Uncertainties in Diffusion MRI

Aasa Feragen

Section for Image Analysis & Computer Graphics, DTU Compute
Technical University of Denmark

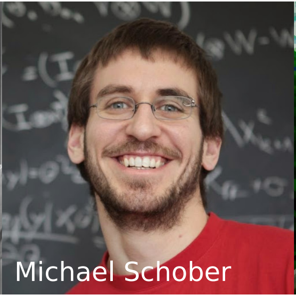
afhar@dtu.dk

DALI/ELLIS workshop on Health

San Sebastian 03.09.2019

Danmarks
Tekniske
Universitet

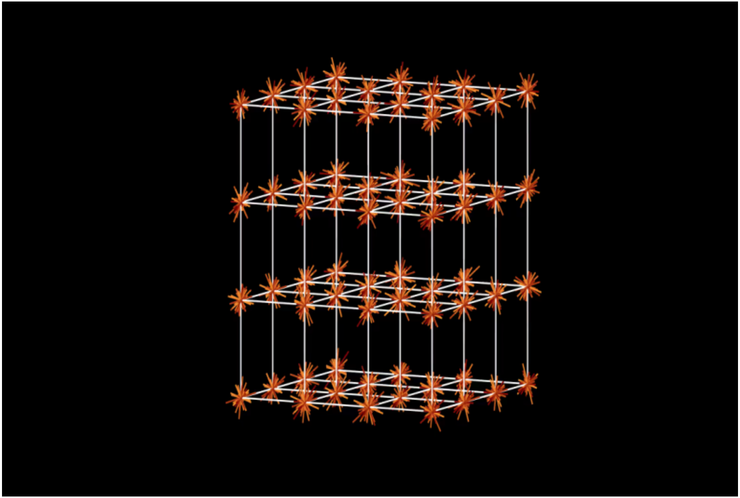
Collaborators



Ingrid (3 months) also helped!

What is diffusion MRI?

What is diffusion MRI?



What is diffusion MRI?

- **DWI hypothesis:** Water diffuses *along* fibers, not across
- Typical DWI pipeline:
  - **Local modelling:** Estimate "fiber orientation distribution function" (fODF) from data
  - **Global modelling:** Integrate local models to obtain long-range connectivity

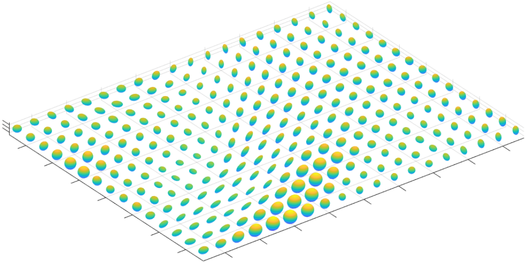


Figure: Field of diffusion tensors estimated from data.

What is diffusion MRI?

- **DWI hypothesis:** Water diffuses *along* fibers, not across
- Typical DWI pipeline:
  - **Local modelling:** Estimate "fiber orientation distribution function" (fODF) from data
  - **Global modelling:** Integrate local models to obtain long-range connectivity

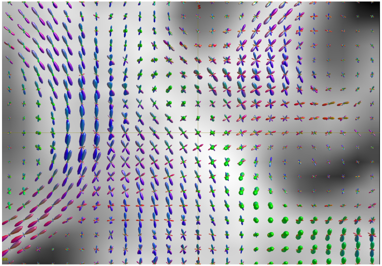


Figure: Field of fODFs estimated via constrained spherical deconvolution.

What is diffusion MRI?

- **DWI hypothesis:** Water diffuses *along* fibers, not across
- Typical DWI pipeline:
  - **Local modelling:** Estimate "fiber orientation distribution function" (fODF) from data
  - **Global modelling:** Integrate local models to obtain long-range connectivity

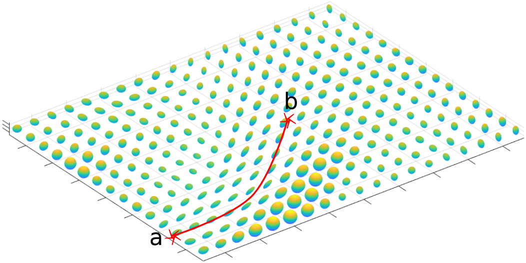
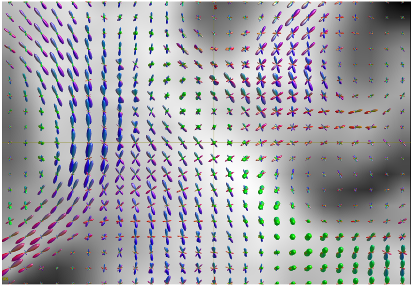


Figure: Estimate of white-matter fiber by integrating the fODF field.

