



# Structural Brain Connectivity Extraction and Analysis

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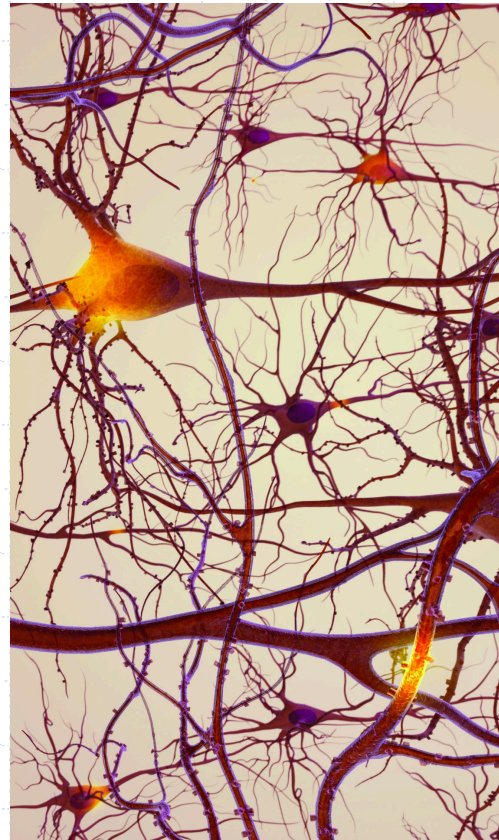
Joint work with Hongtu Zhu, David Dunson Maxime Descoteaux



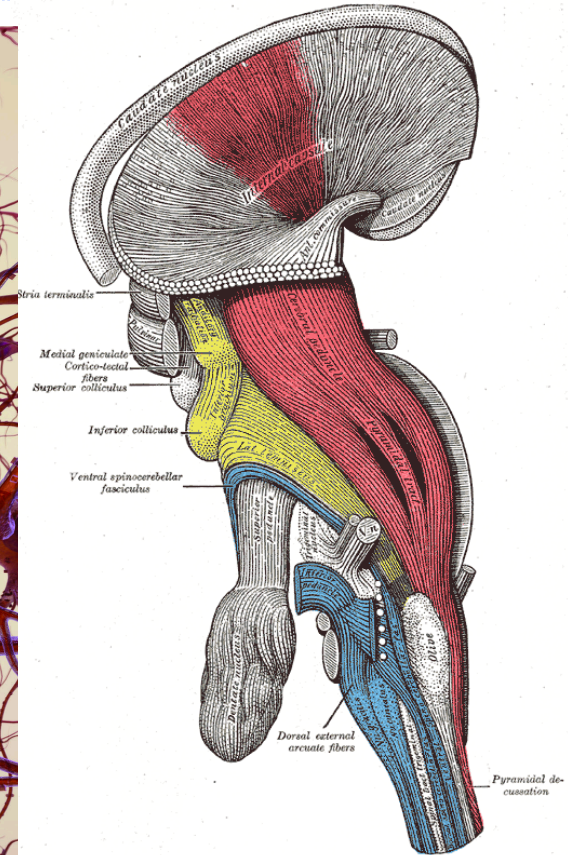


## Diffusion Imaging

- Axons have  $\sim\mu\text{m}$  diameters
- Axons group together in bundles that traverse the white matter in brain
- We can not image individual axon, but we can image bundles with **diffusion MRI**



From UMD website



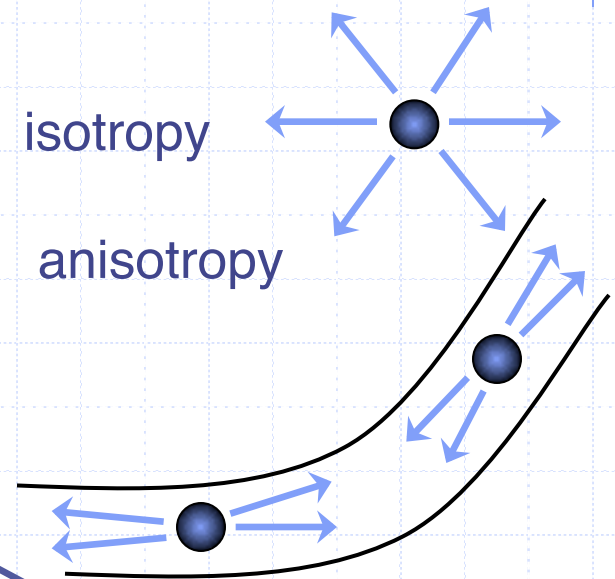
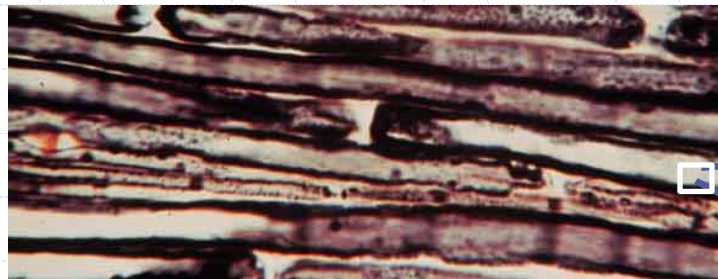
From Gray's Anatomy



## Diffusion in Brain Tissue

➤ Water molecules in different brain tissues have different diffusion properties.

