

# Unbiased longitudinal atlas creation using robust linear registration and log-Euclidean framework for diffeomorphisms

*Antoine Legouhy* <sup>\*a</sup>   *Olivier Commowick* <sup>a</sup>   *François Rousseau* <sup>b</sup>   *Christian Barillot* <sup>a</sup>

<sup>a</sup> Univ Rennes, INRIA, CNRS, INSERM, IRISA UMR 6074, Empenn ERL U-1228, F-35000, Rennes, France

<sup>b</sup> IMT Atlantique, LaTIM U1101 INSERM, UBL, Brest, France

\* antoine.legouhy@irisa.fr

## Atlas:

Average model of the brain in term of shape and intensity.

Useful tool to:

- compute statistics on populations
- understand brain variability
- segment regions
- ...

## Longitudinal atlas:

Average model of the brain in term of shape and intensity.

4D: Time dependent

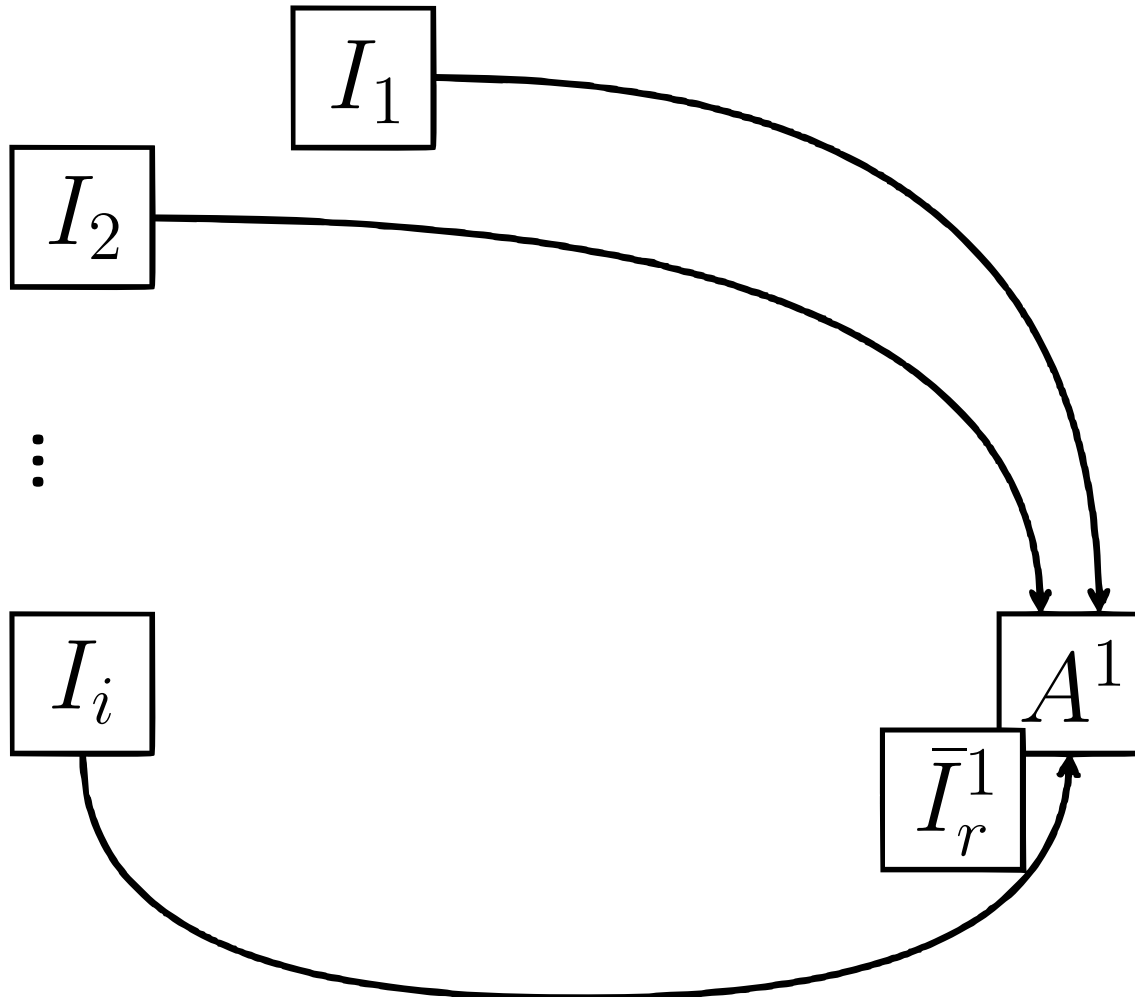
Set of 3-D atlases each for a desired timepoint  
Weight functions modulate subjects contributions according to their age fit with that timepoint.

Useful tool to:

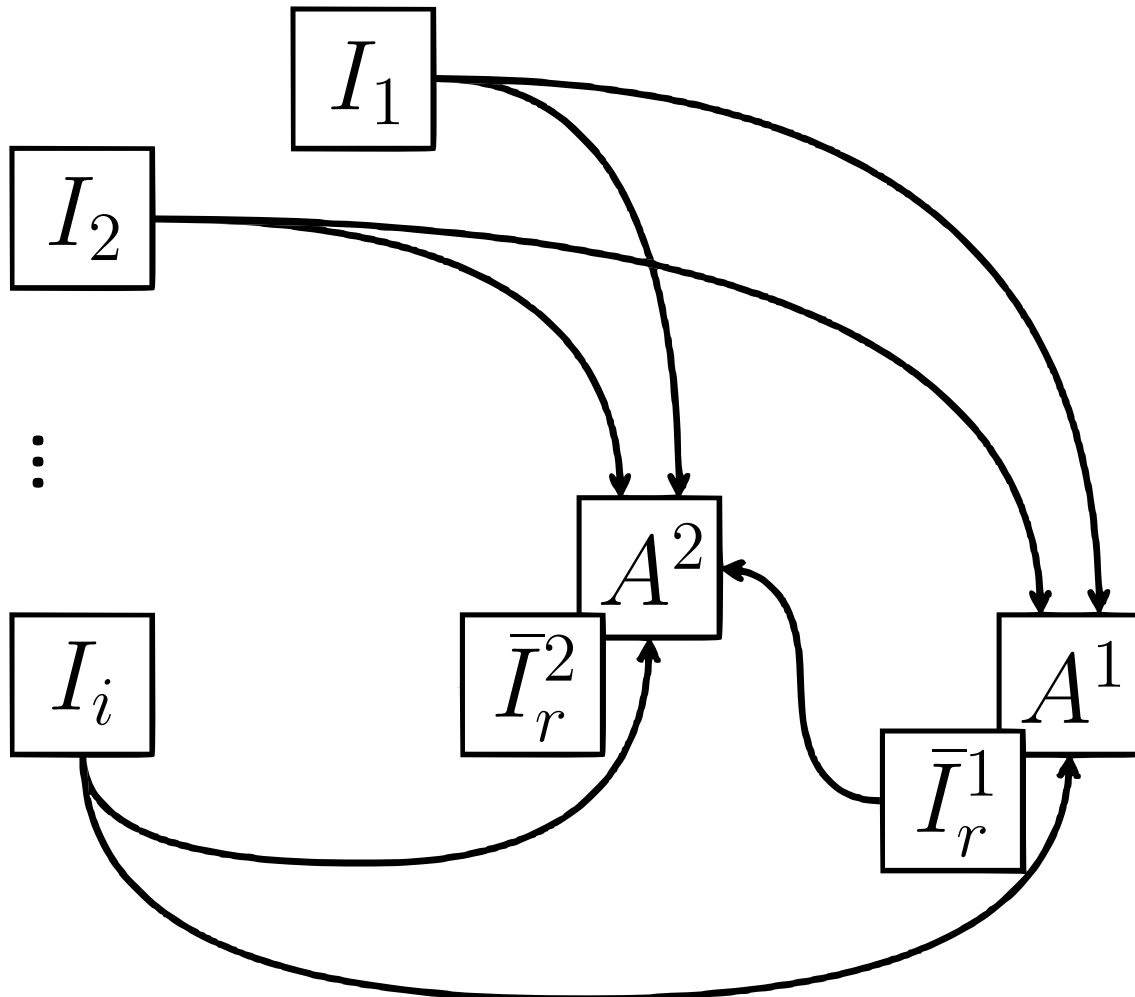
- compute statistics on populations
- understand brain variability
- segment regions
- understand brain development
- highlight changes in growth, shape, structure...
- ...

# Method overview

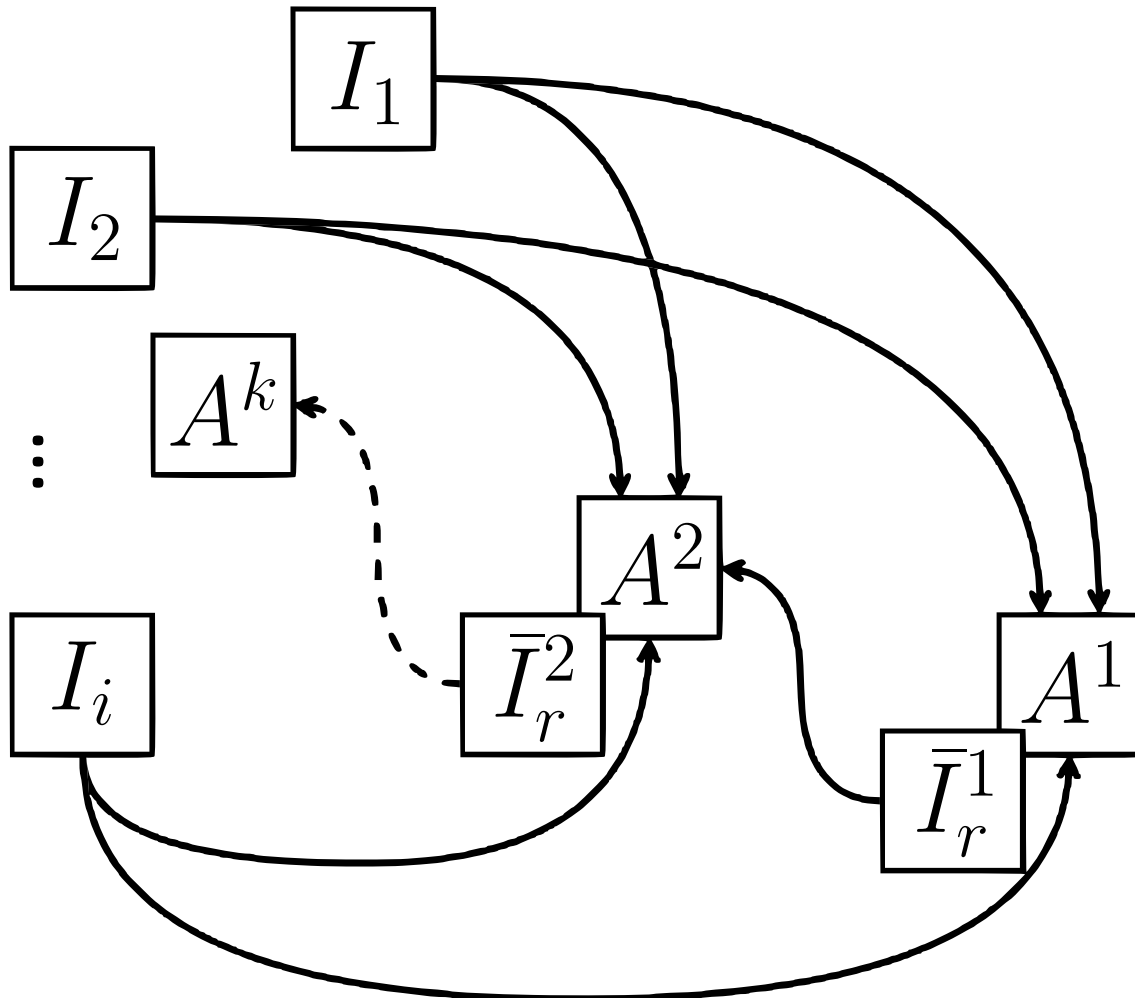




- 1. Registration:** Register all the subjects onto a reference  $A$ .



