# Aging - cognition, brain imaging and genetics

## Multimodal MRI recordings, image processing, and data analysis


Arvid Lundervold MD, PhD

Neuroinformatics and Image Analysis Laboratory
Neural Networks Research Group
Department of Biomedicine, University of Bergen, Norway
https://www.uib.no/rg/neuronet


*Visual Computing Forum*

http://www.ii.uib.no/vis/vcf

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# OUTLINE

- **Multimodal MRI**

  = *Collection of MRI recordings obtained with different MR measurement techniques from the same subject - in the same imaging session*

  - Structural 3D MRI (sMRI)
  - Diffusion tensor imaging (DTI)
  - Functional BOLD MRI (fMRI) in the resting state

    ↑ *Blood Oxygen Level Dependent contrast*

- **Image processing workflows**
  - Brain morphometry (`FreeSurfer`)
  - White matter integrity and fiber tracking (`Diffusion Toolkit` & `TrackVis`)
  - Resting state networks (the `FCON1000 scripts`)

- **Longitudinal data analysis**
  - Linear mixed models (`R`: `lmer` in the `lme4` package)
  - Nonlinear mixed effects estimation (`MATLAB`: `nlmefit`)

- **Data organization**

# The multimodal MRI protocol $\text{Wave1}_{2005}$, $\text{Wave2}_{2008/9}$, $\text{Wave3}_{2011/12}$

1.5 T GE Signa Excite MRI scanner with a standard 8 chn receive only head coil:

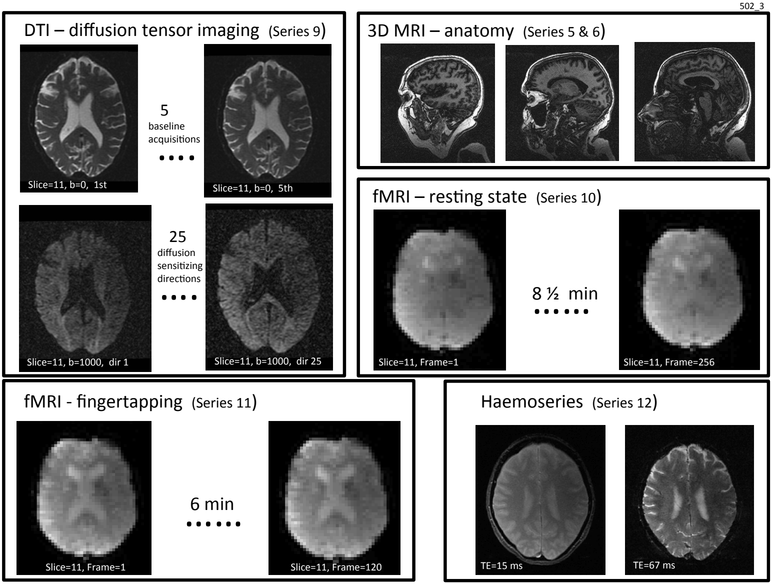
| | *Series* | *Pulse sequence parameters* | *W1* | *W2* | *W3* |
|---|---|---|---|---|---|
| 1 | Localizer 2D | TR/TE = 7.8[ms]/1.7[ms]/30[$^{O}$]; acq.voxel: $1.0 \times 1.0 \times 5.0$ [$mm^3$]; 3 [imgs] | × | × | × |
| 2 | Ax PD/T2 2D FSE | $TR/TE_1/TE_2/FA$ = 3840/12.1/84.9/90; voxel: $0.94 \times 0.94 \times 4.0$; 52 | × | | |
| 3 | Sag T1 3D FSPGR IR preped | TR/TE/TI/FA = 9.45/2.41/450/7; voxel: $0.94 \times 0.94 \times 1.40$; 124 | × | | |
| 4 | Sag T1 3D FSPGR IR preped | [ same as 3 to improve SNR for FreeSurfer segmentation ] | × | | |
| 5 | Sag T1 3D FSPGR IR preped | TR/TE/TI/FA = 9.12/1.77/450/7; voxel: $0.94 \times 0.94 \times 1.40$; 124 | | × | × |
| 6 | Sag T1 3D FSPGR IR preped | [ same as 5 to improve SNR for FreeSurfer segmentation ] | | × | × |
| 7 | Ax DTI, EP SE, 26 slices | TR/TE/FA = 7900/97.1/90; 25 b=1000, 5 b=0; voxel: $0.94 \times 0.94 \times 4.0$; 780 | × | | |
| 8 | Ax DTI, EP SE, 25 slices | TR/TE/FA = 7900/104.8/90; 25 b=1000, 5 b=0; voxel: $0.94 \times 0.94 \times 4.0$; 750 | | × | |
| 9 | Ax DTI, EP SE, 25 slices | TR/TE/FA = 7900/110.5/90; 25 b=1000, 5 b=0; voxel: $0.94 \times 0.94 \times 4.0$; 750 | | | × |
| 10 | Ax fMRI GRE EPI Resting | TR/TE/FA=2000/50/90; voxel: $3.75 \times 3.75 \times 5.5$; 25 slices; 256 volumes; 6400 | | × | × |
| 11 | Ax fMRI GRE EPI Fingertap | TR/TE/FA=3000/50/90; voxel: $3.75 \times 3.75 \times 5.5$; 25 slices; 120 volumes; 3000 | | × | × |
| 12 | Ax GRE Haemoseries | $TR/TE_1/TE_2/FA$=540/15/67/20; voxel: $0.94 \times 0.94 \times 4.0$; 25 slices; 50 | | | × |