- **Gray matter:** Diffusion is unrestricted ↔ isotropy
- **White matter:** Diffusion is restricted ↔ anisotropy



- More diffusion along axon fibers

➤ **Diffusion MRI** measures the water diffusion movement inside brain



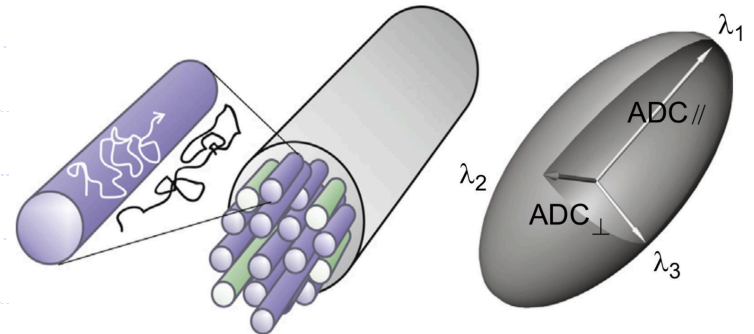
## Representation of Diffusion Direction

- At each voxel, from dMRI we want to know:
  - What is the orientation of the diffusion?
  - What is the magnitude of diffusion?

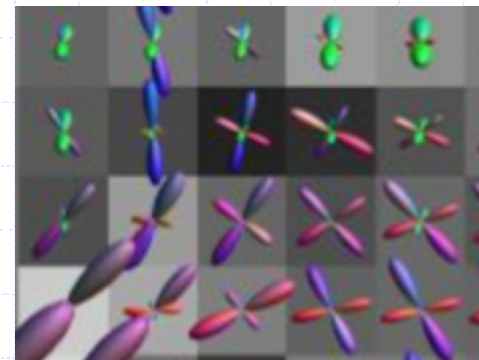
- Two popular representations:

- Diffusion tensor image (DTI)

$$D = \begin{pmatrix} d_{1,1} & d_{2,1} & d_{3,1} \\ d_{2,1} & d_{2,2} & d_{3,2} \\ d_{3,1} & d_{3,2} & d_{3,3} \end{pmatrix}$$



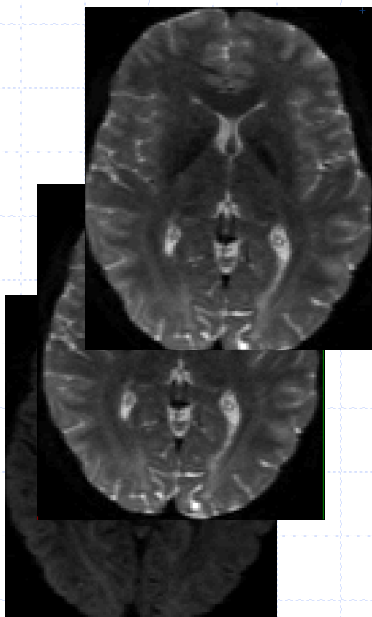
- High angular resolution diffusion imaging (HARDI)
  - Orientation distribution function [Tuch' 04]
  - Diffusion spectrum [Wedeen' 05]
  - Ball-and-stick [Behren's 03]
  - ...



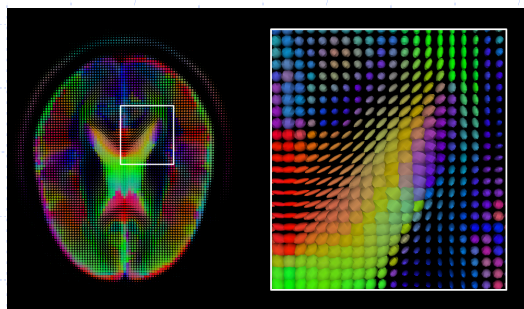


## Diffusion MRI to Connectome

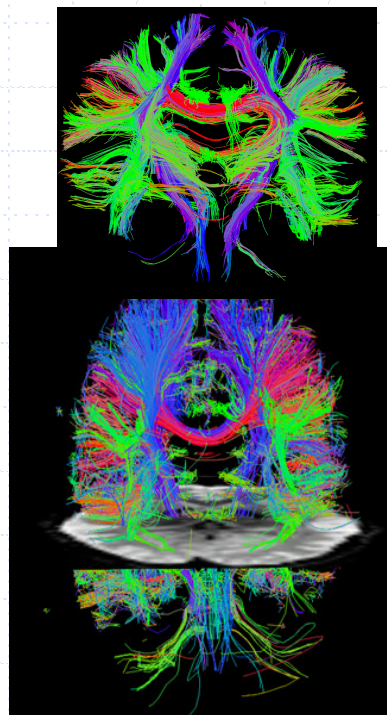
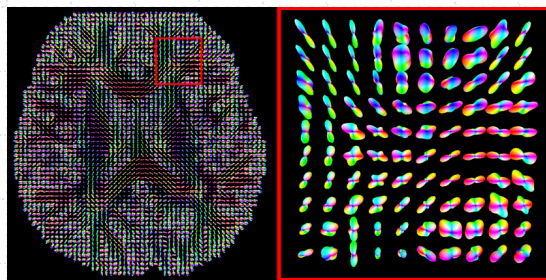
- Pipeline from raw dMRI to structural connectomics



