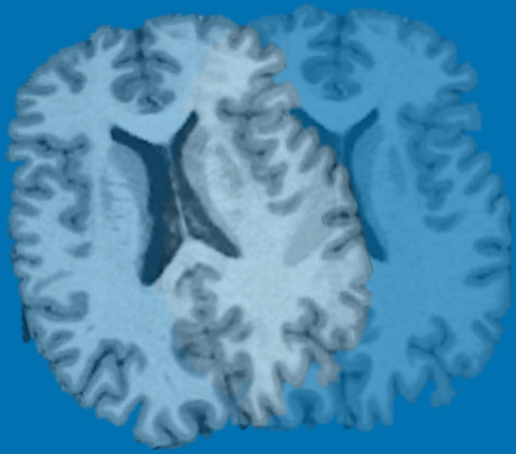
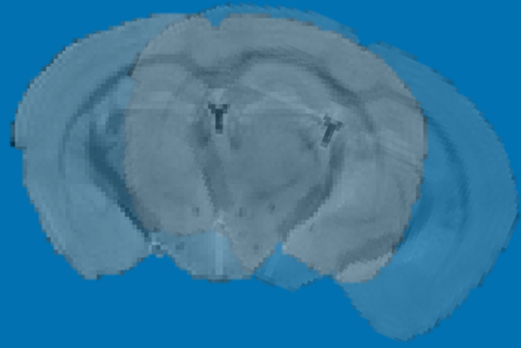




(BRAIN) MR IMAGE REGISTRATION

Meritxell Bach Cuadra[1,2]

[1]CIBM Center for Biomedical Imaging

[2]Radiology Department, Lausanne University Hospital and University of Lausanne

Invited lecture, CIBM translational MR neuroimaging & spectroscopy (PHYS-760), EPFL

UNIL | Université de Lausanne

Medical Image Analysis Laboratory

OBJECTIVES

- Understand the **importance of medical image registration** and **cite some examples.**
- Be able to enumerate the **main actors** of an image registration process.
- Do a good guess on which **type of transformation** could be suitable for a given “problem”.
- Be able to explain the concept of **atlas-based segmentation.**

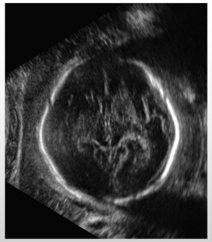
OUTLINE

- General context
- "Definition" and use case scenarios
- Mathematical formulation
  - Features
  - Similarity
  - Transformers: rigid and non-rigid
- In practice !
- New trends

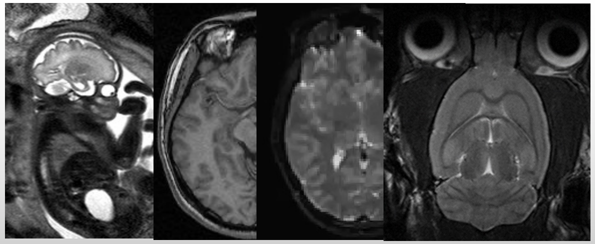
GENERAL CONTEXT

BRAIN IMAGING

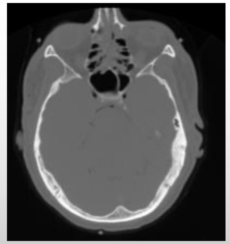
Anatomical Imaging



Ultrasound (US)

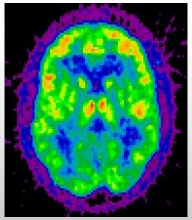


Magnetic Resonance (MR)

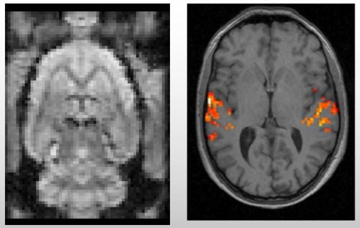


Computer Tomography (CT)

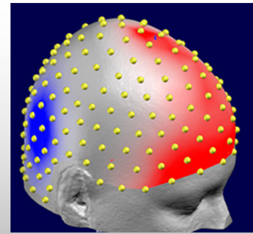
Functional Imaging



Positron Emission Tomography (PET)



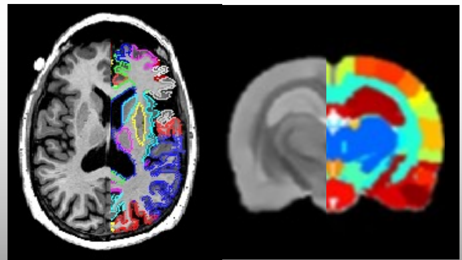
Functional MR (fMR)



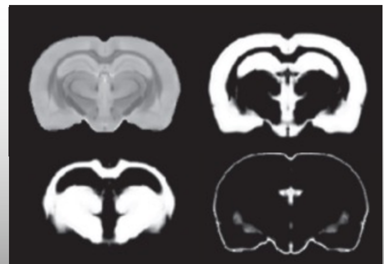
EEG[1] & MEG

Reference Imaging

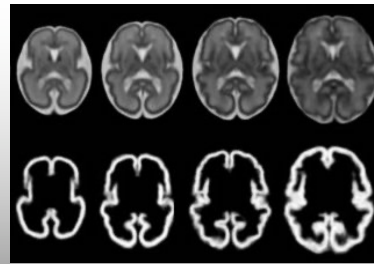
Atlases



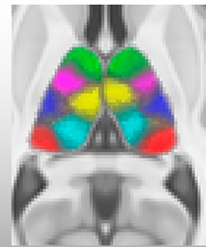
Deterministic[2,3]



Brain tissue[3]



Tissue development [4]



Thalamic nuclei[5]

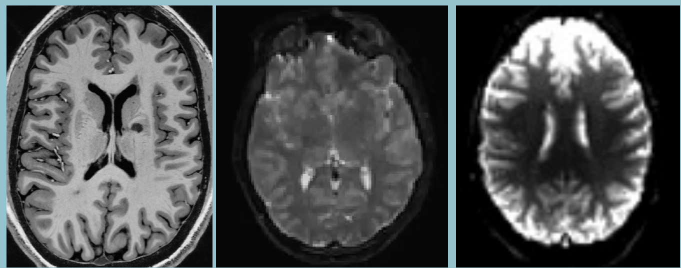
Probabilistic

[1] Michel & Brunet Front. Neurology 2019, [2] Heckemann et al Neuroimage 2010, [3] Barrière et al Nat Com 2019 , [4] Serag et al BMVA 2012 , [5] Najdenovska et al, Scientific Data 2018

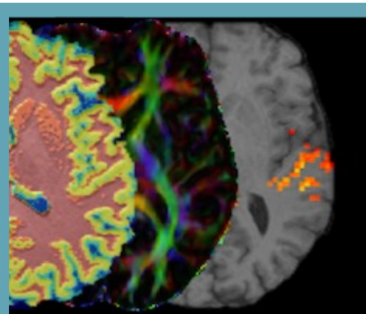
IMAGE ANALYSIS PIPELINE

ACQUISITION

MEASUREMENTS



FEATURE EXTRACTION



RESEARCH/CLINICAL STUDY

SINGLE SUBJECT

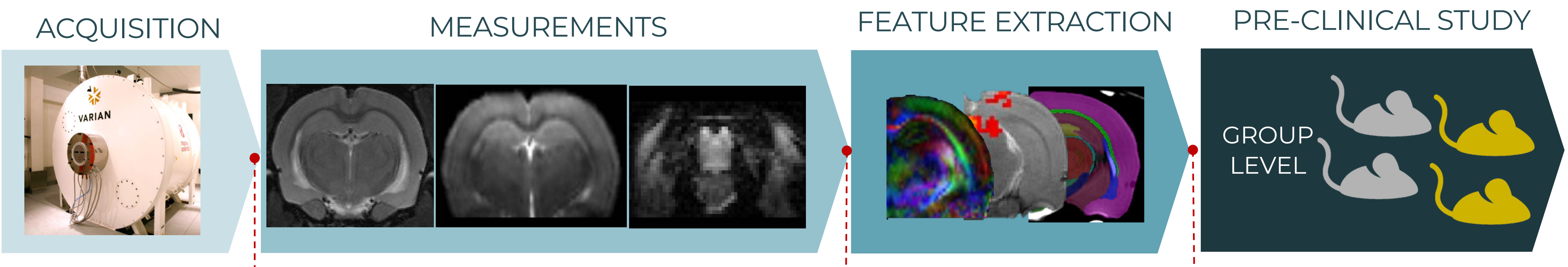
GROUP LEVEL

- Reconstruction
- Distortion correction
- Motion compensation
- Artefact removal
- …

- Denoising, Resolution enhancement,
- Registration, Segmentation,
- Distortion correction
- Model fitting, Fibre tracking, connectivity
- …

- Classification,
- Clustering,
- Regression,
- Voxel- and vertex-wise analysis
- Network analysis
- …

IMAGE ANALYSIS PIPELINE



- Reconstruction
- Distortion correction
- Artefact removal
- ...

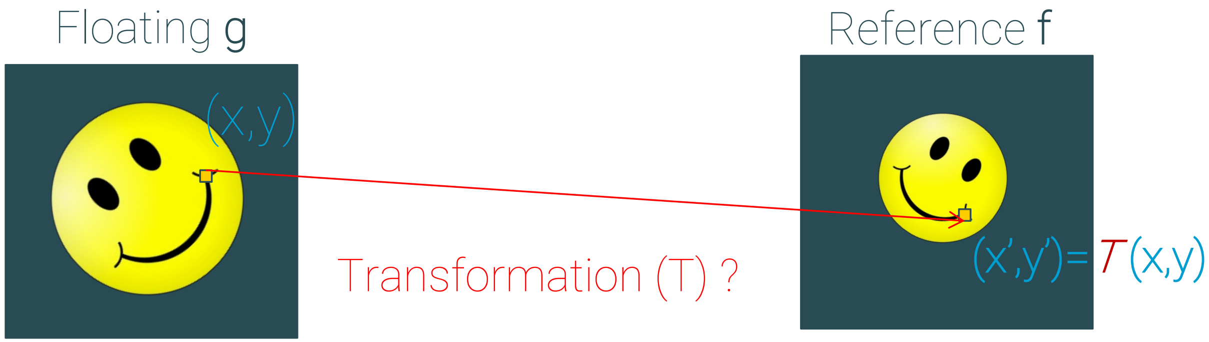
- Denoising,
- Registration, Segmentation,
- Distortion correction
- Model fitting, Fibre tracking, Connectivity
- ...

- Classification,
- Clustering,
- Regression,
- Voxel- and vertex-wise analysis
- Network analysis
- ...

CIBM.CH

DEFINITION AND EXEMPLES

DEFINITION



Registration is the process of **finding the transformation (T)** that put different images into sptaial correspondence

Co-registration, matching, alignment, spatial normalization, etc

QUESTION

- Could you mention one or few image registration application / examples ?

