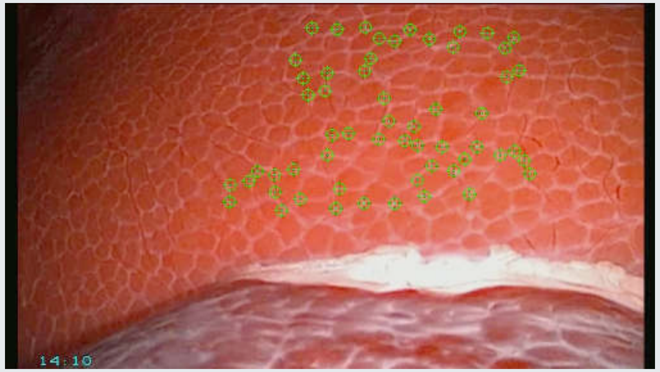
Introduction to Medical Image Registration

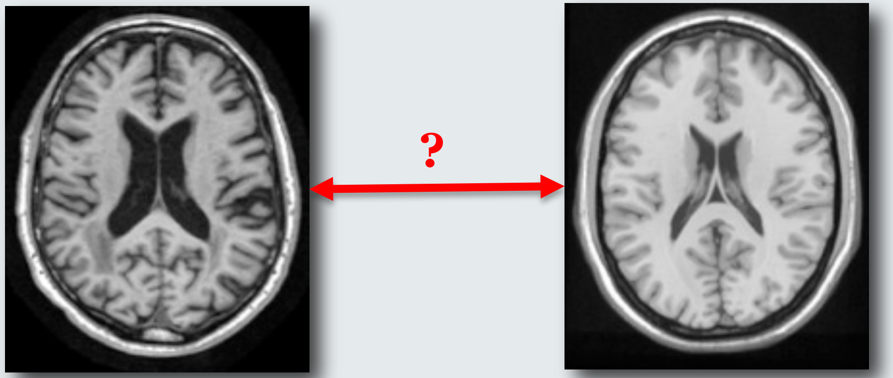
Tom Vercauteren, PhD

Learn2Reg 2019: Tutorial on Deep Learning in Medical Image Registration

MICCAI 2019

Includes slides adapted from Marc Modat, Matt Clarkson and more





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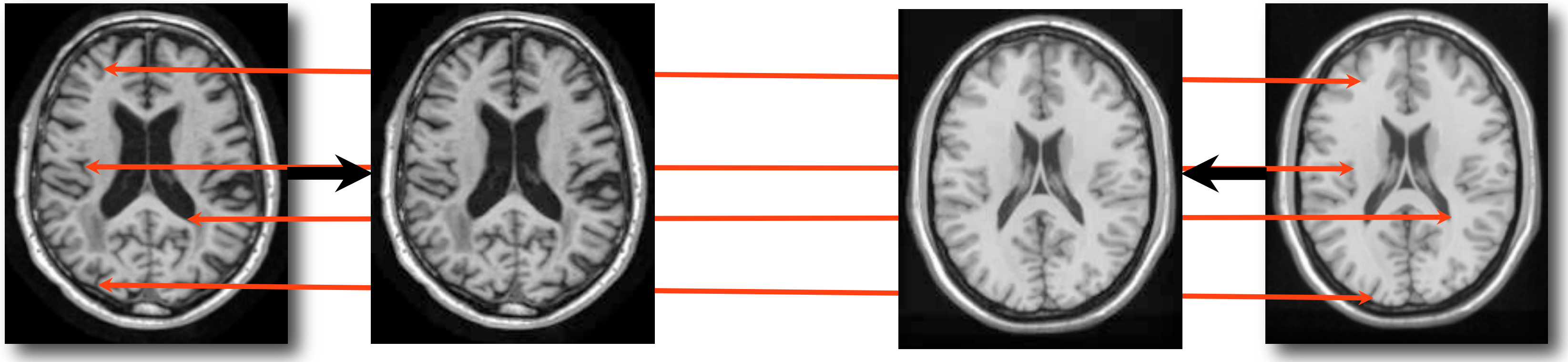
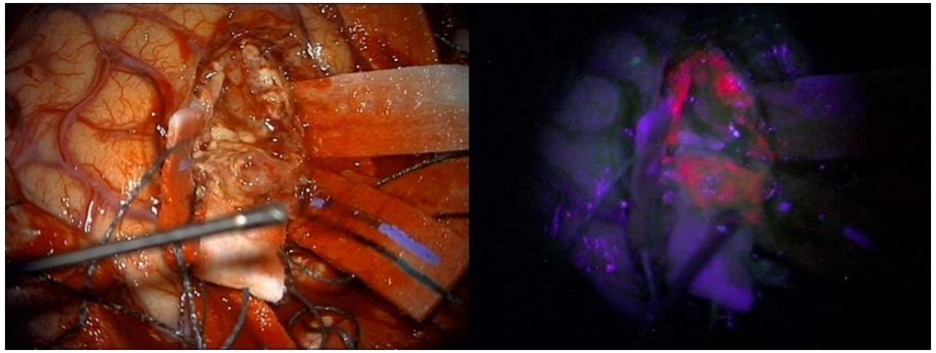
What is medical image registration?