- 1. Registration:** Register all the subjects onto a reference  $A$ .
- 2. Creation of the new reference:**
  - Perform averaging on output images  $\bar{I}_r$ .
  - Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiased transformation.
  - Apply this transformation to  $\bar{I}_r$  to create a new reference image.



- 1. Registration:** Register all the subjects onto a reference  $A$ .
- 2. Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiasing transformation.
  - iii. Apply this transformation to  $\bar{I}_r$  to create a new reference image.

## Requirements

### Longitudinal atlas that is:

- Diffeomorphic
- Unbiased up to a rigid transformation
  - Takes into account global growth
  - Takes into account local displacements
- Temporally accurate
- Robust
  - Sub-atlases are correctly aligned



## Requirements

### Longitudinal atlas that is:

- Diffeomorphic
- Unbiased up to a rigid transformation
  - Takes into account global growth
  - Takes into account local displacements
- Temporally accurate
- Robust
  - Sub-atlases are correctly aligned

## Method

1. **Registration:** Register all the subjects onto a reference  $A$ .
2. **Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiassing transformation.
  - iii. Apply this transformation to to create a new reference image.

# Prerequisites

Robust linear registration

Diffeomorphisms – Log-Euclidean framework

Baker-Campbell-Hausdorff formula

Weight function

## Requirements

### Longitudinal atlas that is:

- Diffeomorphic
- Unbiased up to a rigid transformation
  - Takes into account global growth
  - Takes into account local displacements
- Temporally accurate
- Robust
  - Sub-atlases are correctly aligned

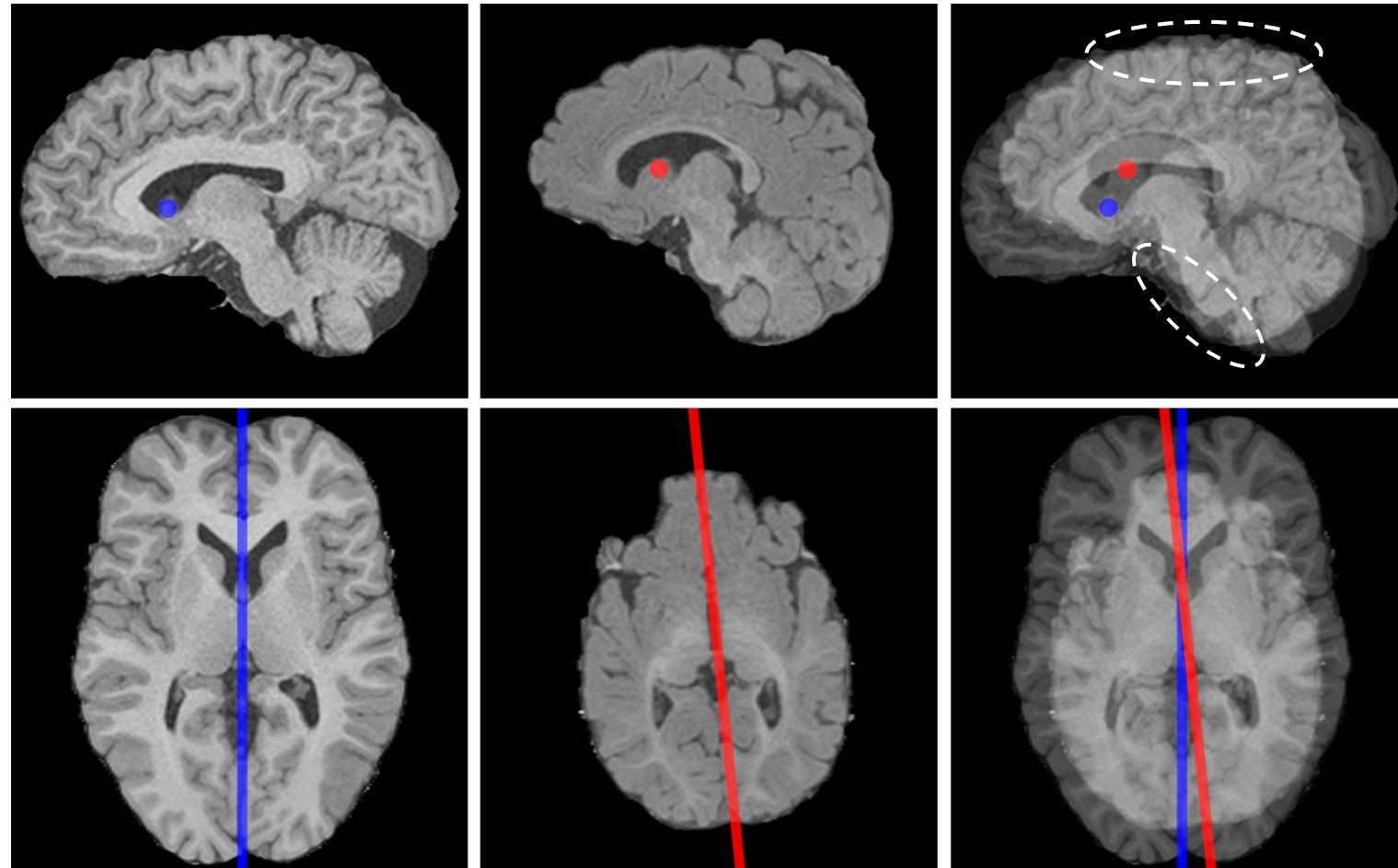
## Method

1. **Registration:** Register all the subjects onto a reference  $A$ .
2. **Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiasing transformation.
  - iii. Apply this transformation to to create a new reference image.

# Robust linear registration

Direct rigid registration can be corrupted for brains of different sizes,  
Strong similarities on the edges of the brain → small one stuck on the edges of the big one:

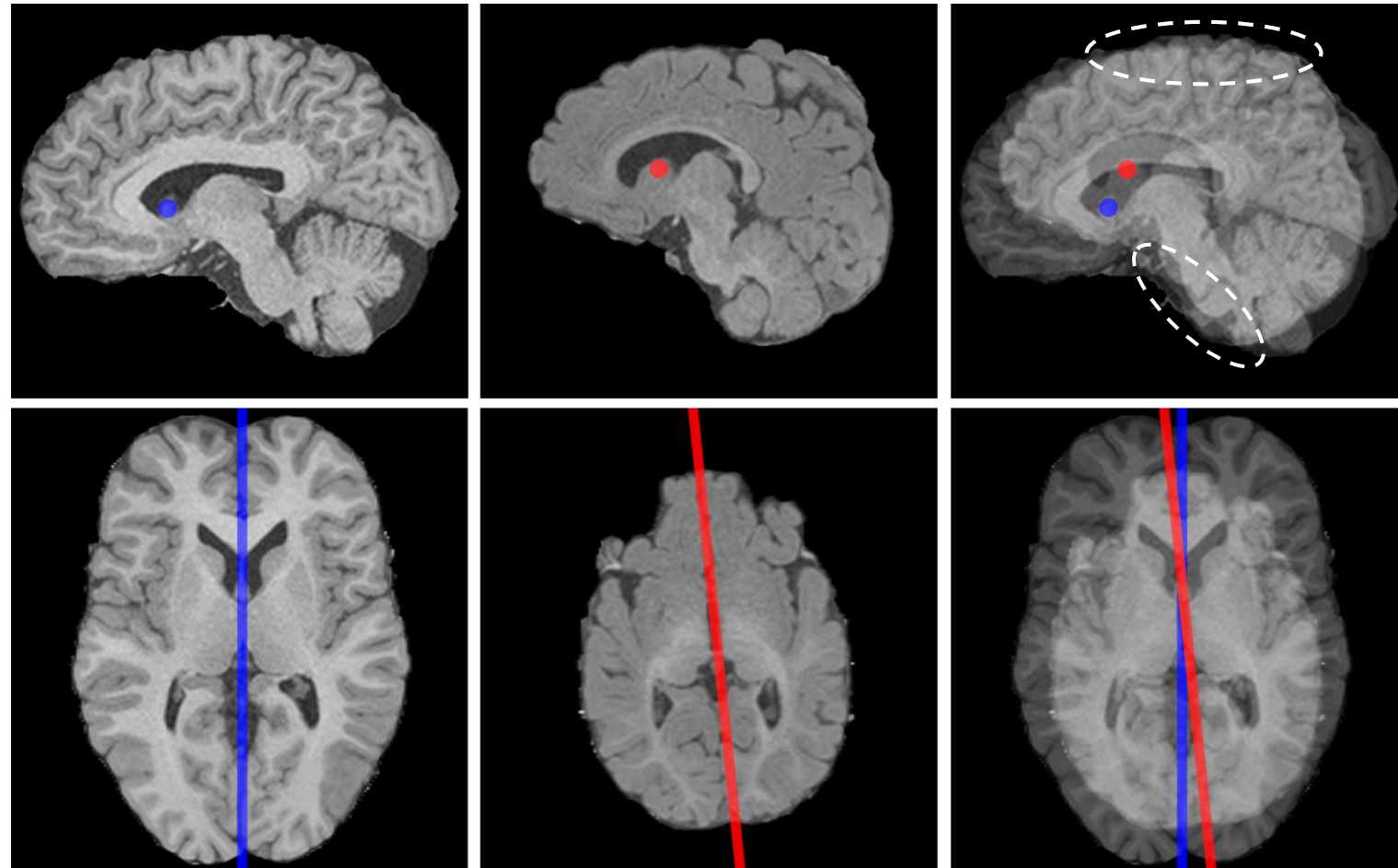
- Shifted brain barycenters
- misaligned sagittal planes



# Robust linear registration

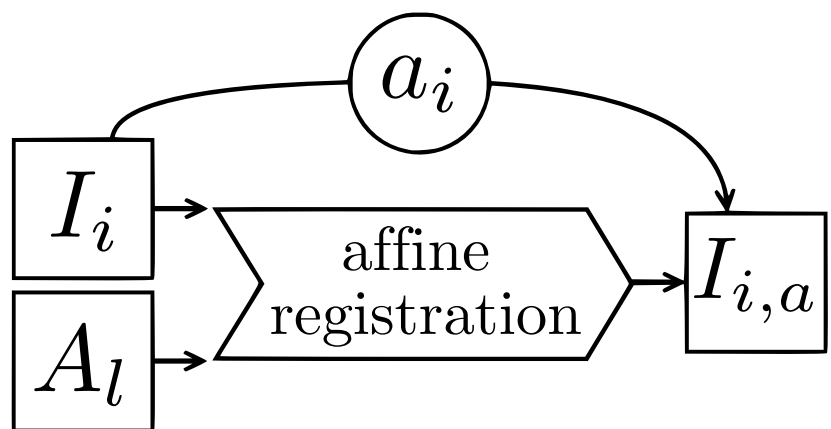
Direct rigid registration can be corrupted for brains of different sizes,  
Strong similarities on the edges of the brain → small one stuck on the edges of the big one:

- Shifted brain barycenters
- misaligned sagittal planes



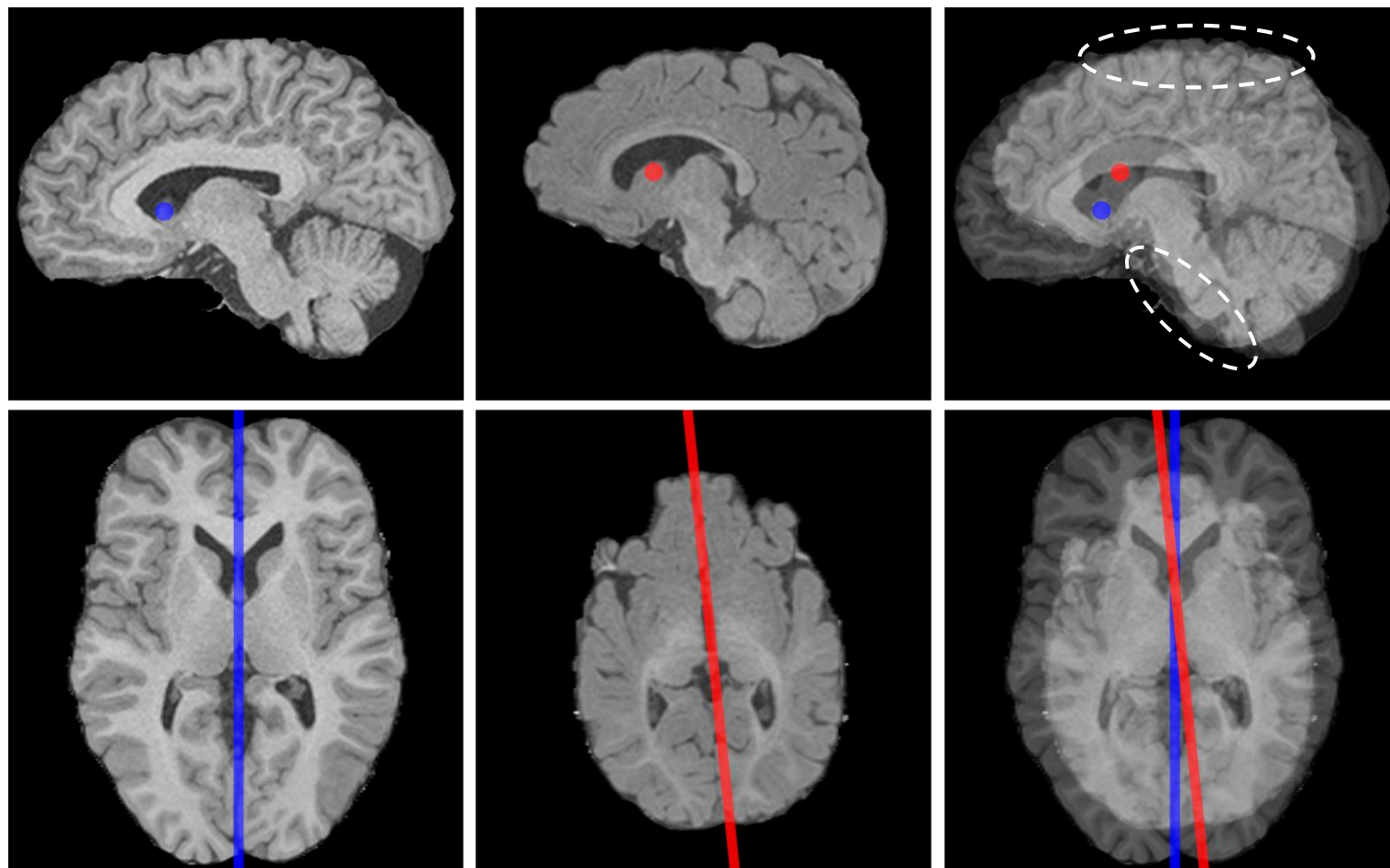
Robust rigid registration:

# Robust linear registration

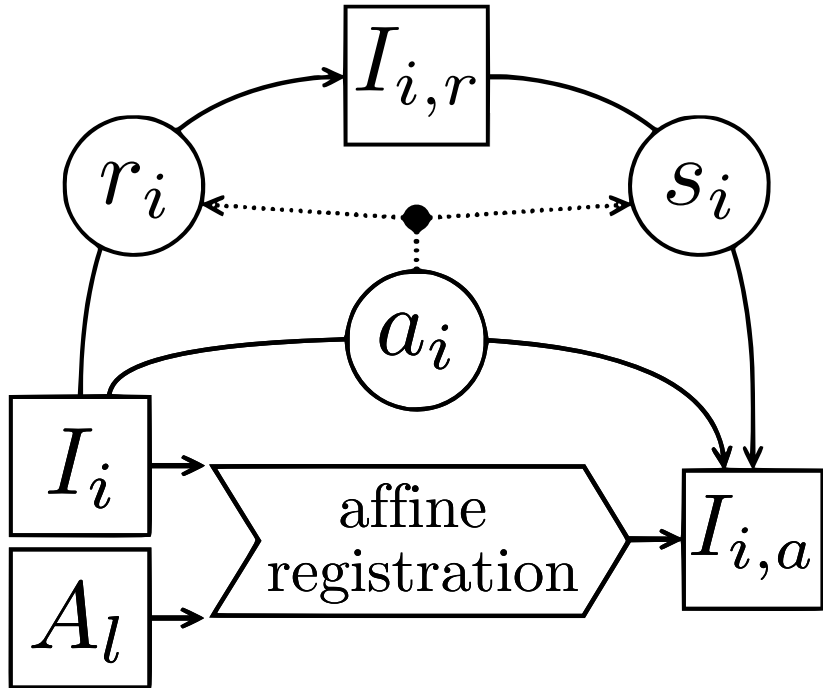


Robust rigid registration:

1. Perform affine registration  
init: PCA on non-zero voxels

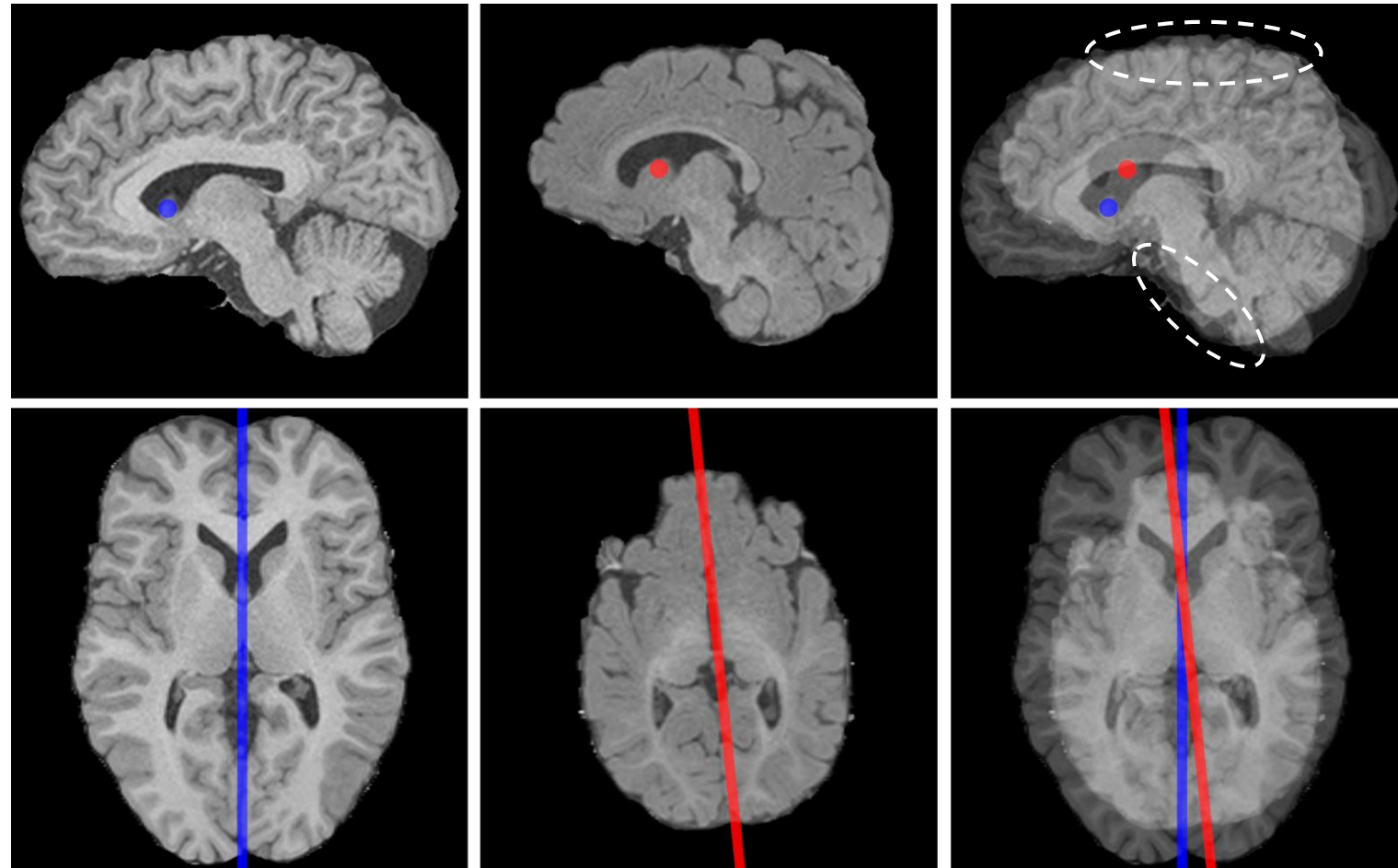


# Robust linear registration

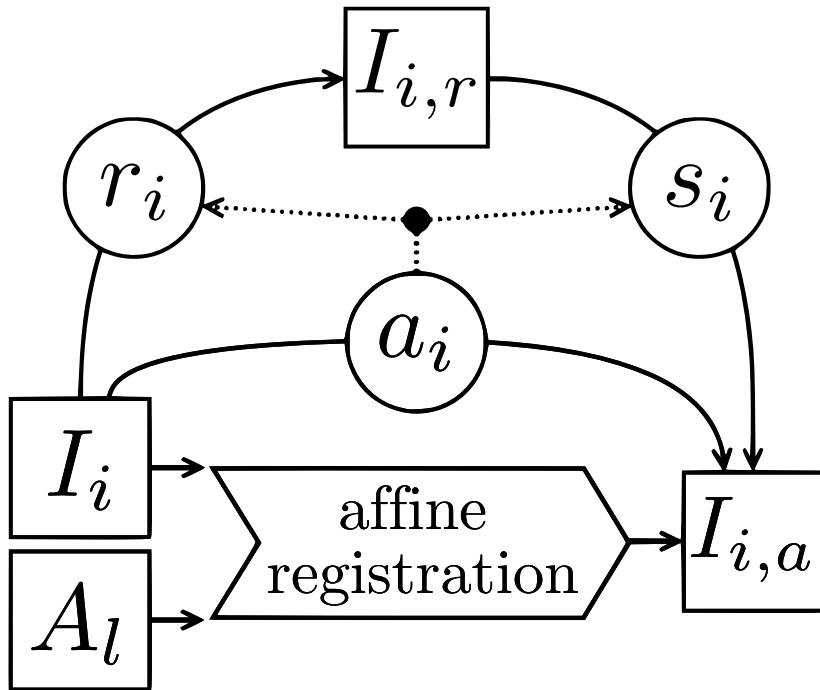


Robust rigid registration:

1. Perform affine registration  
init: PCA on non-zero voxels
2. Extract rigid part using polar decomposition

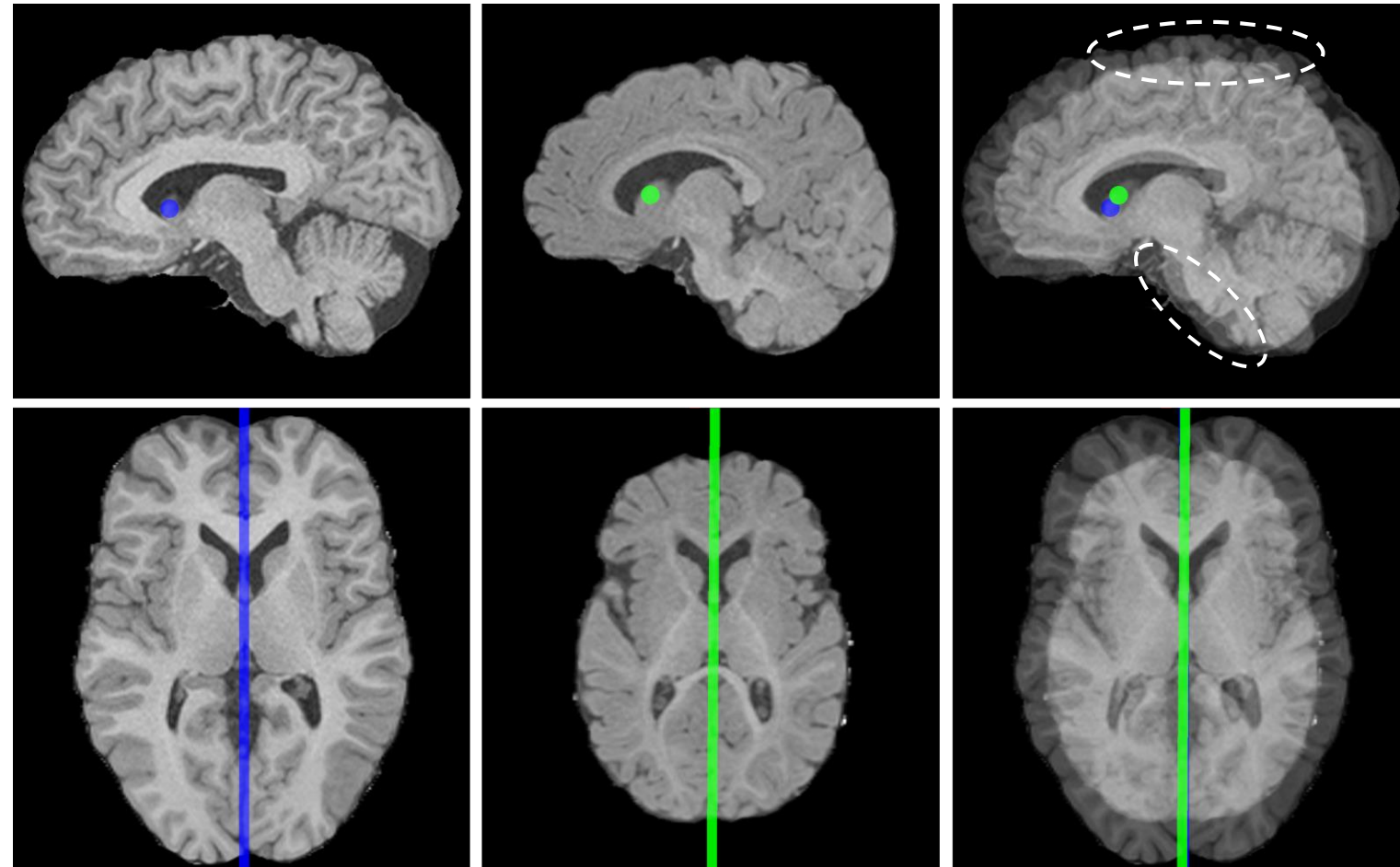


# Robust linear registration



Robust rigid registration:

1. Perform affine registration  
init: PCA on non-zero voxels
2. Extract rigid part using polar decomposition





## Requirements

### Longitudinal atlas that is:

- Diffeomorphic
- Unbiased up to a rigid transformation
  - Takes into account global growth
  - Takes into account local displacements
- Temporally accurate
- Robust
  - Sub-atlases are correctly aligned

## Method

- 1. Registration:** Register all the subjects onto a reference  $A$ .
- 2. Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiassing transformation.
  - iii. Apply this transformation to to create a new reference image.

## **Diffeomorphisms:**

Widely used for non linear registration.

Important properties:

- differentiability
- bijectivity
- differentiability of the inverse map

## Diffeomorphisms:

Widely used for non linear registration.

Important properties:

- differentiability
- bijectivity
- differentiability of the inverse map

But:

Not a group structure for +

→ Computation of Euclidean operations on diffeomorphisms does not yield a diffeomorphism

## Diffeomorphisms:

Widely used for non linear registration.

Important properties:

- differentiability
- bijectivity
- differentiability of the inverse map

But:

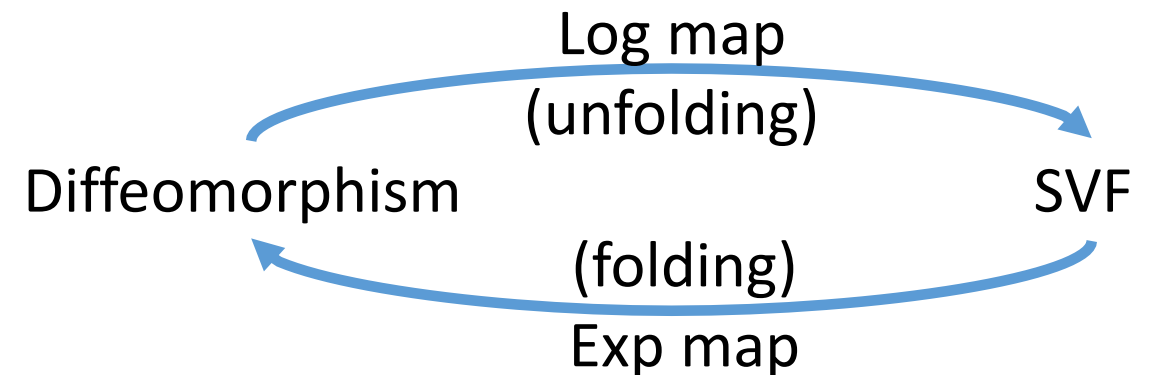
Not a group structure for +  
→ Computation of Euclidean operations on diffeomorphisms does not yield a diffeomorphism

---

## Log-Euclidean framework:

Diffeomorphisms parameterized by Stationary Velocity Fields (SVFs).

→ Euclidean operations on SVFs



## Requirements

### Longitudinal atlas that is:

- Diffeomorphic
- Unbiased up to a rigid transformation
  - Takes into account global growth
  - Takes into account local displacements
- Temporally accurate
- Robust
  - Sub-atlases are correctly aligned

## Method

- 1. Registration:** Register all the subjects onto a reference  $A$ .
- 2. Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiasing transformation.
  - iii. Apply this transformation to to create a new reference image.

# Baker-Campbell-Hausdorff formula



$v$  and  $w$  SVFs, how to compute  $\log(\exp(v) \circ \exp(w))$  ?

*Contributions to 3D Diffeomorphic Atlas Estimation: Application to Brain Images. Bossa et al., 2007*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*

# Baker-Campbell-Hausdorff formula



$v$  and  $w$  SVFs, how to compute  $\log(\exp(v) \circ \exp(w))$  ?

Log computation  $\rightarrow$  very costly

*Contributions to 3D Diffeomorphic Atlas Estimation: Application to Brain Images. Bossa et al., 2007*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*

# Baker-Campbell-Hausdorff formula

$v$  and  $w$  SVFs, how to compute  $\log(\exp(v) \circ \exp(w))$  ?

Log computation  $\rightarrow$  very costly

## Baker-Campbell-Hausdorff formula:

In a BCH-Lie group, for  $v$  and  $w$  small enough :

$$\begin{aligned}\log(\exp(v) \circ \exp(w)) &\approx v + w \\ &+ \frac{1}{2}[v, w] \\ &+ \frac{1}{12}([v, [v, w]] + [[v, w], w]) \\ &+ \dots\end{aligned}$$

Where:

$$[v, w](x) = \text{Jac}(v)(x).w(x) - \text{Jac}(w)(x).v(x)$$



## Requirements

### Longitudinal atlas that is:

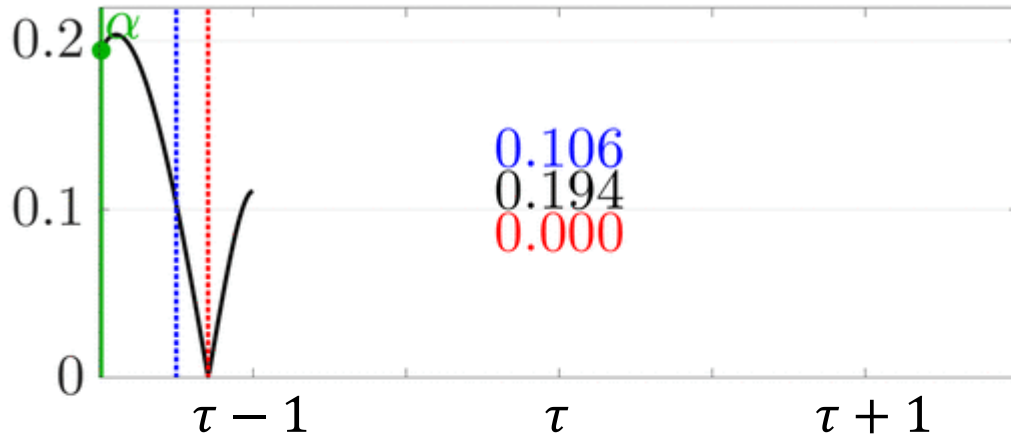
- Diffeomorphic
- Unbiased up to a rigid transformation
  - Takes into account global growth
  - Takes into account local displacements
- Temporally accurate
- Robust
  - Sub-atlases are correctly aligned

## Method

1. **Registration:** Register all the subjects onto a reference  $A$ .
2. **Creation of the new reference:**
  - i. Perform averagings on output images  $\bar{I}_r$ .
  - ii. Perform averagings and inverse map on output transformations  $\rightarrow$  unbiasing transformation.
  - iii. Apply this transformation to create a new reference image.