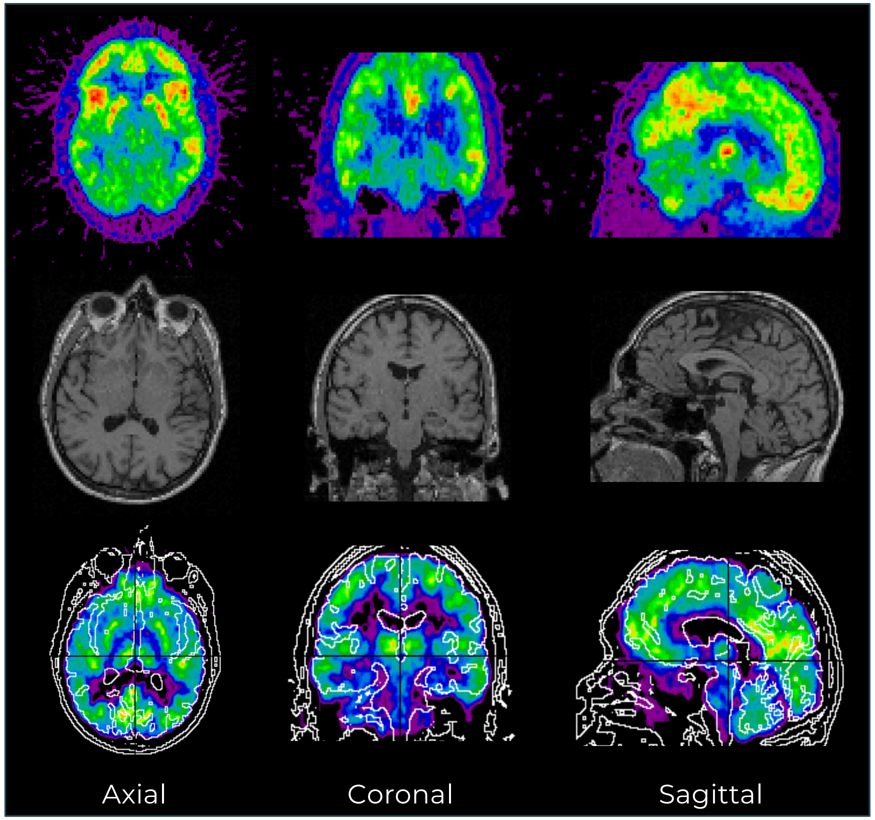
IMAGE FUSION

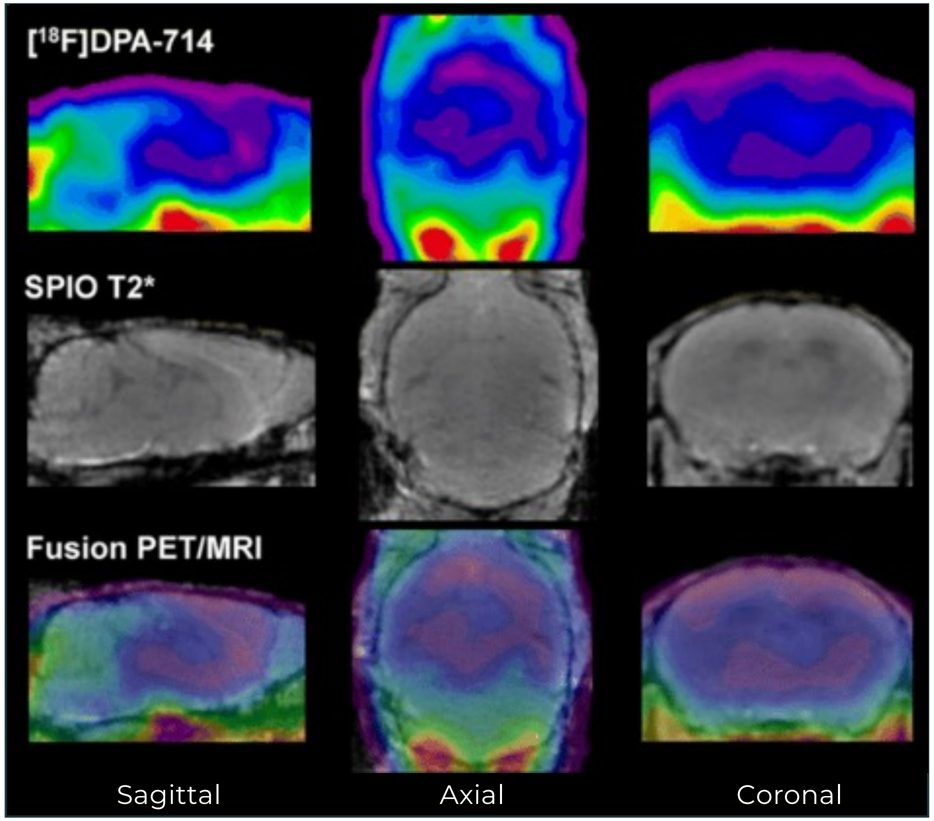
Multi-modal imaging

PET

MRI

Fusion



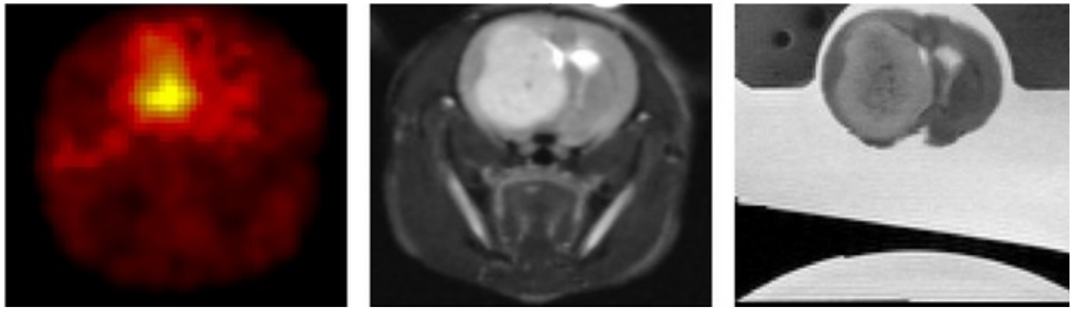


H. Zaidi et al, PET Clinics 2008

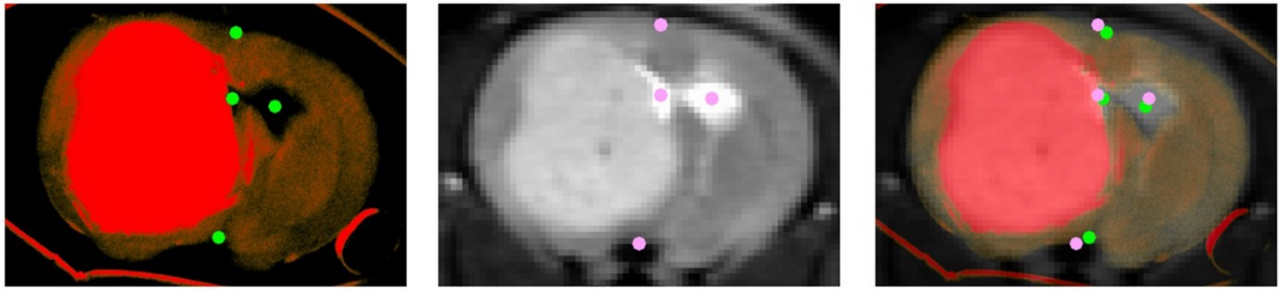
A. R. Coda et al, EJ NM Med and Mol Img, 2021

IMAGE FUSION

Multi-modal



PET, *In vivo* MRI, *ex vivo* MRI



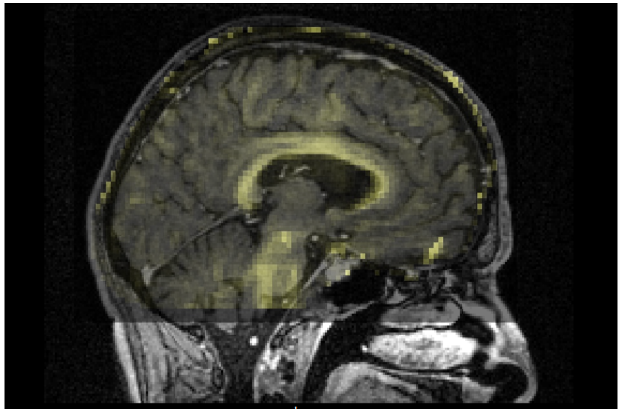
Fluorescence, *In vivo* MRI, Fusion

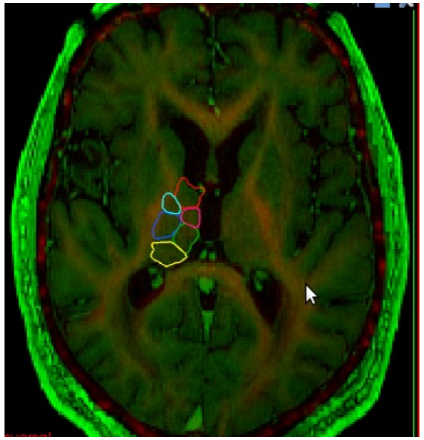
M. L. Scarpelli et al, Scientific Reports, 2020

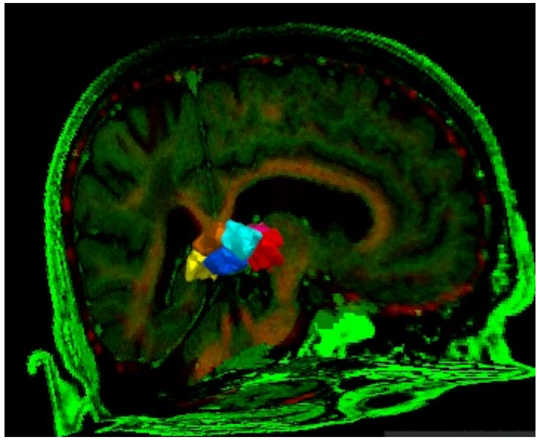
IMAGE FUSION

Treatment planning: VIM targeting for therapy of movement disorders[1]

- T1w thalamus segmentation
- Clustering of the thalamic nuclei in diffusion MRI[2]
- Planning: check internal capsule and thalamus