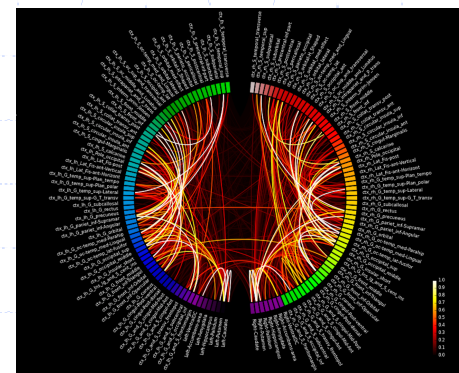
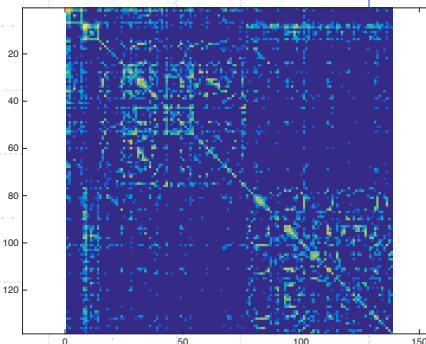
dMRI



diffusion directions



streamlines



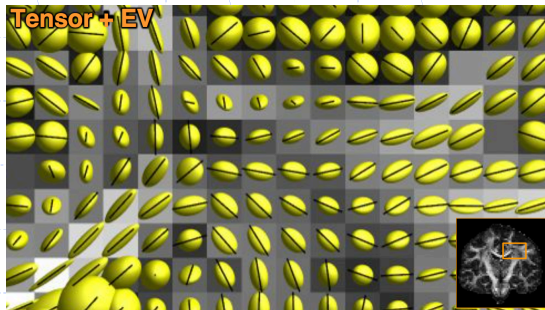
connectivity  
matrix



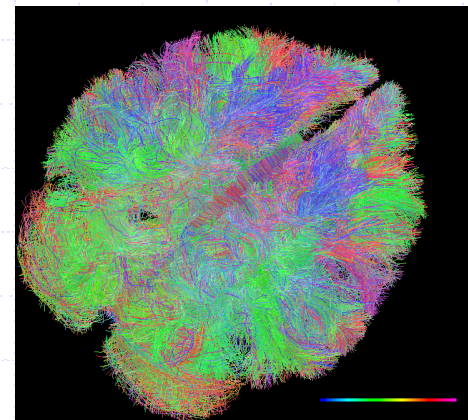
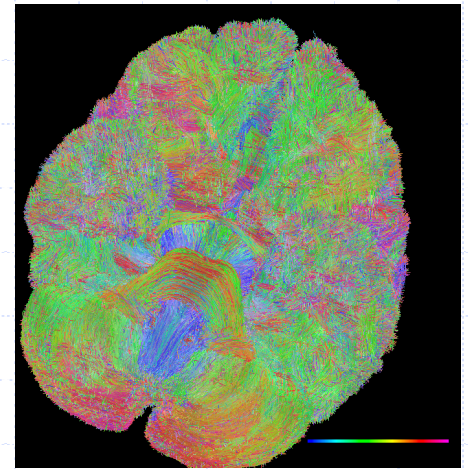
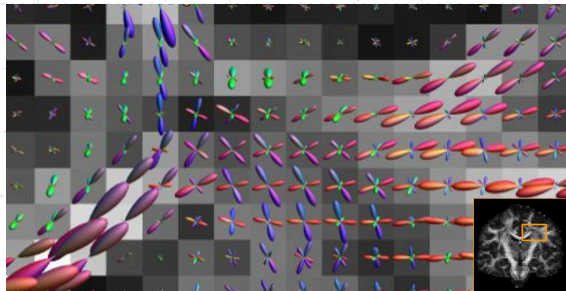
## Streamline Extraction

- Extract the connectome using dMRI and T1 image
- Use tractography algorithm proposed in *Girard et al. 2015*
  - **Step1. Construct HARDI:**  
better than DTI, can handle fiber crossing

DTI:



HARDI:

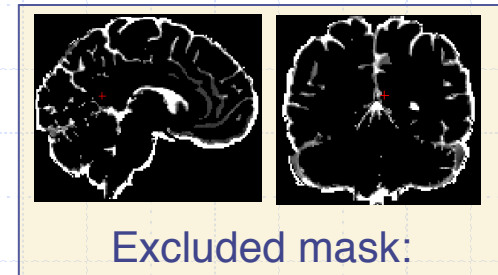
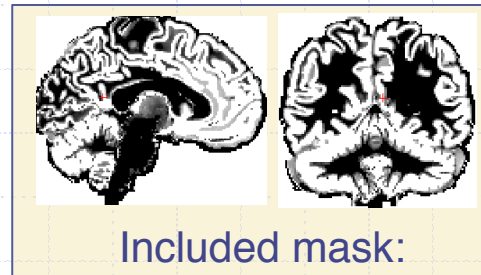




