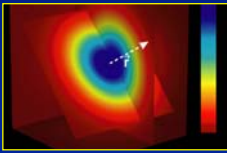
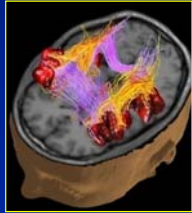




## From Diffusion MR Image Analysis to Whole Brain Connectivity Simulation




Jean-Philippe Thiran

EPFL  
Lausanne, Switzerland




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Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland

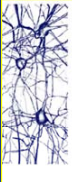


## EPFL - Lausanne



**– HPC in life sciences at EPFL**

- *The Blue Brain project:*
  - create a biologically accurate, functional model of the brain using IBM's Blue Gene supercomputer
  - 8192 processors
- *Several other projects*
- *Including MR image analysis*






**Blue  
Brain  
Project**

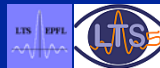
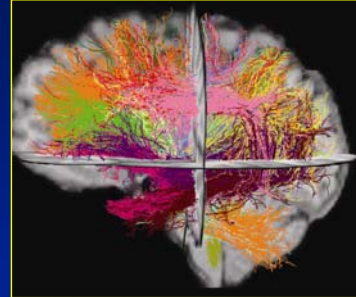



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## Motivation

- **MR imaging** is now established as the most important modality in **neuro-imaging**
- Recent advances allow to obtain *in vivo* information on the **architecture** of the (brain) tissues
  - New MR sequences
  - New algorithmic developments
- This opens **new perspectives in fundamental neurosciences** as well as in clinical practice



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## Outline

- **Basics of diffusion**
- **Imaging the diffusion by MRI**
- **From Diffusion MRI to Fiber Tracking**
- **Applications to Brain Connectivity Analysis**

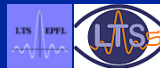


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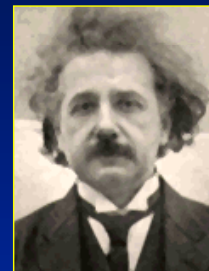


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## Basics of diffusion

- Molecular diffusion – Brownian motion
  - First formally described in 1905 by A. Einstein
  - We will consider **water molecule** diffusion
    - *Example: in a glass of water, molecules diffuse randomly and freely, only constrained by the boundaries of the container*

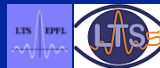
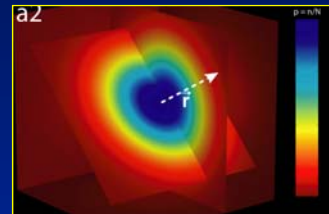


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## Basics of diffusion

- For a **3D volume**,
  - 3D diffusion *pdf*
  - we use here the color-coding of the *pdf*
- For **homogeneous media**, this diffusion is an **isotropic Gaussian**
  - With  $\sigma^2=2D\Delta$
  - **D** is the diffusion coefficient
    - Function of medium viscosity,  $t^\circ$ , ...

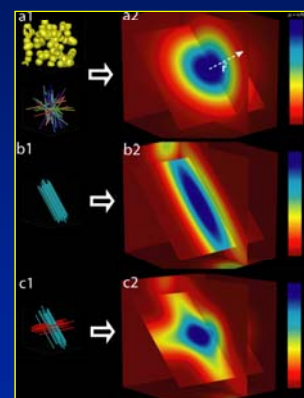
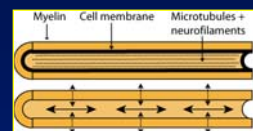


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## Diffusion in complex media

- **Neuronal tissues: fibrillar structure**
  - Tightly packed, coherently aligned axons
  - Diffusion more restricted in direction perpendicular to the axonal orientation than along its parallel direction
  - This is called anisotropic diffusion, as opposed to isotropic diffusion
- fiber crossings:
  - Certainly not a Gaussian pdf then.