FSE=Fast spin-echo; FSPGR=Fast spoiled gradient-echo; EP SE=Echo-planar spin-echo; GRE EPI=Gradient-echo echo-planar; IR=Inversion recovery.

- Image acquisitions being analysed in the project[1]:
  - → Structural 3D Anatomy - $2 \times 124$ images / subject / wave (series 5 & 6)
  - → Diffusion tensor imaging - 750 images / subject / wave (series 9)
  - → Resting state fMRI - 6400 images / subject / wave (series 10)

[1] Up until now ...

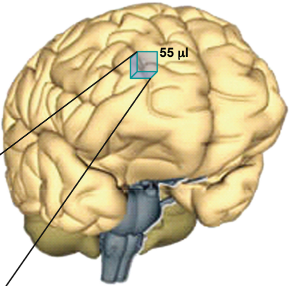
# An example of multimodal MRI recordings



# Voxels and their constituents in brain MRI

Scales:

- Microscopic
- **Mesoscopic** [mm] [s]
- Macroscopic

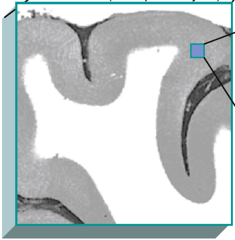



" Given these neuro-statistical data, what are the actual contents of a neuroimaging voxel? An examination of the 300 top-cited cognitive fMRI studies suggests that the commonly used in-plane resolution is 9–16 mm$^2$, for slice thicknesses of 5–7 mm. The average voxel size before any pre-processing of the data is thus 55 μl (or 55 mm$^3$). Often the effective size is 2–3 times larger due to the spatial filtering that most investigators apply to improve the functional SNR. Less than 3% of this volume is occupied by vessels and the rest by neural elements.

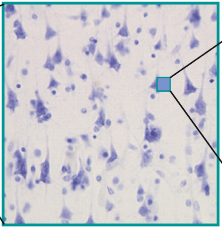
A typical **fMRI voxel of 55 μl** in size thus contains **5.5 million neurons**, **2.2–5.5 x 10$^{10}$ synapses**, **22 km of dendrites** and **220 km of axons**. " !!

**N.K. Logothetis, *Nature* 2008 p.875**

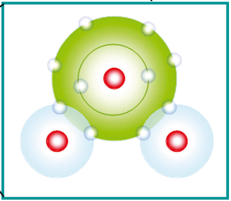
Tissue
(brain parenchyma)



