

# Computing Methods for Experimental Physics and Data Analysis

Data Analysis in Medical Physics

Lecture 5b: Image coregistration

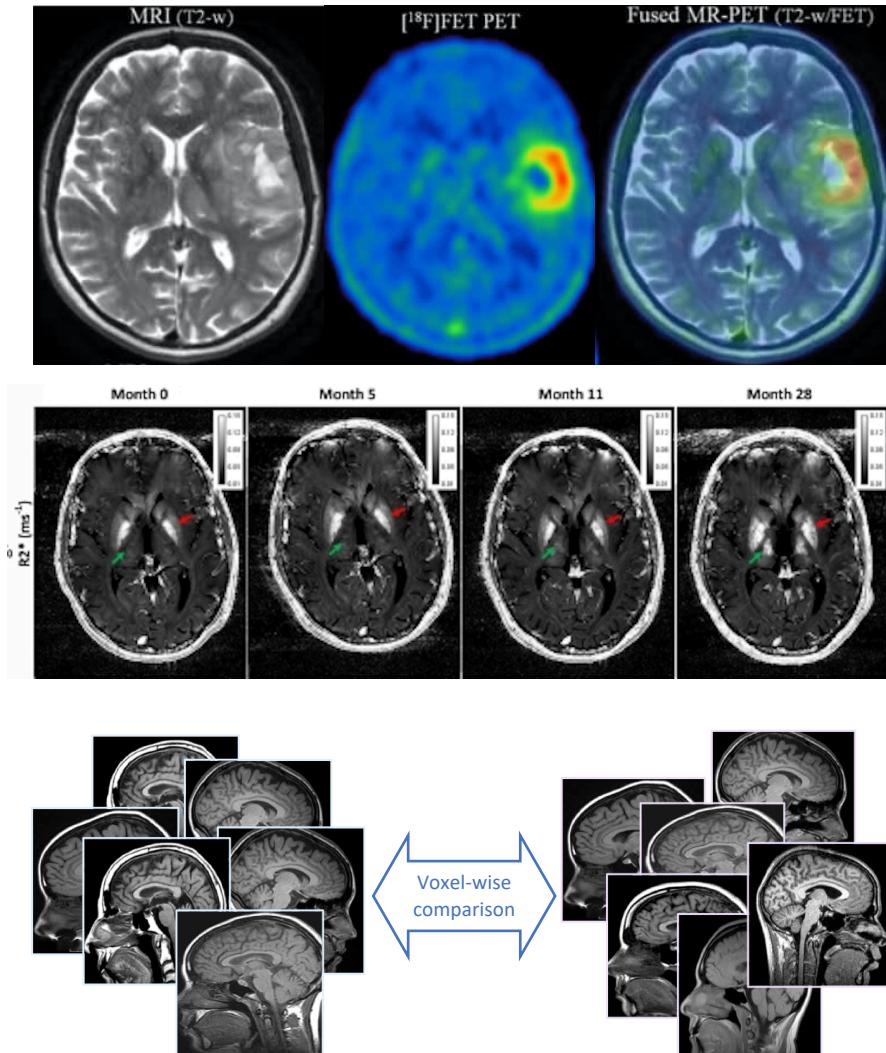
Alessandra Retico

[alessandra.retico@pi.infn.it](mailto:alessandra.retico@pi.infn.it)

INFN - Pisa

# Image registration

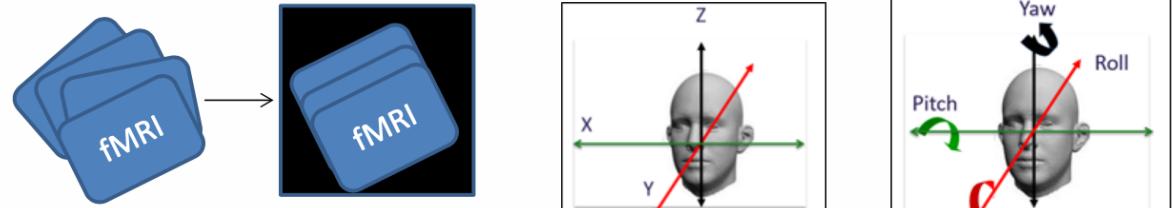
- Image registration is a process that transforms images acquired with different conditions (e.g. geometry of acquisition, resolution, modality) so that they can be put in spatial relation with a reference image
- Registration is necessary to:
  - compare joint information by different imaging modalities of the same subject (multimodal studies)
  - compare image information of the same subjects at different time points (e.g. fMRI data, longitudinal studies)
  - compare image information of different subjects (group analyses)



# Image registration

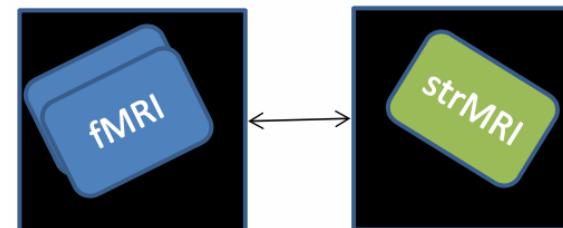
- Realignment:

- Used in motion correction in fMRI; rigid alignment to a template
- Rigid transformation: 6 DoF (3 DoF for translations across axes, 3 DoF for rotations) + interpolation



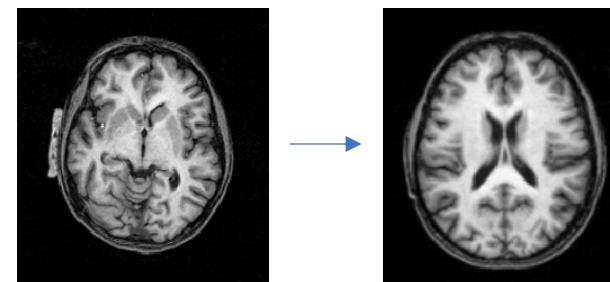
- Coregistration:

- Used to match modalities
- Rigid transformation (6 DoF) + interpolation

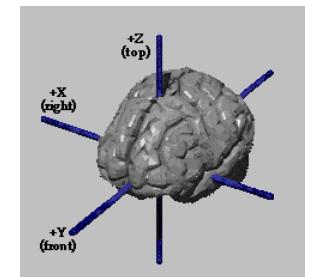


- Normalization

- Used to match images to a template
- Affine transformation (to start): 12 DoF (3 translations, 3 rotations, 3 scaling, 3 skewing)
- Non-linear deformation/warping (to refine the alignment): 1000s DoF

