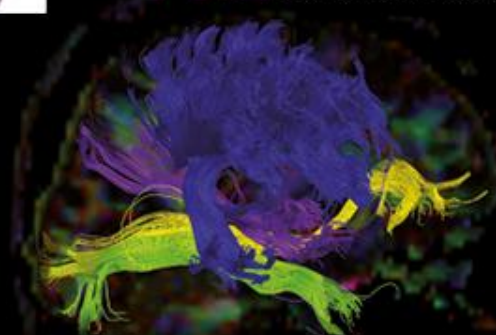


**40<sup>ème</sup> CONGRÈS ANNUEL**  
de la **Société Française**  
de **NeuroRadiologie**



## **Diffusion et connectivité**

**Bernard Mazoyer**

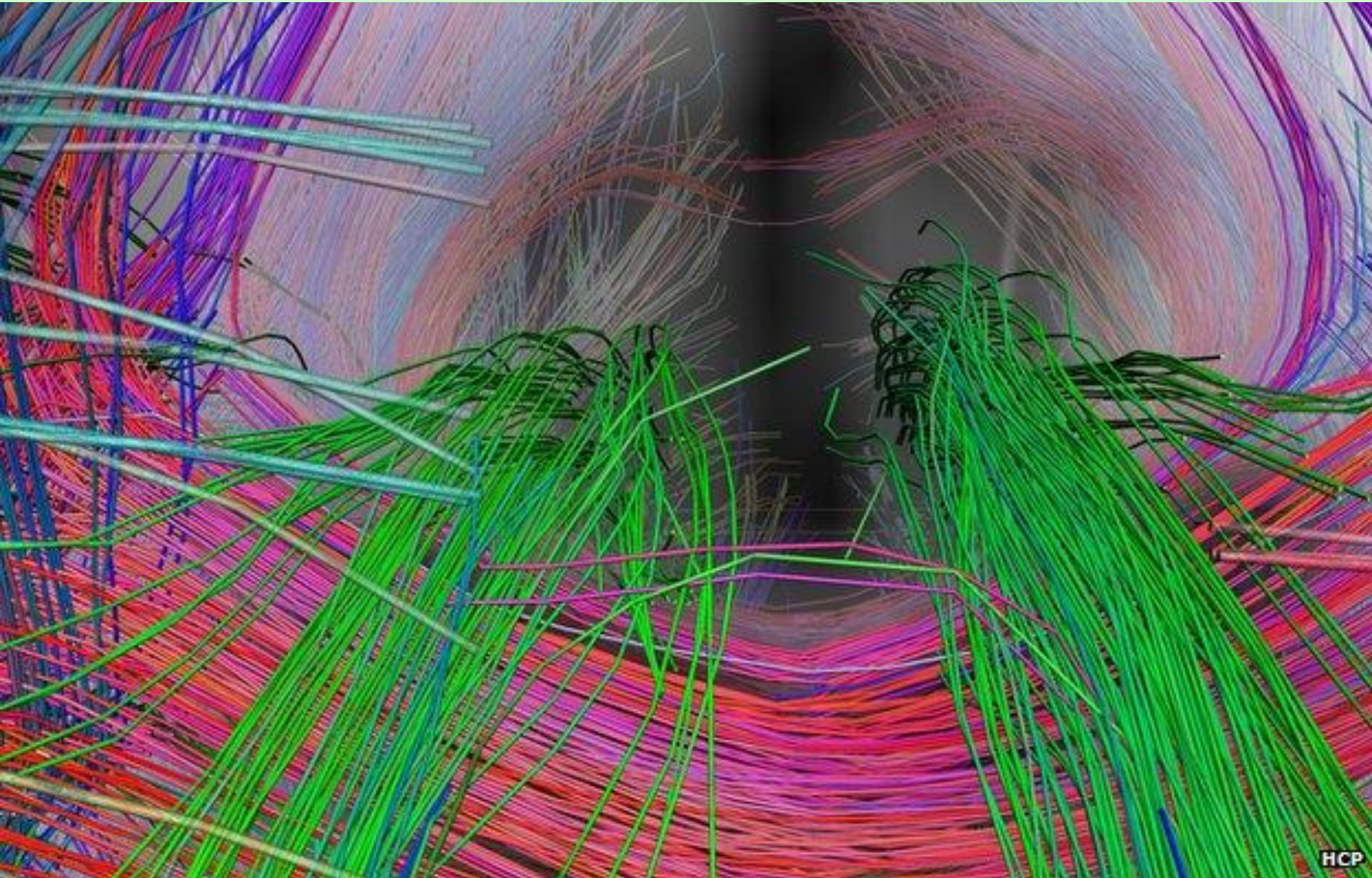
Groupe d'Imagerie Neurofonctionnelle  
UMR5296 CNRS CEA Université Bordeaux Segalen

&

Service de neuroradiologie diagnostique et thérapeutique  
CHU Pellegrin, Bordeaux



# Imagerie de diffusion et de connectivité



HCP



# Imagerie de diffusion et de connectivité

- **Méthodes**

- Diffusion, diffusion apparente, tenseur de diffusion
- Imagerie de diffusion
- Tractographie
- Limites et perspectives

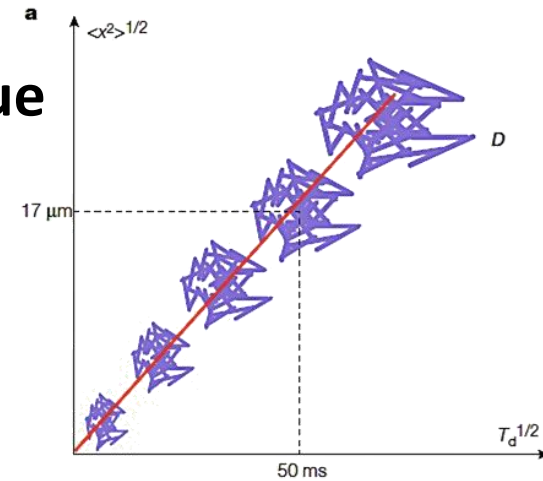
- **Applications**

- Cartographie des fibres blanches: atlas, asymétries
- Développement, vieillissement des faisceaux
- Relation avec les autres imageries de connectivité

# Diffusion, diffusion apparente

- **Mouvement aléatoire dû à l'agitation thermique**

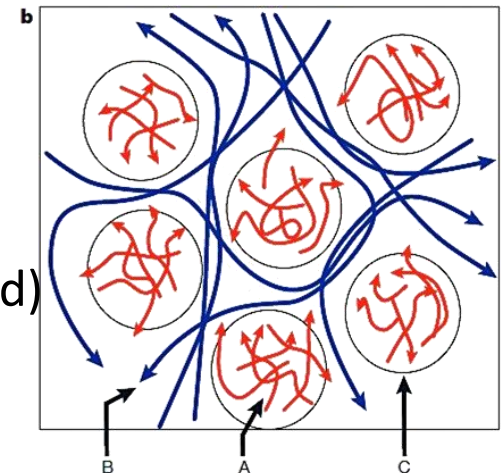
- parcours moyen:  $\langle X^2 \rangle = (6DT_d)^{1/2}$  (en 3D)
- dans l'eau pure à 37°C,  $D = 3 \cdot 10^{-3} \text{ mm}^2 \cdot \text{s}^{-1}$
- $T_d = 10 \text{ ms}$ ,  $\langle X^2 \rangle = 5 \mu\text{m}$



(Lebihan 2003)

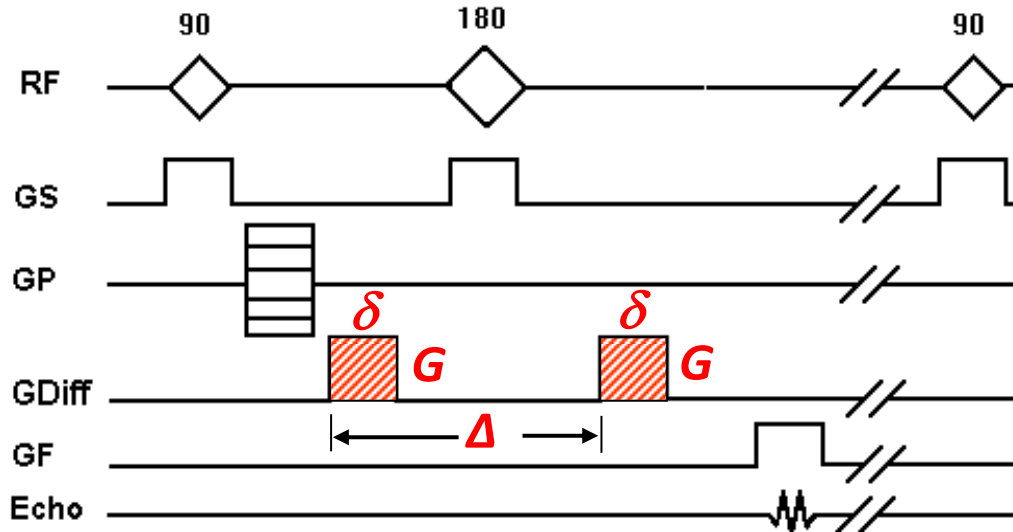
- **Dans le parenchyme cérébral**

- viscosité augmentée (myéline)
- multiples obstacles (microtubules) et compartiments
- diffusion ralentie (hindered) et/ou restreinte (restricted)
- coefficient de diffusion apparente (ADC)  $\ll D(\text{eau})$



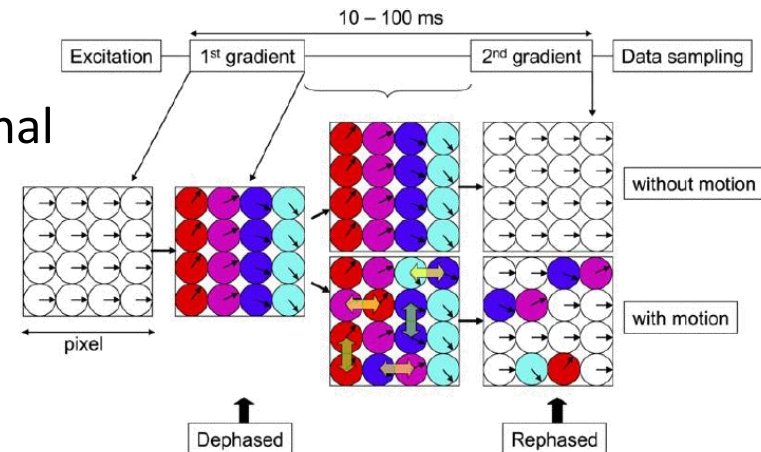
# Imagerie de diffusion

- Imagerie de diffusion en écho de spin (Stejskal-Tanner)