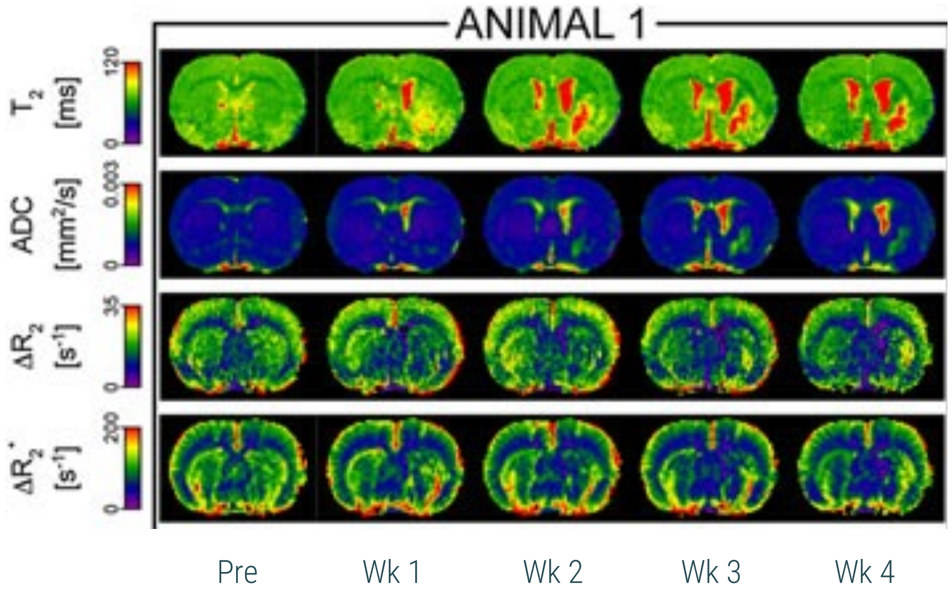




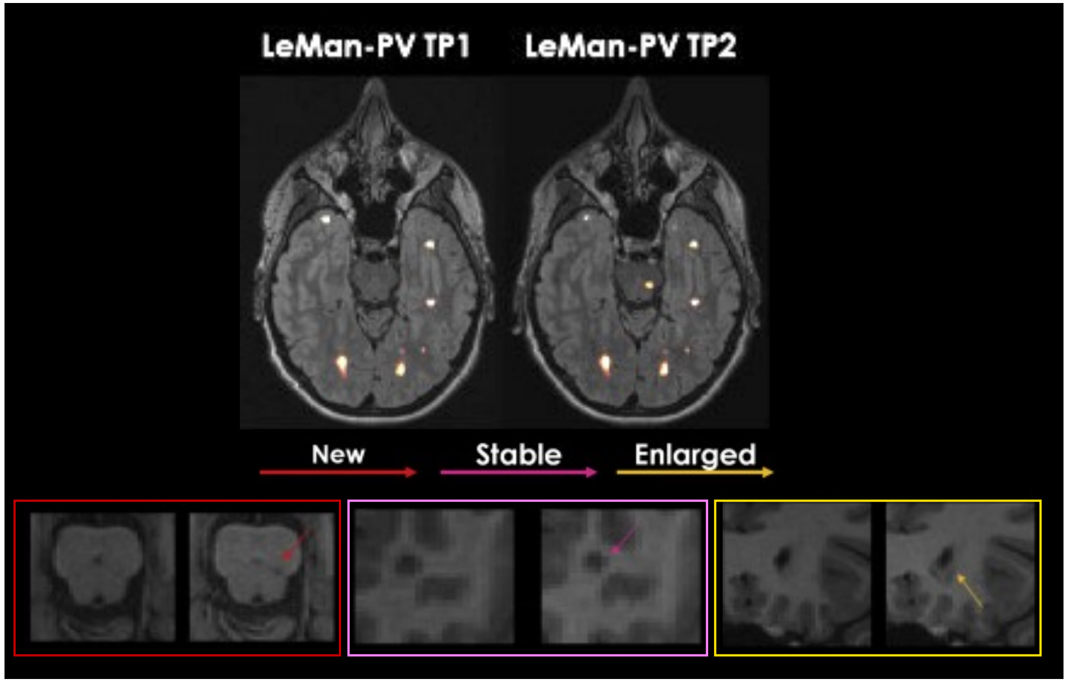
[1] E. Najdenovska*, C. Tuleasca* et al, Scientific Reports 2019, [2] E. Najdenovska*, G Battistella* et al, Brain Structure and Function, 2017.

LONGITUDINAL ANALYSIS

Vascular changes due to stroke[1]



Multiple Sclerosis follow up[2]



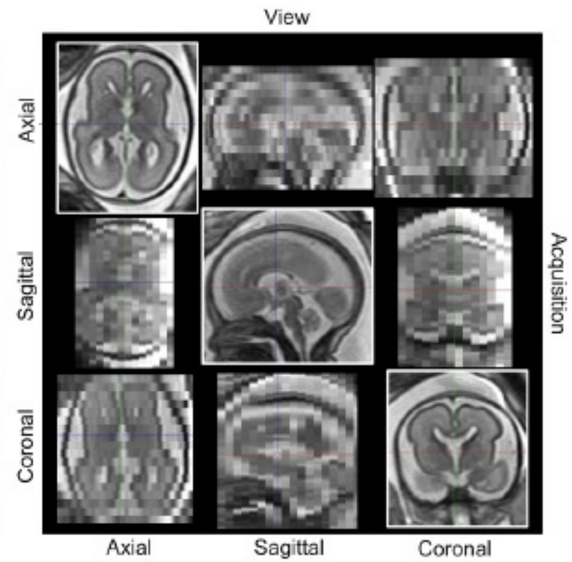
[1] P. Boehm-Sturm et al, Contrast Media & Mol Img, 2012.

[2] M.J. Fartaria et al, NeuroImage Clinical 2019.

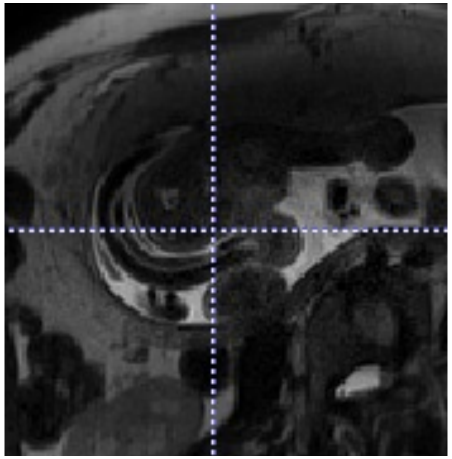
IMAGE RECONSTRUCTION

In-vivo fetal brain 3D high-resolution reconstruction[1]

Clinical acquisition



Motion

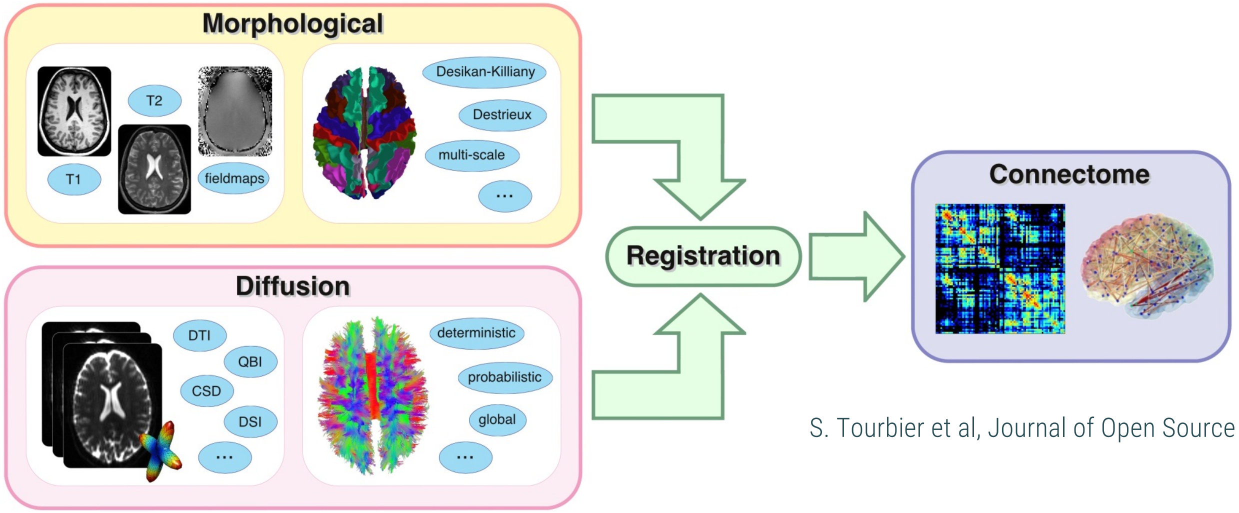


Super-resolution reconstruction[2]

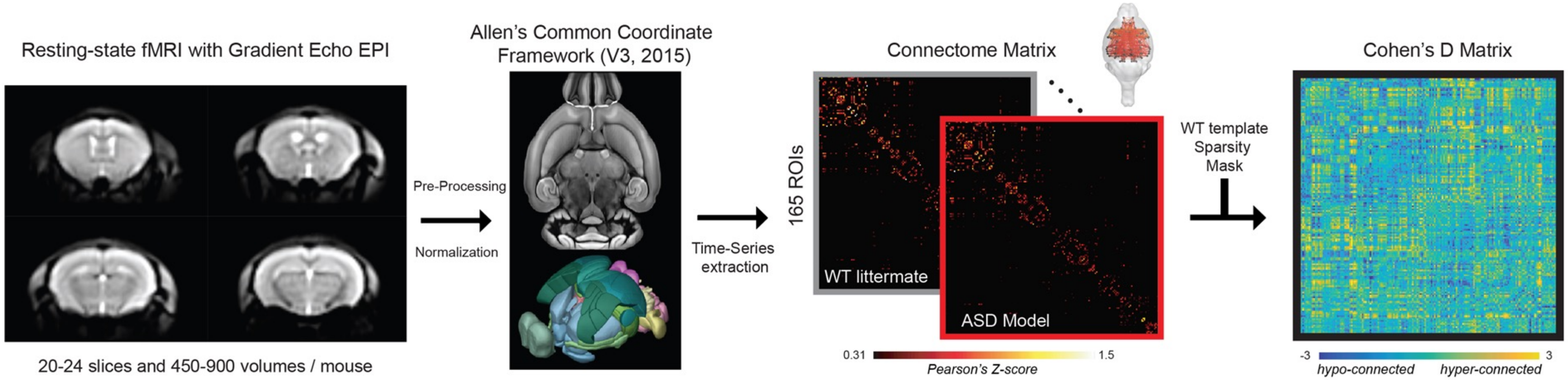
[1] https://wp.unil.ch/mial/research/projects/super-resolution-t2w-foetal-brain-mri/ ,
[2] S. Tourbier et al, Neuroimage, 2015, https://github.com/Medical-Image-Analysis-Laboratory/mialsuperresolutiontoolkit

FNSNF Fonds national suisse de la recherche scientifique
205321-141283
205321-182602