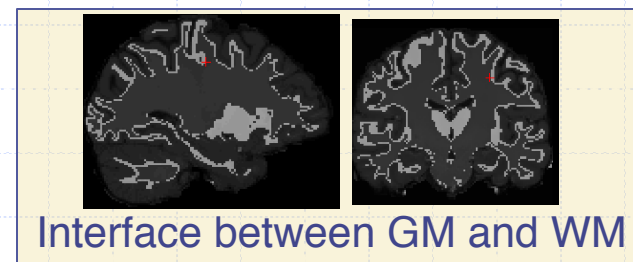
## Streamline Extraction

- Extract the connectome using dMRI and T1 image
- Use tractography algorithm proposed in *Girard et al. 2015*
  - Step 1. Construct HARDI:
  - Step 2. Fiber tracking (incorporate anatomical info):

- Masking:



- Seeding:



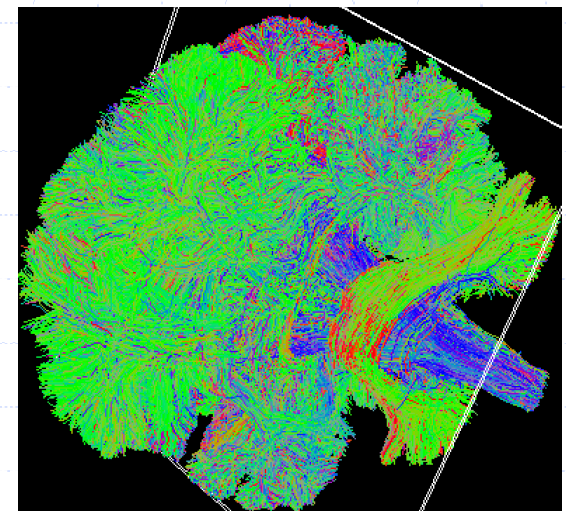
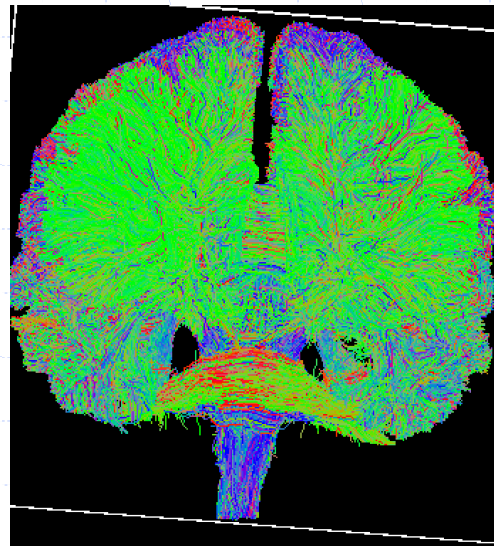
- Streamline growing: probabilistic or deterministic



## Streamline Extraction

- Extract the connectome using dMRI and T1 image
- Use tractography algorithm proposed in *Girard et al. 2015*
  - Step 1. Construct HARDI:
  - Step 2. Fiber tracking (incorporate anatomical info):
  - Step 3. Final output:

1. More than a million streamlines
2. Each streamline has hundreds 3D points
3. Each subject takes > 2.5 GBs



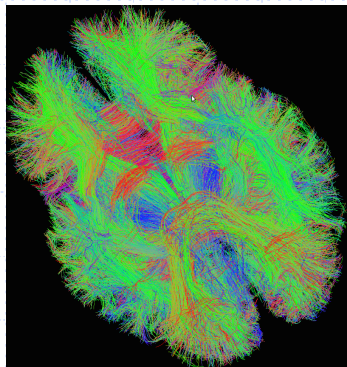




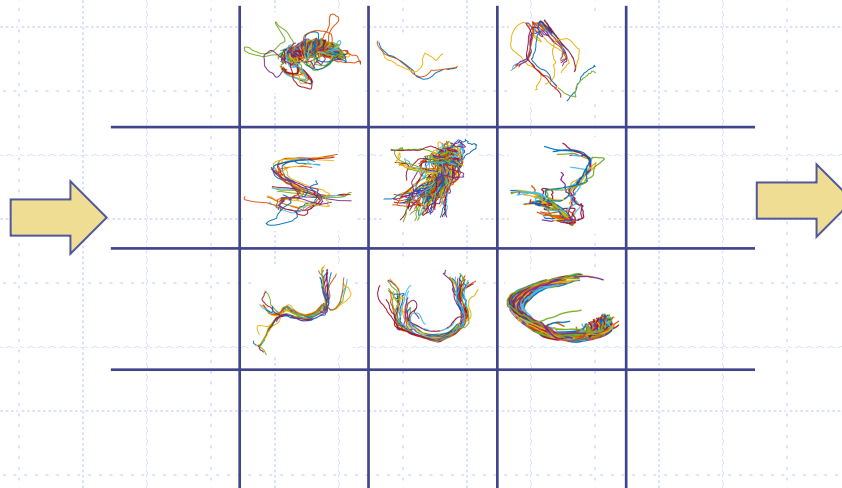
## Connectome Analysis

- Whole brain tractography is complicated
- A new representation: streamline connectivity matrix

