Dept. of Computer Science, University of Copenhagen

Quantifying spatial uncertainty in the space of curves: Streamline tractography

Geometry-Based Methods in Biomedical Image Analysis:
Junior Researchers

Venice 09.04.2019

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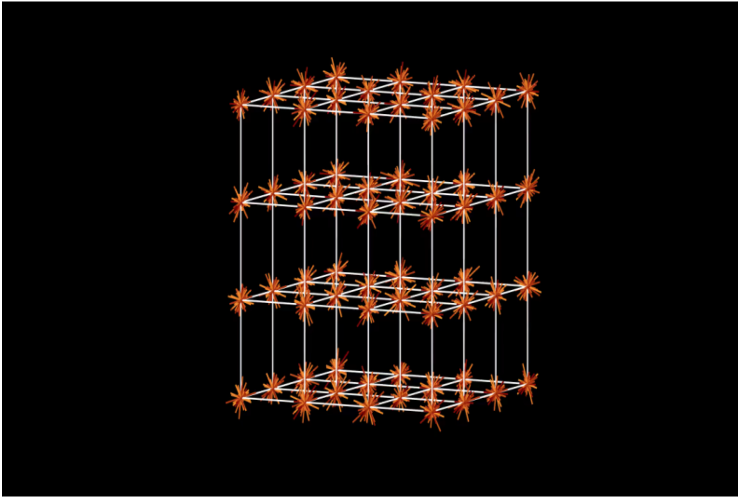
Today's goal

- To convince you that uncertainty quantification is an important and nontrivial problem for data analysis
- This will be exemplified using tractography from medical imaging –
- – but also other, simpler types of data

Part 1: Quantifying spatial uncertainty in tractography

Diffusion MRI

Diffusion MRI



Diffusion MRI

- **DWI hypothesis:** Water diffuses *along* fibers, not across
- Diffusion tensor imaging assumes signal in direction $\boldsymbol{q}$ of form

$$S(\boldsymbol{q}) = e^{-\Delta \boldsymbol{q}^T \boldsymbol{D} \boldsymbol{q}}$$

  for a covariance matrix (diffusion tensor) $\boldsymbol{D}$ (Δ is some constant)

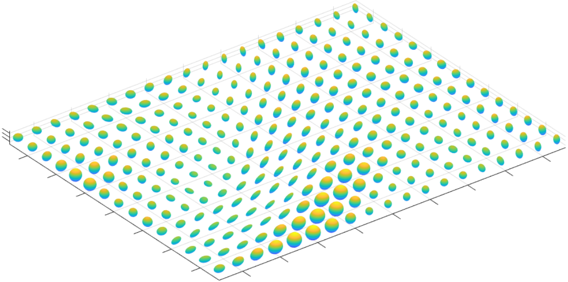


Figure: Field of diffusion tensors estimated from data

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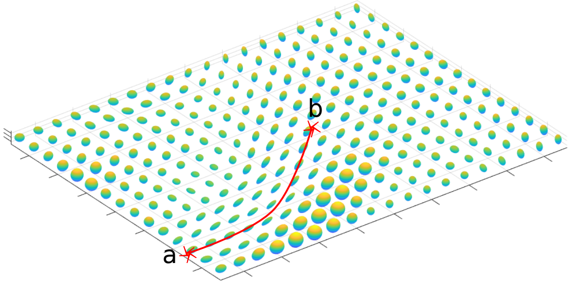
- **Goal of Tractography:** Estimate brain fiber trajectories



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Uncertainty in Tractography

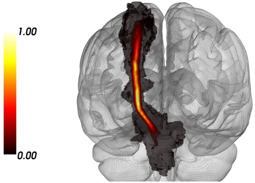


Figure: Voxel-wise heatmap, Kasenburg et al NeuroImage'16.

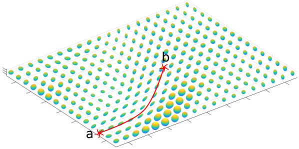
- **What** uncertainty do we quantify?
- Standard heatmaps model probability of connection to a seed point. *Not* spatial uncertainty, although this interpretation is tempting.
- However, for many applications, we *want* spatial uncertainty (e.g. surgical planning)

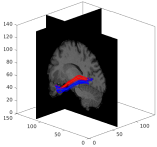
Alternative approach: Tractography via probabilistic numerics (MICCAI'14, MICCAI'15)