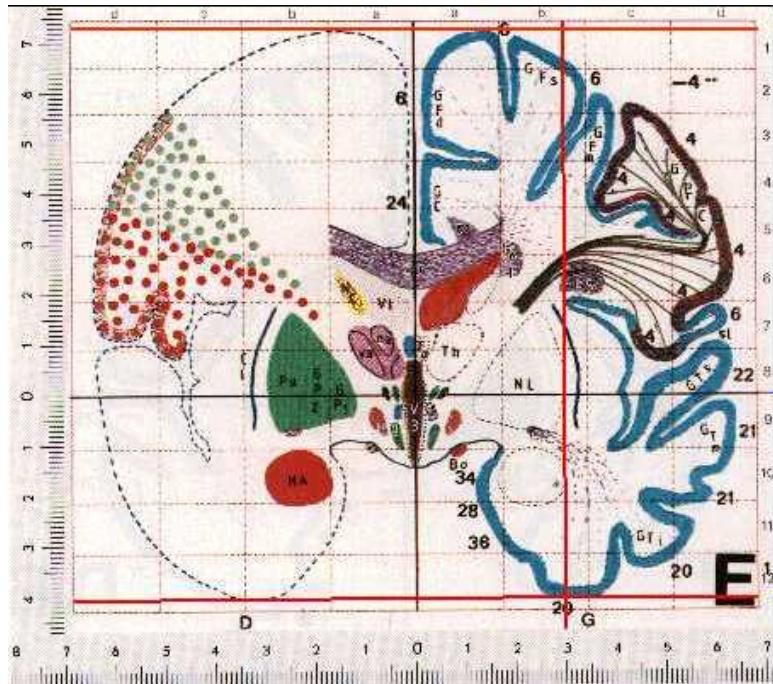


reference orientation

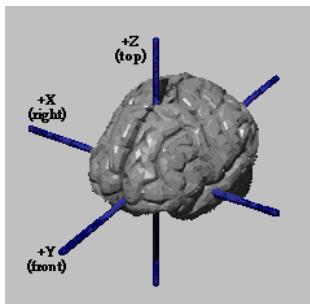
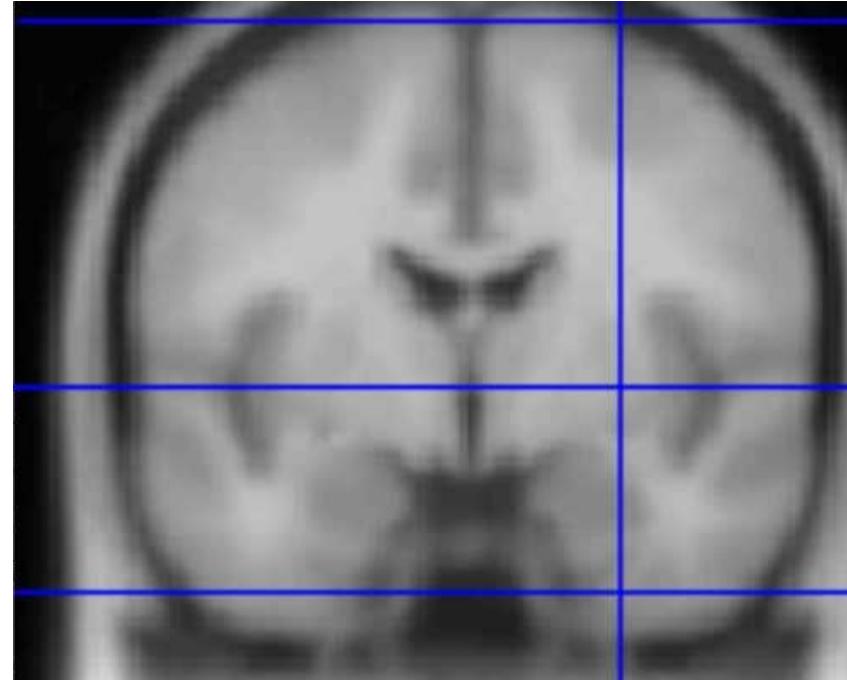


# Standard reference space: Montreal Neurological Initiative (MNI)

The Talairach Atlas



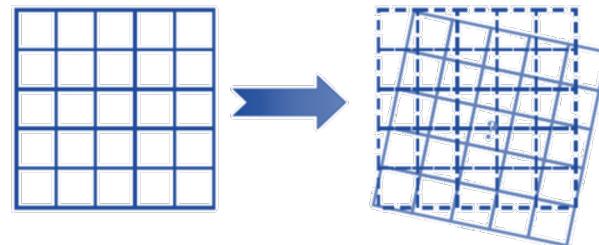
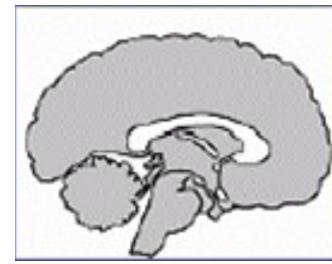
The MNI/ICBM AVG152 Template



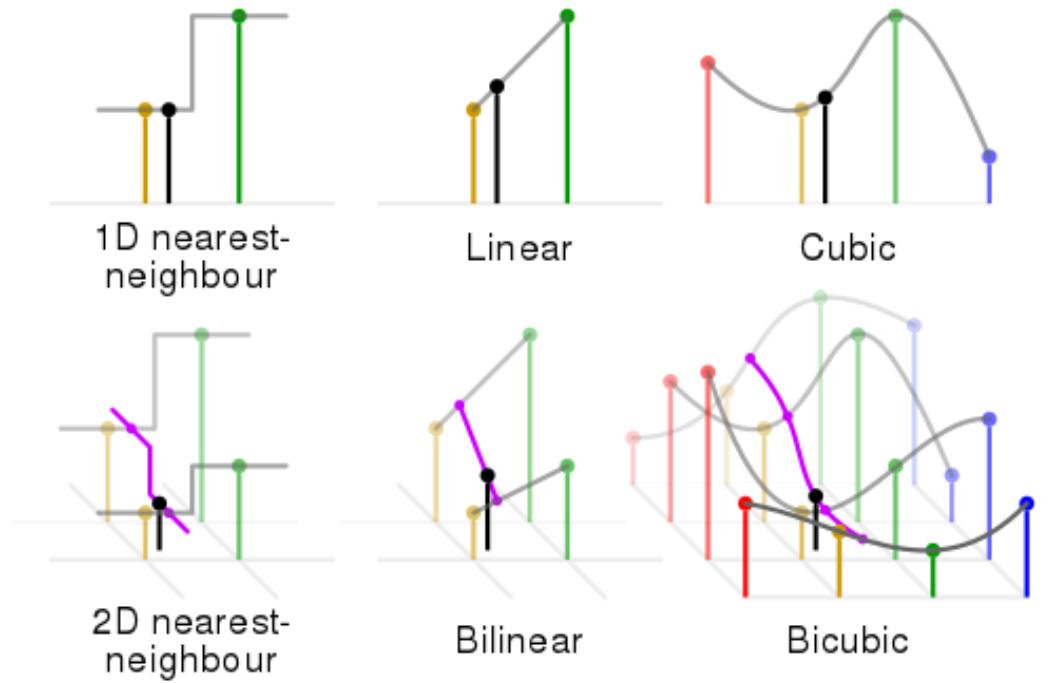
The MNI template follows the *convention* of the Talairach Atlas (Talairach and Tournoux, 1988), but does not match the *particular brain*  
<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>

# Image transformations

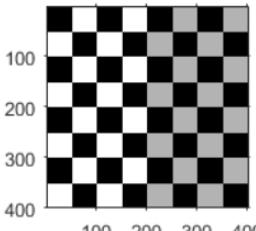
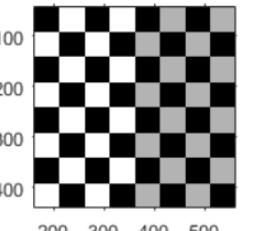
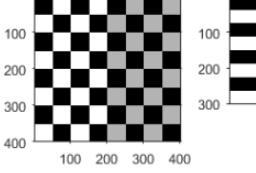
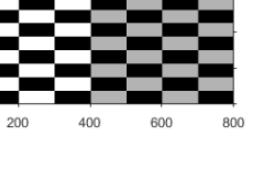
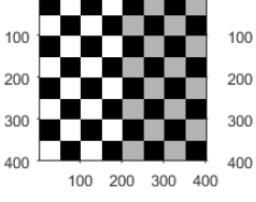
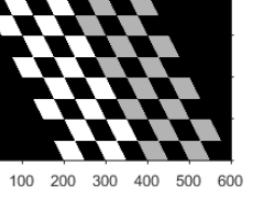
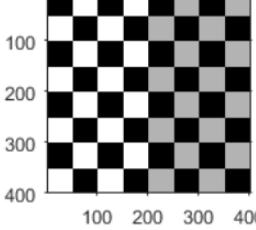
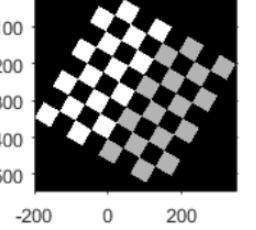
- Geometric transformations: translation, rotation, scaling, shear