- Effet de la diffusion sur le signal RMN

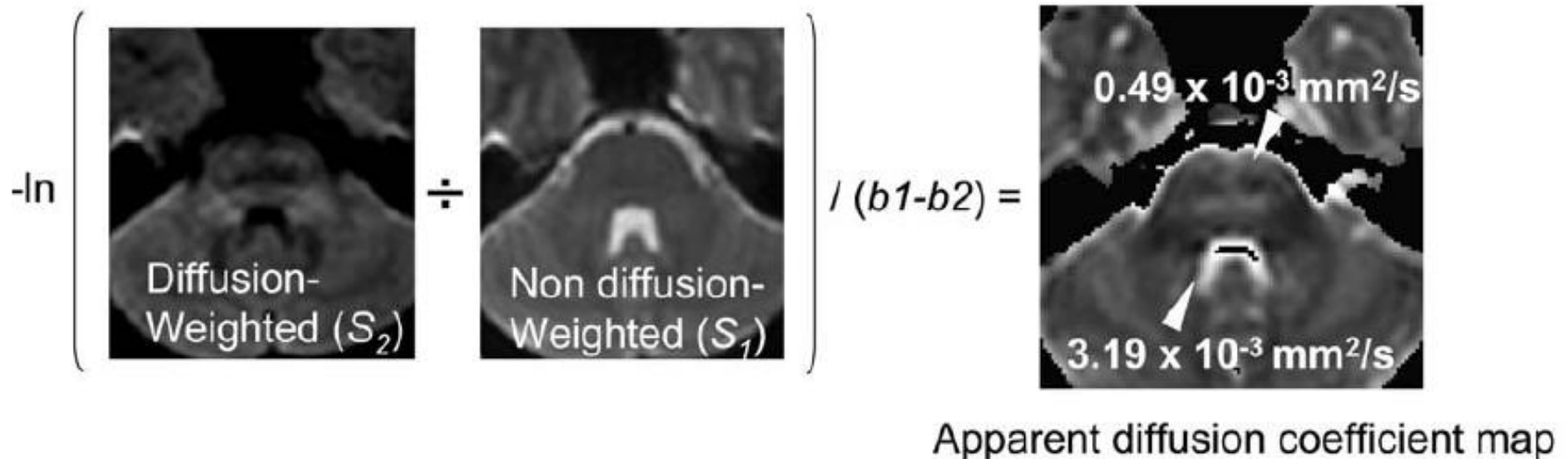
- diffusion des spins > dispersion des phases
- dispersion des phases > atténuation du signal



# Imagerie de diffusion

- Image du coefficient de diffusion apparente (ADC)
  - $S = PD.(1-e^{-TR/T1}).(1-e^{-TE/T2}) e^{-b.ADC}$  ,  $b = -\gamma^2 G^2 \delta^2 (\Delta - \delta/3)$
  - avec 2 valeurs de b:  $S_2/S_1 = \exp(-(b_2-b_1).ADC)$
  - image de coefficient de diffusion apparente:

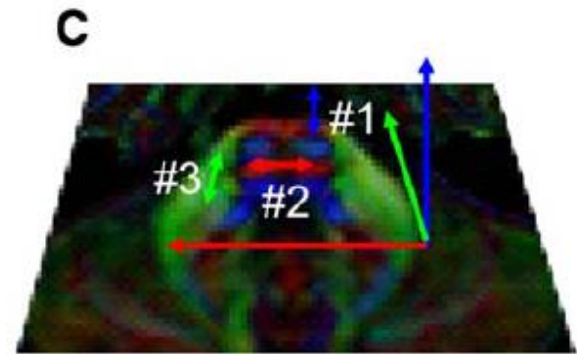
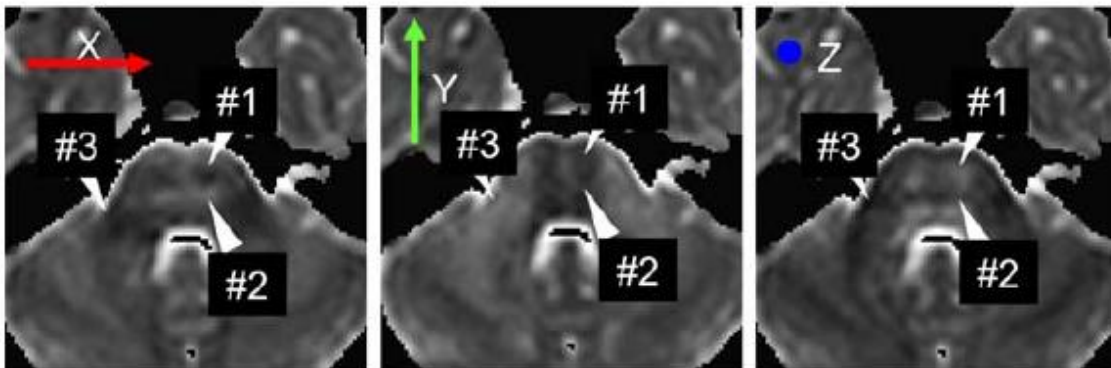
$$ADC_{x,y,z} = -\ln \{S_{x,y,z}(b_2)/S_{x,y,z}(b_1)\} / (b_2-b_1)$$





# Tenseur de diffusion

- La valeur d'ADC varie avec la direction du gradient de diffusion
  - la diffusion dépend de l'organisation spatiale des structures: la présence d'un faisceau de fibres contraint la diffusion dans sa direction
  - ADC donne une information sur la diffusion dans la direction du gradient
  - tous les mouvements de protons contribuent à la perte de signal, sauf ceux strictement perpendiculaires à la direction du gradient



#1	0.49	0.53	1.51 (mm <sup>2</sup> /s)
#2	1.37	0.50	0.54
#3	0.52	1.43	0.37

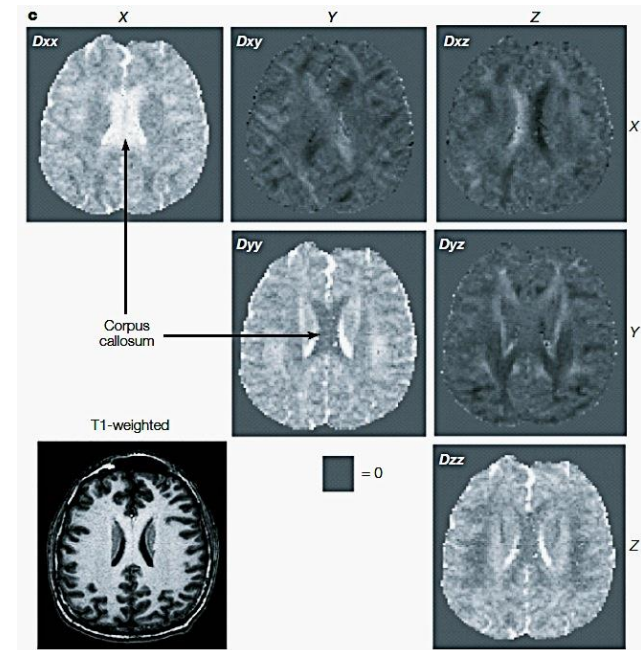
(Mori 2006)

# Tenseur de diffusion

- La description d'une diffusion anisotrope est donc impossible avec un seul scalaire
- Elle peut par contre se faire en 1<sup>ère</sup> approximation par un tenseur caractérisant les mouvements de diffusion dans les trois directions canoniques, ainsi que la corrélation des mouvements orthogonaux:

$$\overline{\overline{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

- En pratique, D est symétrique ( $D_{ij} = D_{ji}$ )
- Le modèle DTI suppose que la distribution des directions de diffusion est gaussienne
- Des modèles plus sophistiqués (multi-tenseurs), et des approches « model-free » (HARDI: Qball, DOT, DSI) sont également possibles

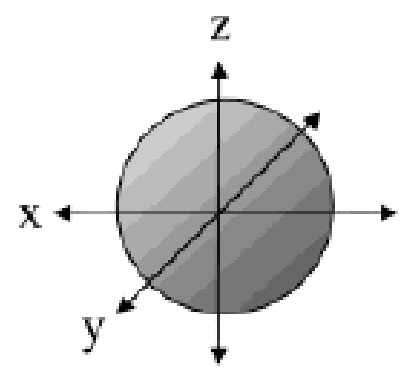
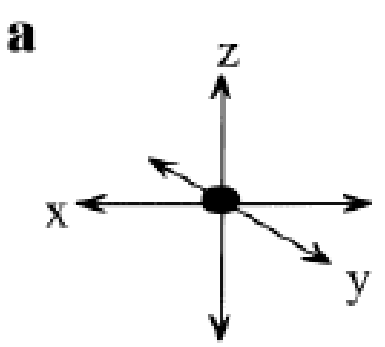


Lebihan 2003



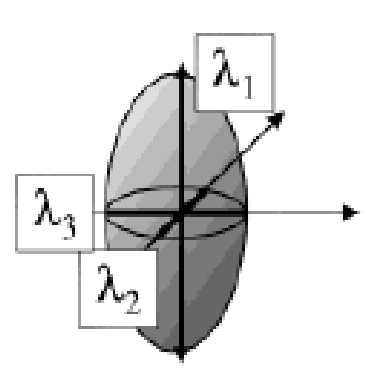
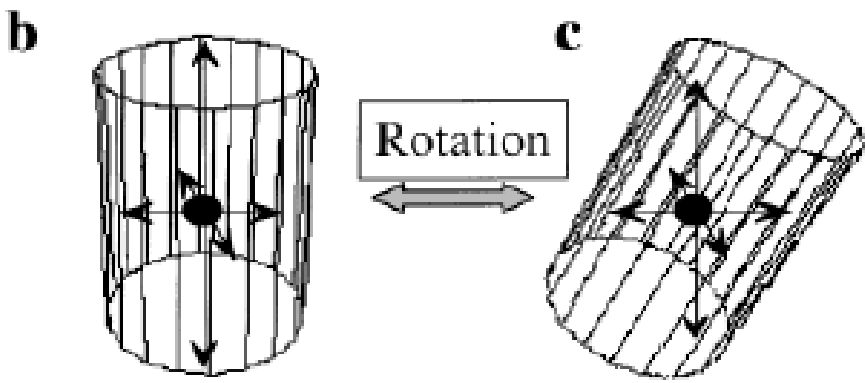
# Représentation du tenseur: ellipsoïde de diffusion