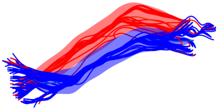
- Tractography reduced to solving the differential equation

$$\ddot{c}_d(t) = -\Gamma_d^T \cdot (\dot{\boldsymbol{c}}(t) \otimes \dot{\boldsymbol{c}}(t)),$$

  with boundary values $\boldsymbol{c}(0) = \boldsymbol{a}$, $\boldsymbol{c}(1) = \boldsymbol{b}$
- Probabilistic numerics view: *Estimate* the curve $\boldsymbol{c}$ from $\ddot{\boldsymbol{c}}$ and $\dot{\boldsymbol{c}}$ using *GP regression*.
- The result is a GP distribution over curve trajectories

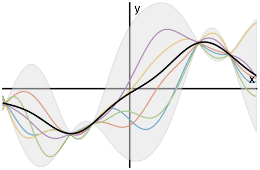






Gaussian Processes

- A Gaussian process (GP) is a collection of random variables, any finite number of which have a joint Gaussian distribution.

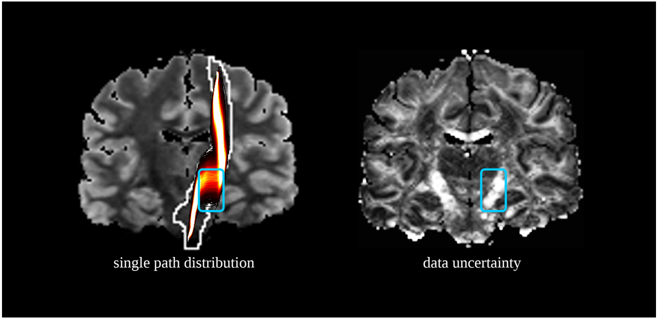


- **Interpretation:** A GP is a distribution in an infinite-dimensional vector space, whose restriction to a finite-dimensional subspace is always a Gaussian distribution.
- A GP f is completely specified by a mean function $c\colon \mathbb{R} \to \mathbb{R}^3$ and covariance function $k\colon \mathbb{R} \times \mathbb{R} \to \mathbb{R}$ with

$$c(t) = \mathbb{E}(f(t))$$
$$k(t, t') = \mathbb{E}((f(t) - c(t))(f(t') - c(t')))$$

- We write $f \sim GP(c, k)$.

Samples from posterior white-matter trajectory



Where did this leave us?

- We got a parametrized model of spatial uncertainty
- However, we are not done:
  - Only worked for DTI
  - Only worked for shortest-path tractography

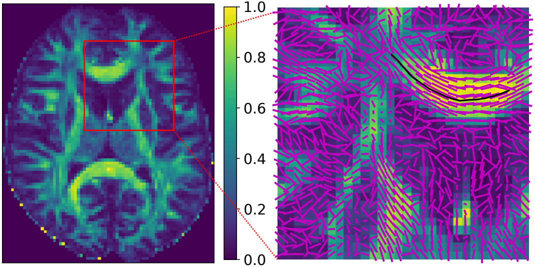
Let's rethink the problem – an IVP solution

- Standard fiber tracking can be thought of as solving the noisy ordinary differential equation (ODE)

$$\dot{\gamma}(t) + \varepsilon = v(\gamma(t))$$

with initial value $\gamma(0) = \mathbf{x}_0$.

- The vector field v is observed via diffusion.



- A simpler ODE, the usual IVP formulation, extends more easily to more complex fODFs.

Let's rethink the problem – an IVP solution

The algorithm (Schober et al, Stat. Comp. 2018):

- Kalman filter tracking, followed by a smoother estimating the final solution covariance utilizing all visited locations.
- Numerically advantageous, as the shortest path problem required a numerically less stable boundary value solver for a more complex, second order, differential equation.

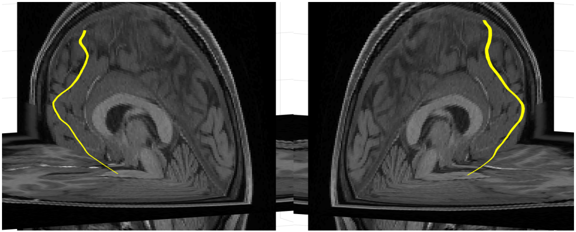
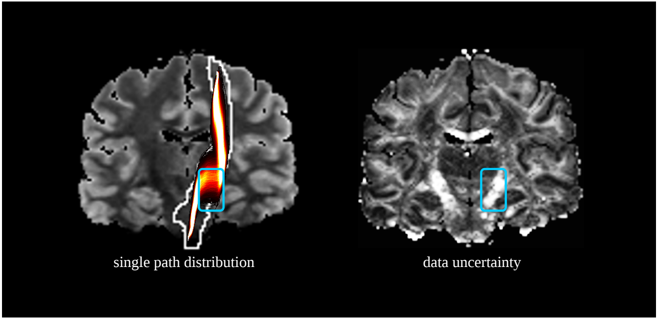


Figure: Two single trajectories from the CST, visualized via GP samples

Part 2:
Outlook for population analysis

Challenge 1: Interpretation.
What does uncertainty measure?