T1w (T2w) & Diffusion/fMRI registration



S. Tourbier et al, Journal of Open Source Software 2022

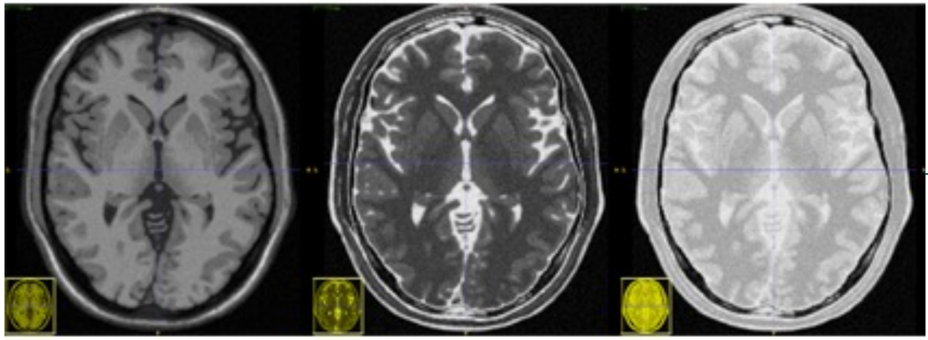


V. Zerbi et al, Mol. Psychiatry 2021

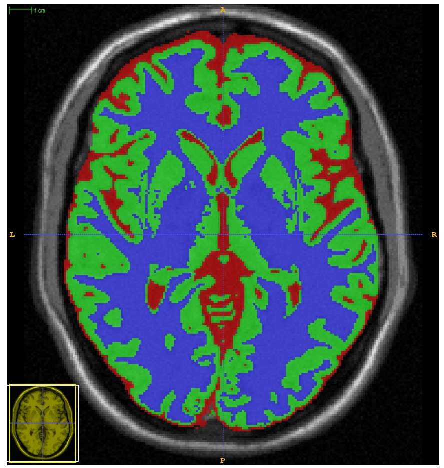
BRAIN MRI TISSUE SEGMENTATION

Multi-spectral segmentation methods

T1w T2w Proton density



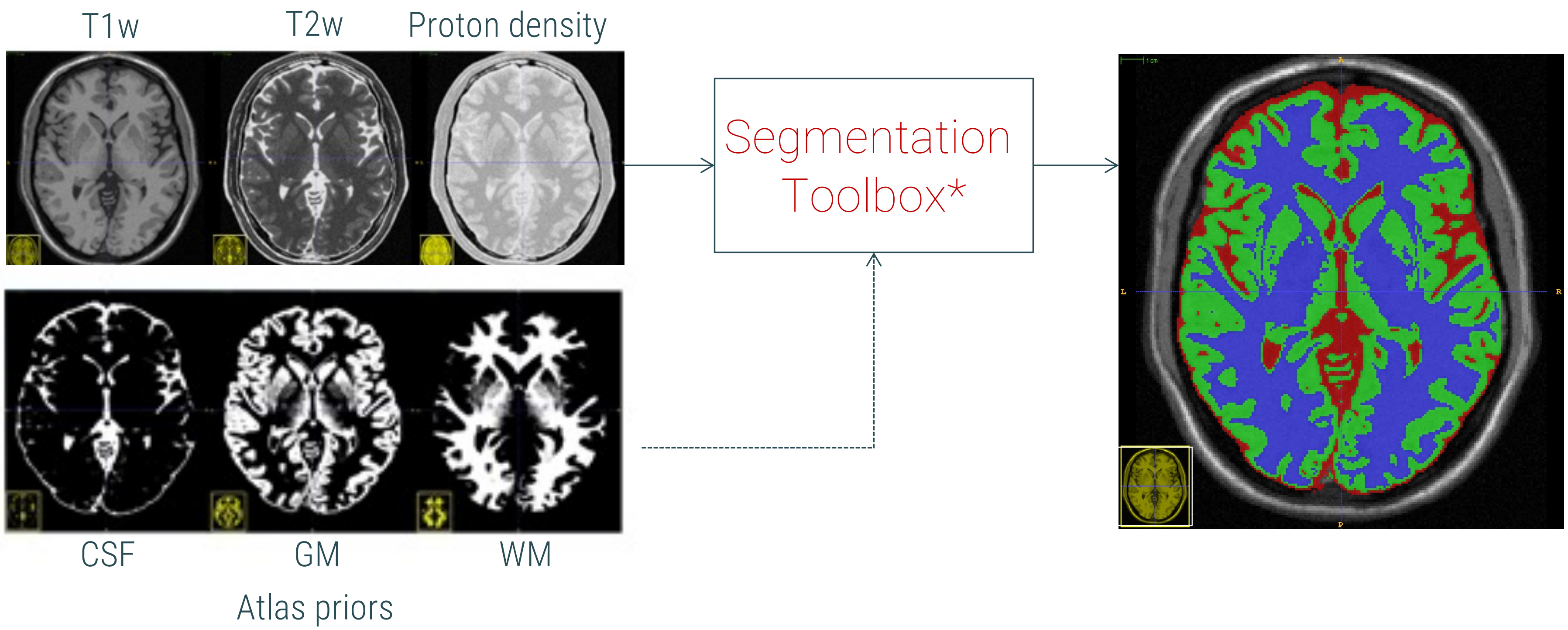
Segmentation method



Adapted from O. Esteban, et al, Comp Meth Prog Biomed, 2014, *Singh et al, Annals of Neuroscience 2021.

BRAIN MRI TISSUE SEGMENTATION

Multi-spectral segmentation methods



Adapted from O. Esteban, et al, Comp Meth Prog Biomed, 2014, *Singh et al, Annals of Neuroscience 2021.

REGISTRATION IN A COMMON SPACE

Spatial normalization

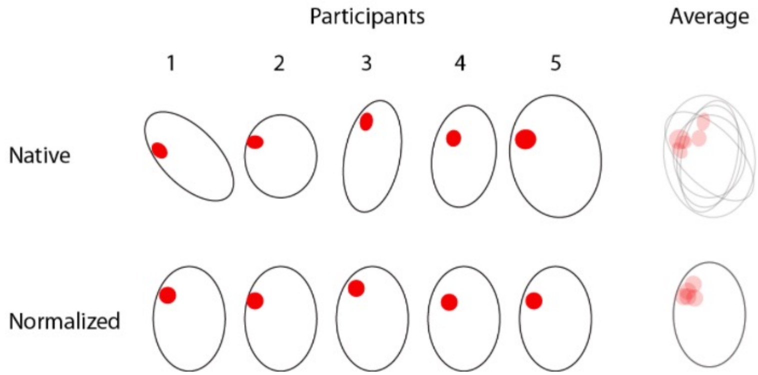


Image from http://jpeelle.net/mri/

- Choice of the «template» [1,2]

Talaraich

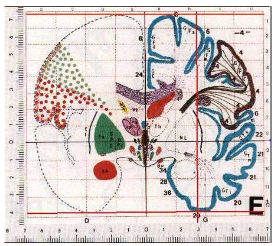
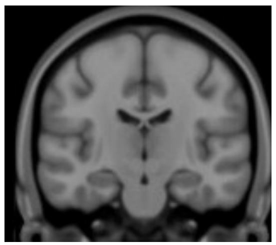


Image from Talaraich Atlas (1988)

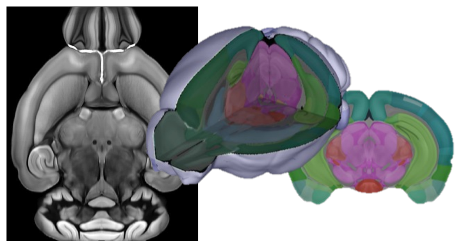
Stereotaxic coordinates

MNI



https://mcin.ca/

Allen Mouse Brain



Wang et al, Cell 2020

- Customized: pediatric, age-matched, disease, etc

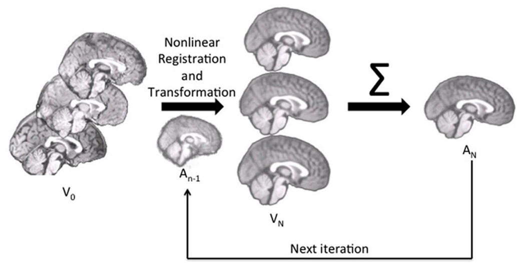
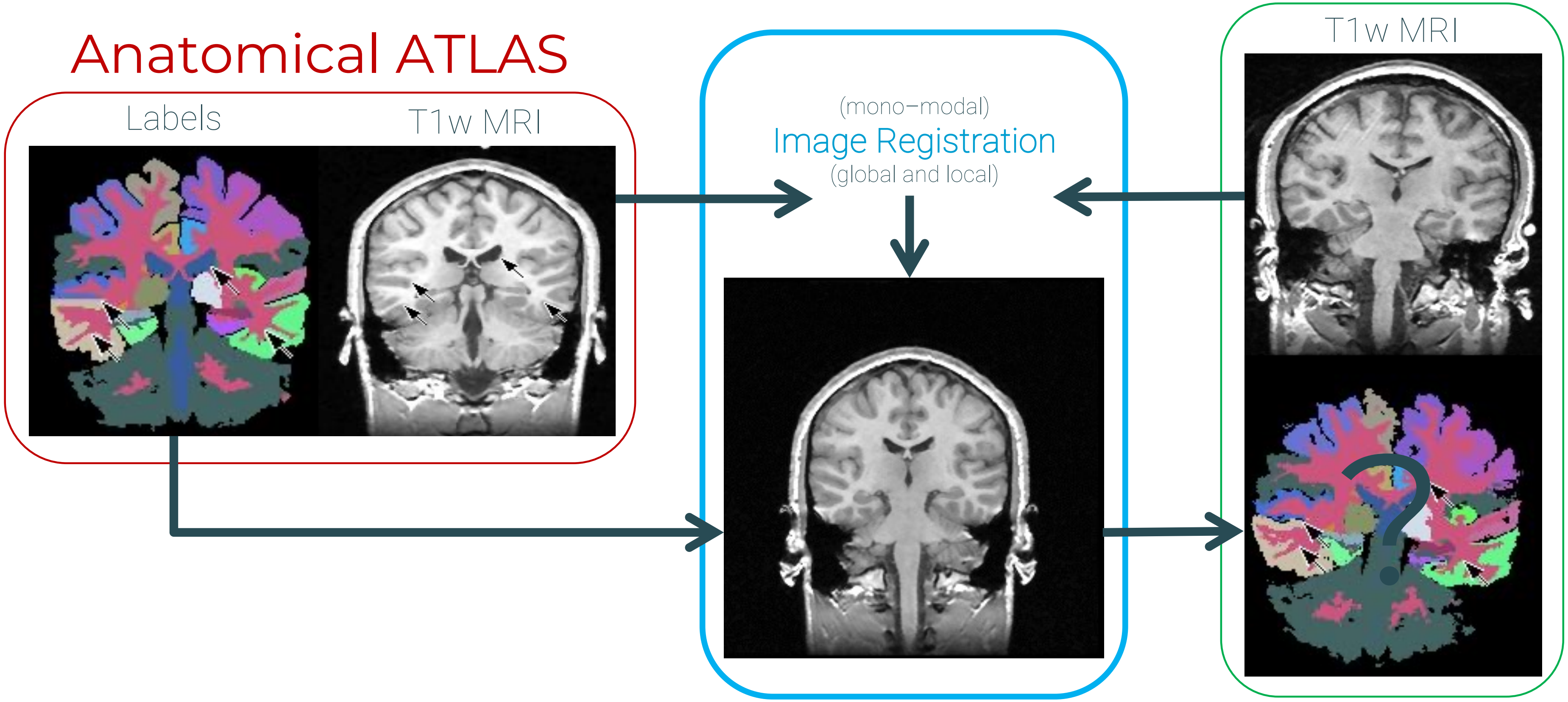


Image from Fillmore et al, Front. Aging Neurosc. 2015

[1] TemplateFlow, https://www.researchsquare.com/article/rs-264855/v1, [2] WL Nowinski, Neuroinformatics, 2021

ATLAS-BASED SEGMENTATION*

Approaching a segmentation problem through image registration



Deformed atlas labels

SEGMENTATION

*Cabezas et al, Review on Atlas-based Segmentation of Magnetic Resonance Brain Images, Computer Methods and Programs in Biomedicine, 2011.

SUMMARY OF REGISTRATION EXAMPLES

Within the same subject

- Co-registration
- Motion/position correction
- Multi-modal imaging
- Longitudinal studies

Between different subjects

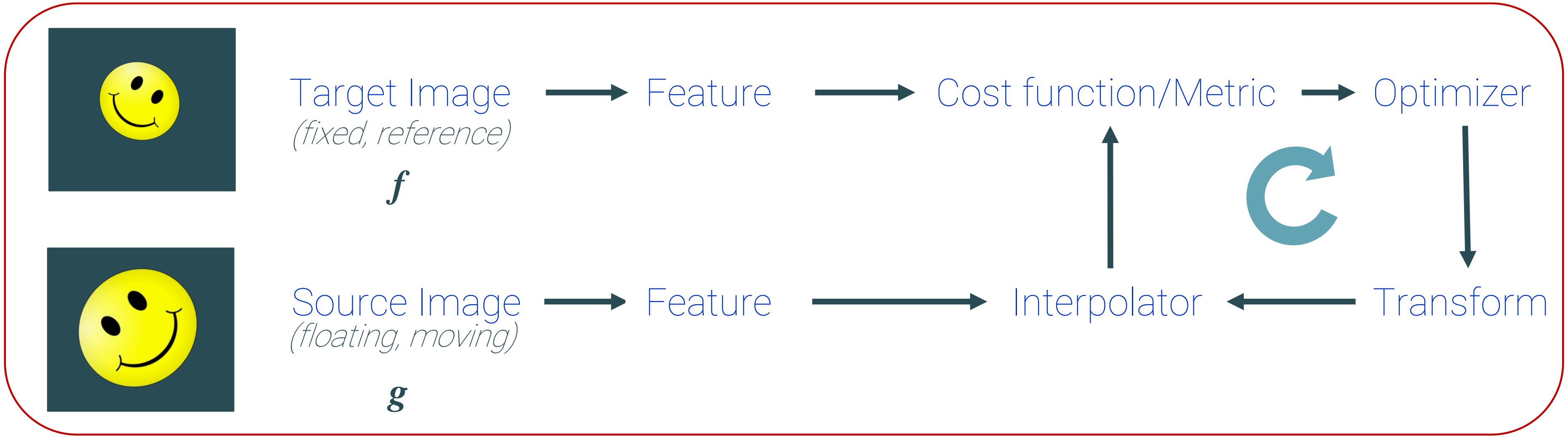
- Spatial normalization
- Capturing anatomical variability between subjects
- Pair of images
- Group studies
- Atlas registration