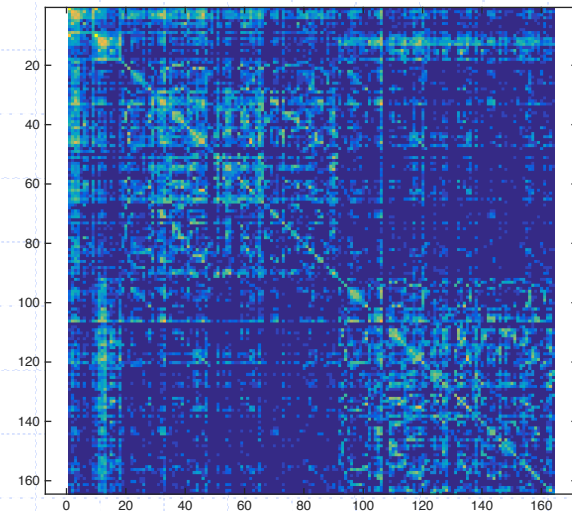
Tractography



Streamline CM



Scalar CM





## Challenges of Analyzing Streamline CM

- The streamline connectivity matrix contains millions of fibers
  - saving, loading, and analyzing are difficult
    - Efficient representation facilitating the comparison is needed (compression)
- Summarize the streamline connectivity matrix
  - Extract robust measure(s) of coupling strength from streamlines



## Efficient Representation of Streamlines

- Fiber representation: **parameterized curves**  $f : [0, 1] \rightarrow \mathbb{R}^3$
- Examples of fibers in  $CM(1, 160)$  for different subjects



- Observations:
  - They have similar **shapes** after alignment
  - These shapes can be efficiently represented



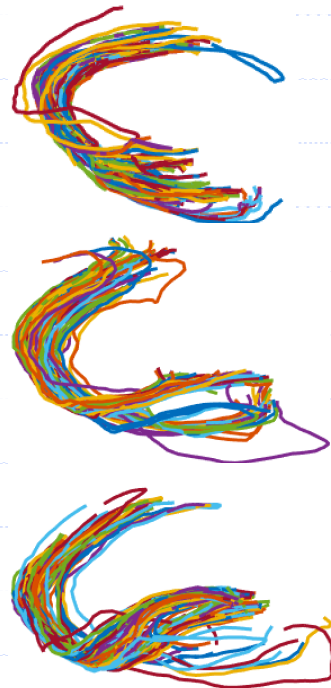


## Efficient Representation of Streamlines

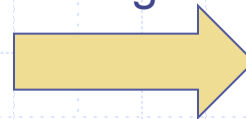
- Represent the streamlines through basis and coefficients
- Basis can be learnt from data to increase its representing power

Step 1. Generate **atlas** for streamlines connecting each pair of regions

Randomly select  
healthy subjects:



Merge





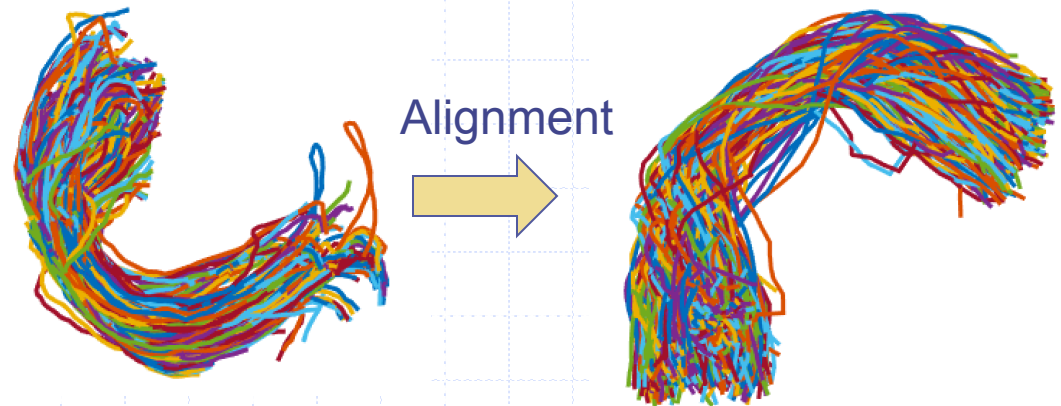
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- Represent the streamlines through basis and coefficients
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Step 1. Generate **atlas** for streamlines connecting each pair of regions

Step 2. Alignment using the **Elastic Shapes Analysis** framework (Srivastava et al. 2012)

- rotation
- translation
- scaling
- re-parameterization



\*K-means clustering may be used if these streamlines have different shapes



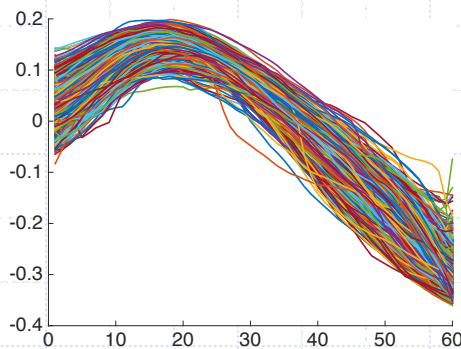
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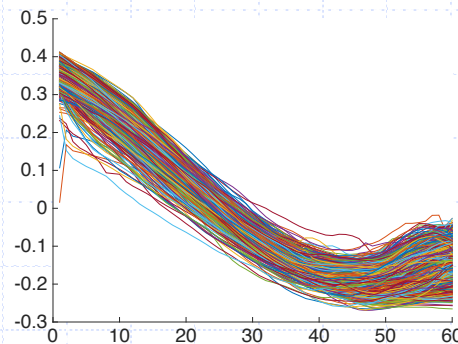
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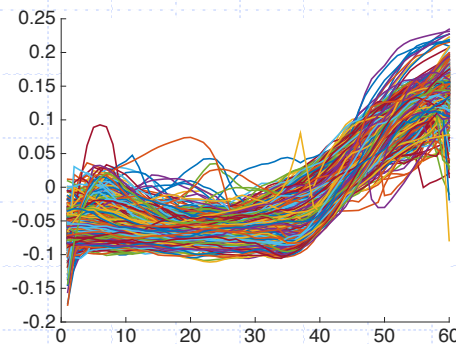
Step 3. Use **fPCA** to learn basis functions for each component