Tractography example:

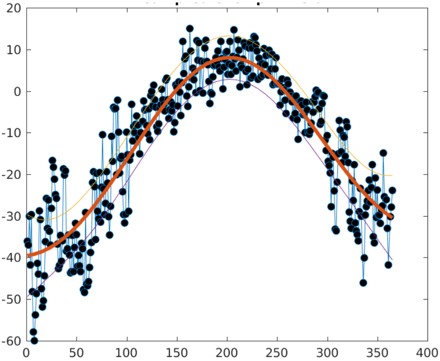


- Uncertainty due to noise
- Signal loss due to anatomical effects
- Poor model fit
- Otherwise lack of support in data

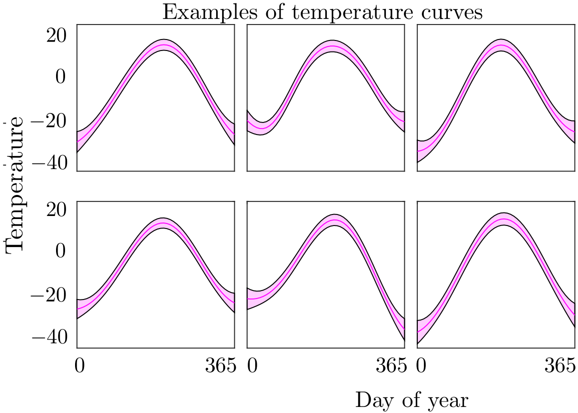
Challenge 1: Interpretation. What does uncertainty measure?

Example: Daily temperature in Siberian city

- Data (temperature curve) is estimated from measurements with high level of variation
- Temperature curve should reflect natural variation – should be represented as *distributions over curves*, not as curves

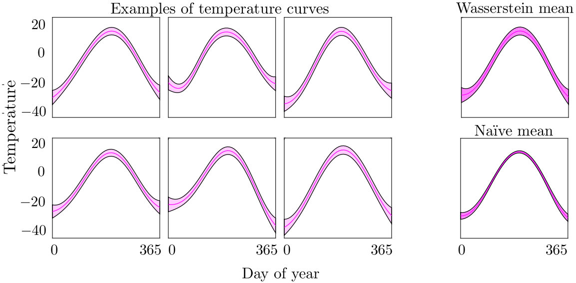


Challenge 1: Interpretation.
What does uncertainty measure?



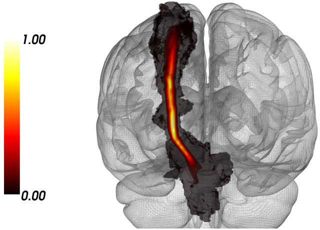
- Uncertainty can also measure of natural variation in the data

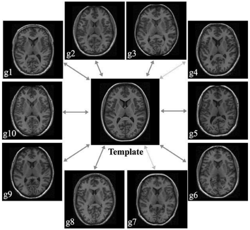
Challenge 2: Ignoring uncertainty in population analysis is a problem

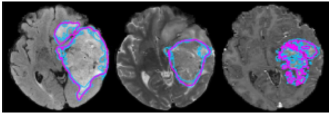


- **Left:** Small sample of uncertain yearly temperature curves represented as Gaussian Processes (GPs) from a Siberian metereological station.
- **Bottom right:** The mean and pointwise standard deviation of the mean temperature curves (the best estimates).
  This is what we routinely do in medical imaging.
- **Top right:** An alternative mean that incorporates the covariance structure of the GP samples (NeurIPS'17).