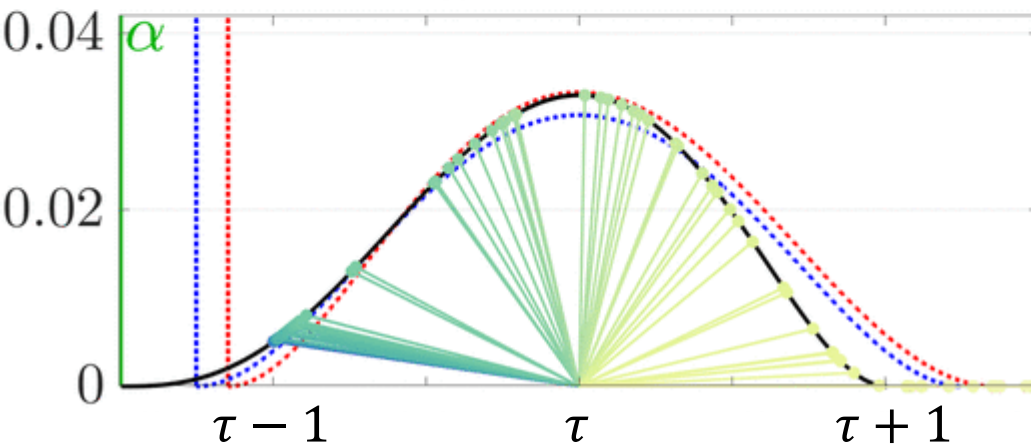
# Weight function

temporal error



**Weight function:** gives more importance to subjects closer in age to  $\tau$ .

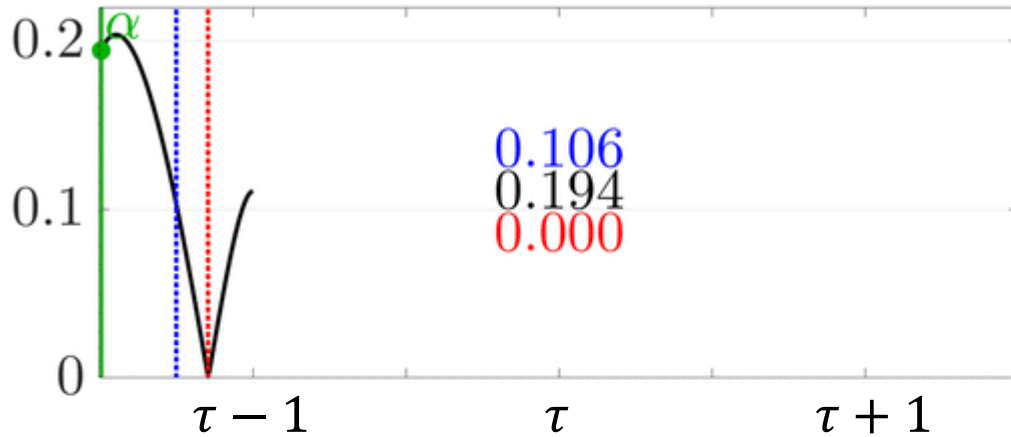
weight function



- $\tau$  : window width
- $\alpha$  : window start

# Weight function

temporal error

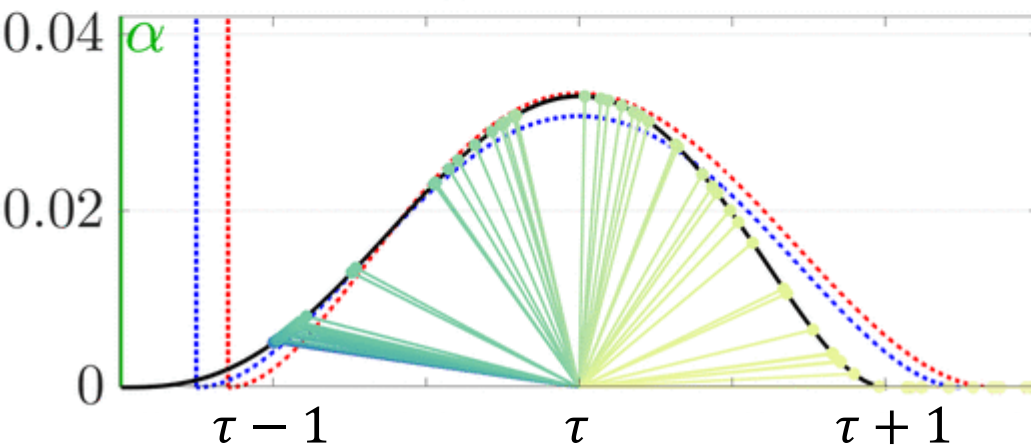


**Weight function:** gives more importance to subjects closer in age to  $\tau$ .

Too few degrees of freedom  $\rightarrow$  temporal error

$$\text{Temporal error: } B = \left| \tau - \sum_{i=1}^n w_i \tau_i \right|$$

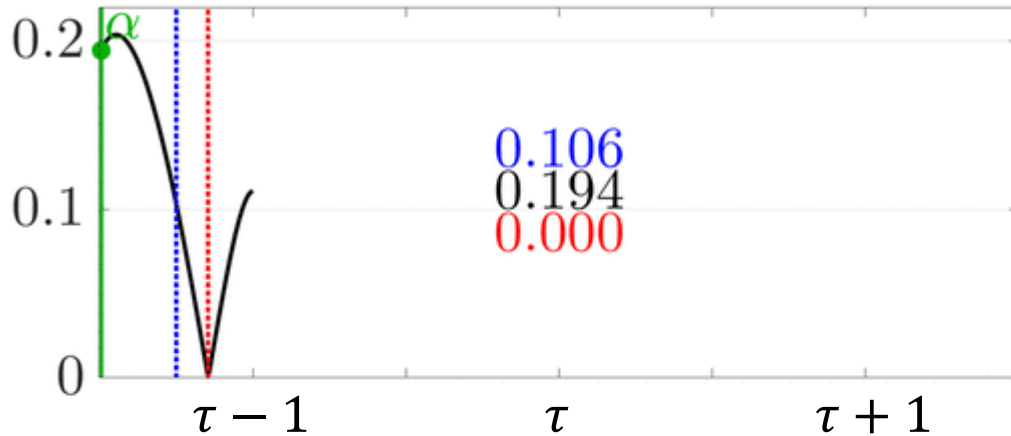
weight function



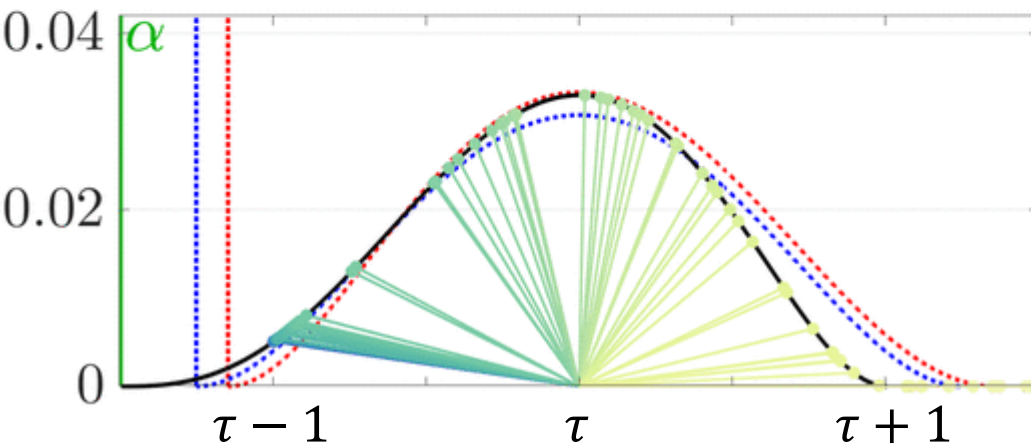
- : window width
- $\alpha$  : window start

# Weight function

temporal error



weight function



**Weight function:** gives more importance to subjects closer in age to  $\tau$ .

Too few degrees of freedom  $\rightarrow$  temporal error

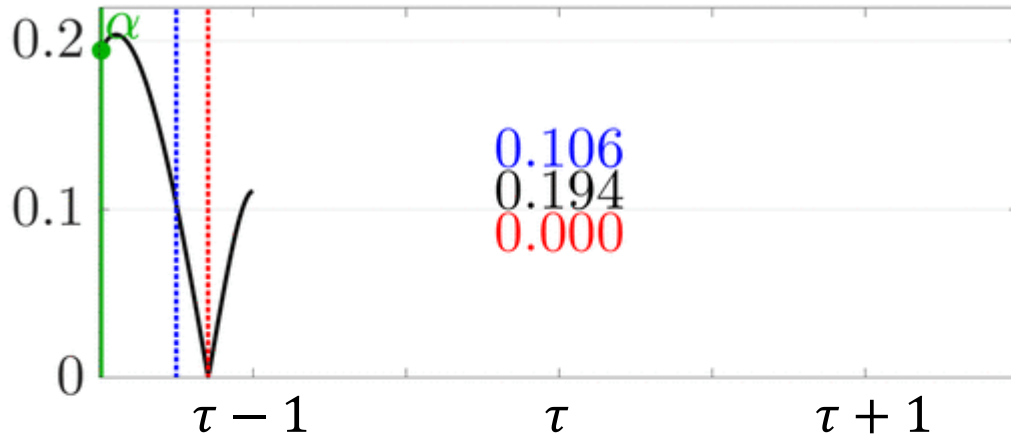
$$\text{Temporal error: } B = \left| \tau - \sum_{i=1}^n w_i \tau_i \right|$$

$\rightarrow$  quintic polynomial weight function

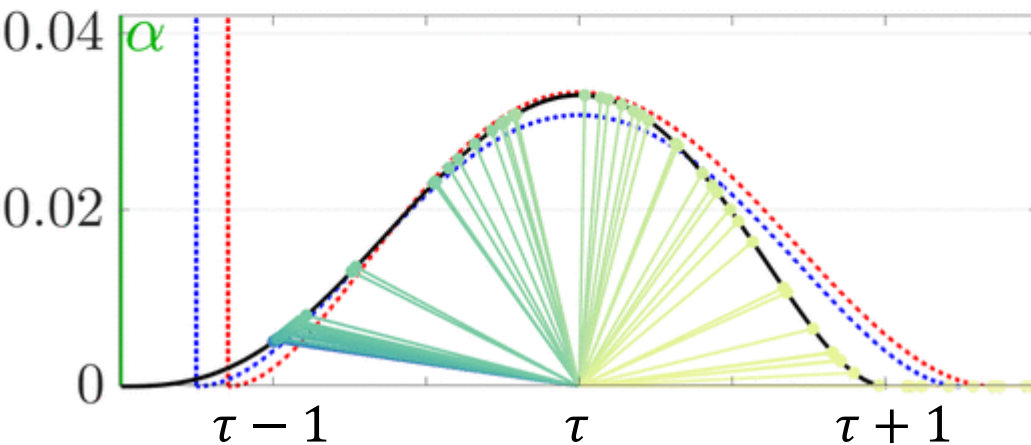
- $\delta$  : window width
- $\alpha$  : window start

# Weight function

temporal error



weight function



**Weight function:** gives more importance to subjects closer in age to  $\tau$ .

Too few degrees of freedom  $\rightarrow$  temporal error

$$\text{Temporal error: } B = \left| \tau - \sum_{i=1}^n w_i \tau_i \right|$$

$\rightarrow$  quintic polynomial weight function

- $\delta$  : window width
- $\alpha$  : window start

- Find  $\alpha$  that minimizes the temporal error
- Modulate window  $\delta$  such to have the desired number of subjects