$j = 1$



$j = 2$



$j = 3$



$\mu_j$   
 $\{\phi_{i,j}\}$



## Efficient Representation of Streamlines

- Represent the streamlines through basis and coefficients
- Basis can be learnt from data to increase its representing power
- Efficient representation (compression): given a new fiber  $f$

Step 1. Align  $f$  to the mean fiber in the atlas

$$\operatorname{argmin}_{O \in SO(3), C \in \mathbb{R}^3} \|O * (f - C) - \mu\|$$

$$g = \boxed{O} * (f - \boxed{C})$$

$\boxed{\phantom{O}}$  rotation

$\boxed{\phantom{C}}$  translation

Step 2. Represent the aligned fiber using basis functions

$$g_j = \mu_j + \sum_{i=1}^{M_j} \boxed{c_{j,i}} \phi_{j,i} + \epsilon_j, j = 1, 2, 3$$

$\boxed{\phantom{c_{j,i}}}$  coefficients

$\|\epsilon_j\|$  determines  $M_j$ , the number of coefficients for representing fibers

Step 3. Parameters need to save  $\{O, C, c_{j,i}\}$



## Efficient Representation of Streamlines

- Represent the streamlines through basis and coefficients
- Basis can be learnt from data to increase its representing power
- Efficient representation (compression): **given a new fiber**  $f$
- Recover  $f$  from saved parameters  $\{O, C, c_{j,i}\}$

$$\hat{f} = O' * \hat{g} + C$$

where each component  $\hat{g}_j = \mu_j + \sum_{i=1}^{M_j} c_{j,i} \phi_{j,i}$

- Comparison of streamlines can be done through saved parameters





## Efficient Representation of Streamlines

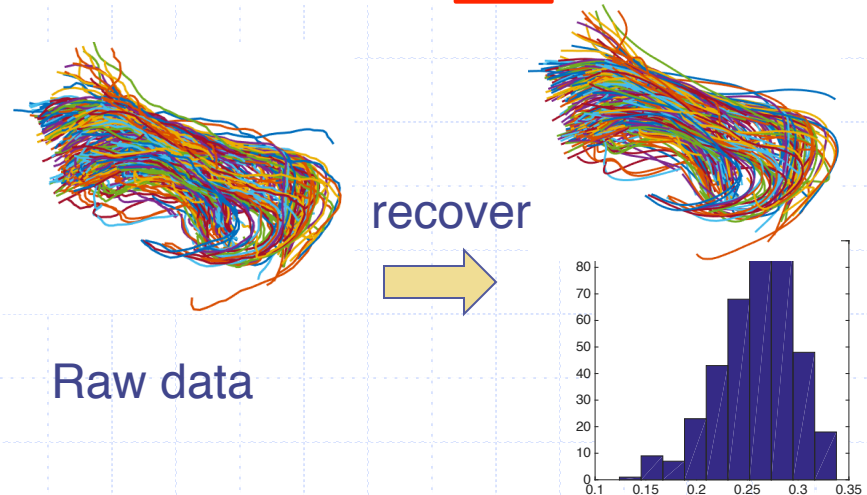
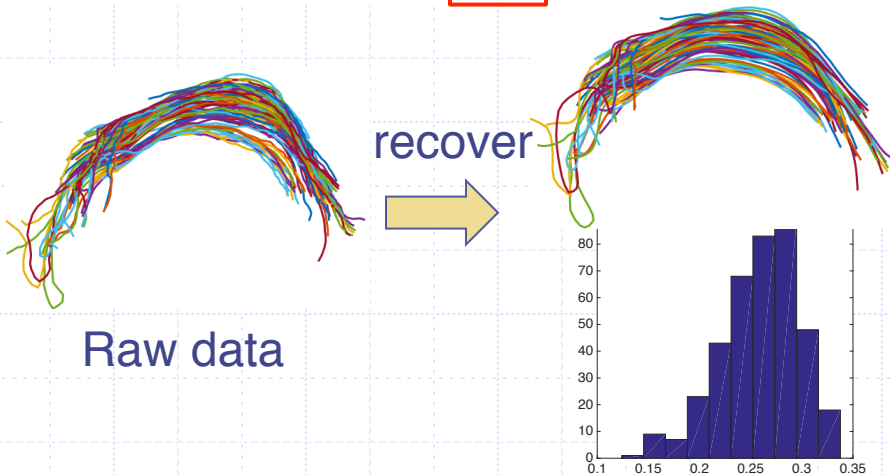
- Compression ratio:  $\rho = 100 * \left(1 - \frac{N_c}{N_r}\right)$