Diffusion isotrope

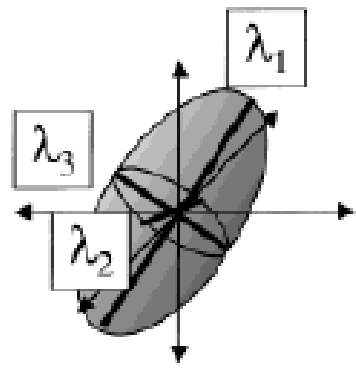


$$\begin{bmatrix} D & 0 & 0 \\ 0 & D & 0 \\ 0 & 0 & D \end{bmatrix}$$

Diffusion anisotrope



$$\begin{bmatrix} \lambda_3 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_1 \end{bmatrix}$$



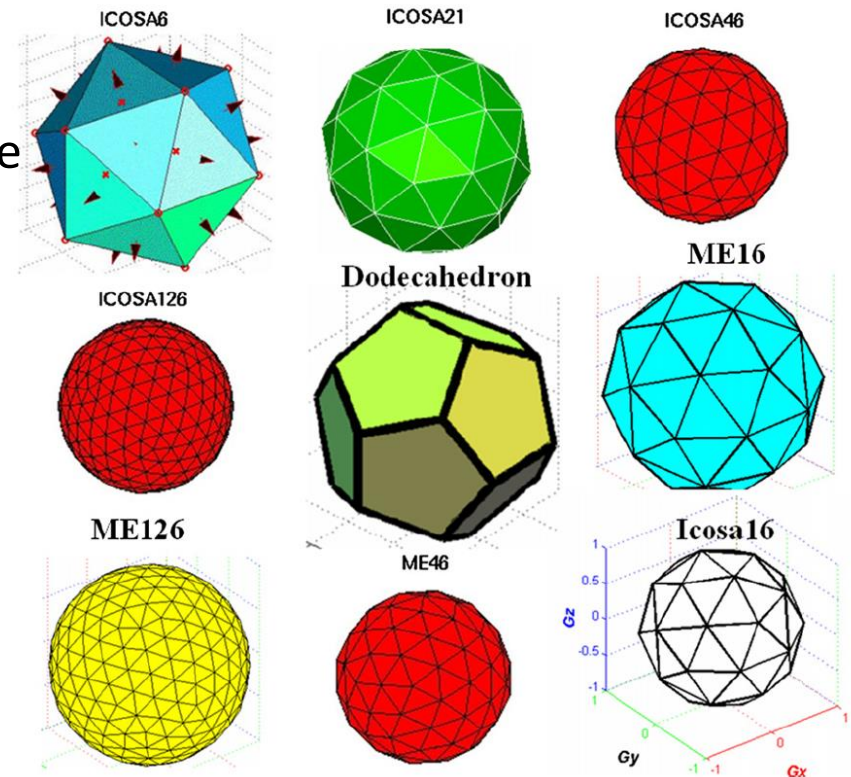
$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

# Imagerie du tenseur de diffusion: acquisition

- $A(x,y,z) = \exp(-\sum_i \sum_j b_{ij} D_{ij}(x,y,z))$ 
  - $b_{ij} = -\gamma^2 G_i G_j \mathcal{D}(\Delta - \delta/3)$  (pour un gradient rectangulaire, Mattiello 1994)
  - en théorie, pour estimer les 6 éléments  $D_{ij}$ , 6 mesures de A avec 6 gradients de directions différentes suffisent (ICOSA6)
  - en pratique, pour obtenir des valeurs précises pour la tractographie, un plus grand nombre de directions sont utilisées (30 ou plus)

- Stratégies d'acquisition

- Avec une seule amplitude maximale de b, les directions doivent être équiréparties sur une sphère
- Plusieurs valeurs d'amplitude de b, moins de directions par valeurs de b



(Hasan 2011)

# Imagerie du tenseur de diffusion: formation de l'image

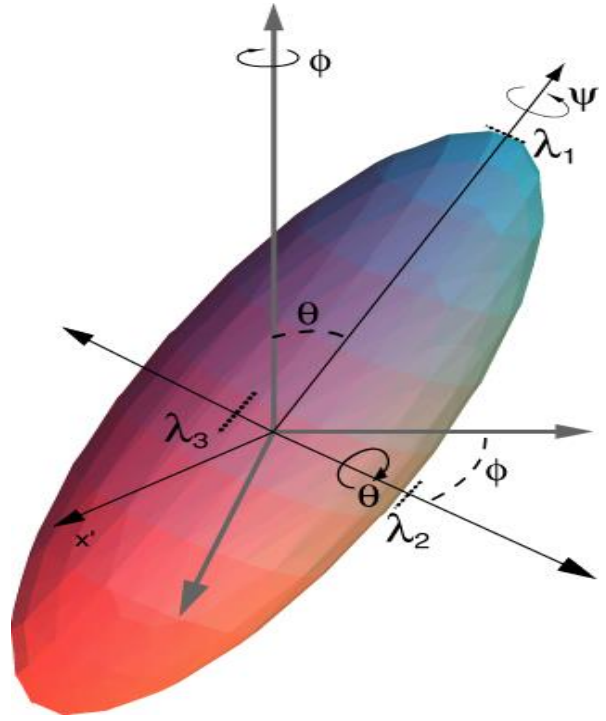
- Données:  $A_k(x,y,z)$ ,  $b_{k,ij}$  pour  $k=1, \dots, N$ ,  $i,j = 1,2,3$ ; tout  $x,y,z$  du volume
- Modèle DTI:  $A_k(x,y,z) = \exp(-\sum_i \sum_j b_{k,ij} D_{ij}(x,y,z))$
- Estimation de  $D_{ij}(x,y,z)$ 
  - Linéarisation:  $\ln(A_k(x,y,z)) = -\sum_i \sum_j b_{k,ij} D_{ij}(x,y,z)$ 
    - *Résolution par moindres carrés ordinaires (OLLS) ou pondérés (WLLS, meilleur)*
  - Non linéaire (*préférable*)  $A_k(x,y,z) = \exp(-\sum_i \sum_j b_{k,ij} D_{ij}(x,y,z))$ 
    - *Résolution par moindres carrés itératifs (NLLS), avec élimination des outliers (RESTORE, la meilleure)*
- Plus il y a de mesures de  $A$ , plus précise est l'estimation des  $D_{ij}$ , et plus fiable sera la tractographie



# Direction principale de diffusion: diagonalisation du tenseur

$$\vec{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} = \begin{pmatrix} V_{1x} & V_{1y} & V_{1z} \\ V_{2x} & V_{2y} & V_{2z} \\ V_{3x} & V_{3y} & V_{3z} \end{pmatrix} \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} \begin{pmatrix} V_{1x} & V_{2x} & V_{3x} \\ V_{1y} & V_{2y} & V_{3y} \\ V_{1z} & V_{2z} & V_{3z} \end{pmatrix}$$

$$\lambda_1 \geq \lambda_2 \geq \lambda_3$$



- Valeur propre principale:  $\lambda_1$
- Vecteur propre principal:  $\begin{bmatrix} V_{1x} & V_{1y} & V_{1z} \end{bmatrix}^T$

Le modèle monoexponentiel de la DTI suppose qu'à l'intérieur de chaque voxel, il n'y a qu'un faisceau de fibres prépondérant:  $V_1$  est sa direction

# Indices d'anisotropie

$$D_{av} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

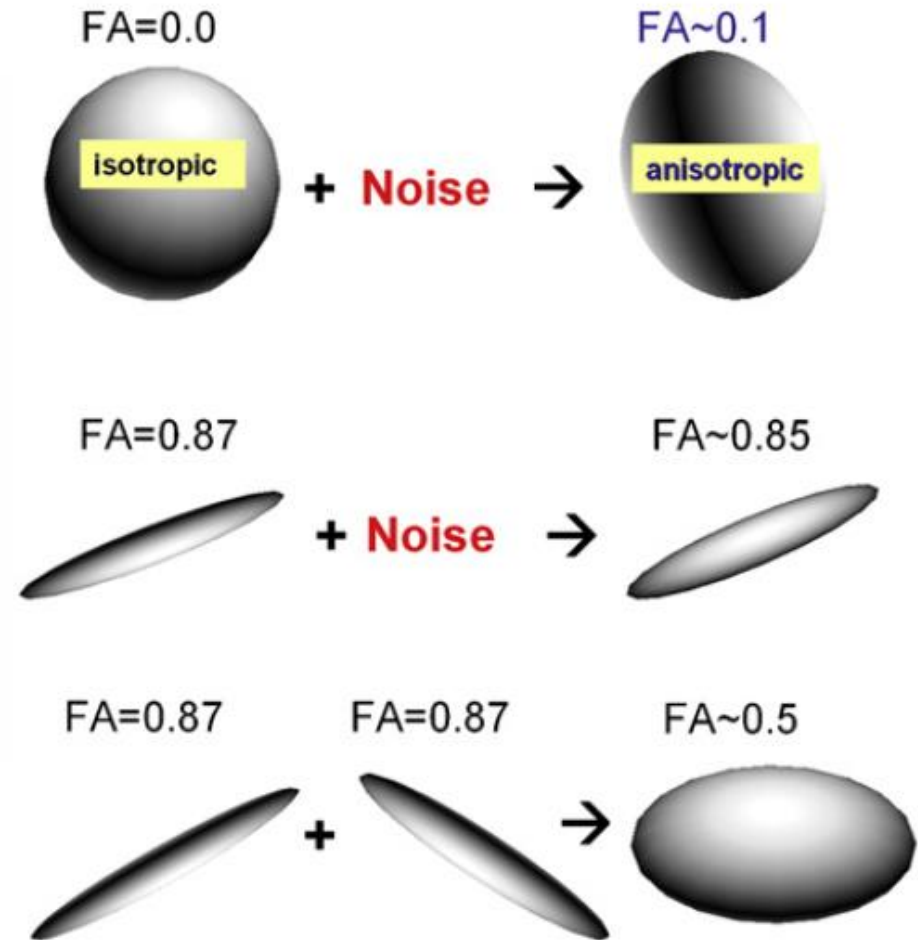
$$RA = \sqrt{\frac{1}{2} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}}{(\lambda_1 + \lambda_2 + \lambda_3)}}$$

$$FA = \sqrt{\frac{1}{2} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}}{\sqrt{(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}}$$