Challenge 3: Ignoring uncertainty in population analysis is a **common** problem

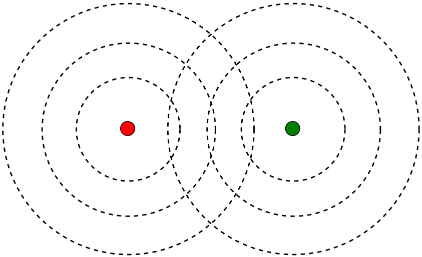




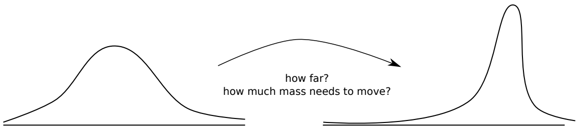


- In most population analysis in medical imaging, the "data" is estimated from data
- Algorithms that quantify uncertainty are starting to appear
- Incorporating uncertainty in population analysis is not currently tackled

Challenge 4: Ignoring uncertainty can lead to incorrect "significant" differences



Is there anything to be done? First steps (NIPS'17)...



- Deriving algorithms for Wasserstein distances and means for GPs, we can use distance-based learning:
  - mean GPs (cluster means)
  - hierarchical clustering
  - permutation tests for equal means

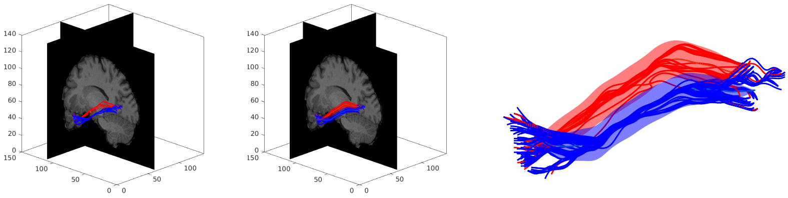


Figure: Clustering, hypothesis testing between populations of GPs

Is there anything to be done? First steps (NIPS'17)...

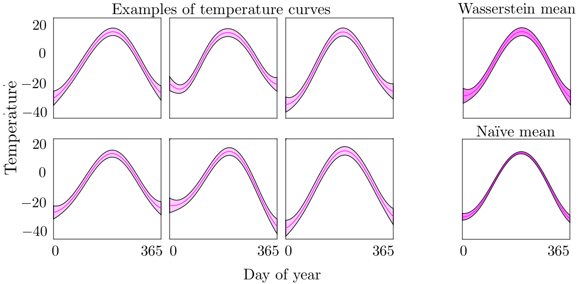


Figure: Wasserstein means utilize the point-wise uncertainty.

NB! Uncertainty is not a bad thing! Can contain highly relevant information. Not clear that we always want to minimize uncertainty in our estimates.

Is there anything to be done? First steps (NIPS'17)...

- With weighted means for GPs, we can perform kernel regression.

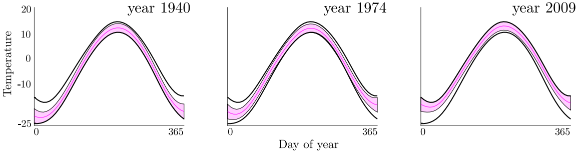
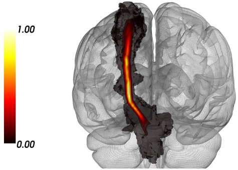
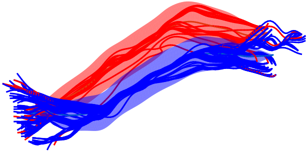


Figure: Kernel regression on GPs: Predicted temperature curve distributions over 30 Russian weather stations in the period 1940-2009

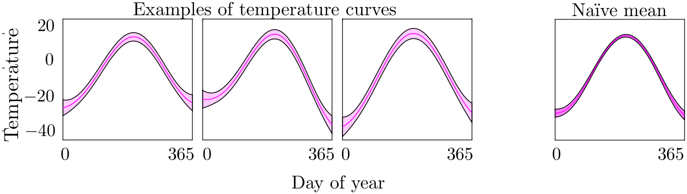
Resulting research challenges

- **What** uncertainty should we quantify? Application dependent.





- **How** do we visualize/communicate uncertainty?
- **How** can we correctly propagate the subject-wise uncertainty into population analysis?



Main points

- Different applications need different uncertainty quantification
  - Take care to interpret uncertainty correctly
  - Exemplified via tractography
  - Tractography models with spatial uncertainty
- Uncertainty covers a number of aspects:
  - Sample size
  - Uncertainty due to noise
  - Signal loss due to anatomical effects
  - Poor model fit
  - Otherwise lack of support in data
- Different aspects need different modelling and communication.
- **Incorporating uncertainty in population analysis** – first steps; many to be taken