$N_c$  -- # para. after compression,  $N_r$  -- # para. before compression

- Example of compressing fibers in  $CM(1,160)$  and  $CM(115,160)$

Error $\epsilon$ (mm)	0.1	0.2	0.5	1.0	2.0
Ratio	95.7	97.3	98.4	98.8	99.1

Error $\epsilon$ (mm)	0.1	0.2	0.5	1.0	2.0
Ratio	93.7	95.6	98.9	97.4	97.6

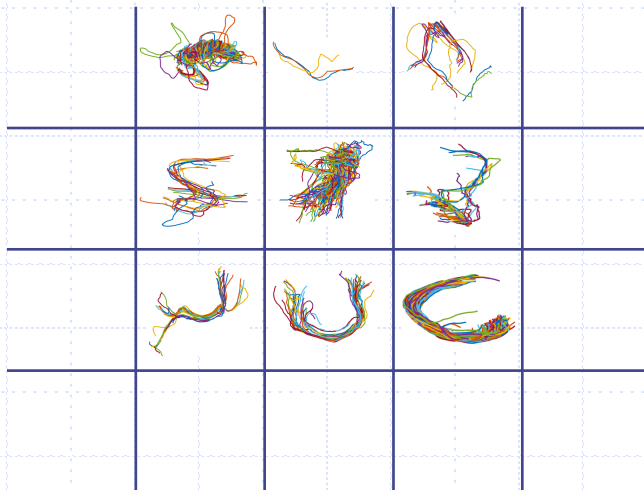




## Structural Network Analysis

- *Unweighted* network analysis:  
from **streamline connectivity matrix** to **binary connectivity matrix**

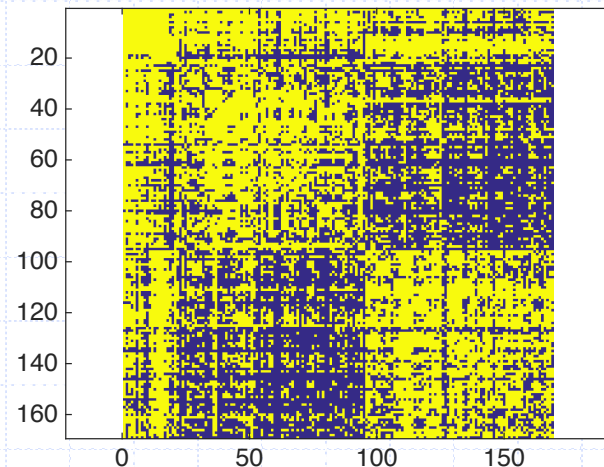
Streamline CM



threshold



Binary CM



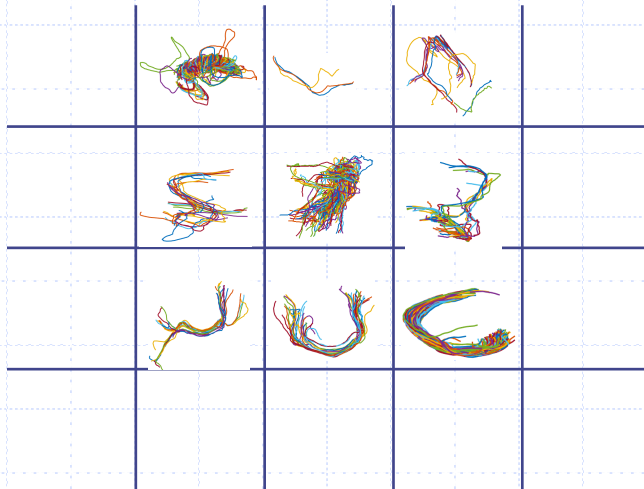


## Structural Network Analysis

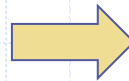
- *Unweighted* network analysis:
- *Weighted* network analysis:

from **streamline connectivity matrix** to **scalar connectivity matrix**

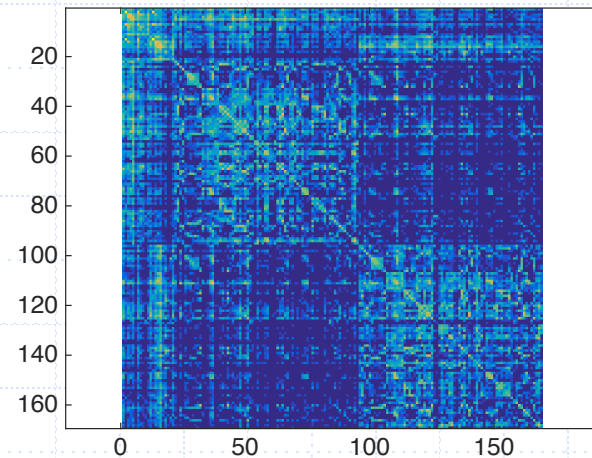
Streamline CM



coupling  
strength  
extraction



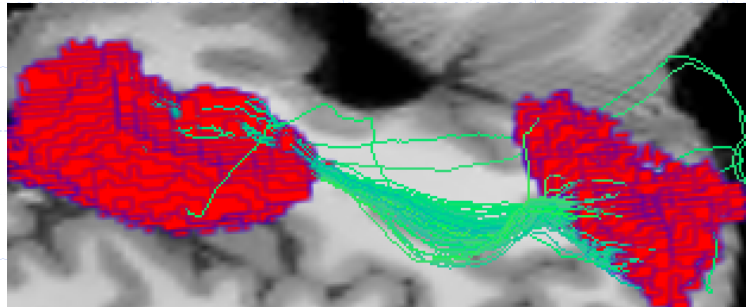
Scalar CM





## Structural Network Analysis

- What is a good measure of the coupling strength between two ROIs



- Most popular measure is the **count**

### Pros:

- Simple to extract
- Reflect the connection strength

### Cons:

- Depends on the resolution of the data
- Changes with the parcellation
- Affected by the fiber shape and curvature