FA = 0 diffusion isotrope

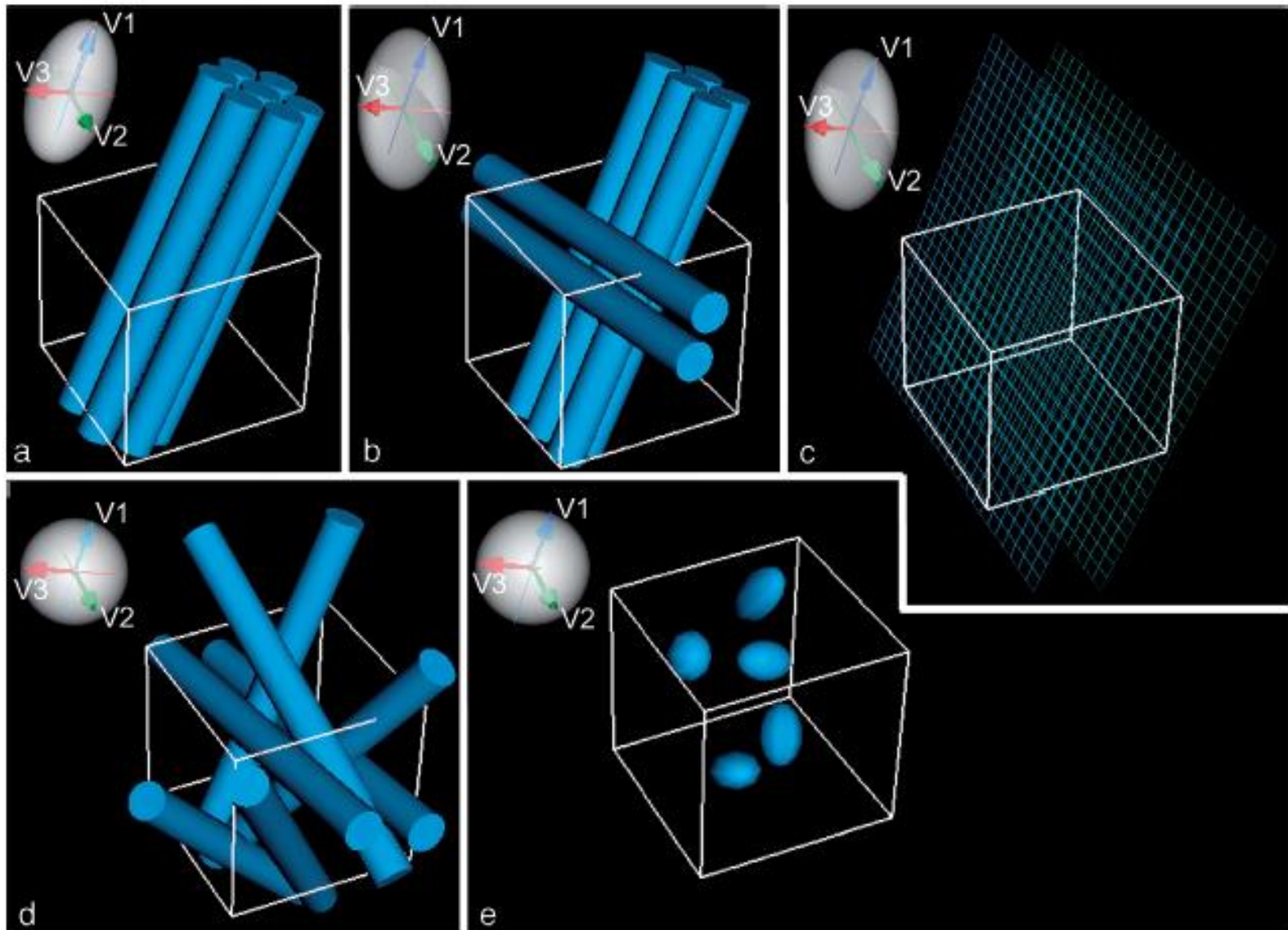
FA = 1 diffusion selon 1 direction

( $\lambda_2 = \lambda_3 = 0$ )



(Hasan 2011)

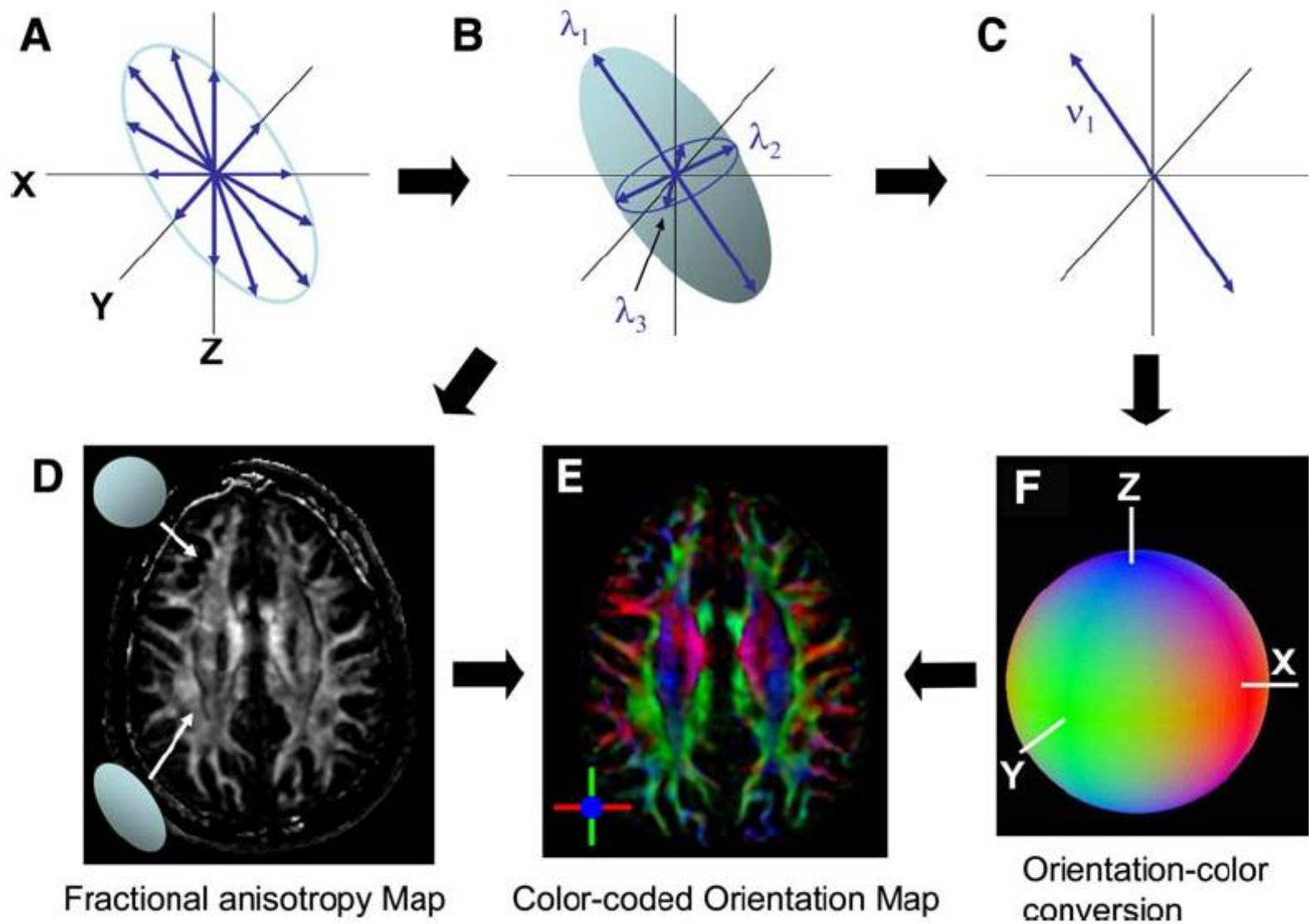
# Différentes configurations et leurs tenseurs de diffusion



(Mori 2006)



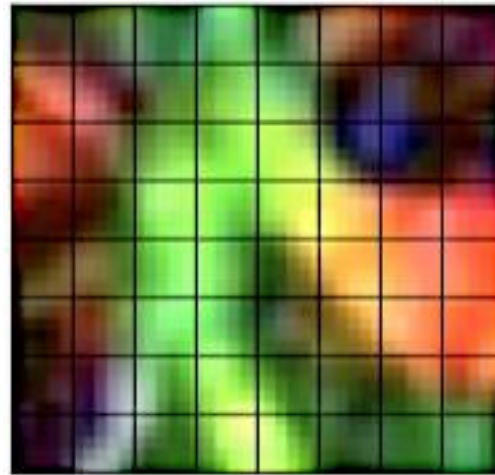
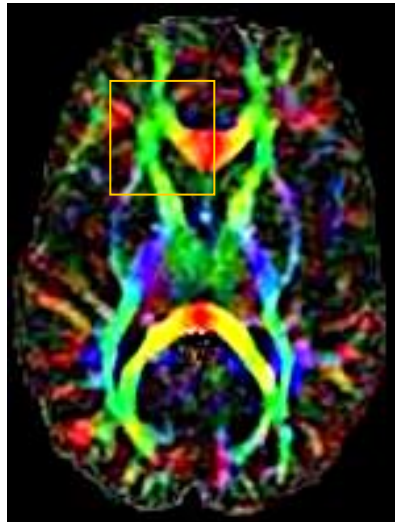
# Visualisation du tenseur de diffusion