- Transformed images often need resampling; an interpolation method should be specified, e.g.:
  - Nearest neighbor
  - Bilinear interpolation
  - Bicubic interpolation

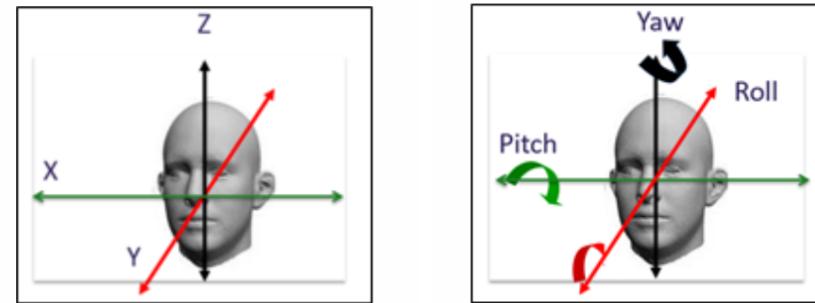
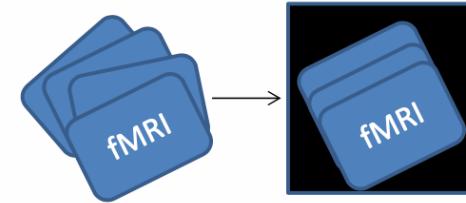


# 2D affine transformation

2-D Affine Transformation	Example (Original and Transformed Image)	Transformation Matrix	
Translation	 	$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ t_x & t_y & 1 \end{bmatrix}$	$t_x$ specifies the displacement along the $x$ axis $t_y$ specifies the displacement along the $y$ axis. For more information about pixel coordinates, see <a href="#">Image Coordinate Systems</a> .
Scale	 	$\begin{bmatrix} s_x & 0 & 0 \\ 0 & s_y & 0 \\ 0 & 0 & 1 \end{bmatrix}$	$s_x$ specifies the scale factor along the $x$ axis $s_y$ specifies the scale factor along the $y$ axis.
Shear	 	$\begin{bmatrix} 1 & sh_y & 0 \\ sh_x & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$	$sh_x$ specifies the shear factor along the $x$ axis $sh_y$ specifies the shear factor along the $y$ axis.
Rotation	 	$\begin{bmatrix} \cos(q) & \sin(q) & 0 \\ -\sin(q) & \cos(q) & 0 \\ 0 & 0 & 1 \end{bmatrix}$	$q$ specifies the angle of rotation about the origin.

# 3D Rigid-body Transformations

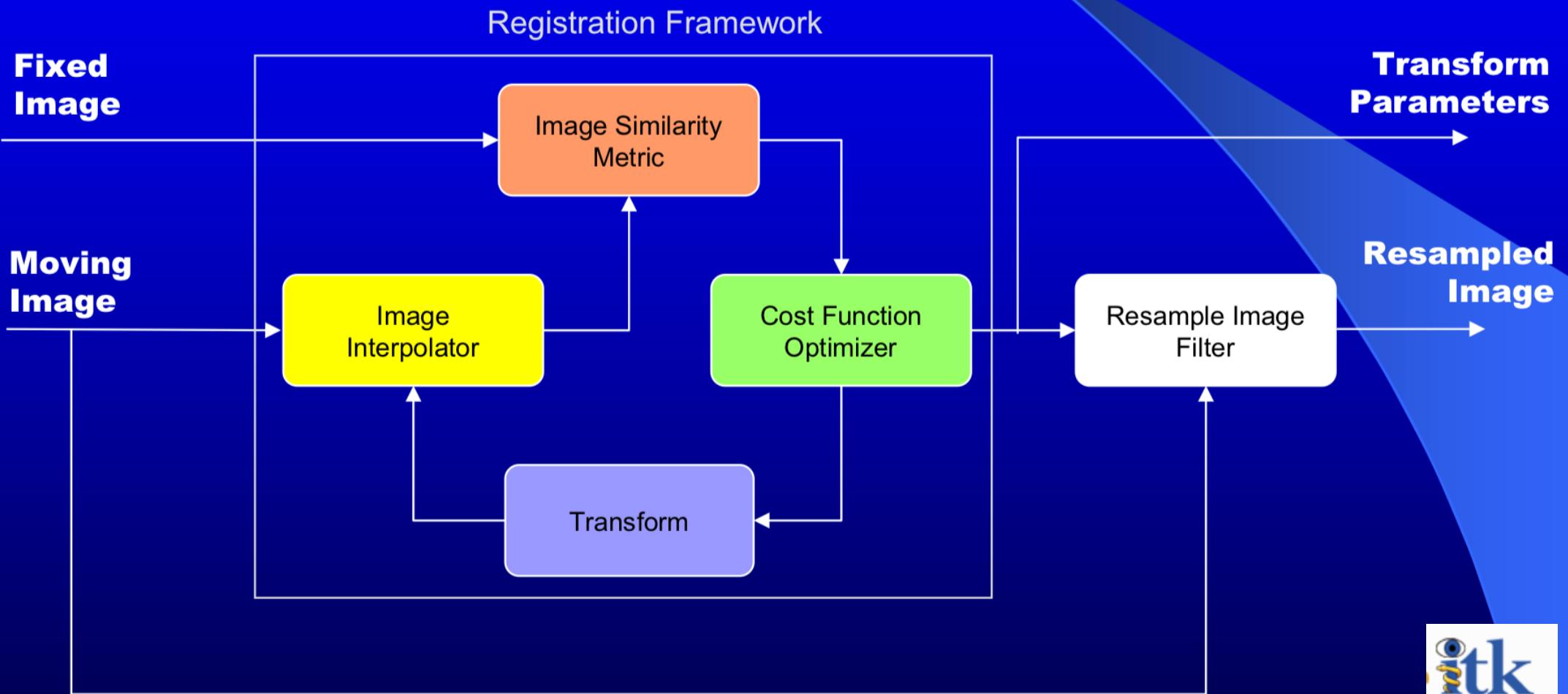
- A 3D rigid body transform is defined by:
  - 3 translations - in X, Y & Z directions
  - 3 rotations - about X, Y & Z axes
- The order of the operations matters



$$\begin{pmatrix} 1 & 0 & 0 & \mathbf{X}_{\text{trans}} \\ 0 & 1 & 0 & \mathbf{Y}_{\text{trans}} \\ 0 & 0 & 1 & \mathbf{Z}_{\text{trans}} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos\Phi & \sin\Phi & 0 \\ 0 & -\sin\Phi & \cos\Phi & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos\Theta & 0 & \sin\Theta & 0 \\ 0 & 1 & 0 & 0 \\ -\sin\Theta & 0 & \cos\Theta & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos\Omega & \sin\Omega & 0 & 0 \\ -\sin\Omega & \cos\Omega & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

Translations                      Pitch about x axis                      Roll about y axis                      Yaw about z axis

# Registration Framework Components



# Image registration key elements

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- To formulate an image registration problem the following elements need to be defined:
  - the feature space – the domain containing the information for matching
    - Focus on intensity-based measures
  - the search space – the class of transformations to be used to establish the correspondence
    - E.g. rigid, affine, diffeomorphisms
  - the search strategy – the optimization process to be conducted to assess the correspondence
  - the similarity metric: the figure of merit chosen in the optimization process
- Then, the registration process consists in the following two operations:
  - Optimise the parameters that describe a spatial transformation between the source (moving) and reference (fixed) images
  - Transforming and resampling the moving images according to the determined transformation parameters

# Voxel-to-world Transforms

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- Affine transform associated with each image
  - Maps from voxels ( $x=1..n_x$ ,  $y=1..n_y$ ,  $z=1..n_z$ ) to some world coordinate system, e.g.,
    - Scanner coordinates
    - Talairach and Tournoux (T&T) or Montreal Neurological Initiative (MNI) coordinates, i.e. spatially normalised images
- Registering image B (moving) to image A (fixed) will update B's voxel-to-world mapping
  - Mapping from voxels in A to voxels in B is by
    - A-to-world using  $M_A$ , then world-to-B using  $M_B^{-1}$ , i.e.  $M_B^{-1} M_A$

# Optimization protocols and cost functions

Image registration is done by optimisation.