- Aim: Establishing spatial correspondences between images
  - Also referred to as **Spatial Normalisation**
- Image registration focuses on finding a **spatial transformation** (or mapping) between the spaces of the images
- Registration is an important question but typically only one component of a clinically relevant solution



Why do we need it? Fuse, track, control

- Patient motion (alignment of temporal series)
- Patient changes (pre- / post-treatment images)
- Patient comparison (atlas-based analysis)
- Information fusion (complementary modalities or timings, planning transfer)
- Motion compensation for improved reconstruction
- Field-of view enlargement (mosaicking)
- Localisation and visual servoing
- Etc.



Some key components

- Spatial transformation model
  - Rigid, affine, local basis function-based, displacement field, etc.
- Image matching driver
  - Sparse paired features, **image intensity comparisons**, etc.
- Regularisation
  - Spatial transformation smoothness prior, etc.
  - Data-driven priors
- Optimisation strategy
  - Gradient descent, derivative-free continuous optimiser, discrete graph-based optimiser, etc.
  - Statistical, machine-learning based

Two main approaches to image registration

- Feature-based matching
  - Identify paired corresponding points, lines or other geometric primitives
  - Fit a spatial transformation model to these correspondences

- Intensity-based registration
  - Define a cost function to compare the similarity between images
  - Warp the images with a spatial transformation
  - Find the spatial transformation that optimises the cost function between the warped images

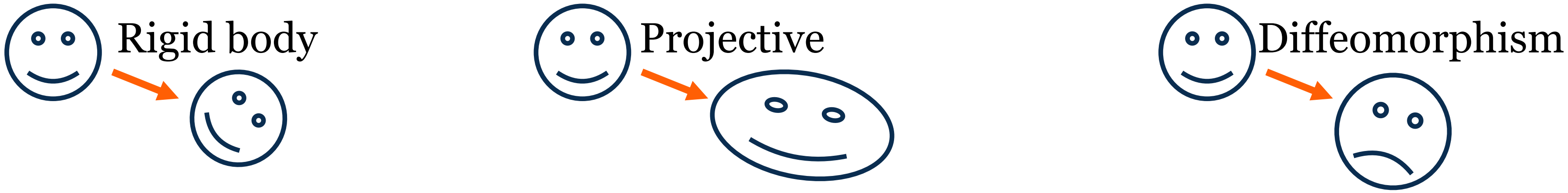
- In this introduction, we focus on intensity-based registration

Classical intensity-based registration: An optimization problem

- Note that notations vary widely in the field

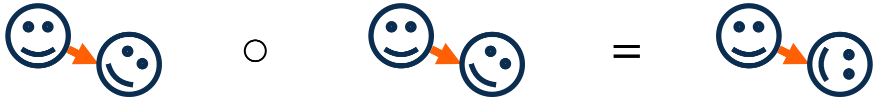
- F : Fixed image
  - Spatial transformation leaves from its domain Ω_F
- M : Moving image
  - Spatial transformation arrives to its domain Ω_M
- $s*$: Sought spatial transformation
  - From Ω_F to Ω_M
  - $x \in \Omega_F$
- G : Transformation model
  - Space of the spatial transformations s
- $\mathrm{Sim}(\cdot, \cdot)$: Image similarity measure
- $\mathrm{Reg}(\cdot)$: (Optional) regularization term

Examples of spatial transformations spaces and related complexity



- Spatial transformations do not necessarily form vector spaces
- Addition: no geometric meaning
  - $s1, s2 \in G \quad \Rightarrow \quad s = s1 + s2 \notin G$

- Natural operation: composition
  - $s1, s2 \in G \quad \Rightarrow \quad s = s1 \circ s2 \in G, \quad s\colon p \in \Omega,\ s(p) = s1(s2(p))$