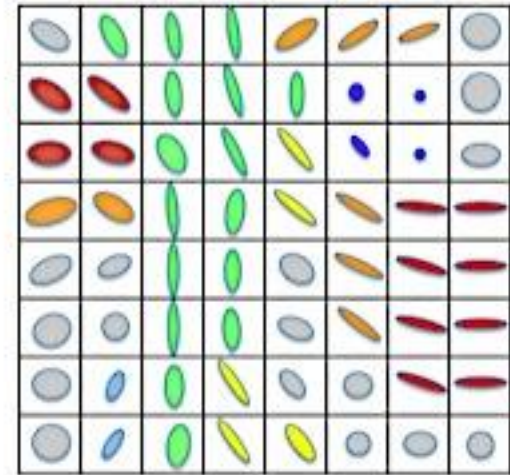
(Mori 2006)

# Tractographie en DTI

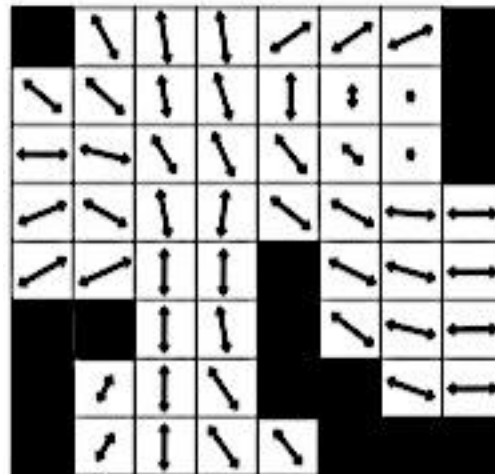
- Objectif: reconstruction des faisceaux de fibres en utilisant les données des images de diffusion



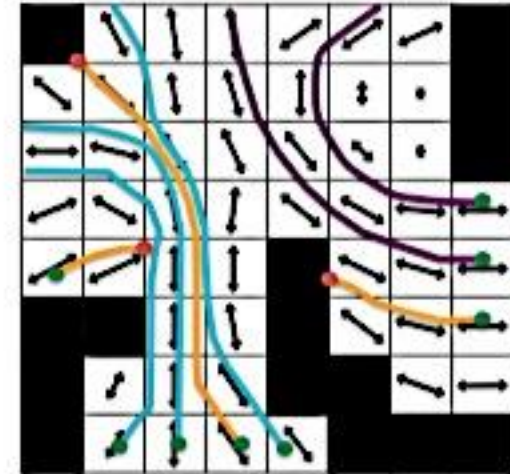
a



b



c



d

# Tractographie: freewares

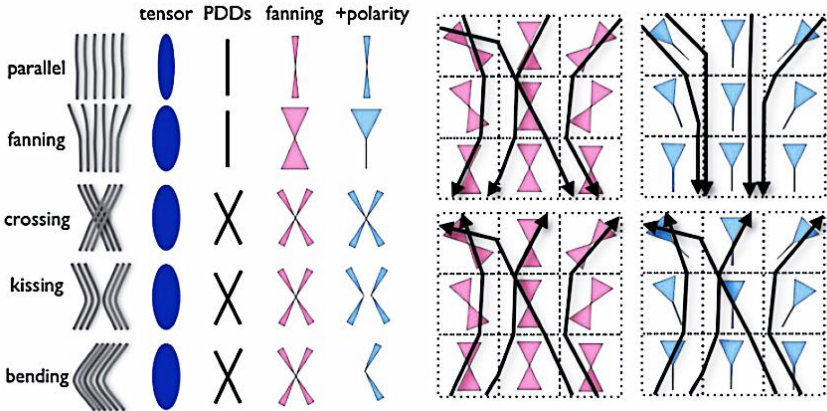
DTI software	Purpose	Web location
<b>CATNAP</b>	Coregistration, adjustment, and tensor-solving—a nicely automated program	<a href="http://www.nitrc.org/projects/jist/">http://www.nitrc.org/projects/jist/</a>
<b>CAMINO</b>	Diffusion MRI toolkit	<a href="http://www.nitrc.org/plugins/mwiki/index.php/jist:MainPage#Diffusion_Tensor_Imaging">http://www.nitrc.org/plugins/mwiki/index.php/jist:MainPage#Diffusion_Tensor_Imaging</a> <a href="http://web4.cs.ucl.ac.uk/research/medic/camino/pmwiki/pmwiki.php?n=Main.HomePage">http://web4.cs.ucl.ac.uk/research/medic/camino/pmwiki/pmwiki.php?n=Main.HomePage</a>
<b>DipY</b>	Diffusion imaging in Python	<a href="http://nipy.sourceforge.net/dipy/theory/dicom.html">http://nipy.sourceforge.net/dipy/theory/dicom.html</a>
<b>DoDTI</b>	DTI	<a href="http://neuroimage.yonsei.ac.kr/dodti/">http://neuroimage.yonsei.ac.kr/dodti/</a>
<b>DTIStudio</b>	DTI processing, deterministic fiber tracking	<a href="https://www.mristudio.org/wiki/installation">https://www.mristudio.org/wiki/installation</a>
<b>DiffeoMap &amp; ROIEditor</b>		<a href="https://www.mristudio.org/wiki/user_manual">https://www.mristudio.org/wiki/user_manual</a>
<b>DSIStudio</b>	Handles QBI, DSI, DTI	<a href="http://graphics.stanford.edu/projects/dti/software/">http://graphics.stanford.edu/projects/dti/software/</a> <a href="http://dsi-studio.labsolver.org/Manual/Reconstruction">http://dsi-studio.labsolver.org/Manual/Reconstruction</a>
<b>DTI-TK</b>	Tracking	<a href="http://www.nitrc.org/projects/dtitk">http://www.nitrc.org/projects/dtitk</a>
<b>DTI-Query</b>	DTI	<a href="http://graphics.stanford.edu/projects/dti/">http://graphics.stanford.edu/projects/dti/</a>
<b>DTI-Toolbox</b>	Data prep Interpolation, smooth/process ROI/Atlas-based segment	<a href="http://www.uth.tmc.edu/radiology/faculty/hasan.html">http://www.uth.tmc.edu/radiology/faculty/hasan.html</a>
<b>ExploreDTI</b>	DTI-tracking	<a href="http://www.exploredti.com/animations/">http://www.exploredti.com/animations/</a>
<b>FDT</b>	FSL diffusion tools	<a href="http://www.fmrib.ox.ac.uk/fslcourse/lectures/practicals/fdt/index.htm#tbss">http://www.fmrib.ox.ac.uk/fslcourse/lectures/practicals/fdt/index.htm#tbss</a>
<b>TBSS</b>	Voxel-based	<a href="http://www.fmrib.ox.ac.uk/fsl/tbss/index.html">http://www.fmrib.ox.ac.uk/fsl/tbss/index.html</a>
<b>Probtrack</b>	Prob. tracking	<a href="http://www.fmrib.ox.ac.uk/fslcourse/lectures/fdt.pdf">http://www.fmrib.ox.ac.uk/fslcourse/lectures/fdt.pdf</a>
<b>INRIA</b>	DTI	<a href="http://www-sop.inria.fr/asclepios/software/MedINRIA/">http://www-sop.inria.fr/asclepios/software/MedINRIA/</a>
<b>MedINRIA</b>		
<b>SepINRIA</b>		
<b>Quantitative DTI</b>	DTI	<a href="http://www.nitrc.org/projects/quantitivedti/">http://www.nitrc.org/projects/quantitivedti/</a>
<b>SATURN</b>	Single tensor DTI	<a href="http://www.lpi.tel.uva.es/saturn">http://www.lpi.tel.uva.es/saturn</a>
<b>SLICER-DTMRI</b>	DTI	<a href="http://www.na-mic.org/Wiki/index.php/Slicer:DTMRI">http://www.na-mic.org/Wiki/index.php/Slicer:DTMRI</a>
<b>SPM</b>	fMRI, spatial normalization registration	<a href="http://www.fil.ion.ucl.ac.uk/spm/">http://www.fil.ion.ucl.ac.uk/spm/</a> <a href="http://www.fil.ion.ucl.ac.uk/spm/ext/#toolboxes">http://www.fil.ion.ucl.ac.uk/spm/ext/#toolboxes</a> <a href="http://users.ioni.ucla.edu/~narr/protocol.php?q=vbm_spm">http://users.ioni.ucla.edu/~narr/protocol.php?q=vbm_spm</a>
<b>TrackVis</b>	Q-ball, DTI, DSI	<a href="http://www.trackvis.org/">http://www.trackvis.org/</a>
<b>TracTor</b>	DTI	<a href="http://code.google.com/p/tractor/">http://code.google.com/p/tractor/</a> <a href="http://www.nitrc.org/projects/tractor">http://www.nitrc.org/projects/tractor</a>
<b>Volume-One dTV</b>	Diffusion tensor visualizer	<a href="http://www.volume-one.org/">http://www.volume-one.org/</a> <a href="http://www.ut-radiology.umin.jp/people/masutani/dTV/dTV_frame-e.htm">http://www.ut-radiology.umin.jp/people/masutani/dTV/dTV_frame-e.htm</a>

(Hasan 2011)

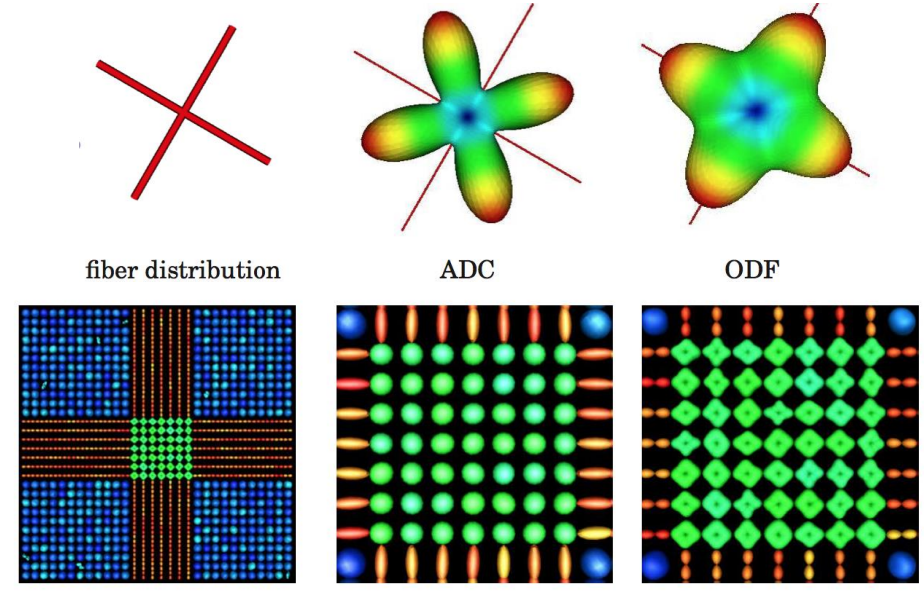


# Diffusion et tractographie: limites, perspectives

- DTI suppose que la direction principale de diffusion est alignée avec celle d'un faisceau de fibres
  - mais le profil de diffusion n'est pas la géométrie de la matière blanche
  - À  $2 \times 2 \times 2 \text{mm}^3$  de résolution, 90% des voxels sont inhomogènes
- Recours à des modèles plus complexes



