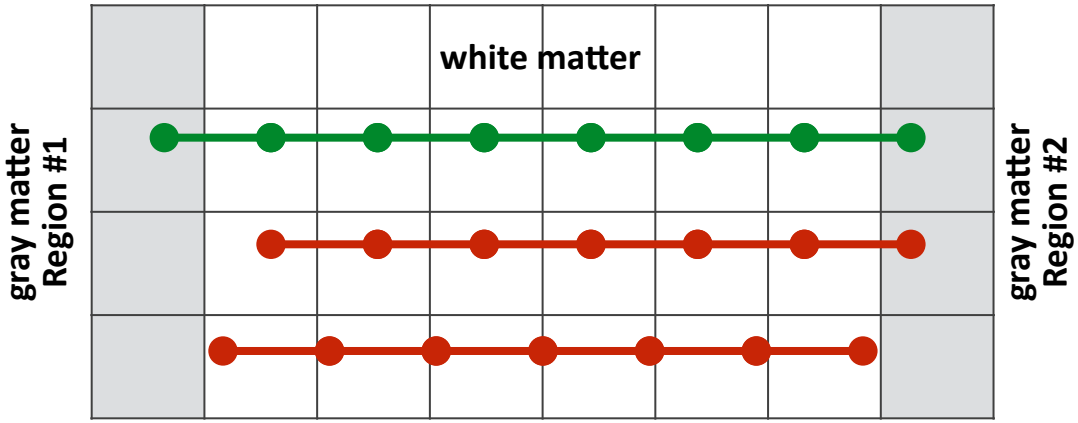
  - **Partial fibers**: do not form a full trajectory/fiber







  - **Orphan fibers**: do not reach the gray matter

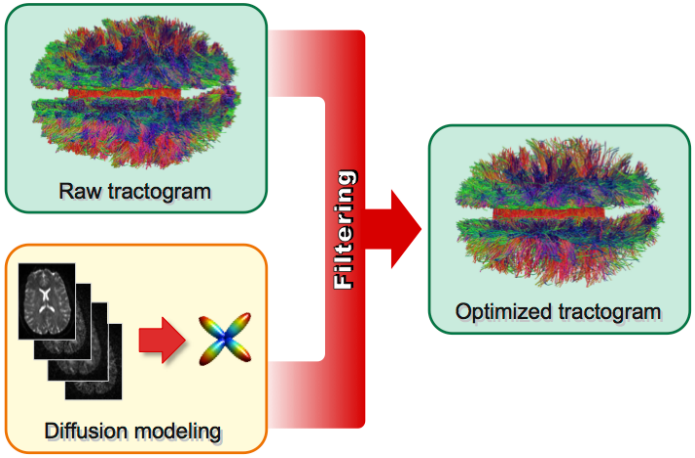


Global inverse problem: top-down (1/2)

Top-down strategy [Sherbondy et al., 2009]

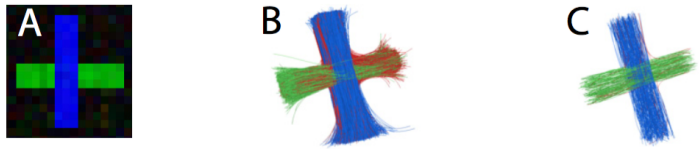
$$\mathcal{F} = \text{argmax } \mathcal{E}\left(S, \hat{S}(\mathcal{F})\right)$$

- $\mathcal{F}$ is a *large* **superset of fibers** estimated combining standard methods
- Fibers **removed** from $\mathcal{F}$ based on $\mathcal{E}(\cdot,\cdot)$



BlueMatter algorithm [Sherbondy et al., 2009]

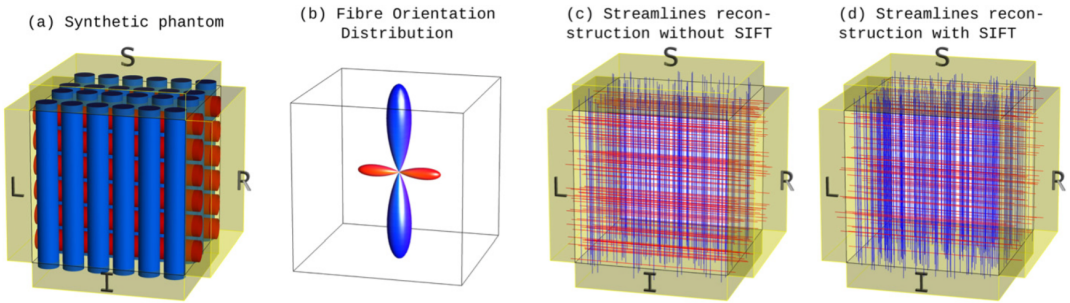
- $\mathcal{F}$ consists of ≃**180 billion candidate fascicles** (mixes many algorithms, e.g. deterministic and probabilistic)
- $\mathcal{E}(\cdot,\cdot)$ **simultaneously accounts** for:
  - how well the acquired dMRI signal is explained
  - volume occupied by fascicles in a voxel
- Optimal subset of fibers searched using a *parallel stochastic hill climbing algorithm*
- Requires a **BlueGene/L supercomputer**

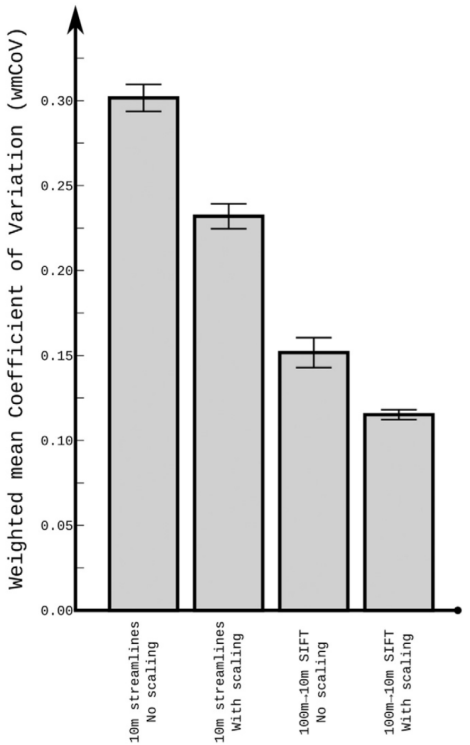


Global inverse problem: top-down (2/2)

- **NB**: it represents only a **proof of concept**
  - ≃ **9 days/brain** on a supercomputer (2048 cores + 500 GB ram), but…
  - …showed a **different perspective** to approach tractography

- **Notes**
  - Since then, **optimized techniques** have been developed
    - *SIFT*: ≃ 15-20 hours/brain, 100M fibers, 26 GB ram [Smith et al., 2013]
    - *SIFT2*: ≃ few hours/brain, 10M fibers, few GB ram [Smith et al., 2015]
  - Optimized tractograms are more **biologically meaningful**
    [Smith et al., 2015; Yeh et al., 2016]





  - Still **room for improvement** (coming lecture)
    e.g. adding biophysical models might give access to features like *actual density* or the *axon caliber* of each bundle

Questions?

Comments?

Suggestions?