MATHEMATICAL FORMULATION

MATHEMATICAL DEFINITION

Image registration as an energy optimization problem

$$T^* = \underset{T \in \mathrm{T}}{argmin}\ \mathrm{cost}(f, T \circ g)$$



TAXONOMY OF REGISTRATION METHODS

How to classify the different registration methods ?*

$$\boxed{T^{*} = \underset{T \in \mathrm{T}}{argmin}\ \mathrm{cost}(f, T \circ g)}$$

A. Image features

B. Cost function: Similarity/Distance

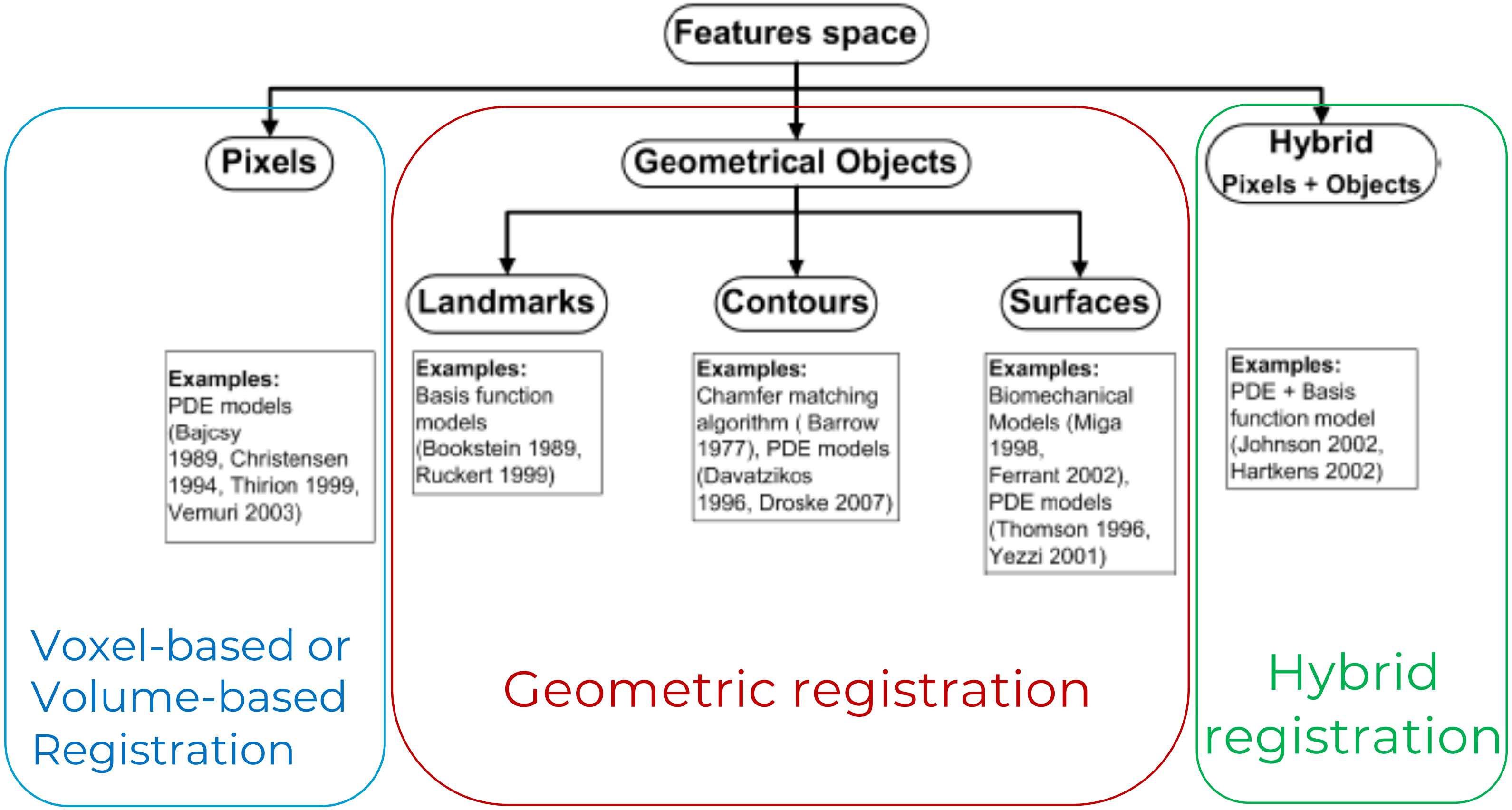
C. Nature and domain of possible transformation

Interpolation and optimizer

- Image modality available?
- Ultimate goal?

*Maintz et al, "A survey of medical image registration", Medical Image Analysis, 1998.

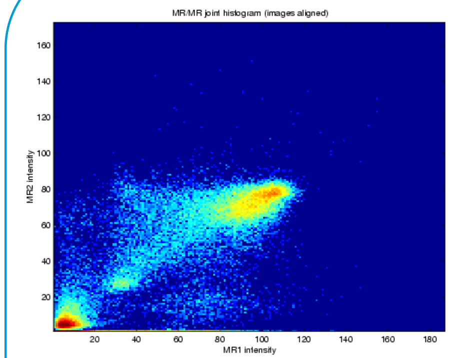
A. CLASSIFICATION BASED ON FEATURES



B. CLASSIFICATION BASED ON COST FUNCTION

Similarity Metrics

- **Intensity-based**
  - **Mono-modal**
    - Absolute or squared intensity difference
    - Correlation
  - **Multi-modal**
    - Absolute or squared gradient difference
    - Joint entropy
    - Mutual information
- **Distance-based**
  - **Geometrical features**
    - Euclidean distance
    - Procrustean metric
    - Curvature



Intensity-based registration

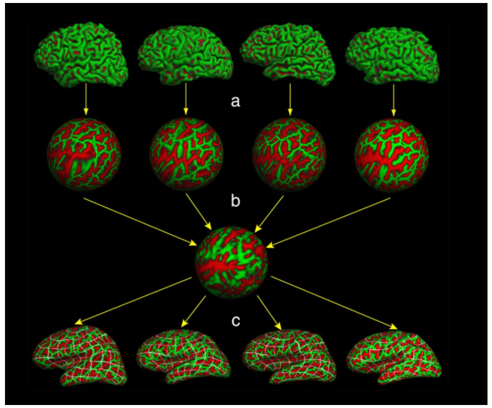
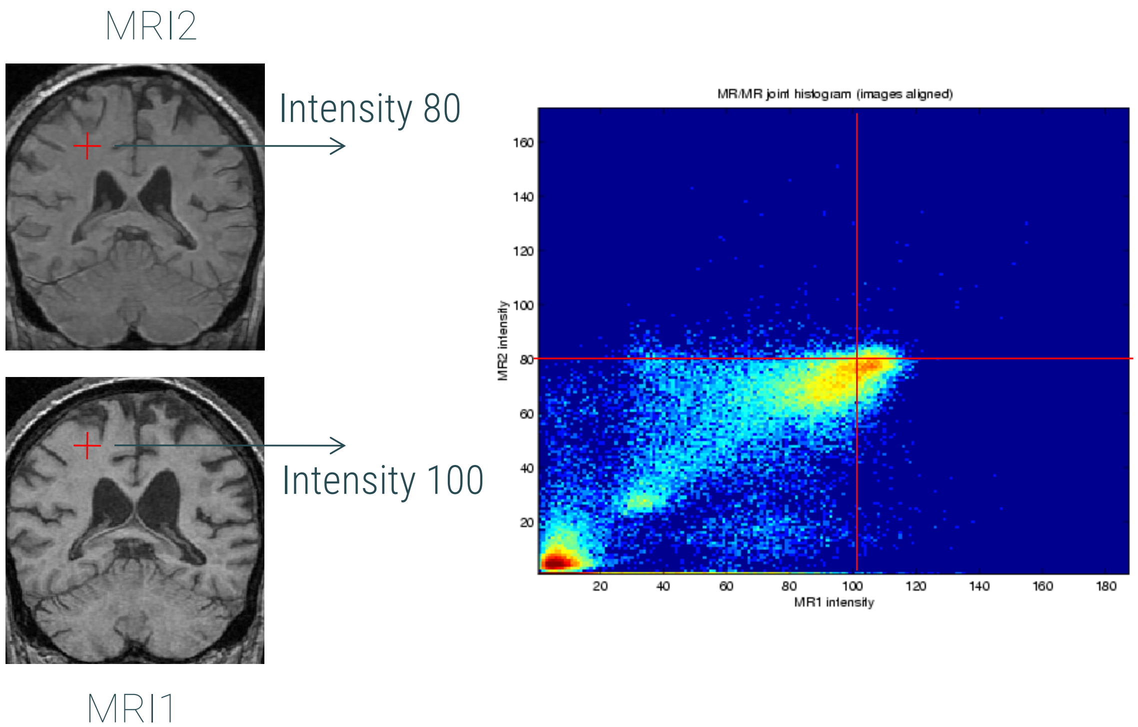


Image from Freesurfer, B. Fischl

INTENSITY-BASED REGISTRATION

Joint image histogram



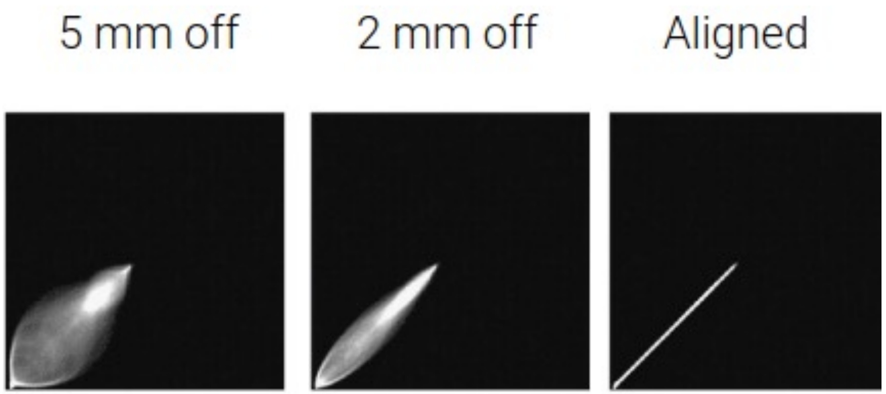
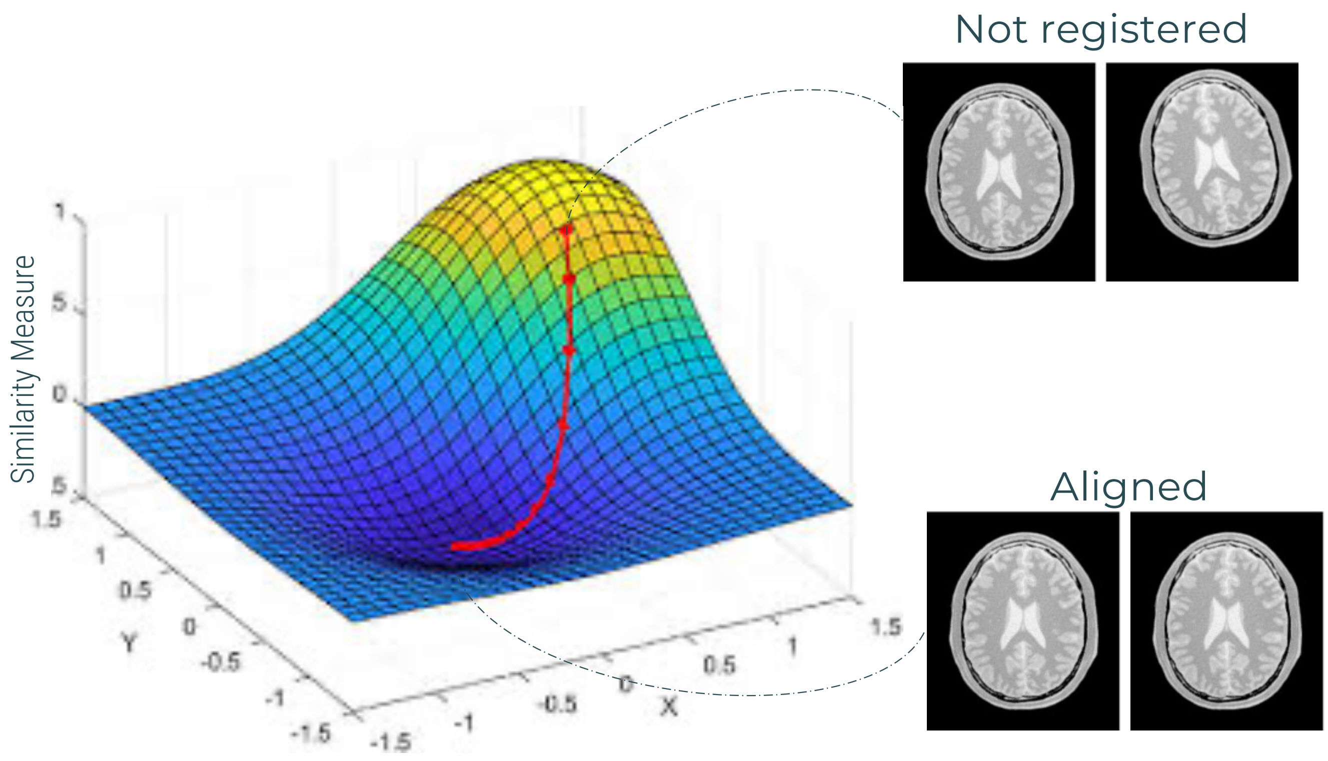