## Structural Network Analysis

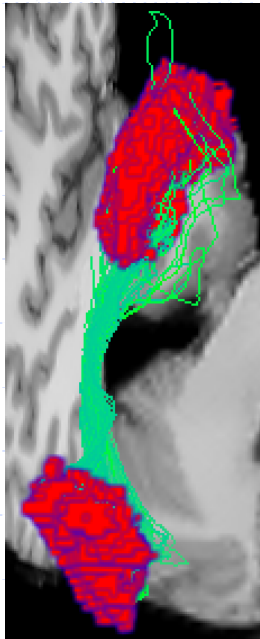
- Example of streamlines between two regions in the brain

Right-Putamen (16)

ctx\_rh\_G\_occipital\_sup(115)

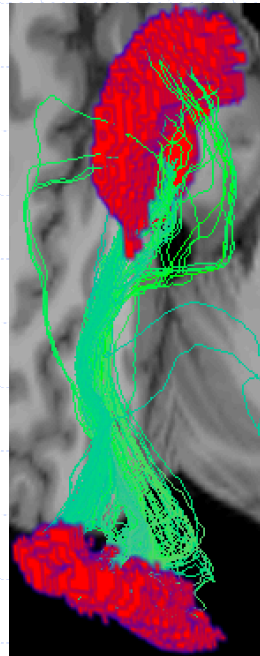
ID: 104820

|  $CM(16,115)$  | = 483



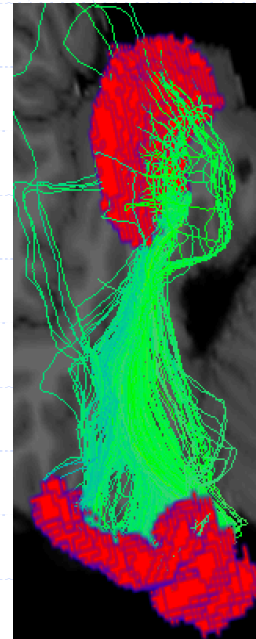
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|  $CM(16,115)$  | = 758



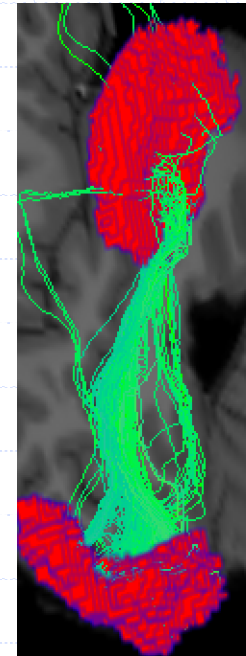
ID: 102311

|  $CM(16,115)$  | = 614



ID: 145836

|  $CM(16,115)$  | = 429





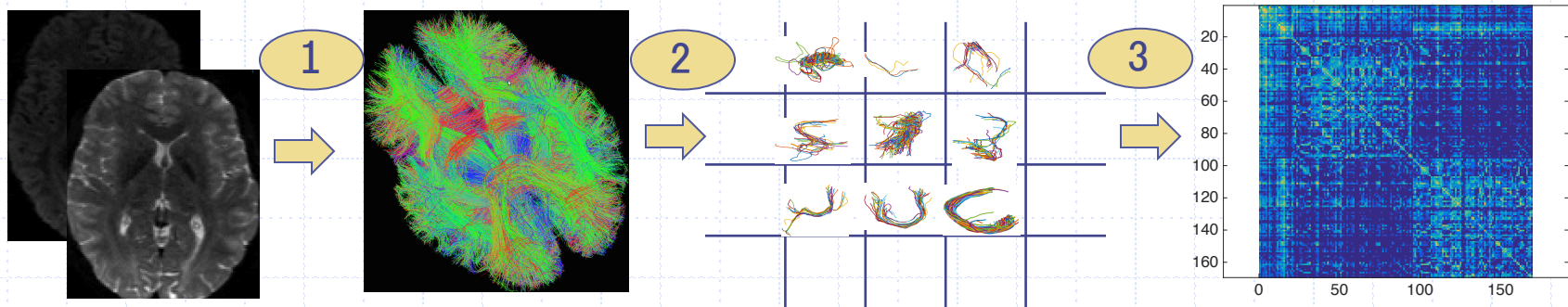
## Robust Coupling Strength Measures

- More robust coupling strength measures
  - Diffusion properties: FA values, AFD values along fibers
  - Geometry properties: Shapes, Loops, Clusters
  - Nodes information: Volume of nodes, Connected surface areas
  - ...



## Conclusions

- We have developed a pipeline to process the dMRI



1. State-of-the-art tractography algorithm: incorporating the anatomical prior to reduce the bias in the reconstructed streamlines
2. Streamlines analysis framework: comparing and efficient representing streamlines
3. Robust coupling strength measures: enable better network analysis



HUMAN  
**Connectome**  
PROJECT

Mapping structural and functional connections in the human brain

**Thank You**