Cells & capillaries



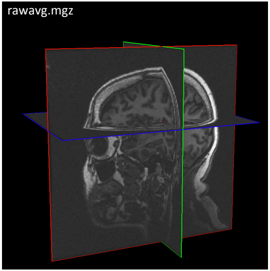
Water molecules / protons

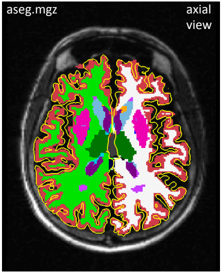


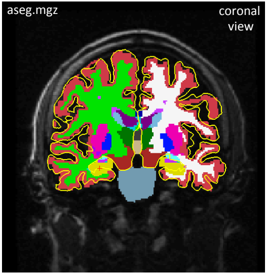
From Baars & Gage: *Cognition, Brain, and Consciousness* (2010)

# Image processing workflows - FreeSurfer

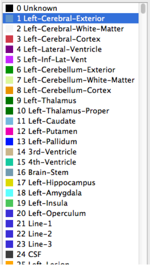
Brain segmentation:



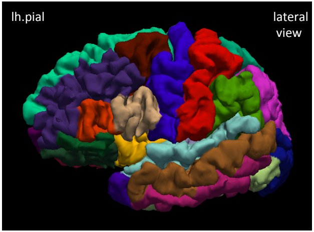



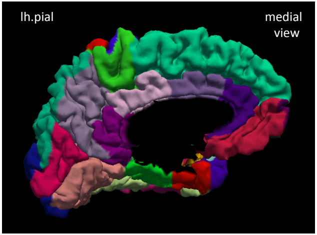




FreeSurferColorLUT




Brain surface reconstruction and cortical parcellation:

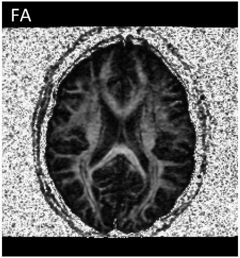


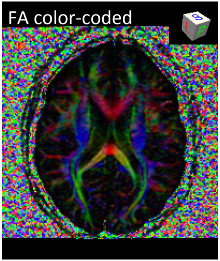



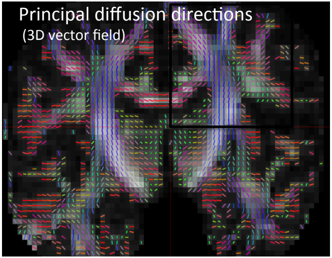

507_3

FreeSurfer 5.1 & Freeview

# Image processing workflows - Diffusion Toolkit




From: Are Losnegård, In prep.

The diffusion tensor:

$$\mathrm{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix}$$

Eigen decomposition:

$$\mathrm{D}\,\varepsilon_1 = \lambda_1 \varepsilon_1$$
$$\mathrm{D}\,\varepsilon_2 = \lambda_2 \varepsilon_2$$
$$\mathrm{D}\,\varepsilon_3 = \lambda_3 \varepsilon_3$$

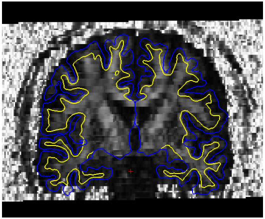
$$\lambda_1 \geq \lambda_2 \geq \lambda_3 \geq 0$$

Principal diffusion direction: $\varepsilon_1 = (\varepsilon_{1x}, \varepsilon_{1y}, \varepsilon_{1z})$

Fractional anisotropy (“white matter integrity”):

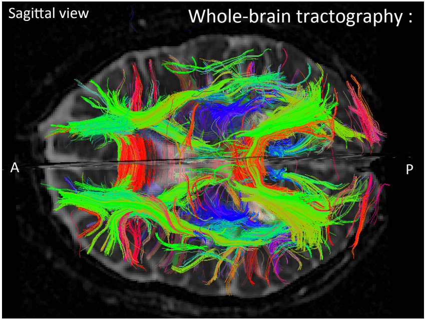
$$\mathrm{FA} = \sqrt{\frac{1}{2}}\,\frac{\sqrt{(\lambda_1-\lambda_2)^2+(\lambda_1-\lambda_3)^2+(\lambda_2-\lambda_3)^2}}{\sqrt{(\lambda_1^2+\lambda_2^2+\lambda_3^2)}} \qquad 0 \leq \mathrm{FA} \leq 1$$