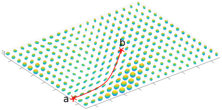
Uncertainties in local modelling

- Reflection symmetric probability distribution on S^2 modelling probability of tangential white matter bundle
- E.g. used for quantifying microstructural properties
- *Does* quantify uncertainty – but in an ad hoc way, based on a single noisy measurement
- **Limitations:** Angular resolution, scale of measurement vs anatomy, model assumptions, ...



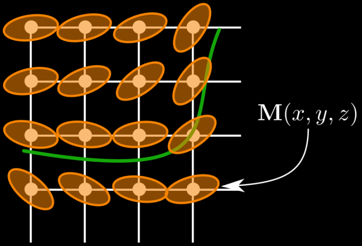
Uncertainties in global modelling

Geometrize the brain:
Interpolated diffusion tensors define Riemannian geometry;
Shortest paths = estimates of white matter trajectories
(O'Donnel et al'02; Lenglet et al'04)



Uncertainties in global modelling

A local distance is estimated from a Gaussian approximation to the diffusion process.



Shortest paths are found by optimization

$$\text{Shortest paths} = \arg\min_{\mathbf{c}} \int_0^1 \sqrt{\dot{\mathbf{c}}(t)^\intercal \mathbf{M}(\mathbf{c}(t)) \dot{\mathbf{c}}(t)} \mathrm{d}t$$

Such paths are solutions to the differential equation

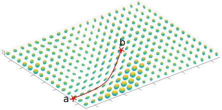
$$\ddot{c}_d(t) = f_d(t, \mathbf{c}, \dot{\mathbf{c}}) = -\boldsymbol{\Gamma}_d^\intercal \cdot (\dot{\mathbf{c}}(t) \otimes \dot{\mathbf{c}}(t)),$$

$$\boldsymbol{\Gamma}_d = \frac{1}{2} \sum_{k=1}^{D} \left[\mathbf{M}_{\mathbf{c}(t)}^{-1}\right]_{d,k} \left(\frac{\partial \operatorname{vec} \mathbf{M}_{\mathbf{p}}}{\partial p_k} \right)_{\mathbf{p}=\mathbf{c}(t)}$$

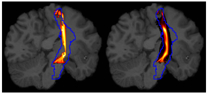
which can be solved numerically.

Uncertainties in global modelling

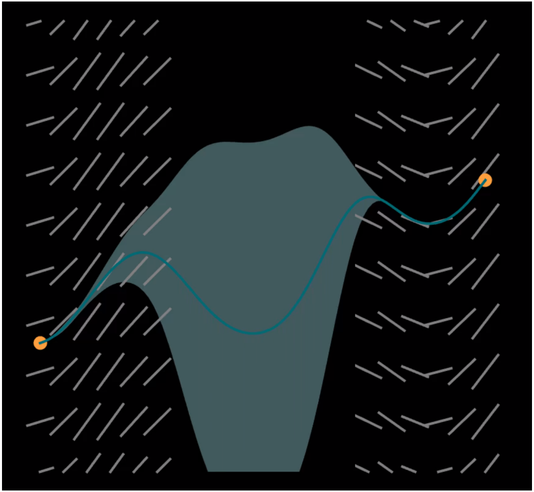
Geometrize the brain:
Interpolated diffusion tensors define Riemannian geometry;
Shortest paths = estimates of white matter trajectories
(O'Donnel et al'02; Lenglet et al'04)



Utilize probabilistic numerics:
Riemannian shortest paths are solutions to a 2nd order diff-EQ
Numerical uncertainty quantified by solving the diff-EQ
it using GP regression
(Schober et al, MICCAI'14)

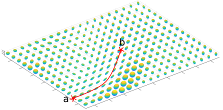


Uncertainties in global modelling



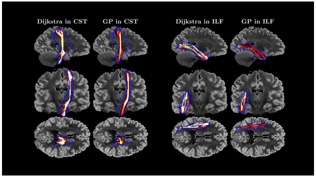
Uncertainties in global modelling

Geometrize the brain:
Interpolated diffusion tensors define Riemannian geometry;
Shortest paths = estimates of white matter trajectories
(O'Donnel et al'02; Lenglet et al'04)

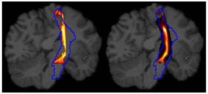


Incorporate measurement uncertainty:
Modern DWI has "high" angular resolution;
DTI requires far less
Bootstrap the data to obtain uncertain diffusion tensors
= stochastic Riemannian metric