Optimisation involves finding some best parameters according to a cost function, which is either minimised or maximised

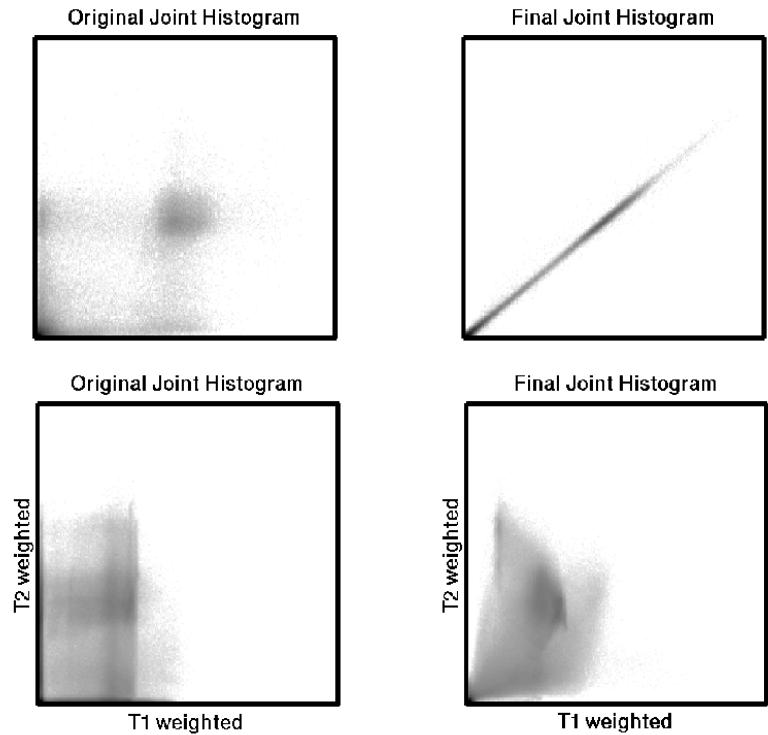
## Optimization methods

- Gradient descent
- Genetic algorithms

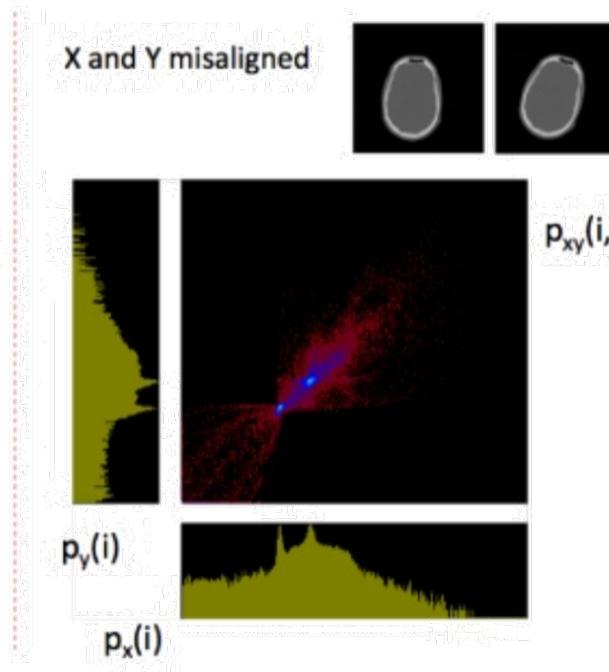
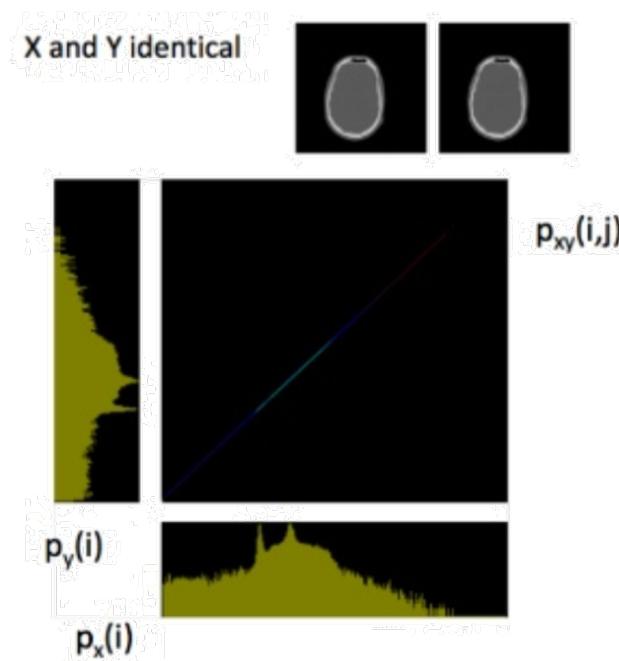
## Cost functions

- Intra-modal (e.g. realignment in fMRI)
  - Mean squared difference (minimise)
  - Normalised cross correlation (maximise)
- Inter-modal (or intra-modal)
  - Mutual information (maximise)
  - Normalised mutual information (maximise)
  - Entropy correlation coefficient (maximise)

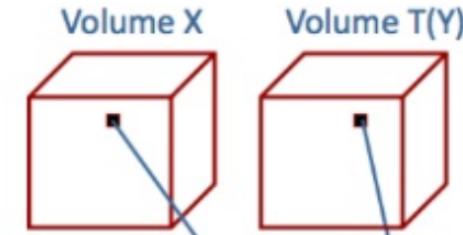
The joint histogram is a useful tool for visualizing the relationship between the intensities of corresponding voxels in two or more images.