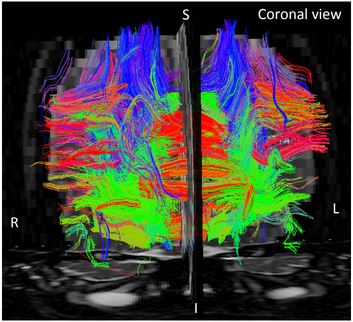
Checking goodness of co-registration between Anatomy and DTI (FA)

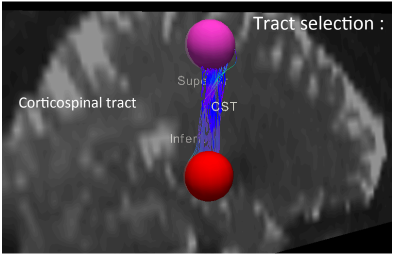


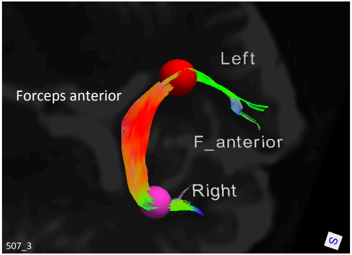
aging_anatomy_dti_integration_centos_macos_al20130228.m

# Image processing workflows - TrackVis



# Image processing workflows - `FCON1000 scripts`

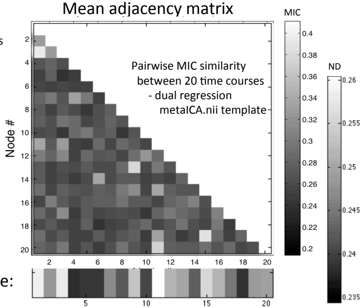
Graph analysis of resting state functional connectivity:

(Eikeland et al, HBM 2013)

Wave 2 & 3: 80 subjects

MIC =
Maximal
Information
Coefficient

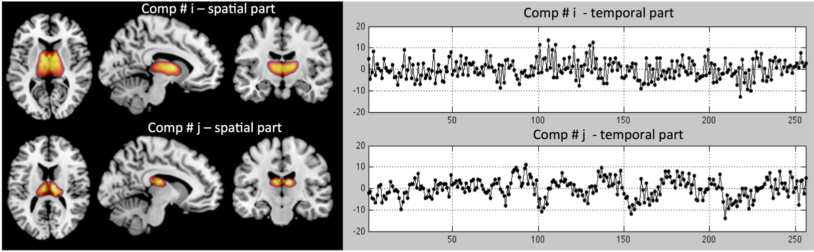
(Reshef et al, 2011)




Node degree:

- Name
- 0_preprocess.sh
- 1_anatpreproc.sh
- 2_funcpreproc.sh
- 3_registration.sh
- 4_segment.sh
- 5_nuisance.sh
- 6_singlesubjectRSFC.sh
- 7_singlesubjectfALFF.sh
- 8_singlesubjectDR.sh
- batch_list.txt
- batch_process.sh
- example_seed_list.txt
- Fox_seed_list.txt
- seeds
- templates
- tissuepriors

http://www.nitrc.org/plugins/mwiki/index.php/fcon_1000:ScriptUse



## Longitudinal data analysis (LDA) - Linear mixed-effect models

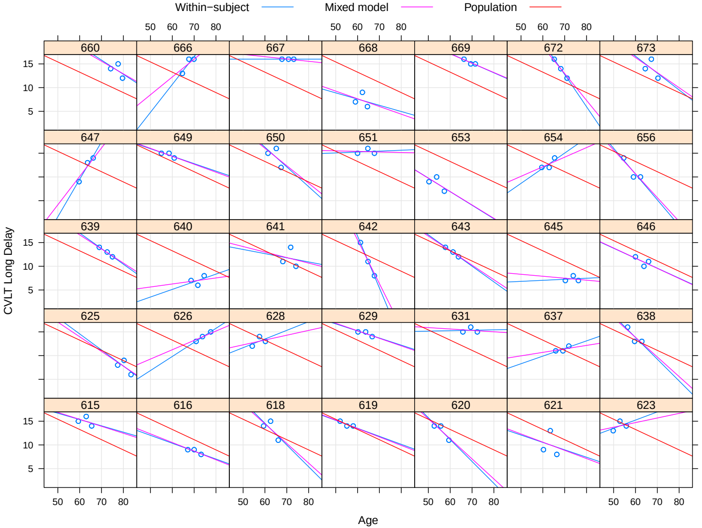
Let $y_{ij}$ denote the response at the $j$th observation of the $i$th subject; $i = 1, \ldots, N$, $j = 1, \ldots, n_i$, and $x_{ij}$ be the corresponding value of the explanatory (covariate) variable $x$, then the standard linear mixed-effects model with random intercept $b_{0i}$ and random slope $b_{1i}$ is:

$$y_{ij} = \beta_0 + \beta_1 x_{ij} + (b_{0i} + b_{1i} x_{ij}) + \epsilon_{ij}$$

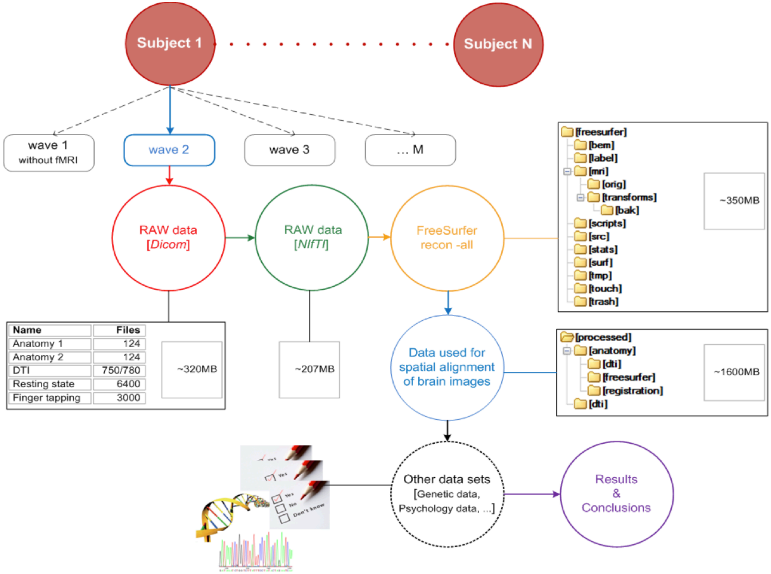
- the $\beta_k$s are fixed effect parameters
- the $b_{ki}$s are random effect parameters
- $\epsilon_{ij}$ is the error for observation $j$ in subject $i$, where the errors for subject $i$ are assumed to be multivariate normally distributed

# CVLT LongDelay - fit a linear mixed-effect model

$\texttt{Age}_{ij}$ as a predictor for $y_{ij} = \texttt{LongDelay}_{ij}$ across subjects $i = 1, \ldots, 106$ and waves $j = 1, 2, 3$: $\quad y_{ij} = \beta_0 + \beta_1 \mathrm{Age}_{ij} + (b_{0i} + b_{1i}\mathrm{Age}_{ij}) + \epsilon_{ij}$ (CVLT_analysis_long_al20130213.R)



# Data organisation (SVN/mySQL - Sebastian Bablock, 2009)



# Thanks !

UiB project members

and collaborators:

| | |
|---|---|
| Erlend Hodneland | **Biomed/math,** post doc |
| Martin Ystad | **Biomed**, MD, PhD |
| Steinunn Adolfsdottir | **IBMP,** PhD student |
| Judit Haasz | **Biomed,** MD PhD student |
| Erling Tjelta Westlye | **Biomed,** MD PhD student |
| Alexandra Vik | **IBMP,** PhD |
| Rune Eikeland | **IBMP**, PhD |
| Erik Hanson | **Math,** PhD |
| Martin Andersson | **IBMP,** PhD |
| Jonn-Terje Geitung | **Radiology,** HDS |
| Tom Eichele | **Neurology/IBMP**, MD, PhD |
| Eike Wehling | **IBMP,** post doc |
| Are Losnegård | **Biomed,** PhD student |
| Ivar Reinvang | **UiO** |
| Thomas Espeseth | **UiO / IBMP** |
| Tessa Welte | **Tu/E, Eindhoven, Netherlands** |
| Clément de Ribet | **ISIMA, Blaise Pasacal University, FR** |
| | |
| MedViz | **UiB / HUS / CMR** |
| The Vis Group | **UiB / Informatics** |

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