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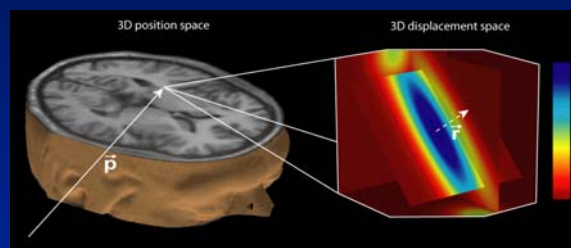


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## Diffusion imaging

- Imaging the diffusion of the 3D volume would ideally give a 6D data set

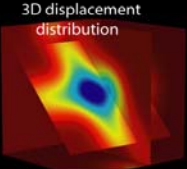


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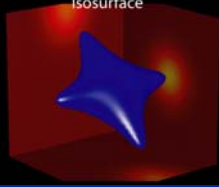





### Diffusion imaging

- But this information is too complex to be analyzed and visualized
- Simplified representations
  - Isosurfaces
  - Orientation Distribution Functions (ODF)
    - + color code for the orientation




Data reduction










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### Diffusion imaging

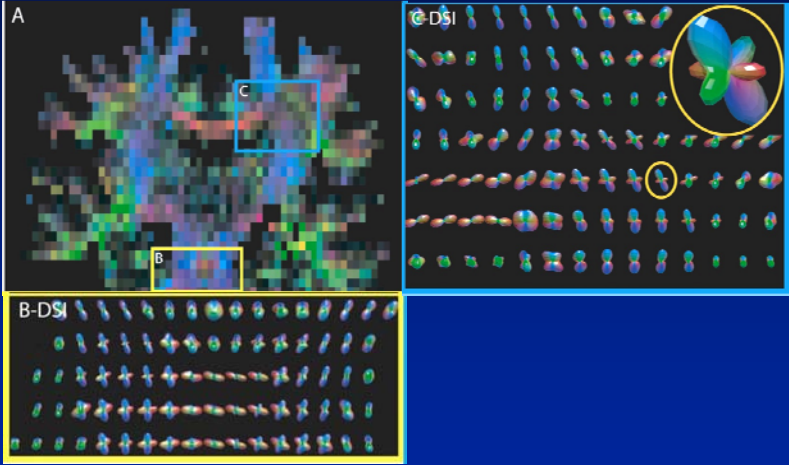


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### Diffusion imaging



The figure displays diffusion imaging results. Panel A shows a 3D fiber tracking visualization of white matter tracts in a brain slice, with regions B and C highlighted by yellow and blue boxes respectively. Panel B-DSI shows a grid of diffusion tensor maps corresponding to region B. Panel C-DSI shows a grid of diffusion tensor maps corresponding to region C, with a magnified view of a single tensor map showing its principal components as colored lobes.


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### Outline

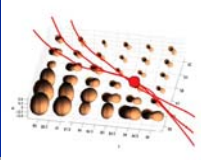
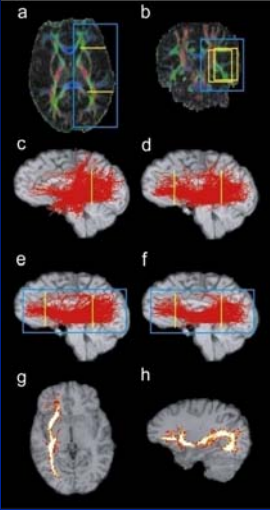
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

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### Tractography

- **Fibre tracking**
  - Infer axonal trajectories i.e. brain connectivity
  - Computation of trajectories following principal directions of diffusion
- **Whole brain simulation**
  - Trajectories are initiated all over the brain's WM
  - Result is an estimate of the whole brain connectivity (~100'000 lines)
- **Tract selection, virtual dissection**
  - Fibre selection using ROIs