# Longitudinal atlas creation method

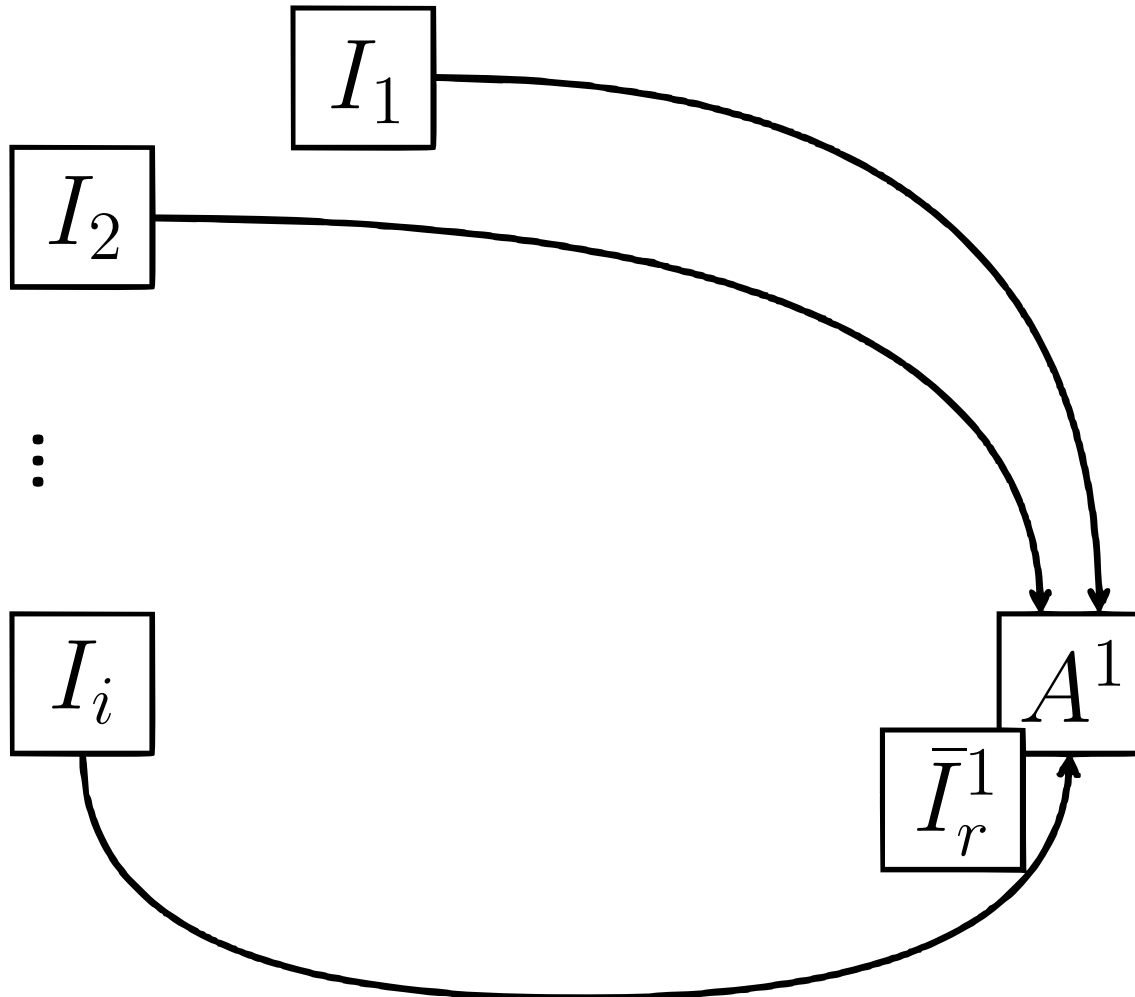
Classical version overview

Registration

Creation of the new reference image

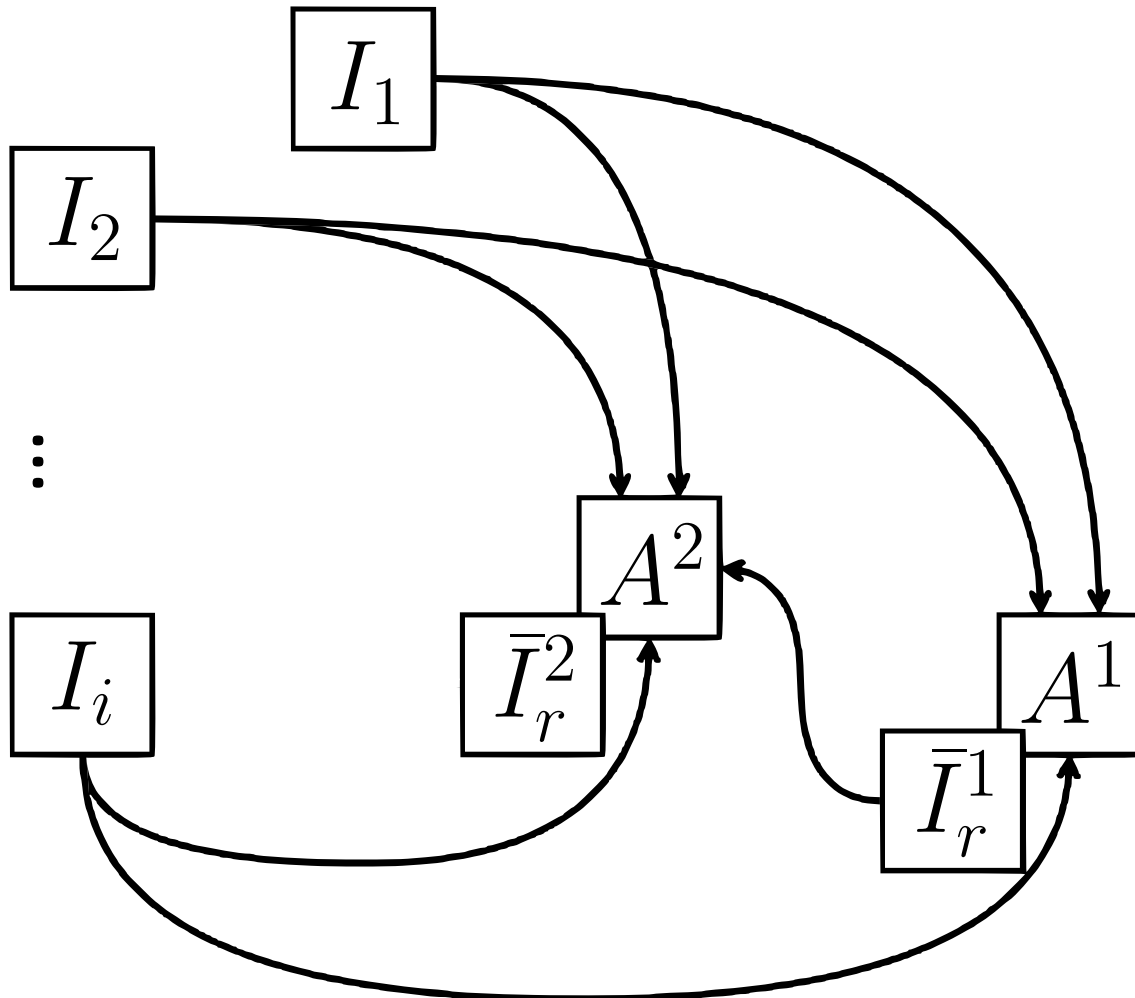
# Method overview



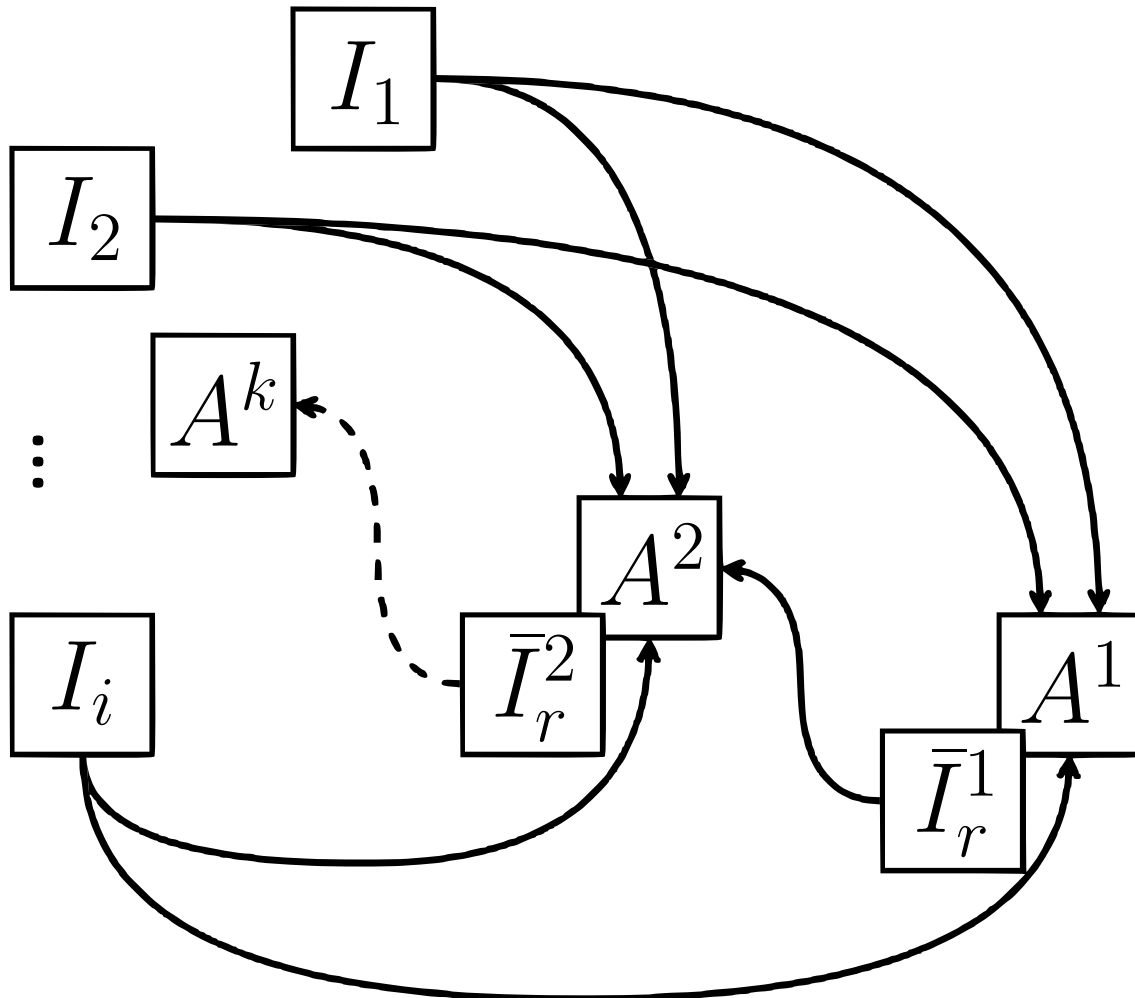


- 1. Registration:** Register all the subjects onto a reference  $A$ .





- 1. Registration:** Register all the subjects onto a reference  $A$ .
- 2. Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiasing transformation.
  - iii. Apply this transformation to  $\bar{I}_r$  to create a new reference image.