Obtain uncertain GP estimates of white matter tracts
solving the geodesic diff-EQ using GP regression
(Hauberg et al, MICCAI'15)

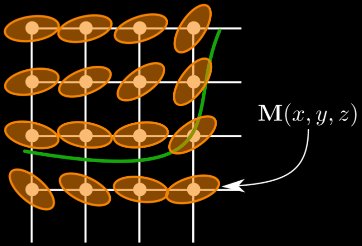


Utilize probabilistic numerics:
Riemannian shortest paths are solutions to a 2nd order diff-EQ
Numerical uncertainty quantified by solving the diff-EQ
it using GP regression
(Schober et al, MICCAI'14)



Uncertainties in global modelling

A local distance is estimated from a Gaussian approximation to the diffusion process.



Shortest paths are found by optimization

$$\text{Shortest paths} = \arg\min_{\mathbf{c}} \int_0^1 \sqrt{\dot{\mathbf{c}}(t)^\intercal \mathbf{M}(\mathbf{c}(t))\dot{\mathbf{c}}(t)}\mathrm{d}t$$

Such paths are solutions to the differential equation

$$\ddot{c}_d(t) = f_d(t, \mathbf{c}, \dot{\mathbf{c}}) = -\boldsymbol{\Gamma}_d^\intercal \cdot (\dot{\mathbf{c}}(t) \otimes \dot{\mathbf{c}}(t)),$$

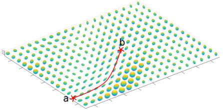
$$\boldsymbol{\Gamma}_d = \frac{1}{2}\sum_{k=1}^{D} \left[\mathbf{M}_{\mathbf{c}(t)}^{-1}\right]_{d,k} \left(\frac{\partial \operatorname{vec} \mathbf{M}_{\mathbf{p}}}{\partial p_k}\right)_{\mathbf{p}=\mathbf{c}(t)}$$

which can be solved numerically.

Uncertainties in global modelling

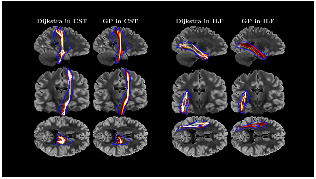
Uncertainties in global modelling

Geometrize the brain:
Interpolated diffusion tensors define Riemannian geometry;
Shortest paths = estimates of white matter trajectories
(O'Donnel et al'02; Lenglet et al'04)

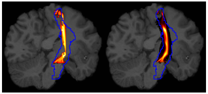


Incorporate measurement uncertainty:
Modern DWI has "high" angular resolution;
DTI requires far less
Bootstrap the data to obtain uncertain diffusion tensors
= stochastic Riemannian metric

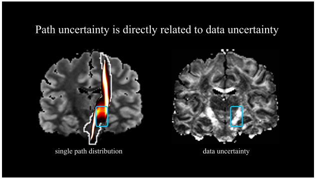
Obtain uncertain GP estimates of white matter tracts
solving the geodesic diff-EQ using GP regression
(Hauberg et al, MICCAI'15)



Utilize probabilistic numerics:
Riemannian shortest paths are solutions to a 2nd order diff-EQ
Numerical uncertainty quantified by solving the diff-EQ
it using GP regression
(Schober et al, MICCAI'14)



A number of problems remain:
* Propagation of uncertainty with distance to endpoints:
A ProbNum problem
* Proper modelling of local uncertainty
* Propagation of uncertainty throughout imaging pipeline
* More flexible fODF models; avoid inflated uncertainty
due to poor model fit
* Uncertain fiber tracking (not shortest-path tractography)



Uncertainties in population modelling

State-of-the-art in population modelling is to represent the tract by a fixed prototype and perform population analysis on scalar properties measured along the prototype.

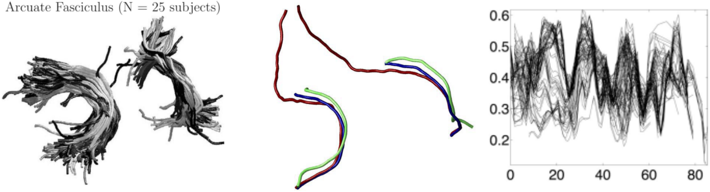


Figure: O'Donnel et al, NeuroImage'09.

This ignores the variance in the estimated tract on every level (estimation uncertainty, population variance, ...)

Uncertainties in population modelling

State-of-the-art in population modelling is to represent the tract by a fixed prototype and perform population analysis on scalar properties measured along the prototype.