(Jbabdi 2011)



ODF spherical functions    DTs in crossing area    ODFs in crossing area

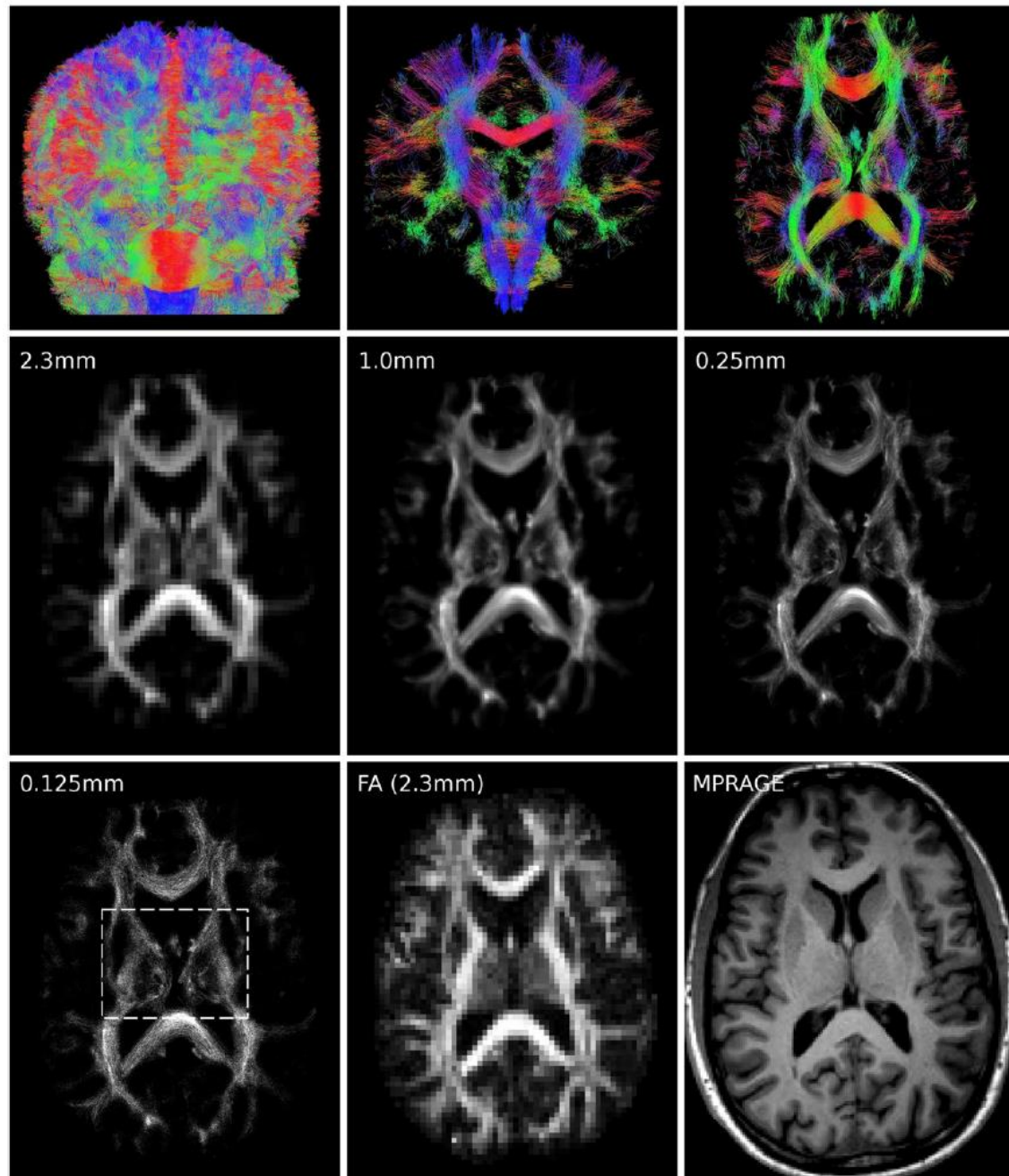
(Descoteaux 2008)

# Tractographie: super résolution à 3T

- Tractographie probabiliste de fibres (Behrens 2005) combinée à une modélisation multi-faisceaux (Tournier 2007)
- Reconstruction de 2,5 millions de fibres
- Calcul d'une carte de densité de fibres (TDI) sur des voxels plus petits que ceux des images de diffusion

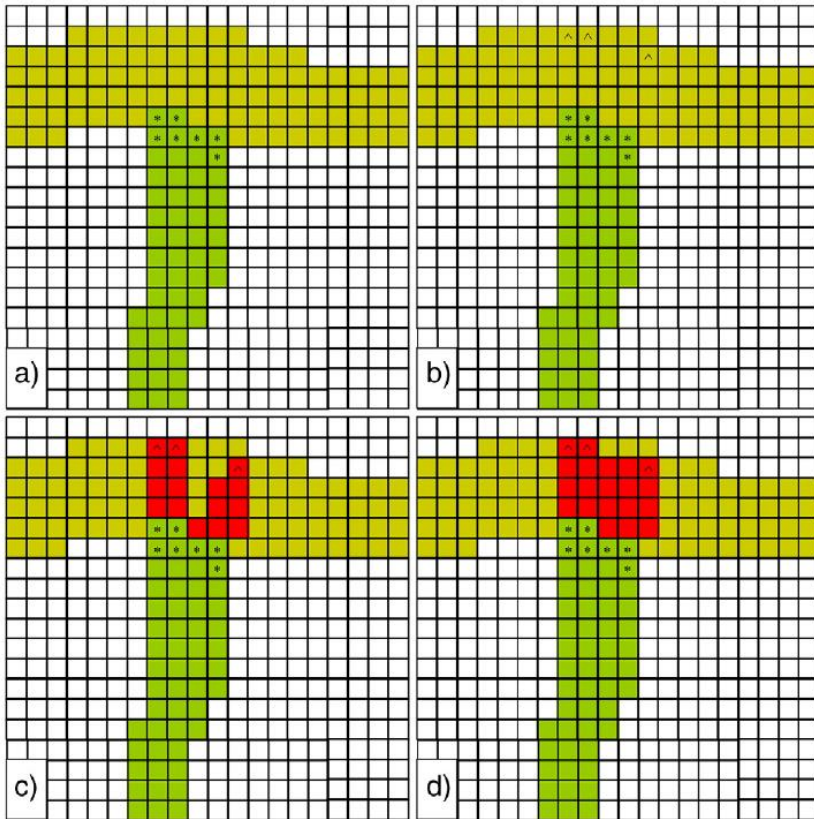
DWI data were acquired from 5 healthy volunteers on a 3 T Siemens Trio system, using a twice-refocused SE-EPI sequence (Reese et al., 2003) ( $b = 3000 \text{ s/mm}^2$ ). Three subjects (subjects S1-S3) were scanned with 150 DWI-directions, 54 contiguous slices, voxel size  $2.3 \times 2.3 \times 2.3 \text{ mm}^3$ , and acquisition time: 20.5 min. A further subject (S4) was scanned with 60 DWI-directions, 60 contiguous slices, voxel size  $2.5 \times 2.5 \times 2.5 \text{ mm}^3$ , and acquisition time: 9.4 min. The final subject

(Calamante 2010, 2011)

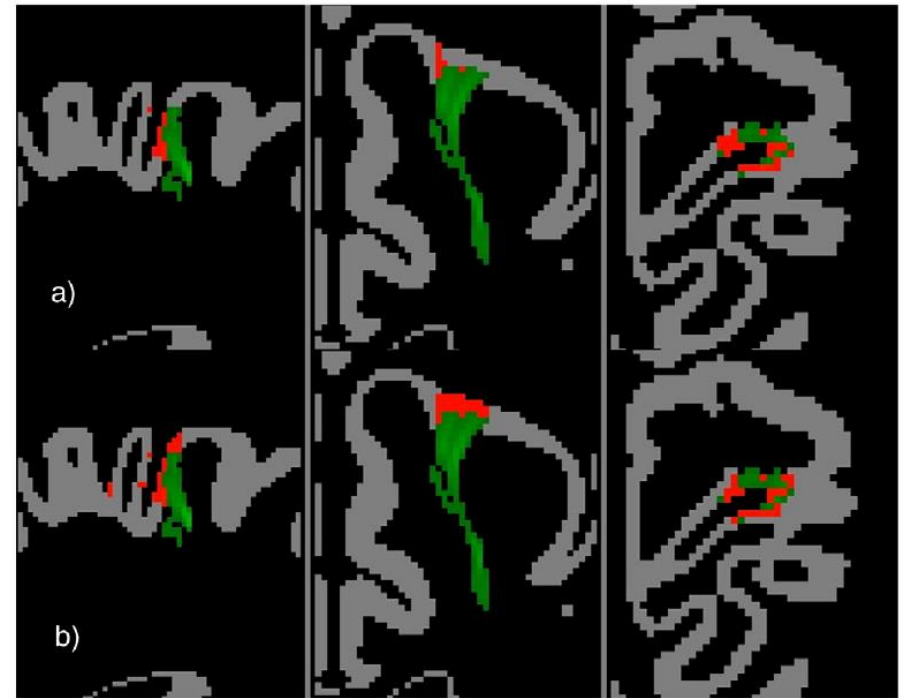


# Diffusion et tractographie: limites, perspectives

- Absence de précision radiale et transversale
- Quelles sont les terminaisons corticales des faisceaux?
  - Où se terminent et commencent les faisceaux de fibres? Dans quelles couches? Sur quelles extensions? qui est connecté à qui?