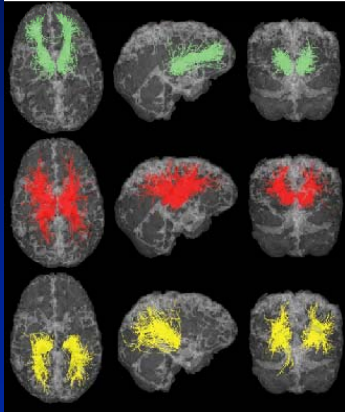
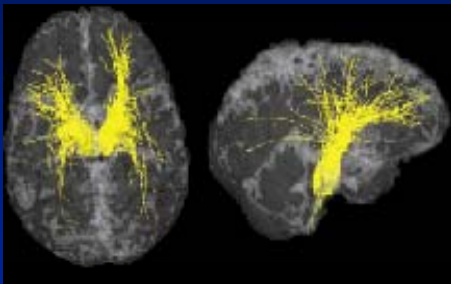





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### Fibre-tracking, results

- Thalamic projections
- Cortico-spinal and cortico-bulbar tracts

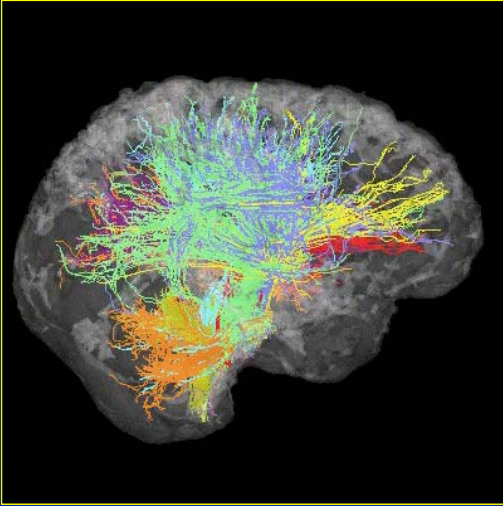





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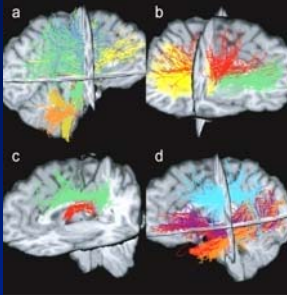





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
### References






Hagmann et al. 2003





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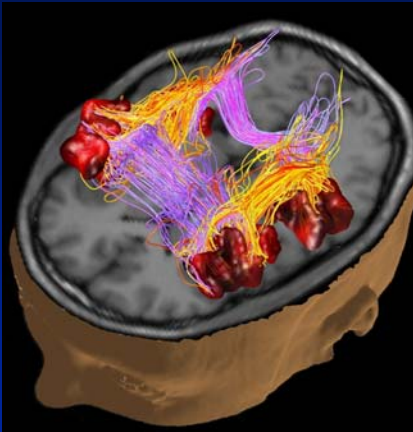


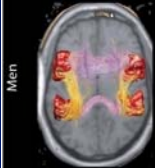
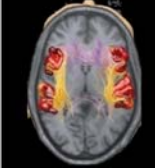
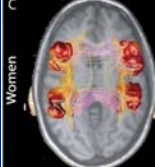
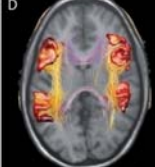
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- From Diffusion MRI to Fiber Tracking
- **Applications to Brain Connectivity Analysis**

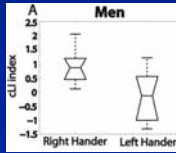
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### Application: study of language networks



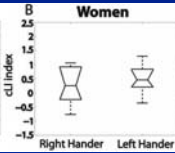
|              |  |   |
|--------------|--|---|
|              | <b>A Right Hander</b>  | <b>B Left Hander</b>  |
| <b>Men</b>   |  |  |
| <b>Women</b> |  |  |