Figure adapted from *Handbook of Medical Image Processing and Analysis (Second Edition), 2009*

OPTIMIZATION PROBLEM

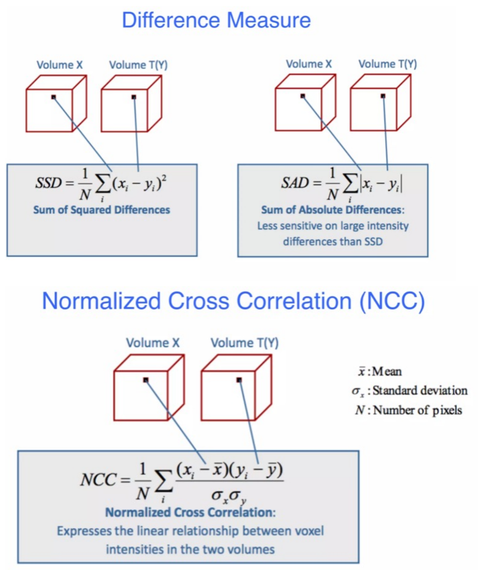
CIBM Center for Biomedical Imaging

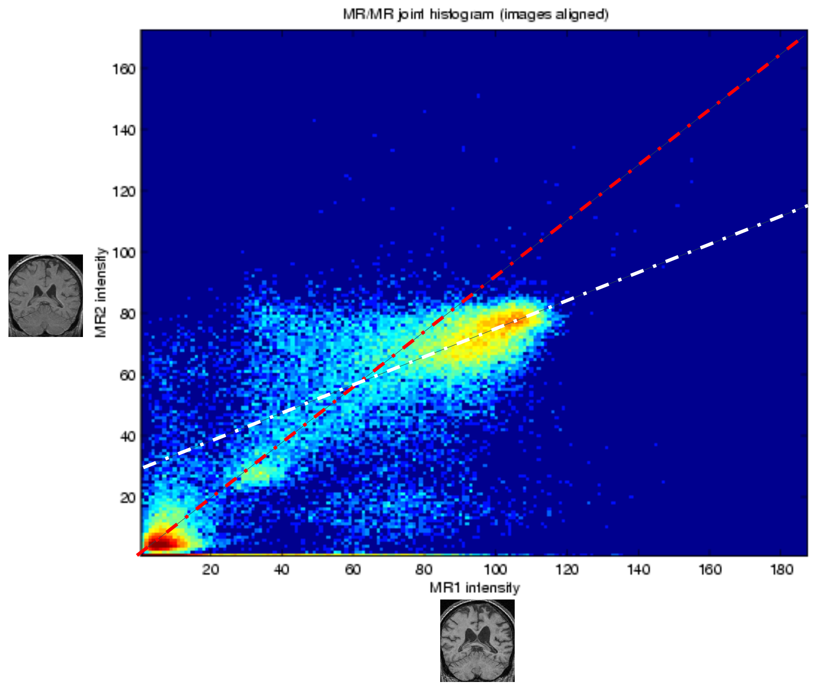


INTENSITY-BASED SIMILARITY MEASURES

Mind the relation between floating and target intensities

Similarity	Assumption on intensities in f and g
Sum of squared differences	Exact
Cross-correlation	Linear relationships



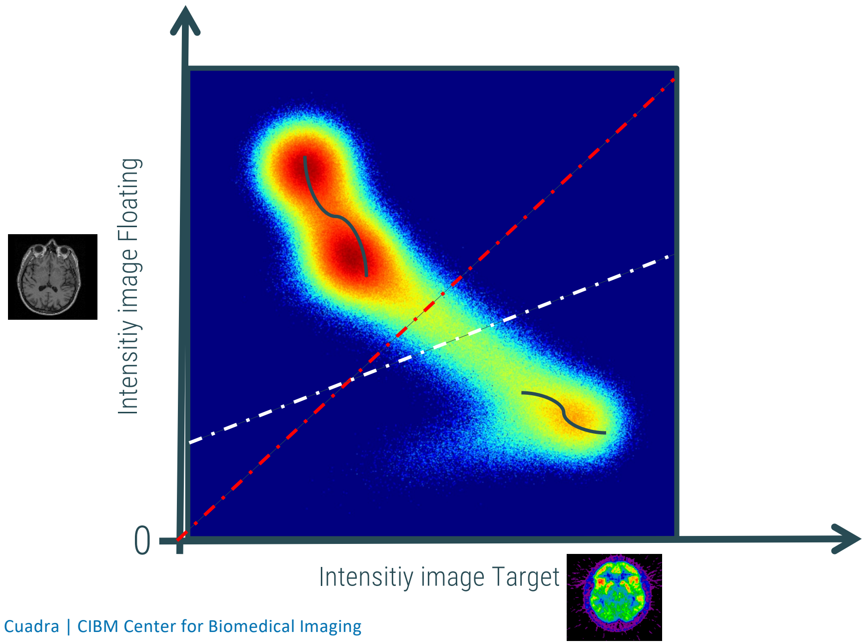


Figures adapted from Prof Ulas Bagci

INTENSITY-BASED SIMILARITY MEASURES

Mind the relation between floating and target intensities

Similarity	Assumption on intensities in f and g
Sum of squared differences	Exact
Cross-correlation	Linear relationships
Entropy, mutual information	Satistical relationship



Mutual Information (Viola & Wells 1994)

$$\boxed{MI(f,T(g)) = H(f) + H(T(g)) - H(f,T(g))}$$

where, H is Shannon Entropy

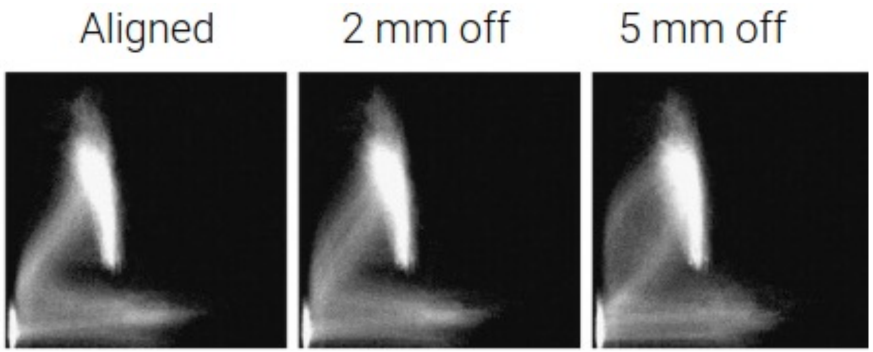
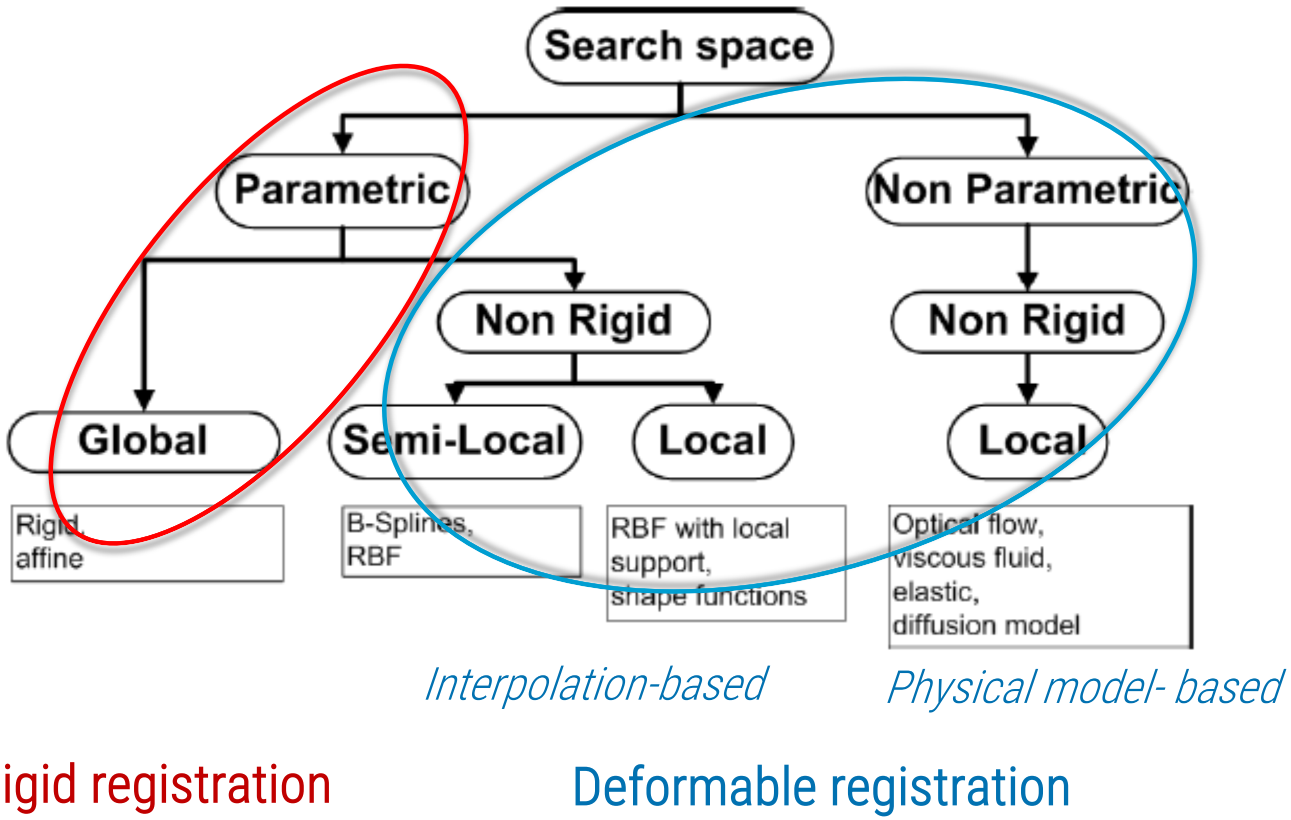


Figure from *Handbook of Medical Image Processing and Analysis (Second Edition), 2009*