« grey matter extension approach »

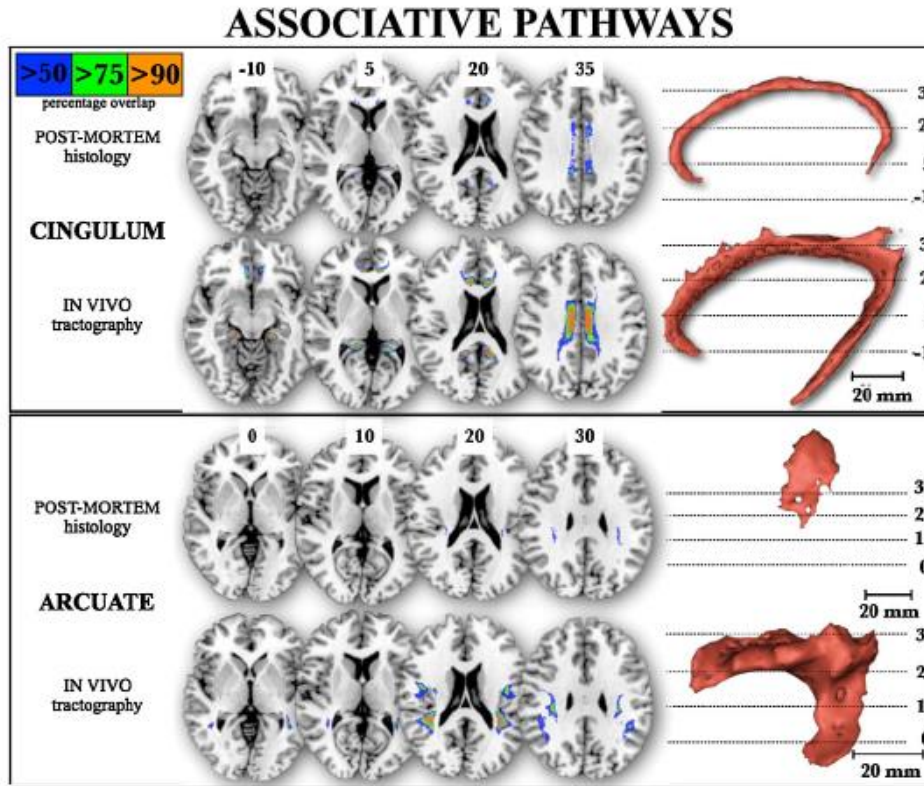
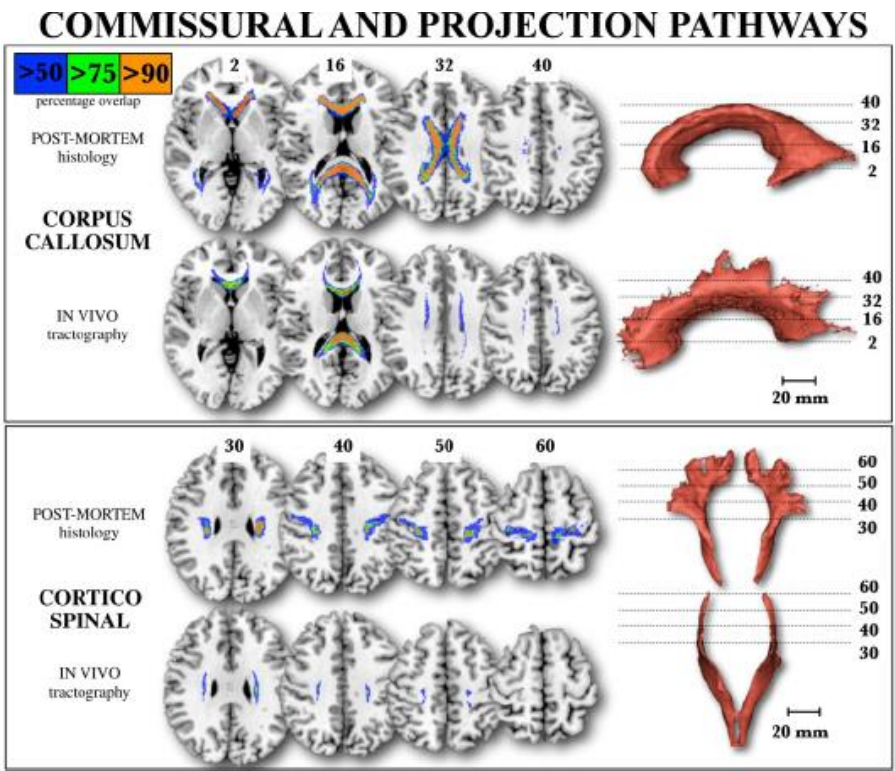


(Tozer 2012)



# Diffusion et tractographie: limites, perspectives

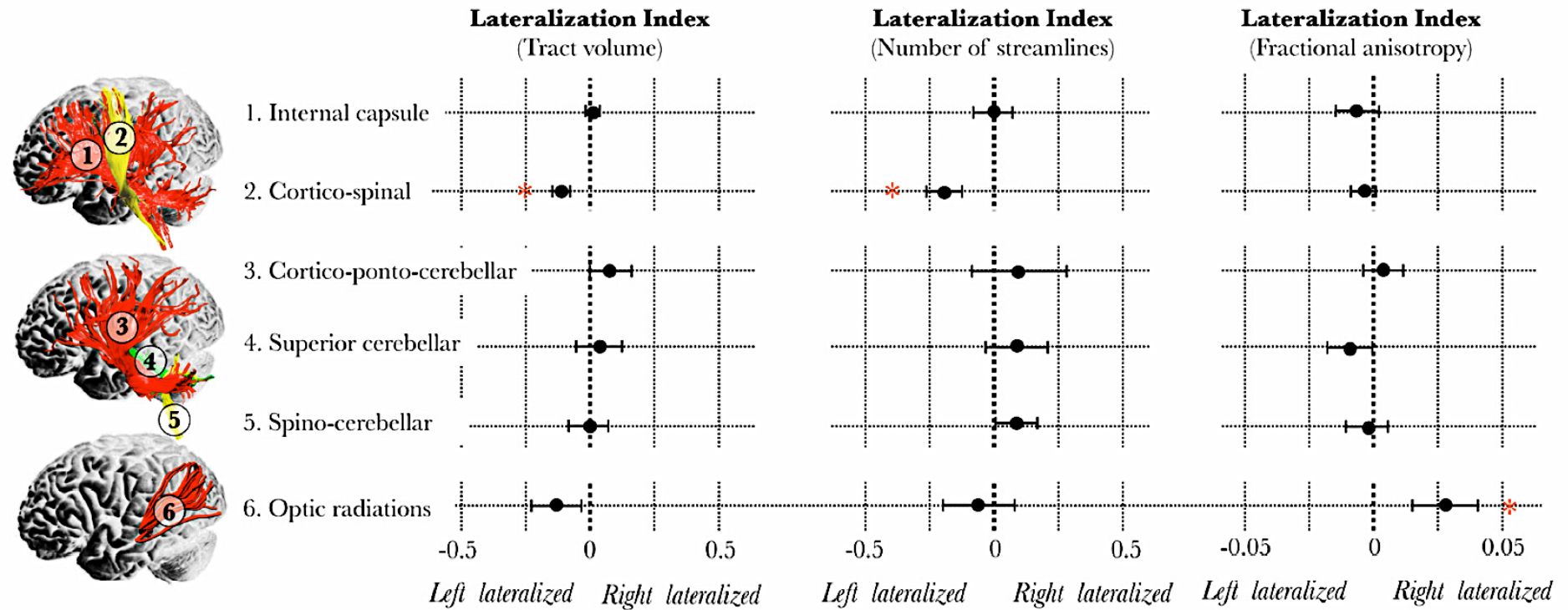
- Validation difficile
  - Fantôme: bas niveau, peu réaliste
  - Animaux: neuroanatomie différente
  - Post-mortem: dissection possible mais pas le traçage



(Thiebaut de Schotten 2011)