**A Men**



Right Hander   Left Hander

**B Women**

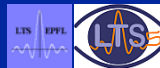
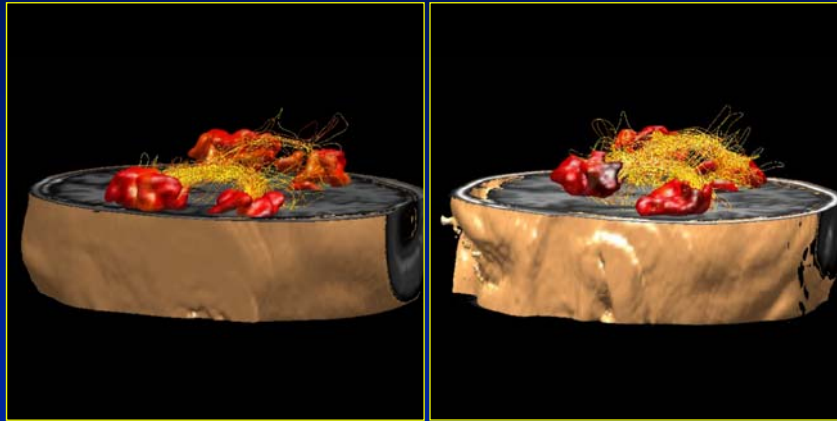


Right Hander   Left Hander

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### Application: study of language networks

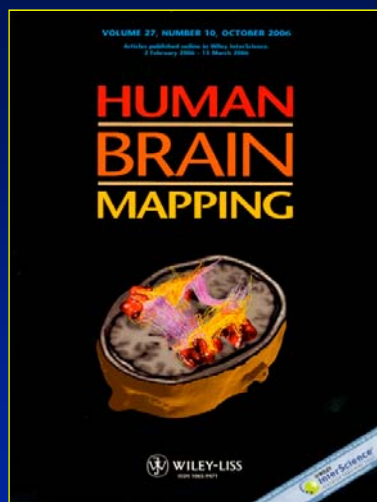
- Language networks in right and left handers



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### Application: study of language networks



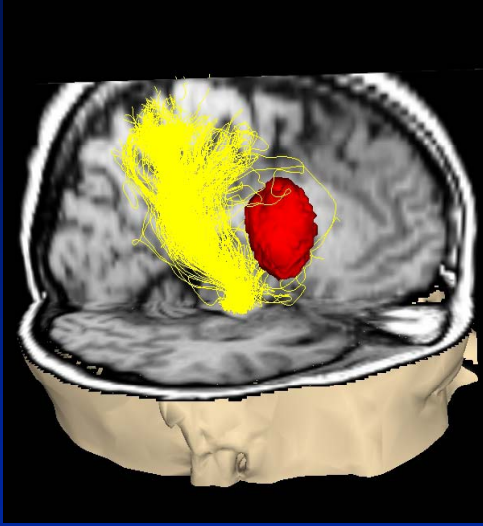
Hagmann et al. Human Brain Mapping, 2006





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### Application: diagnosis and therapy




A 3D visualization of a brain scan showing fiber tractography. A red, textured mass is visible in the center, surrounded by yellow fiber-like structures representing neural pathways. The brain is shown in a coronal section, with a 3D model of the skull overlaid.

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

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### Fast-Marching Tractography (Fast-TraC)



A visualization of an Orientation Distribution Function (ODF) map in a coronal section. The map shows a dense grid of small, multi-colored arrows (vectors) representing the orientation of white matter fibers. The colors range from red to blue, indicating different fiber orientations.

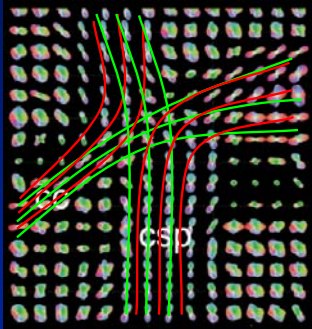
*Orientation Distribution Function map (coronal section)*



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### Fast-Marching Tractography (Fast-TraC)

- **Motivation**
  - Classical tractography algorithms: not accurate in complex fiber crossings regions, because fibers follow locally the most linear trajectories.
- **Goal**
  - Design a tractography algorithm able to map complex fiber crossings in the brain WM using a Fast-Marching approach.