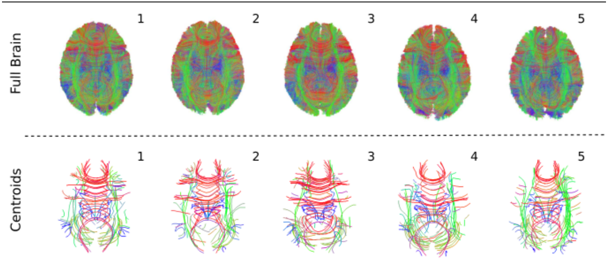
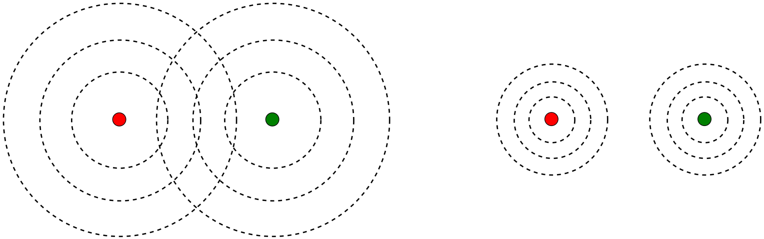


Figure: Garyfalldis et al, Front Neurosci'12

This ignores the variance in the estimated tract on every level (estimation uncertainty, population variance, ...)

Ignoring uncertainty in population modelling is a problem

- The more clinical your paper is, the more likely you are to have to support your claims by p-values (my experience)
- Ignoring uncertainty can lead to incorrect "significant" differences



- **Conclusion:** If your final output includes an uncertainty, then it needs to be propagated from the uncertainty of your "data"

Back to population analysis of white matter tracts

- Different tracts are *not* independent observations of one phenomenon, they are highly dependent observations of highly dependent phenomena
- The noise is in the image. New observation = new image = unavailable.

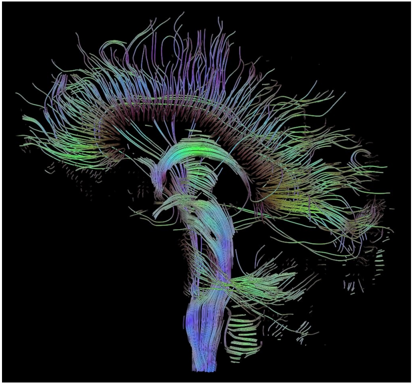
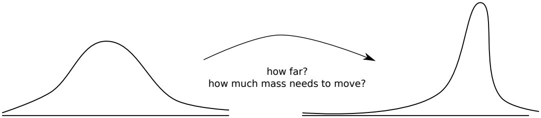


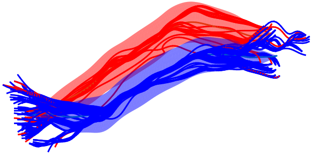
Figure: By Thomas Schultz

Learning from uncertain curves via Wasserstein distances between GPs (Mallasto and **F**, NeurIPS'17)

- Derived analytical approximations of Wasserstein distances, geodesics and barycenters for GPs via GD approximations
- Enables tractable distance-based learning



- **Pros:** Computationally tractable; resembles state-of-the-art methods without uncertainties
- **Cons:** Strict model assumptions; limited scope
- **Thus:** Very open problem



Discussion and outlook

- Diffusion MRI offers a rich pool of problems in modelling, quantifying and communicating uncertainty
- We have first solutions based on GPs in global modelling and population analysis
- A wide range of open problems remain

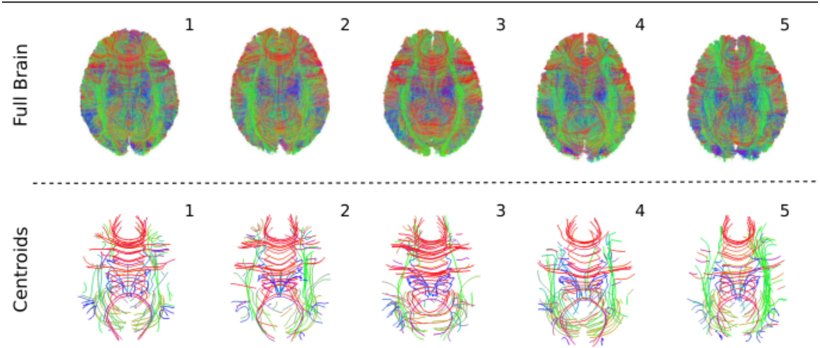


Figure: From Garyfalldis et al, Front Neurosci'12