# Intra-modal registration



## Normalized Cross Correlation (NCC)

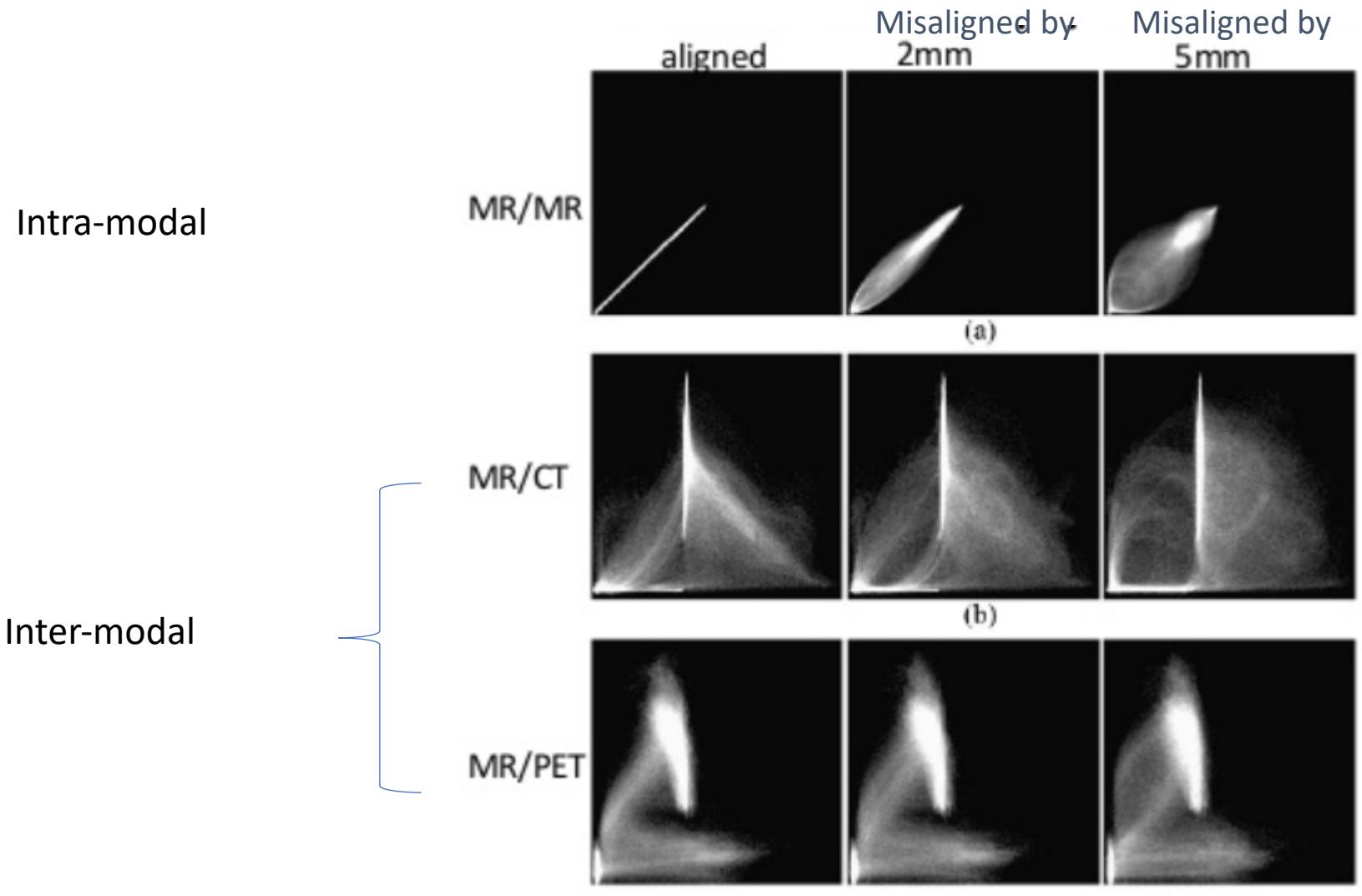


$$NCC = \frac{1}{N} \sum_i \frac{(x_i - \bar{x})(y_i - \bar{y})}{\sigma_x \sigma_y}$$

**Normalized Cross Correlation:**  
Expresses the linear relationship between voxel intensities in the two volumes

$\bar{x}$  : Mean  
 $\sigma_x$  : Standard deviation  
 $N$  : Number of pixels

# Joint histograms



# Inter-modal registration

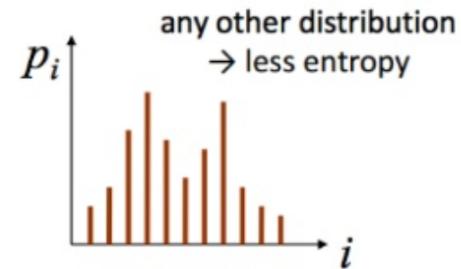
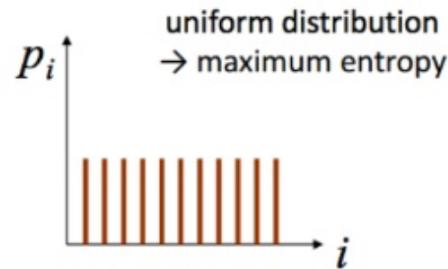
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- Image registration is considered as to maximize the amount of shared information in two images
  - reducing the amount of information in the combined image
- Algorithms used
  - Joint entropy
    - Joint entropy measures the amount of information in the two images combined
  - **Mutual information**
    - A measure of how well one image explains the other, and is maximized at the optimal alignment
  - Normalized Mutual Information

# Entropy for image registration

Shannon Entropy, developed in the 1940s  
(communication theory)

$$H = -\sum_i p_i \log p_i$$



- **Shannon's Entropy**

$$H = \sum_i p_i \cdot \log \frac{1}{p_i}$$

- weighs the information based on the probability that an outcome will occur
- second term shows the amount of information an event provides is inversely proportional to its probability of occurring

## Entropy for Image Registration

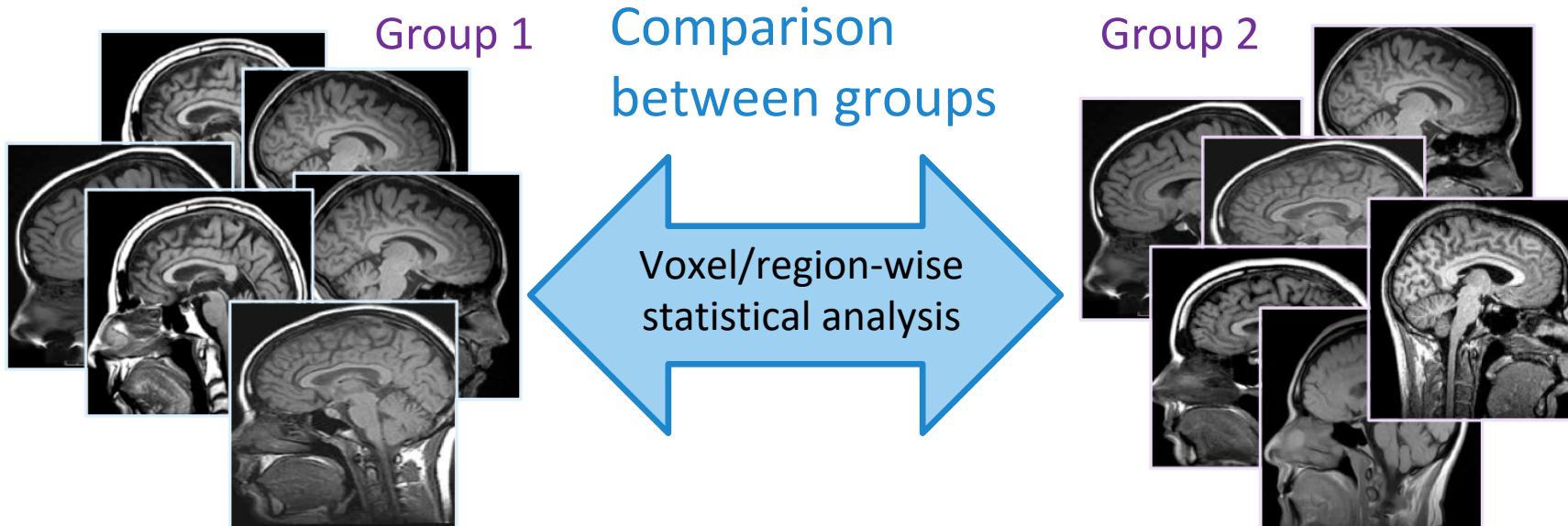
- Using joint entropy for registration
  - Define joint entropy to be:

$$H(A, B) = -\sum_{i,j} p(i, j) \cdot \log[p(i, j)]$$

- Images are registered when one is transformed relative to the other to minimize the joint entropy
- The dispersion in the joint histogram is thus minimized