C. NATURE OF THE TRANSFORMATION



GLOBAL AND PARAMETRIC

From rigid to affine transformations

- **Rigid:** $T(x) = \mathbf{R}x + \mathbf{t}$
  - Rotation ($\mathbf{R}$) and translation ($\mathbf{t}$): 6 parameters
  - Invariants: distances (isometric), curvature, angles, lines

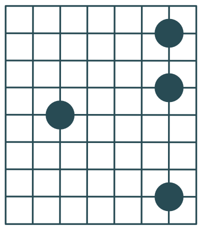
- **Similitude:** $T(x) = \mathbf{sR}x + \mathbf{t}$
  - Adds a scaling factor ($\mathbf{s}$): 9 parameters
  - Invariants: distance ratios, angles, line

- **Affine:** $T(x) = \mathbf{A}x + \mathbf{t}$
  - $\mathbf{A}$ includes shearing: 12 parameters
  - Invariants: lines, parallelism

DEFORMABLE REGISTRATION*

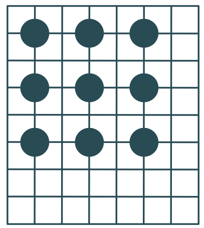
Also non-rigid, based on interpolation

- Initialization through global registration
- Parametric: $T(x) = f(\theta_i)$
  - Representation in basis functions: ~ 100's parameters
  - A **grid** (regular or irregular) of **nodes** is required
  - Local polynomials / Locally affine transformations



Irregular grid

Radial	Non-radial
Thin-plate Splines Gaussian	Trigonometric Wavelets B-splines



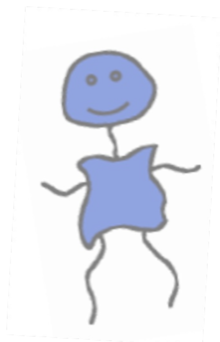
Regular grid

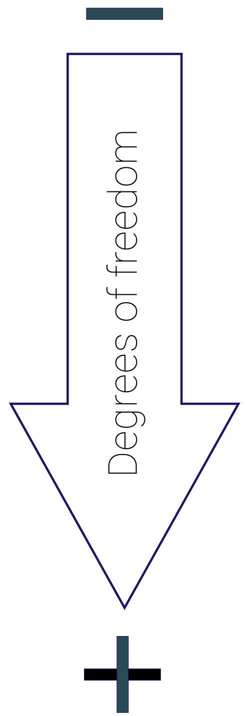
*Review of deformable registration, Sotiras et al, IEEE TMI, 2013.

DEFORMABLE REGISTRATION*

Also non-rigid, based on physical models

- Initialization through global registration
- Parametric: T(x) = f(θ_i)
  - Representation in basis functions: ~ 100's parameters
  - A **grid** (regular or irregular) of **nodes** is required
  - Local polynomials / Locally affine transformations
- Non-parametric: T(x) = x + u(x)
  - Voxel-wise parametrization
  - ~ 10000's parameters
  - REGULARIZATION needs to be explicitly ensured





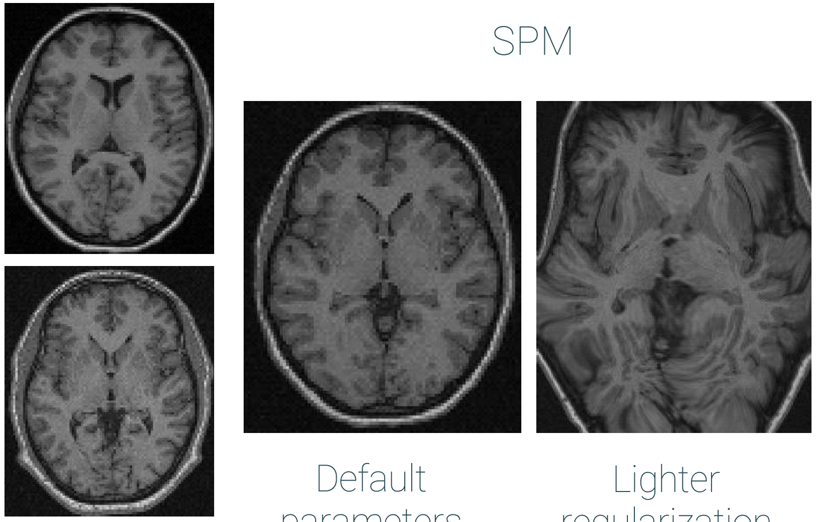
*Review of deformable registration, Sotiras et al, IEEE TMI, 2013.

REGULARIZATION

$$u^* = argmin\ cost(f, u \circ g) + R(u)$$

Source

SPM

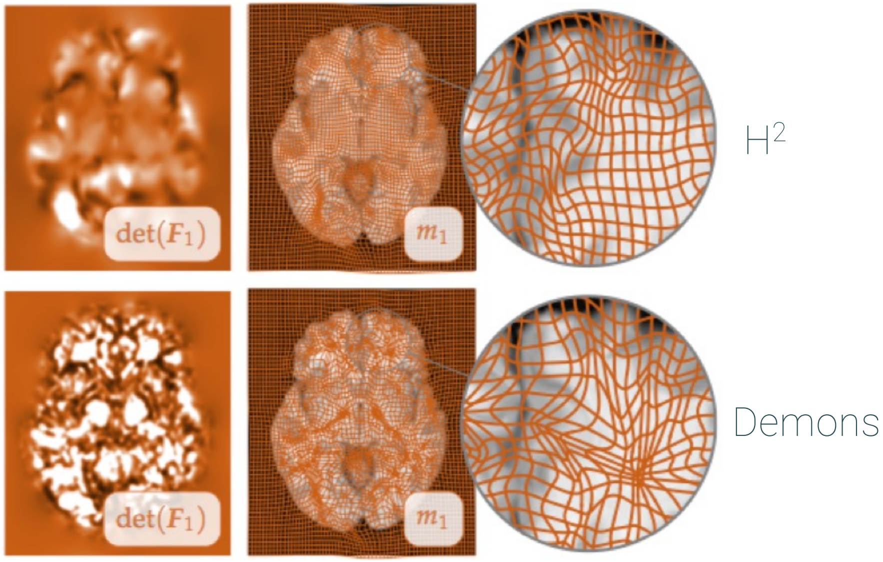


Target

Default parameters

Lighter regularization

Exemple from "Elastic Registration of Medical MR Images", PhD Thesis, L. Kristian Nielsen, 2003



Adapted from Mang et al, Imaging Sci, 2016.

DIFFEOMORPHIC TRANSFORMATIONS

- Powerful and mathematically elegant transformations that ensure a one-to-one **smooth, continuous and invertible** mapping

- Bijective, Differentiable, Inverse Differentiable
- Preserve topology: **prevent folding/crossings**
- Jacobian determinant never goes to zero (>0) : non-singular
- Allow large deformations
- Many diffeomorphic registration: B-splines[1], demons[2,3], LDDMM[4], Symmetric Lagrangian[5], etc
- Publicly available: ITK, Matlab, SPM etc

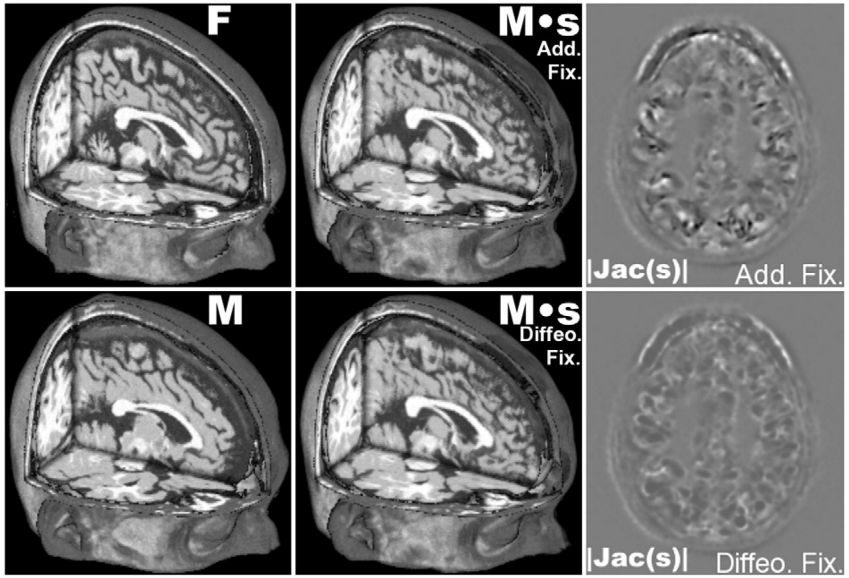


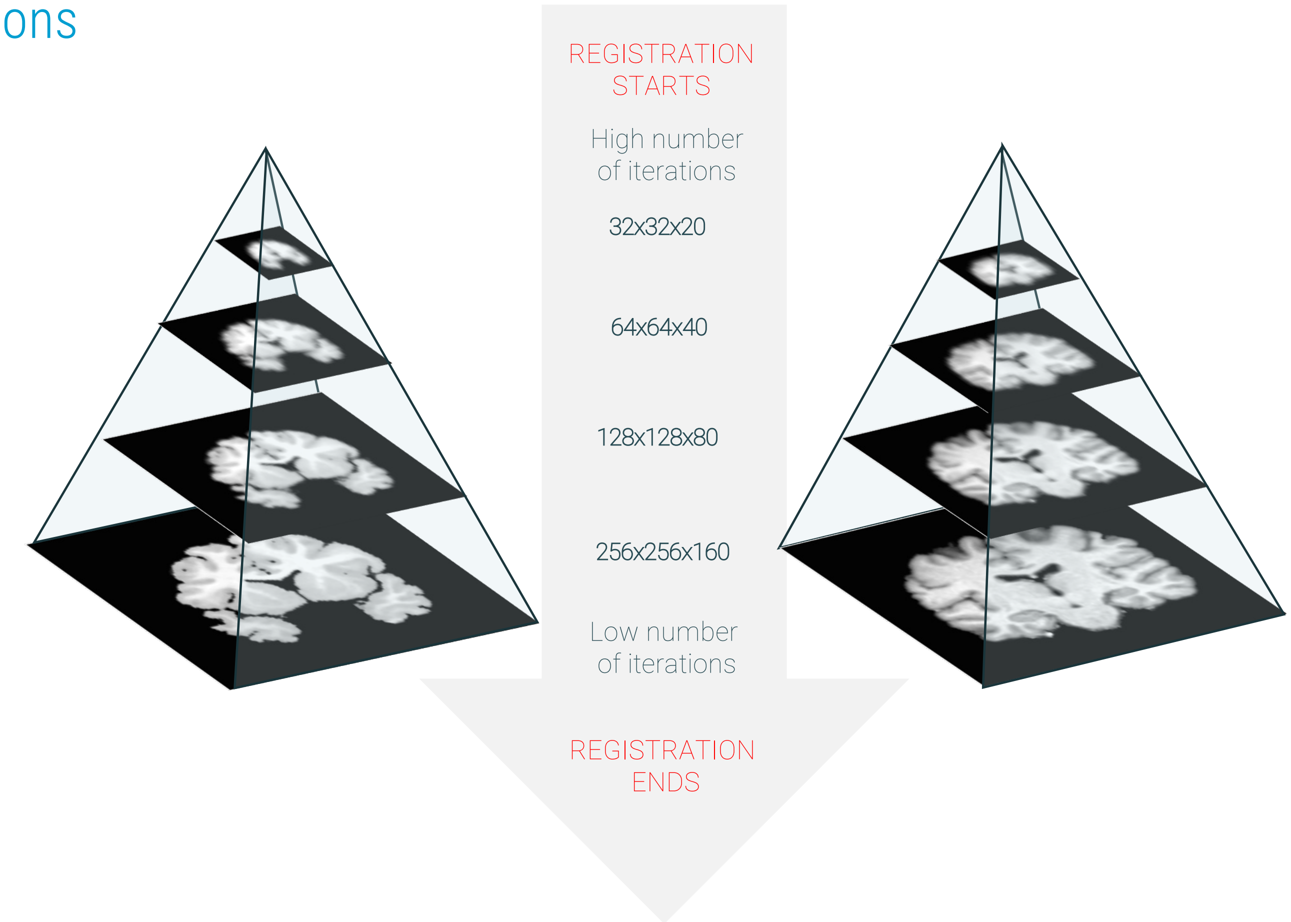
Figure from T. Vercauteren et al., NeuroImage 2009.