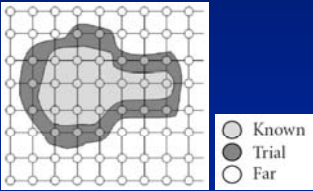



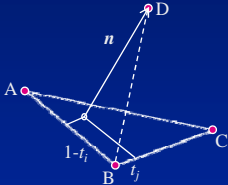
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

- **Front propagation**
  - 3D Anisotropic Fast Marching (shifted grid, 26 neighbors, Qingfen Lin 2003)








$$u_D = (1-t_i)u_A + (t_i-t_j)u_B + t_j u_C + \min\{|n \times s_1|, \dots, |n \times s_N|\}$$

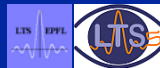
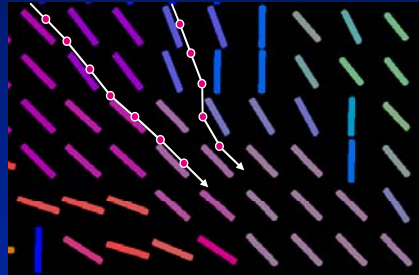



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### Fast-Marching Tractography (Fast-TraC)

- Back propagation of the fibers
  - Gradient descent through cost map  $u(\mathbf{r})$
  - Initialization points: one in each GM voxel

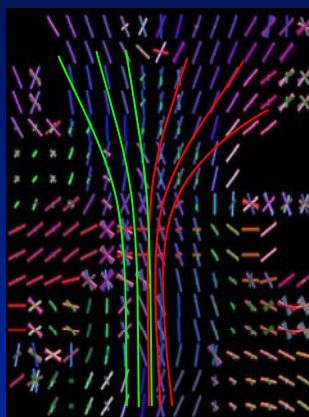


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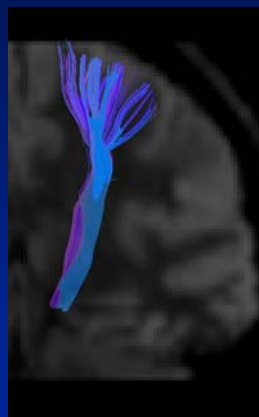


### Fast-Marching Tractography (Fast-TraC)

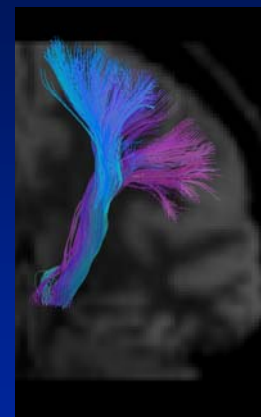
- Results: cortico-spinal tract



Local maxima  
of the ODF map



Classical streamline  
tractography (posterior view)