# A typical task in neuroimaging studies: voxel-wise comparison between groups of subjects

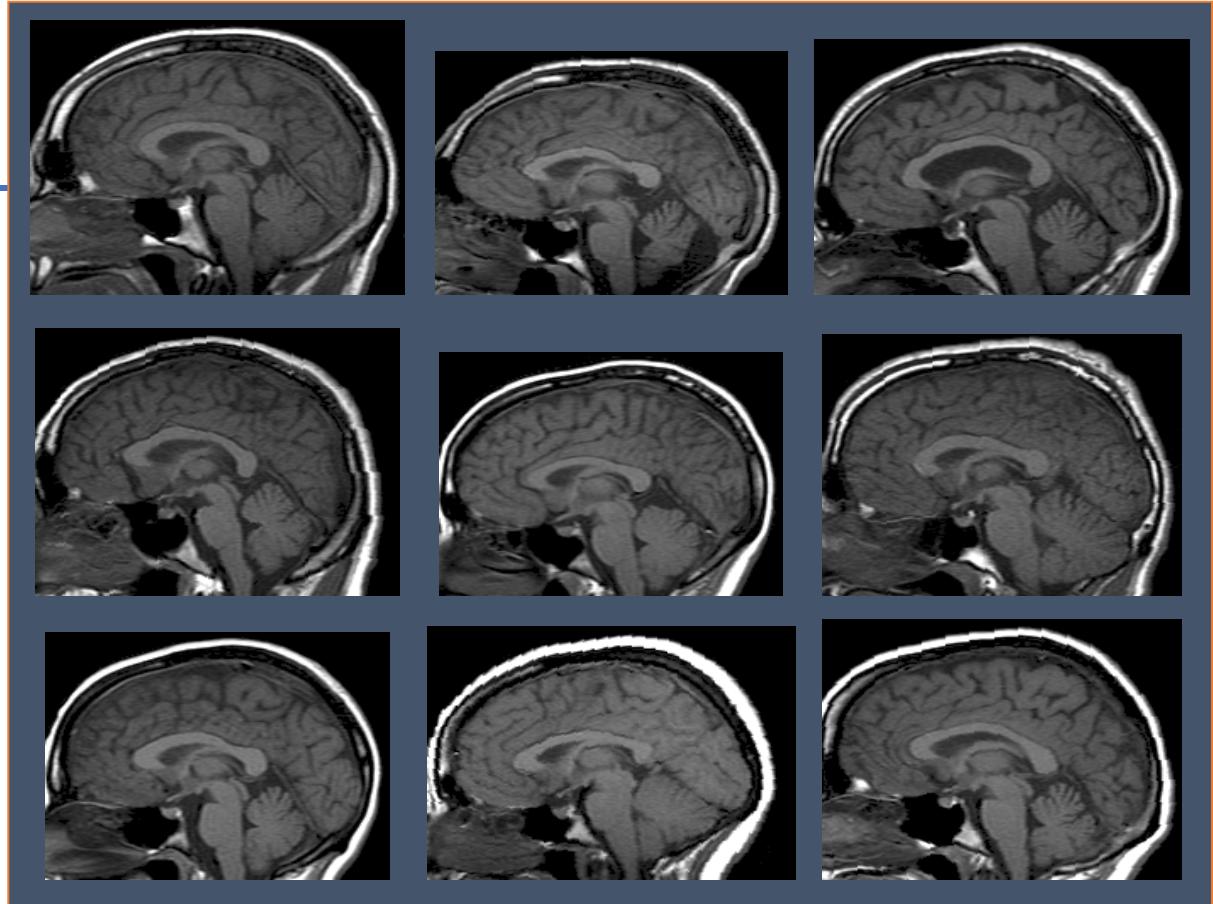
The inter-subject coregistration is necessary if we want to compare local brain characteristics of different subjects



- Comparison between Patients (group 1) and Controls (group 2):
  - to detect pathology specific brain alterations
- Need to bring them all into a common anatomical space.
  - Examine homologous regions across subjects
  - Report findings in a common anatomical space (e.g. MNI space)

# Coregister to a template

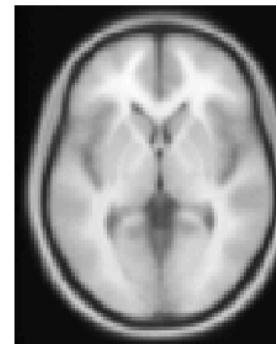
- How can we carry out a voxel-wise comparison of brains of different subjects?
- Images need to be **spatially aligned**



Each image is registered to a  $T_1$  template



12 DoF affine transformation, to match the size and position, possibly + non-linear warping

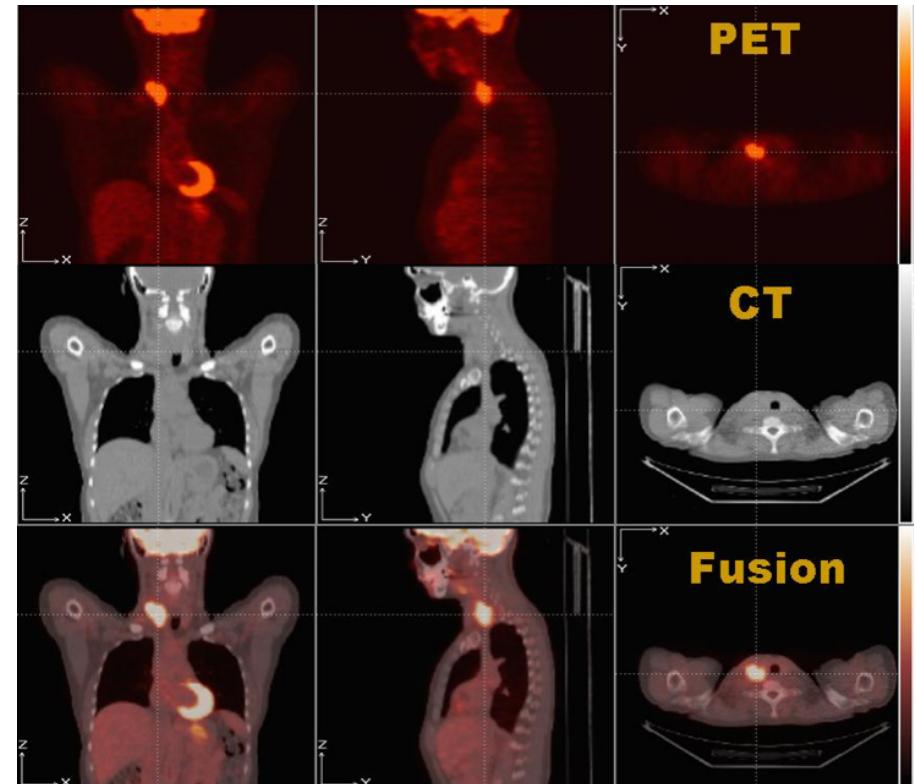


This is a necessary preliminary step in all template-based segmentation software

# Coregister different images of the same subject

The intra-subject *coregistration* is useful:

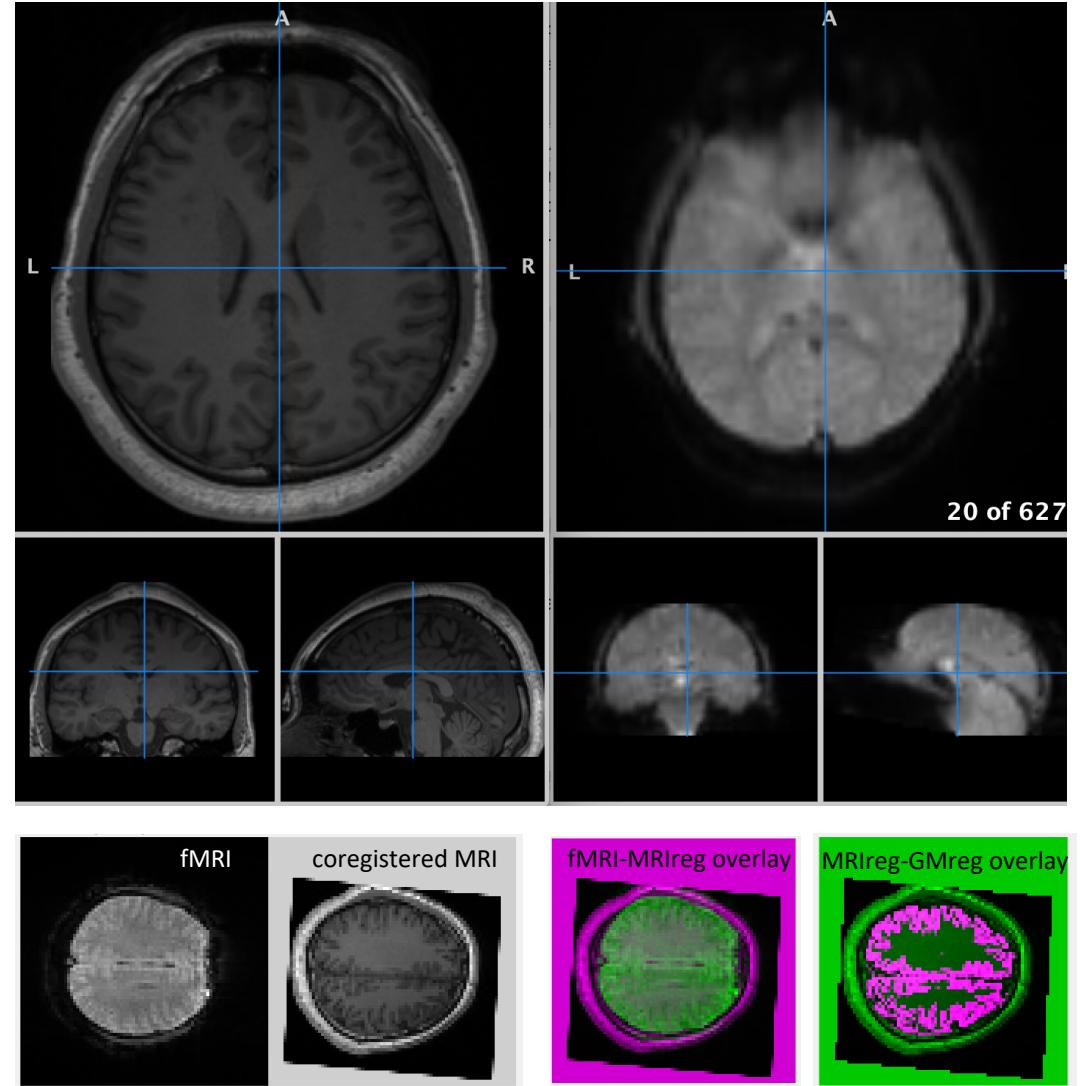
- To reduce motion artifact during sequential acquisitions (e.g. fMRI)
- To detect changes in longitudinal studies (e.g. to study the effect of age or of a disease)
- To *overlay* information acquired with different image modalities (image fusion)



See demo code Lecture5\_demo\_image\_registration mlx

# Lecture5\_demo\_image\_registration mlx

- We will coregister the structural MRI and fMRI data of one subjects
- The volumes of the two different modalities are very roughly similarly oriented
- The voxel size are different
- We move the higher resolution image to match the lower resolution one to avoid a strong resampling of the functional signal
- Once the two modalities are aligned, the same transformation can be applied for example to GM segmented volume, which is originally aligned with the structural MRI volume



# The imregdemons function is based on

## Image matching as a diffusion process: an analogy with Maxwell's demons

J.-P. Thirion\*

INRIA, Equipe Epidaure, 2004 Route des Lucioles BP93, 06902 Sophia-Antipolis, France

### Abstract

In this paper, we present the concept of diffusing models to perform image-to-image matching. Having two images to match, the main idea is to consider the objects boundaries in one image as semi-permeable membranes and to let the other image, considered as a deformable grid model, diffuse through these interfaces, by the action of effectors situated within the membranes. We illustrate this concept by an analogy with Maxwell's demons. We show that this concept relates to more traditional ones, based on attraction, with an intermediate step being optical flow techniques. We use the concept of diffusing models to derive three different non-rigid matching algorithms, one using all the intensity levels in the static image, one using only contour points, and a 1-synthesized deformation field.

Keywords: image registration, non-rigid registration, non-rigid transformation

Received October 2000; accepted July 2001



## A fast diffeomorphic image registration algorithm

John Ashburner

Wellcome Trust Centre for Neuroimaging, 12 Queen Square, London, WC1N 3BG, UK

Received 26 October 2006; revised 14 May 2007; accepted 3 July 2007

Available online 18 July 2007

Comput.

This paper describes DARTEL, which is an algorithm for diffeomorphic

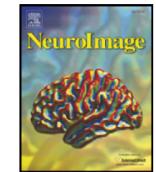
Many registration approaches still use a small deformation

NeuroImage 45 (2009) S61–S72

Contents lists available at ScienceDirect

NeuroImage

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



ELSEVIER

## Diffeomorphic demons: Efficient non-parametric image registration

Tom Vercauteren <sup>a,\*</sup>, Xavier Pennec <sup>b</sup>, Aymeric Perchant <sup>a</sup>, Nicholas Ayache <sup>b</sup>

<sup>a</sup> Mauna Kea Technologies, 9 rue d'Enghien, 75010 Paris, France

<sup>b</sup> INRIA Sophia Antipolis, Asclepios Research Project, 2004 route des Lucioles - BP 93, 06902 Sophia Antipolis Cedex, France

### ABSTRACT

We propose an efficient non-parametric diffeomorphic image registration algorithm based on Thirion's demons algorithm. In the first part of this paper, we show that Thirion's demons algorithm can be seen as an optimization procedure on the entire space of displacement fields. We provide strong theoretical roots to the different variants of Thirion's demons algorithm. This analysis predicts a theoretical advantage for the symmetric forces variant of the demons algorithm. We show on controlled experiments that this advantage is confirmed in practice and yields a faster convergence. In the second part of this paper, we adapt the optimization procedure underlying the demons algorithm to a space of diffeomorphic transformations. In contrast to many diffeomorphic registration algorithms, our solution is computationally efficient since in practice it only replaces an addition of displacement fields by a few compositions. Our experiments show that in addition to being diffeomorphic, our algorithm provides results that are similar to the ones from the demons algorithm but with transformations that are much smoother and closer to the gold standard, available in controlled experiments, in terms of Jacobians.

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NeuroImage

[www.elsevier.com/locate/ynimg](http://www.elsevier.com/locate/ynimg)  
NeuroImage 38 (2007) 95–113

# Image processing and analysis resources



The screenshot shows the homepage of the Insight Toolkit (ITK) website. At the top, there's a navigation bar with the Kitware logo, a search bar, and links for PROJECT, RESOURCES, HELP, and OPEN SOURCE. Below the navigation is a large banner featuring the ITK logo and the URL <https://itk.org/itkindex.html>. The main content area starts with a welcome message about ITK, its goals, and a list of supporting organizations. To the right, there's a detailed section about ITK, a 3D image segmentation visualization, and a summary box.