[1]Rueckert MICCAI 2006, [2]Vercauteren et al., NeuroImage 2009, [3]Lorenzi et al Neuroimage, 2013, [4] Ashburner et al, Neuroimage 2011, 5 Avants et al MedIA 2008.

MULTI-SCALE STRATEGY

For deformable/non-rigid deformations

- Support convergence
- Capture larger-scale information efficiently
- Improves convergence, speed, accuracy and robustness



ASSESSMENT OF THE REGISTRATION

- Biological validity
- Requirements of a validation system:
  - Accuracy
  - Robustness
  - Complexity
- Validation made by*:
  - comparison with landmarks
  - visual validation by expert criteria
  - physical phantom
  - simulated data

Deep brain stimulation treatment for Parkinson Disease

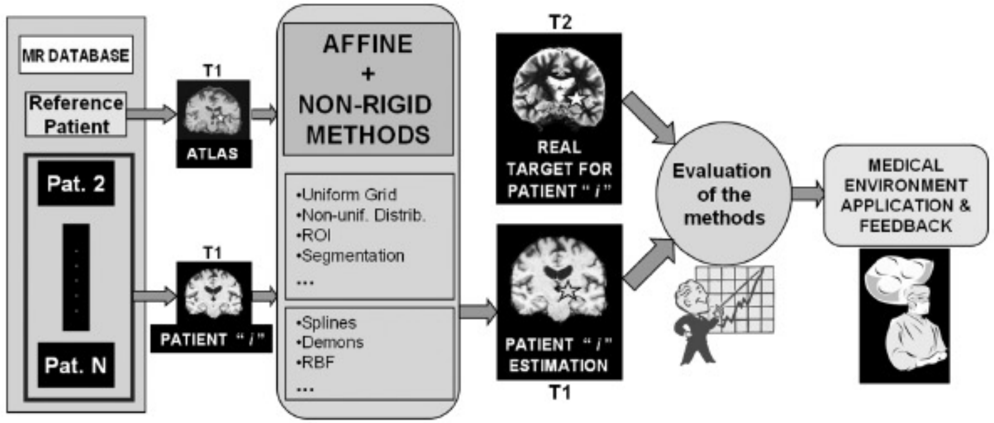


Figure from Sanchez-Castro el al IEEE TMI 2006

*West et al J. Compt Ass. Tom. 2007, Fitzpatrick et al, TMI 2001, Sanchez-Castro et al, TMI 2006, Ou et al, TMI 2014, Datteri et al, TMI 2015

IN PRACTICE !

ROADMAP OF (BRAIN) IMAGE REGISTRATION TOOLS

Human

- ITK
- ANTS (Advanced noramlization tool)
- CAVASS
- NiftReg
- Elastix
- 3D Slicer
- FAIR
- FSL
- SPM12, CAT
- … Collection of available resources: https://en.wikipedia.org/wiki/List_of_neuroimaging_software https://www.nitrc.org

Pre-clinical

Adhoc-solution to use "human" tools:

- ITK
- ANTS (Advanced noramlization tool)
- FSL

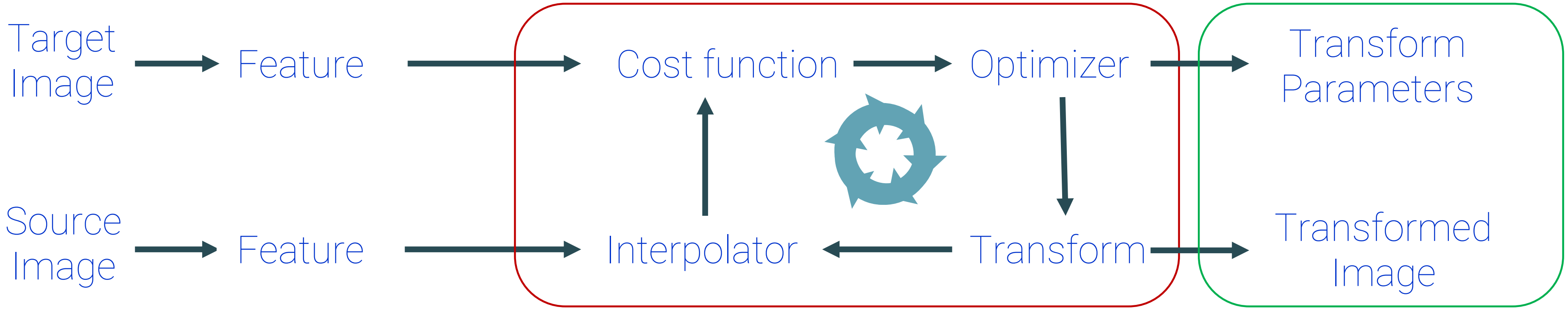
- SAMBA
- Sammba-MRI
- AIDAmri
- SAMRI

DEEP LEARNING REGISTRATION

IMAGE REGISTRATION AS AN OPTIMIZATION

Limitations

- Hand-crafted features
- Optimization is ill-posed and high-dimensional
- Multi-scale and iterative processes: time-consuming
- Task-sensitive parameter tuning
- Requires prior knowledge/hypothesis on transformation type



TAXONOMY OF IMAGE REGISTRATION

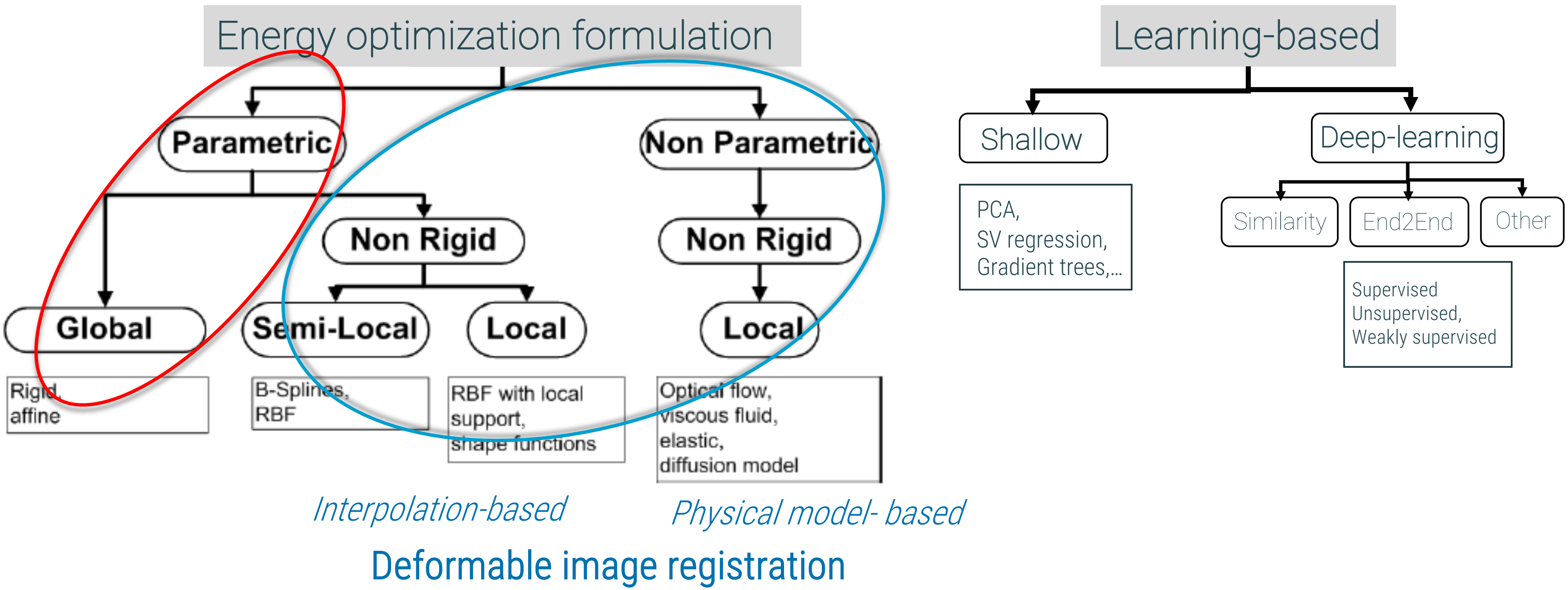
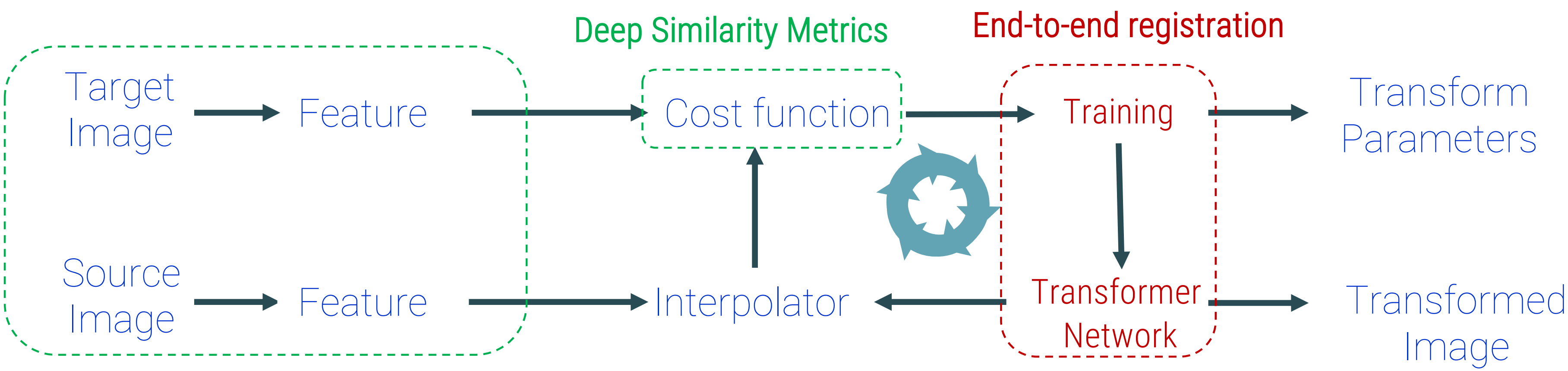


IMAGE REGISTRATION BASED ON LEARNING

- Statistical/Shallow: PCA, SV regression, gradient trees.
- Deep Learning[1,2]:
  - counterparts for cost, optimization and transformation
  - many image pairs not only one pair of images
  - fast inference but… training time



[1] Haskins et al, Machine Vision and Applications, 2020, [2] Chen et al, Progress in Biomedical Engineering, 2021

ROOM FOR IMPROVEMENT

And some questions remain open !

- Re-inventing the wheel?
- Deep Learning (-registration):
  - Include prior-knowledge
  - Generalization and domain adaptation
  - Interpretability and explainability
- How accurate/good image registration is?
- Still check on application constrains:
  - Image modality available?
  - Ultimate goal?

Deep learning

TAKE HOME QUESTIONS

- Can you cite some applications where image registration is needed?
- Which are the **main actors** of the registration framework ?
- **Types of transformation** know so far?

Center for Biomedical Imaging

THANK YOU FOR YOUR ATTENTION

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LEMANIC NEURO SCIENCE

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