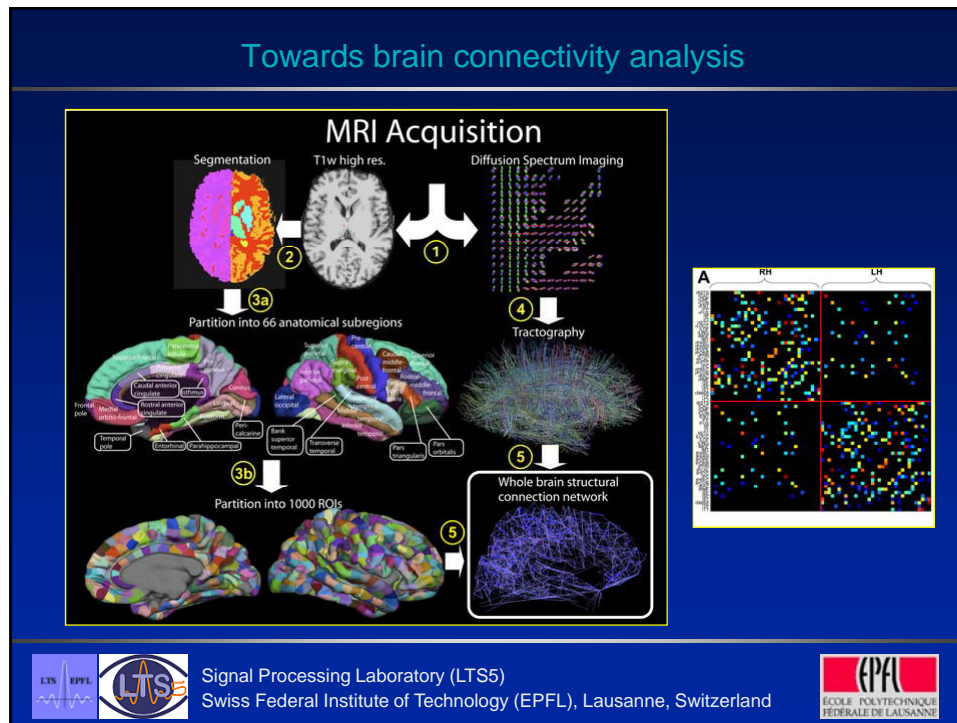


Fast-TraC  
(posterior view)



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### Computational complexity

- **Front propagation**
  - Volume of interest (WM):  $\sim 450\text{cm}^3$
  - Resolution:  $1 \times 1 \times 1 \text{ mm}^3$
  - => Number of voxels :  $\sim 450'000$
  - In each of these voxels, we have to minimize  $u_D$
  - Regions of Interest:  $\sim 1000$
  - One front propagation per ROI
  - => 998 front propagations
- **Back propagation**
  - Computed trajectories: 1 – 20 millions

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## Computational complexity

- **Computation time**
  - Approx. 20 hours (P4 3.8GHz, C++ code)
  - Each front propagation is independent, the algorithm is highly parallelizable
- **What would we gain with HPC ?**
  - Ideally, we should perform **one front propagation for every voxel** of the WM-GM interface
  - WM-GM interface: ~200'000 voxels
  - Estimated computation time without parallelization: 4000 hours!



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## Fast-Marching Tractography (Fast-TraC)

- **Discussion**
  - New methodology for whole brain tractography, able to solve fiber crossings and branchings
  - Increases the global connectivity in the brain WM
  - Preliminary results obtained on the premotor cortex show a strong improvement of tractography results compared to classical streamline
  - Need for HPC to improve the resolution of the tractography



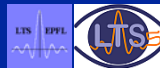
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## Conclusions

- Diffusion MRI & adapted tractography are useful tools to study brain connectivity analysis *in vivo*
- **The *connectome*** gives both a visual and quantitative representation of the brain connectivity
  - Normal subjects
  - Pathologies
    - Schizophrenia
    - Epilepsy
    - ...
  - Brain development



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## Acknowledgments

- **At the EPFL**
  - Dr Leila Cammoun
  - Mr Xavier Gigandet
  - Miss Elda Fisci
  - Dr Lisa Jonasson
  - Dr Xavier Bresson
  - The CIBM
    - Gilles Puy
- **At the CHUV**
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  - Prof. Reto Meuli
  - Dr Claudio Pollo
- **And also**
  - Prof. Van J Wedeen  
(Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Harvard Medical School)
  - Prof. Olaf Sporns (Indiana University, Bloomington, Indiana)
  - Siemens
- **Supports:**
  - Swiss SNF
  - Lausanne-Geneva Center for Biomedical Imaging (CIBM)



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