Welcome to the **Insight Toolkit (ITK)**. ITK is an open-source, cross-platform system that provides developers with an extensive suite of software tools for image analysis. Developed through extreme programming methodologies, ITK employs leading-edge algorithms for registering and segmenting multidimensional data. The goals for ITK include:

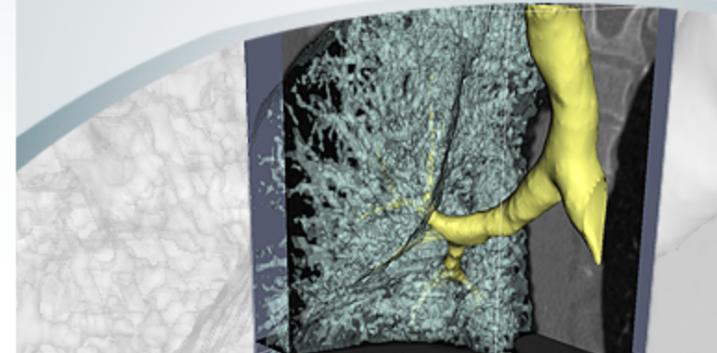
- Supporting the Visible Human Project.
- Establishing a foundation for future research.
- Creating a repository of fundamental algorithms.
- Developing a platform for advanced product development.
- Support commercial application of the technology.
- Create conventions for future work.
- Grow a self-sustaining community of software users and developers.

[Start Using ITK ▶](#)



**NIMH** **NIDCD** **NIDCR**

**ITK**  
ITK provides leading-edge segmentation and registration algorithms in two, three, and more dimensions; it is distributed as an open-source software package.



**ITK: Insight Segmentation and Registration Toolkit, a C++ open source image analysis toolkit**

# SimpleITK: simplified, open source, interface to ITK

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Search docs

## TABLE OF CONTENTS

- Installation
- Fundamental Concepts
- Registration Overview
- Common Conventions
- Reading and Writing for Images and Transforms
- SimpleITK Filters
- Building SimpleITK
- Setting Up Eclipse and Visual Studio
- Tutorials and Courses
- Frequently Asked Questions
- Examples
  - Hello World

## DemonsRegistration1

### Overview

This example illustrates how to use the [classic Demons registration algorithm](#). The user supplied parameters for the algorithm are the number of iterations and the standard deviations for the Gaussian smoothing of the total displacement field. Additional methods which control regularization, total field smoothing for elastic model or update field smoothing for viscous model are available.

The underlying assumption of the demons framework is that the intensities of homologous points are equal. The example uses histogram matching to make the two images similar prior to registration. This is relevant for registration of MR images where the assumption is not valid. For other imaging modalities where the assumption is valid, such as CT, this step is not necessary. Additionally, the command design pattern is used to monitor registration progress. The resulting deformation field is written to file.

See also: [DemonsRegistration2](#).

### Code

C++

Python

R

Search

TABLE

Install

Fundam

Registr

Commu

Readin

Transfo

Simple

Fundamental Concepts

Registration Overview

Common Conventions

Reading and Writing for Images and  
Transforms

SimpleITK Filters

Building SimpleITK

Setting Up Eclipse and Visual Studio

Tutorials and Courses

Frequently Asked Questions

Examples

Hello World

CSharp Integration

DemonsRegistration1

Overview

Code

DemonsRegistration2

Read Image Meta-Data Dictionary  
and Print

Dicom Series Reader

Dicom Series Read Modify Write

Read the Docs

v: master ▾

C++

Python

R

```
#!/usr/bin/env python

from __future__ import print_function

import SimpleITK as sitk
import sys
import os

def command_iteration(filter):
    print("{0:3} = {1:10.5f}".format(filter.GetElapsedIterations(),
                                    filter.GetMetric()))

if len( sys.argv ) < 4:
    print( "Usage: {0} <fixedImageFilter> <movingImageFile> <outputTransformFile>".format(sys.argv[0]))
    sys.exit ( 1 )

fixed = sitk.ReadImage(sys.argv[1], sitk.sitkFloat32)

moving = sitk.ReadImage(sys.argv[2], sitk.sitkFloat32)

matcher = sitk.HistogramMatchingImageFilter()
matcher.SetNumberOfHistogramLevels(1024)
matcher.SetNumberOfMatchPoints(7)
matcher.ThresholdAtMeanIntensityOn()
moving = matcher.Execute(fixed)

# The basic Demons Registration Filter
# Note there is a whole family of Demons Registration algorithms included in SimpleITK
demons = sitk.DemonsRegistrationFilter()
demons.SetNumberOfIterations( 50 )
# Standard deviation for Gaussian smoothing of displacement field
demons.SetStandardDeviations( 1.0 )
```

# Widely used software suites for coregistration in neuroimaging

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Help Login  
**FSL**

<https://fsl.fmrib.ox.ac.uk/fsl/>

FSL is a comprehensive library of analysis tools for FMRI, MRI and DTI brain imaging data.

## FMRIB Software Library v6.0

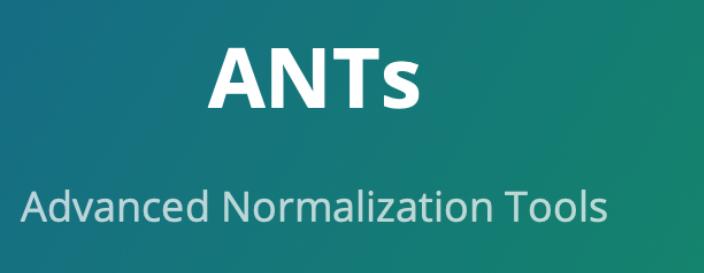
Created by the [Analysis Group](#), FMRIB, Oxford, UK.

<https://www.fil.ion.ucl.ac.uk/spm/software/>



SPM is made freely available to the [neuro]imaging community, to promote collaboration and a common analysis scheme across laboratories. The software represents the implementation of the theoretical concepts of Statistical Parametric Mapping in a complete analysis package.

The SPM software is a suite of MATLAB ([The MathWorks, Inc](#)) functions and subroutines with some externally compiled C routines. SPM was written to organise and interpret our functional neuroimaging data. The distributed version is the same as that we use ourselves.



University of Pennsylvania    <http://stnava.github.io/ANTs/>  
Richards Medical Research Laboratories

Advanced Normalization Tools (ANTs) extracts information from complex datasets that include imaging. ANTs development is led by Brian Avants and supported by other researchers and developers at PICSL and other institutions.



<https://afni.nimh.nih.gov>  
**AFNI** (**A**nalysis of **F**unctional **N**euro**I**mages) is a leading software suite of C, Python, R programs and shell scripts primarily developed for the analysis and display of anatomical and functional MRI (FMRI) data. It is freely available (both in source code and in precompiled binaries) for research purposes. The software is made to run on virtually an Unix system with X11 and Motif displays. Binary Packages are provided for MacOS and Linux systems including Fedora, Ubuntu (including Ubuntu under the Windows Subsystem for Linux)

# References and sources

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- Image processing and analysis resources
  - ITK - <https://itk.org/itkindex.html>
- Neuroimaging coregistration software
  - FSL - <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki>
  - AFNI - <https://afni.nimh.nih.gov>
  - SPM - <https://www.fil.ion.ucl.ac.uk>
  - ANTs - <http://picsl.upenn.edu/software/ants/>
- Sources
  - <https://simpleitk.readthedocs.io/en/master/Documentation/docs/source/tutorialsAndCourses.html>
  - <https://itk.org/CourseWare/Training/RegistrationMethodsOverview.pdf>
  - <https://simpleitk.readthedocs.io/en/master/Documentation/docs/source/registrationOverview.html>