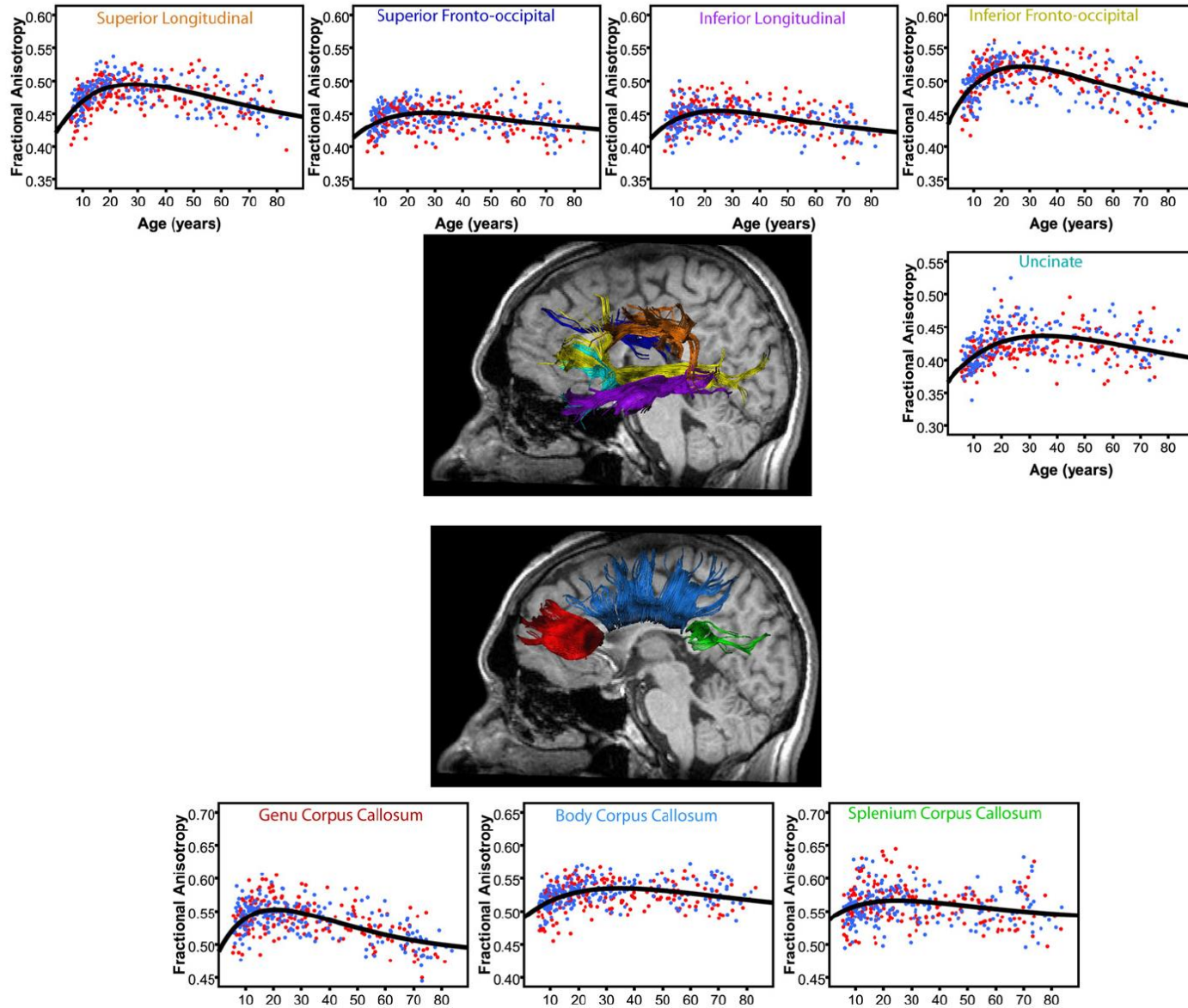


# Applications: organisation des faisceaux, variabilité



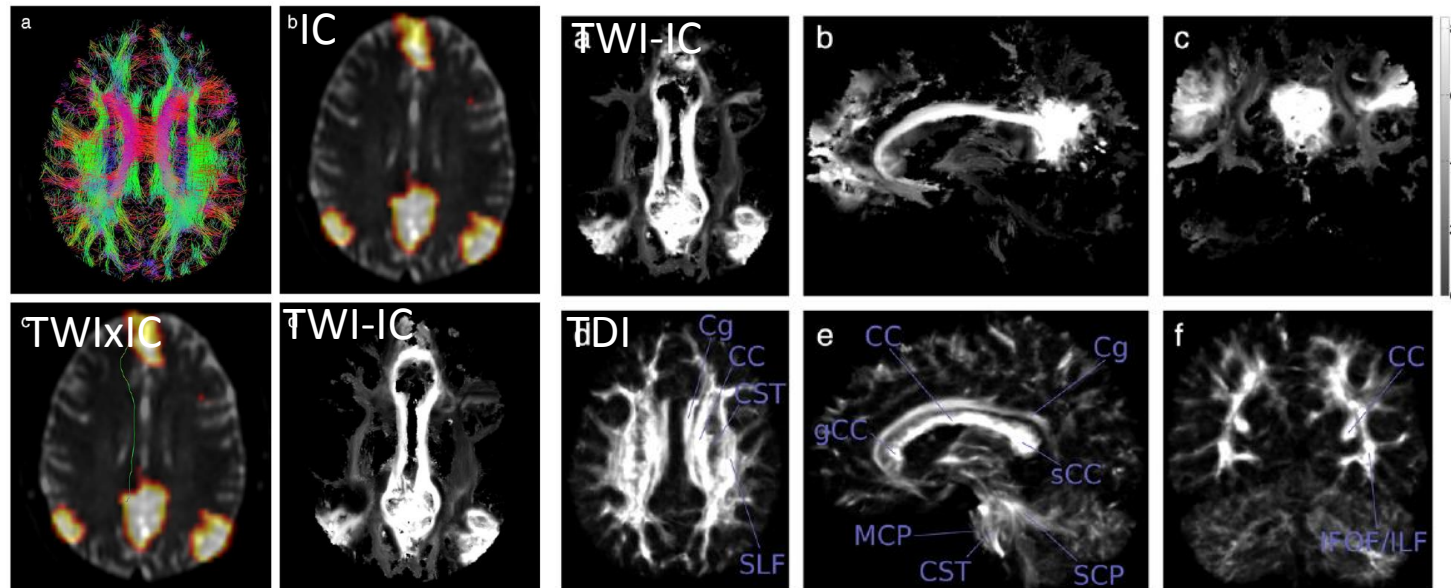
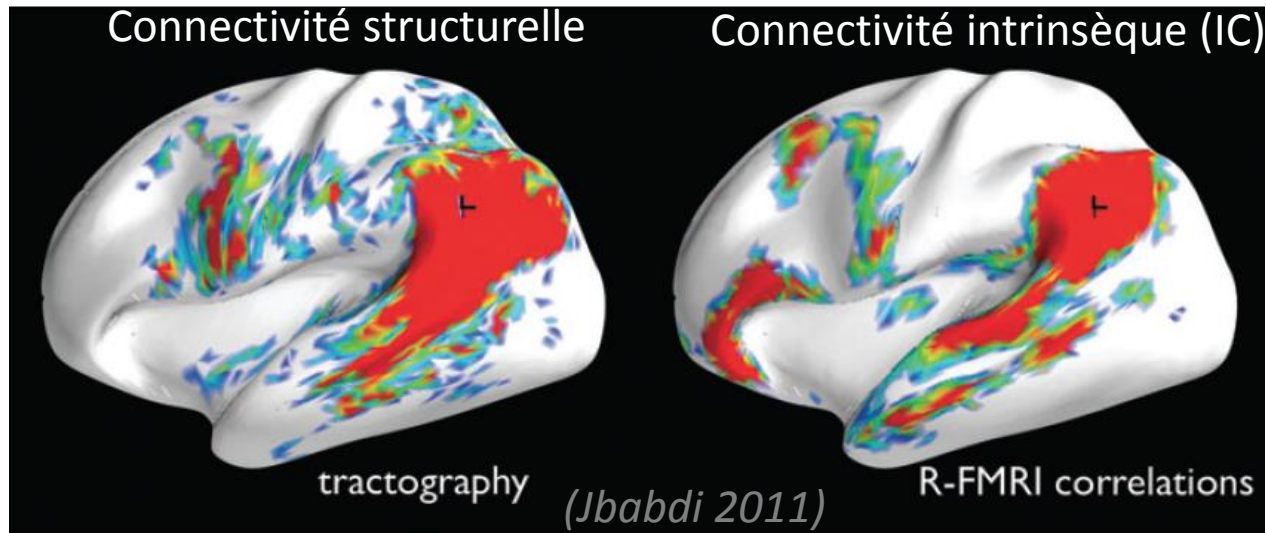
(Thiebaud de Schotten 2011)

# Applications: maturation et vieillissement



(Lebel 2011)

# Tractographie et connectivité intrinsèque



(Calamante 2013)





# HUMAN Connectome PROJECT

Mapping structural and functional connections in the human brain

## Human Connectome

The NIH Human Connectome Project is an ambitious effort to map the neural pathways that underlie human brain function. The overarching purpose of the Project is to acquire and share data about the structural and functional connectivity of the human brain. It will greatly advance the capabilities for imaging and analyzing brain connections, resulting in improved sensitivity, resolution, and utility, thereby accelerating progress in the emerging field of human connectomics.

Altogether, the Human Connectome Project will lead to major advances in our understanding of what makes us uniquely human and will set the stage for future studies of abnormal brain circuits in many neurological and psychiatric disorders.

## Consortia

The Blueprint has funded two major cooperative agreements that will take complementary approaches to deciphering the brain's complex wiring diagram. For more information see the NIH press release, "[\\$40 million awarded to trace human brain's connections.](#)"

Use the box at the right to search the consortium sites or browse the sites directly using the links below.

### [The WU-Minn Project](#)

**The Human Connectome Project**  
Understanding the human brain is one of the great scientific challenges of the 21st century. The Human Connectome Project (HCP) represents a concerted attack on a key aspect of this challenge: elucidating the neural pathways that underlie brain function. Deciphering this amazingly complex wiring diagram will reveal much about what makes us uniquely human and what makes every person different from all others.

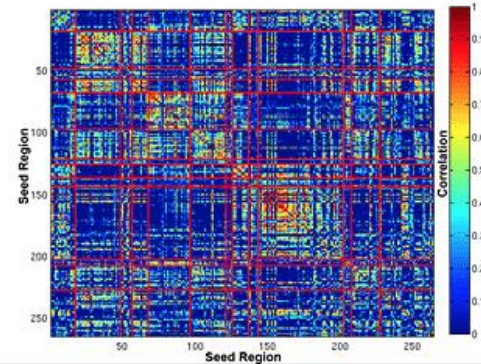
The HCP will comprehensively map human brain circuitry in 1,200 healthy adults using state-of-the-art methods of brainwave neuroimaging. It will yield invaluable information about brain connectivity, its relationship to behavior, and the contributions of genetic and environmental factors to individual differences in brain circuitry.

Results will be made freely available to the scientific community via the ConnectomeDB database and the Connectome Research Visualization Platform. This will include unprecedented "through" capabilities for navigating brain pathways and identifying neural circuits associated with different behavioral capacities.

**PROJECT SPOTLIGHT**  
**Brain function divided by time**  
A new approach for defining functional modules in the brain using temporally distinct differences in fMRI activity. [Read More](#)

## Connectome News and Announcements

- [Brain wiring a no-brainer?](#) March 29, 2012



## Search the Human Connectome Project


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### [The Harvard/MGH-UCLA Project](#)

**Human Connectome Project**

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**The Human Connectome Project**  
Navigate the brain in a way that was never before possible. Follow major brain pathways, compare essential circuits, identify regions to explore the cells that comprise it, and the functions that depend on it.

The Human Connectome Project aims to provide an unparalleled compilation of neural data, an interface to graphically navigate that data and the opportunity to explore neural pathways before realized. Connectome: about the brain, human brain.

Image © by the Laboratory of Human Imaging, LQILA

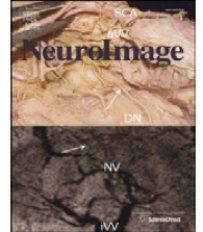




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## NeuroImage

journal homepage: [www.elsevier.com/locate/ynimg](http://www.elsevier.com/locate/ynimg)



Comments and Controversies

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