- 1. Registration:** Register all the subjects onto a reference  $A$ .
- 2. Creation of the new reference:**
  - i. Perform averaging on output images  $\bar{I}_r$ .
  - ii. Perform averaging and inverse mapping on output transformations  $\rightarrow$  unbiasing transformation.
  - iii. Apply this transformation to  $\bar{I}_r$  to create a new reference image.

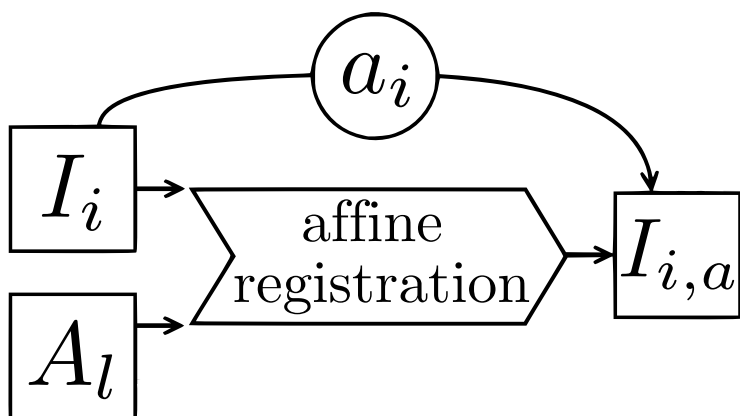
2-step registrations using block-matching algorithms:

*Block-matching strategies for rigid registration of multimodal medical images. Commowick et al., 2012*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*

2-step registrations using block-matching algorithms:

- affine

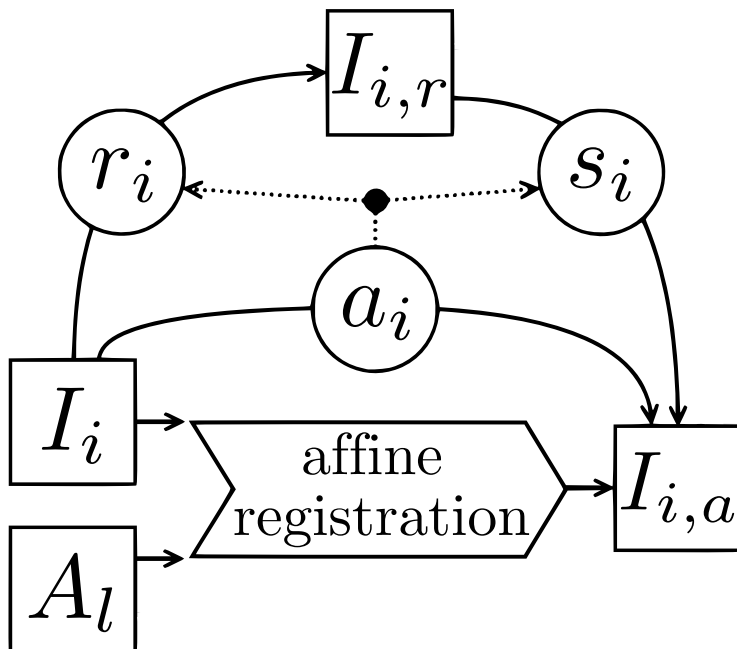


*Block-matching strategies for rigid registration of multimodal medical images. Commowick et al., 2012*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*

2-step registrations using block-matching algorithms:

- affine
  - decomposed into a rigid and a stretching part

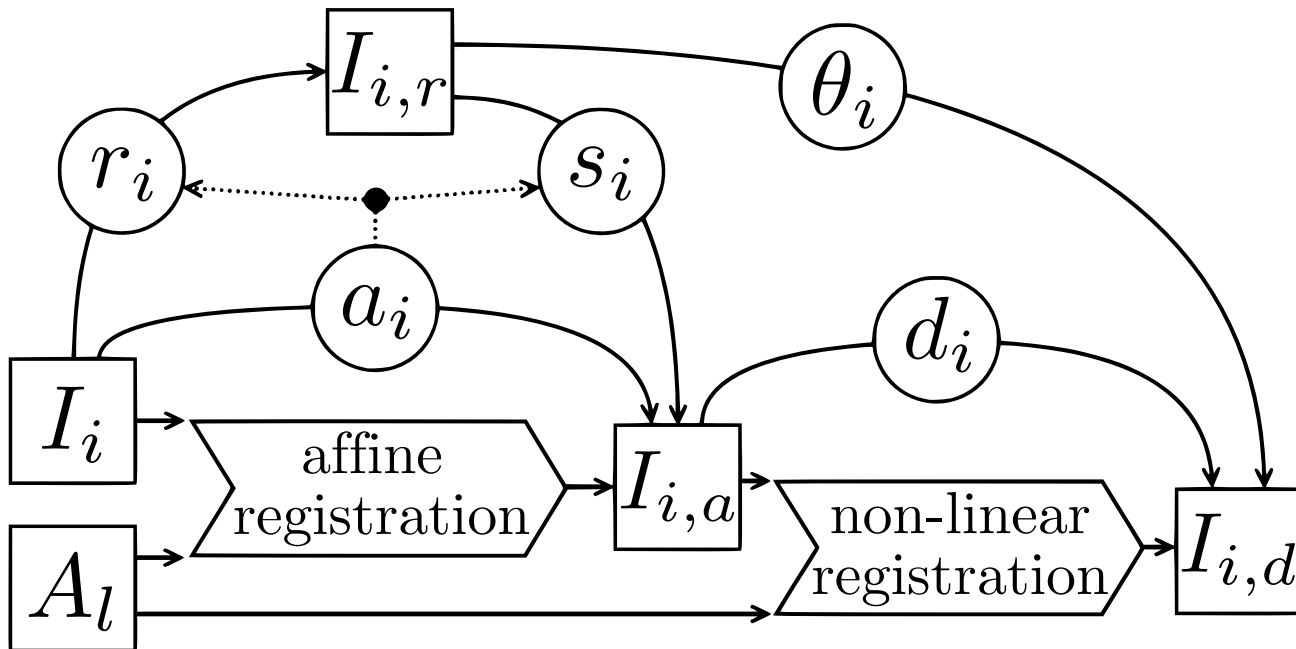


*Block-matching strategies for rigid registration of multimodal medical images. Commowick et al., 2012*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*

2-step registrations using block-matching algorithms:

- affine
  - decomposed into a rigid and a stretching part
- Diffeomorphic (made such as it outputs SVF)

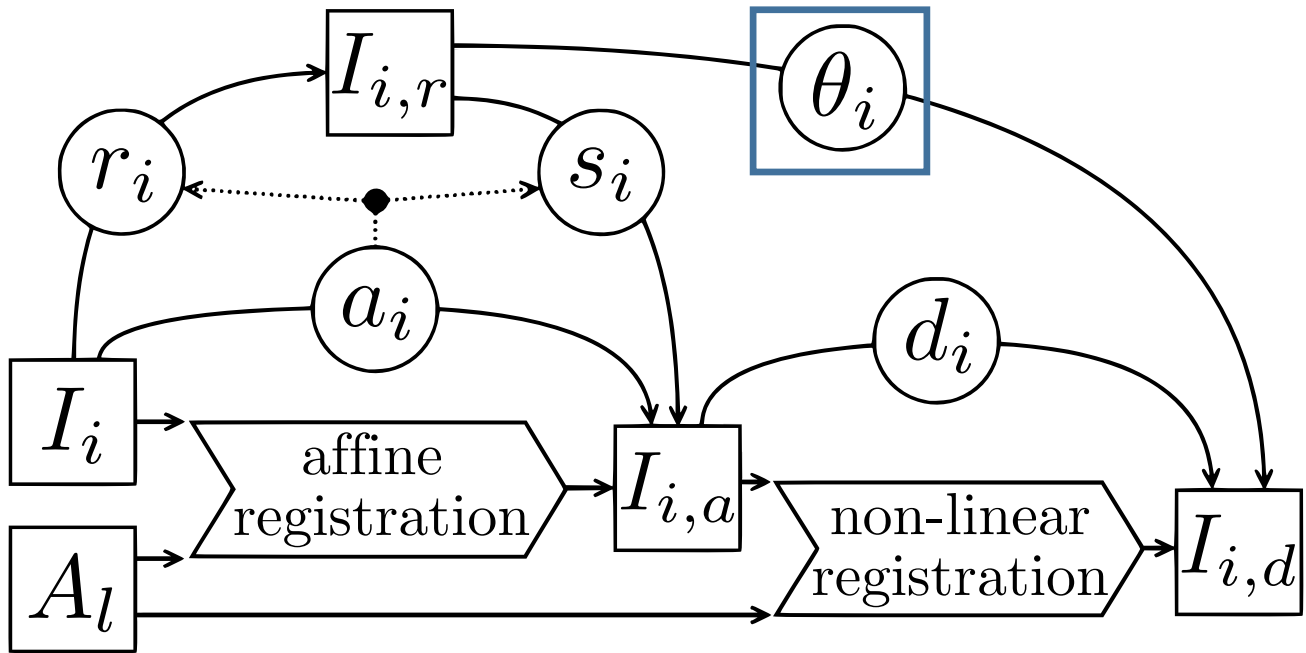


*Block-matching strategies for rigid registration of multimodal medical images. Commowick et al., 2012*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*

2-step registrations using block-matching algorithms:

- affine
  - decomposed into a rigid and a stretching part
- Diffeomorphic (made such as it outputs SVF)

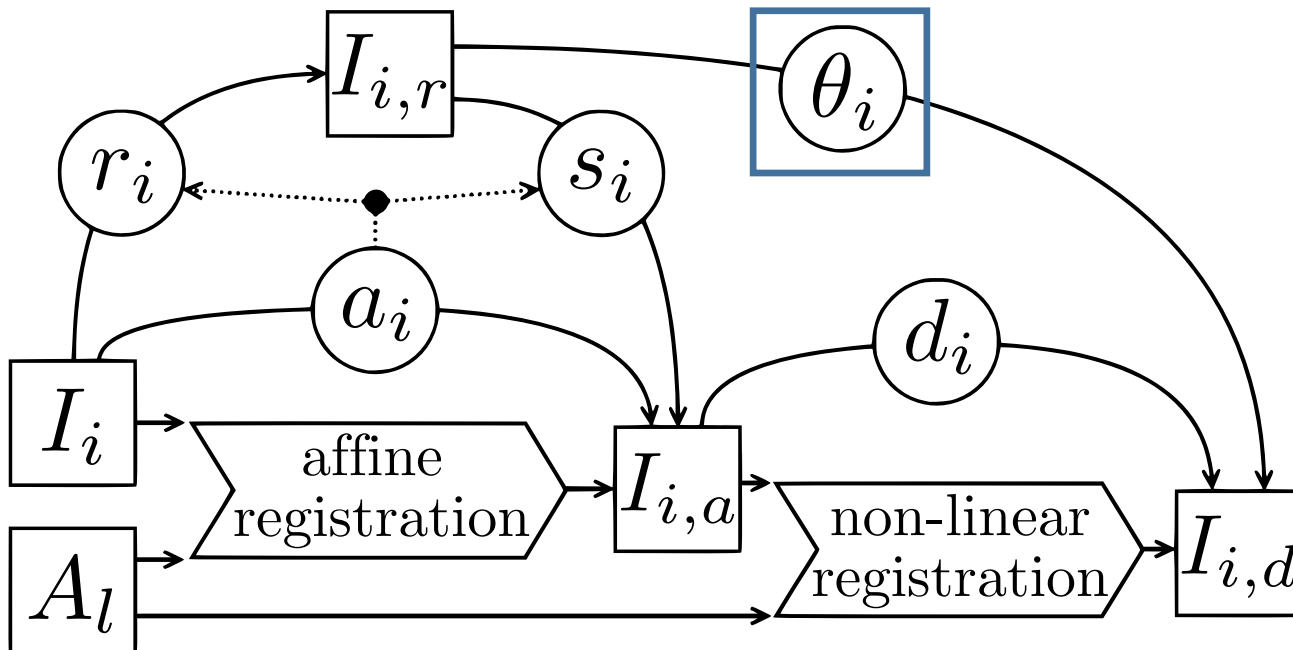


Block-matching strategies for rigid registration of multimodal medical images. Commowick et al., 2012

Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012

2-step registrations using block-matching algorithms:

- affine
  - decomposed into a rigid and a stretching part
- Diffeomorphic (made such as it outputs SVF)



Create SVF from  $s_i$ :

- Compute  $\log(s_i)$  (matrix)
- Apply  $\log(s_i)$  to each spatial point  
→  $\log(s_i)$  (SVF)

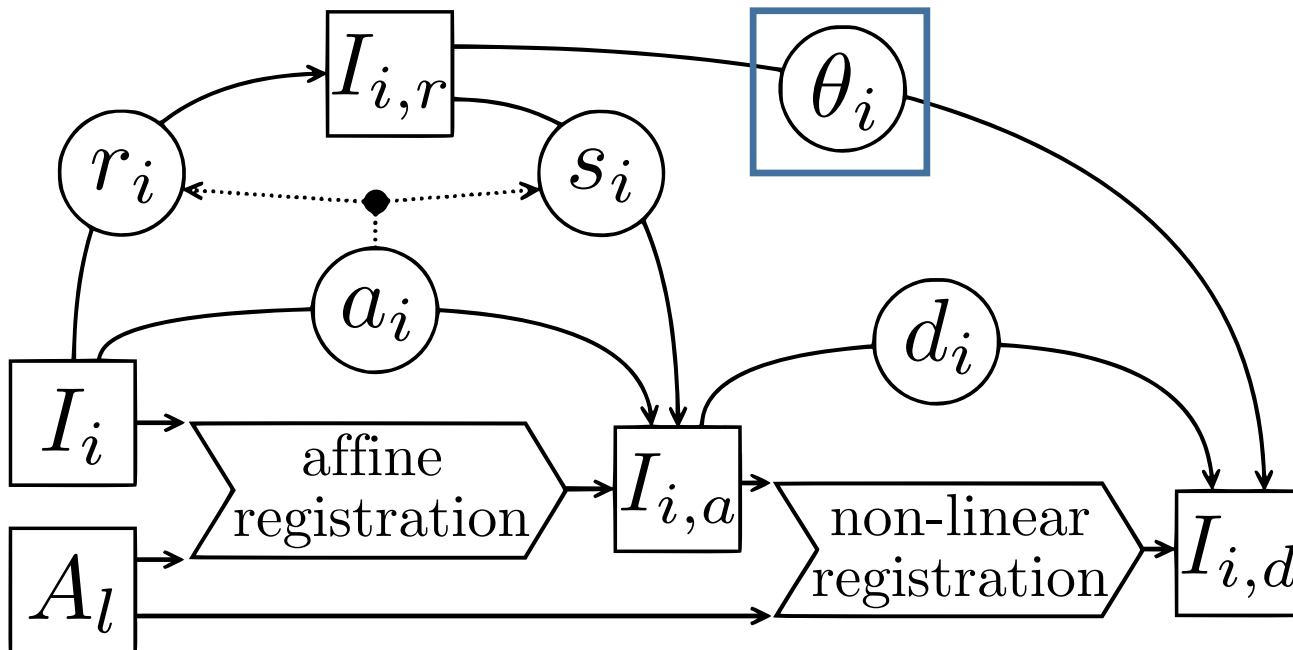
*Block-matching strategies for rigid registration of multimodal medical images. Commowick et al., 2012*

*Automated diffeomorphic registration of anatomical structures with rigid parts: application to dynamic cervical MRI. Commowick et al., 2012*



2-step registrations using block-matching algorithms:

- affine
  - decomposed into a rigid and a stretching part
- Diffeomorphic (made such as it outputs SVF)



Create SVF from  $s_i$  :

- Compute  $\log(s_i)$  (matrix)
- Apply  $\log(s_i)$  to each spatial point  
→  $\log(s_i)$  (SVF)

$$\log(\theta_i) = \text{BCH}(\log(s_i), \log(d_i))$$

# Creation of the new reference image



- Creation of the unbiasing transformation:  
Inverse of transformation average (through weight function):

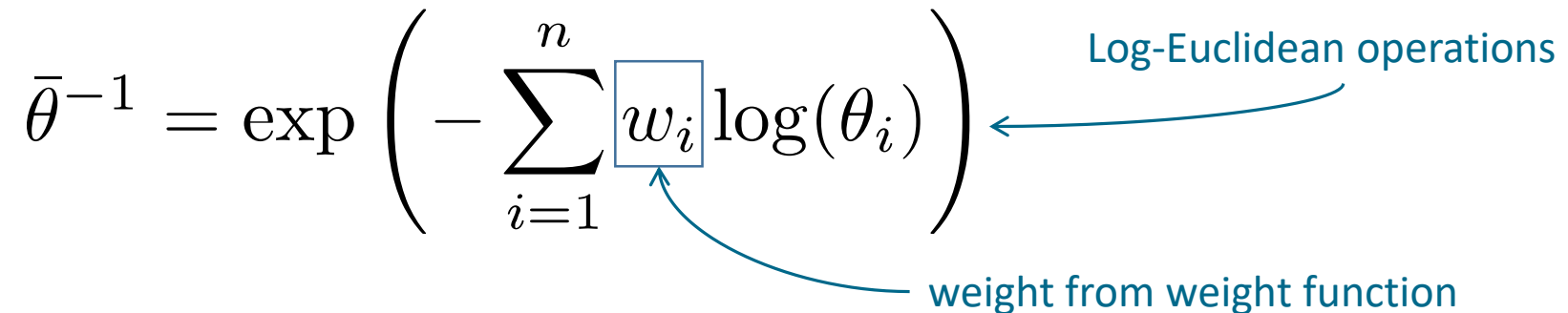
$$\bar{\theta}^{-1} = \exp \left( - \sum_{i=1}^n w_i \log(\theta_i) \right)$$

- Creation of the unbiasing transformation:  
Inverse of transformation average (through weight function):

$$\bar{\theta}^{-1} = \exp \left( - \sum_{i=1}^n w_i \log(\theta_i) \right)$$

Log-Euclidean operations

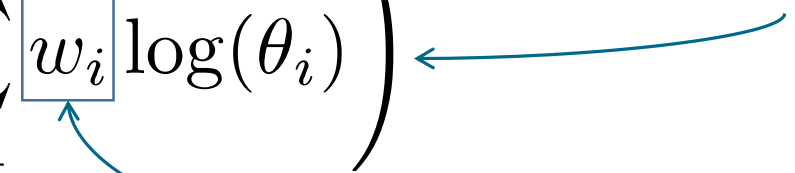
weight from weight function

The equation is presented with two blue annotations. One arrow points from the text 'Log-Euclidean operations' to the logarithm function in the sum. Another arrow points from the text 'weight from weight function' to the weight variable  $w_i$ , which is enclosed in a small blue square.

- Creation of the unbiasing transformation:  
Inverse of transformation average (through weight function):

$$\bar{\theta}^{-1} = \exp \left( - \sum_{i=1}^n w_i \log(\theta_i) \right)$$

Log-Euclidean operations



- Transform and average the initial images:

$$A = \sum_{i=1}^n w_i I_i \circ R_i \circ \theta_i \circ \bar{\theta}^{-1}$$

- Creation of the unbiasing transformation:  
Inverse of transformation average (through weight function):

$$\bar{\theta}^{-1} = \exp \left( - \sum_{i=1}^n \boxed{w_i} \log(\theta_i) \right)$$

Log-Euclidean operations

weight from weight function

- Transform and average the initial images:

new reference image

$$\boxed{A} = \sum_{i=1}^n \boxed{w_i} I_i \circ \boxed{R_i \circ \theta_i} \circ \boxed{\bar{\theta}^{-1}}$$

weight from weight function

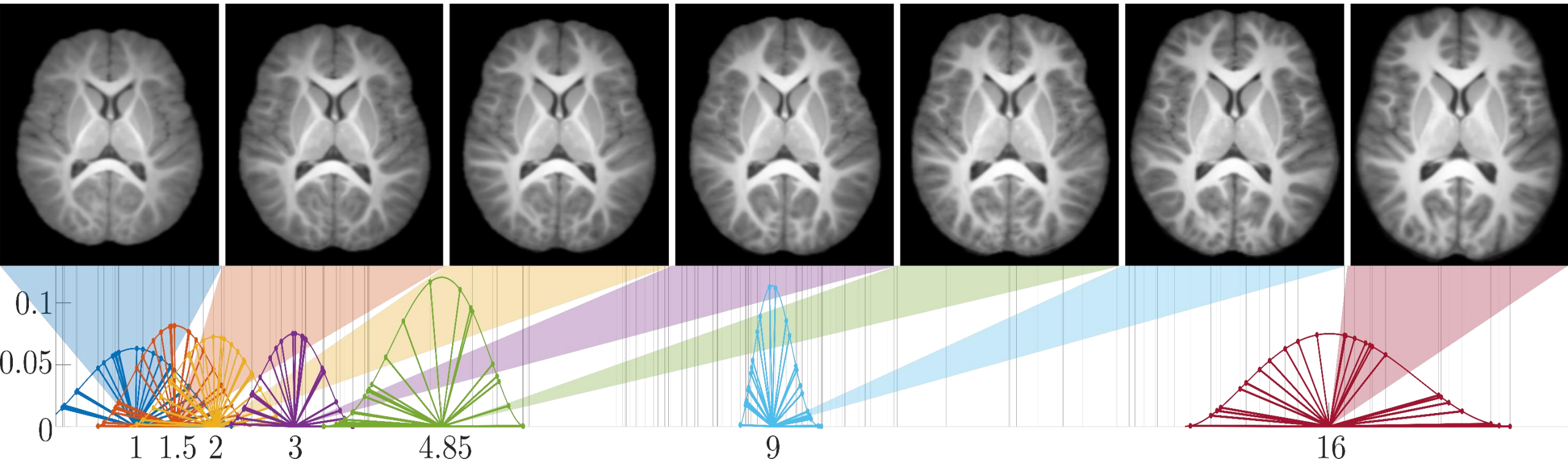
transformations from registration

unbiasing transformation

# Constructed atlas

# Results

197 healthy subjects from C-MIND database  
T1 weighted images 1mm iso  
about 25 subjects per sub-atlas



C-MIND database: <https://research.cchmc.org/c-mind>



# Code provision

- Anima: Open source software for medical image processing from the Empenn team

<https://github.com/Inria-Visages/Anima-Public>

Registration, transformation composition...



- Anima-Scripts: Open source processing scripts using Anima tools

<https://github.com/Inria-Visages/Anima-Scripts-Public>

Atlasing script





Thank you for your attention !  
Question ?

Contact: [antoine.legouhy@irisa.fr](mailto:antoine.legouhy@irisa.fr)