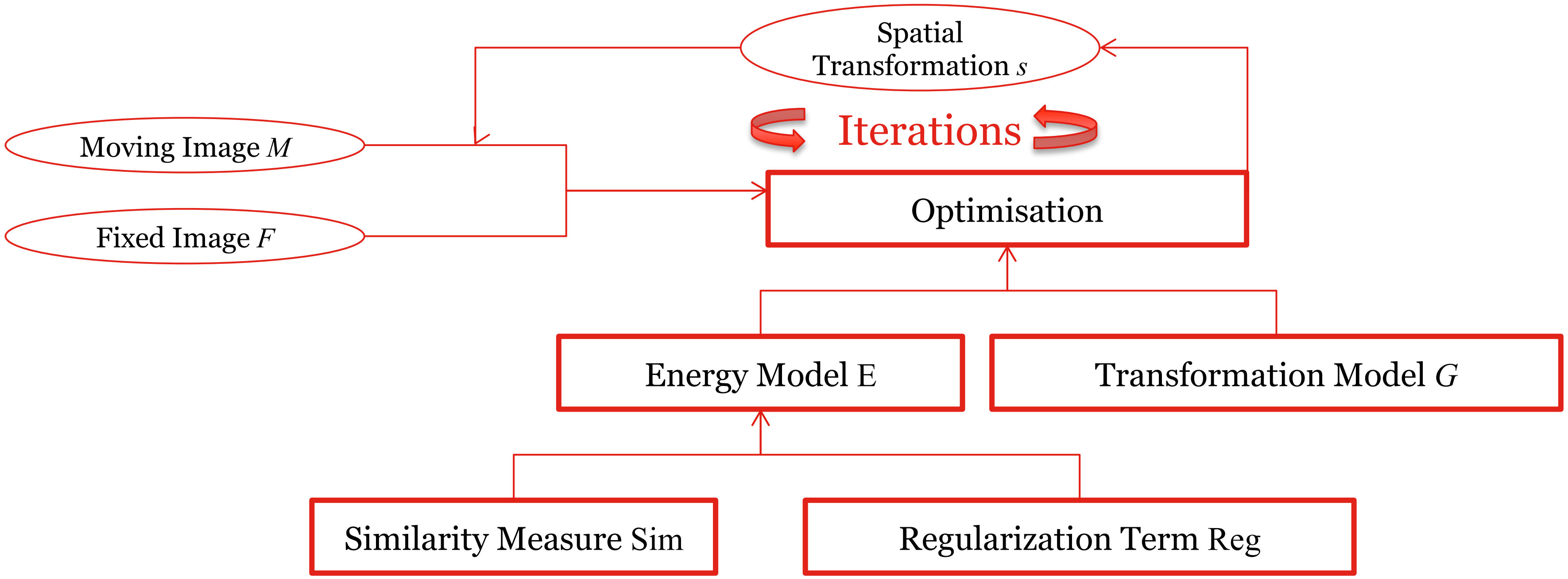


- *Lie group* structure
  - Need to find a good intrinsic parameterization of the space or use constrained optimisation

Classical intensity-based registration: An optimization problem

- Optimisation problem to solve (omitting weighting factors)
- $s^* = \arg\min_s \ \mathrm{Sim}(F, M \circ s) + \mathrm{Reg}(s)$

  $= \arg\min_s \ \mathrm{E}(s)$
- Typically solved iteratively



From classical to learning-based approaches

- Classical approach
  - Rely on one pair or images F and M
  - $s^* = \arg\min_s \ \mathrm{Sim}(F, M \circ s) + \mathrm{Reg}(s)$

- Extension to learning-based approach (omitting weighting factors)
  - Exploit many image pairs F_i and M_i
  - Potentially use extra information E available only at training time (annotations, simulated ground-truth)
    - Define a supervised loss SuppLoss
  - Use a function approximator (e.g. a CNN) $f_\theta(\cdot)$ parameterised by θ to encode s
    - $s = f_\theta(F, M)$
  - Optimise over all training set
  - $\theta^* = \arg\min_\theta \mathrm{E}_{\mathrm{P}(F, M)}[\ \mathrm{Sim}(F, M \circ f_\theta(F,M)) + \mathrm{Reg}(f_\theta(F,M)) + \mathrm{SupLoss}(E, F, M, f_\theta(F,M))\ ]$
  - Many other learning-based options possible (e.g. learn Sim or learn the update step)

Intensity-based registration: hidden difficulties

- Many choices to make
  - Sim, Reg, G, optimiser, parameters, weighting, etc.
  - Most choices should be problem specific
  - Many of these can be difficult to learn from the data
    - Little ground truth available
  - No magic recipe!

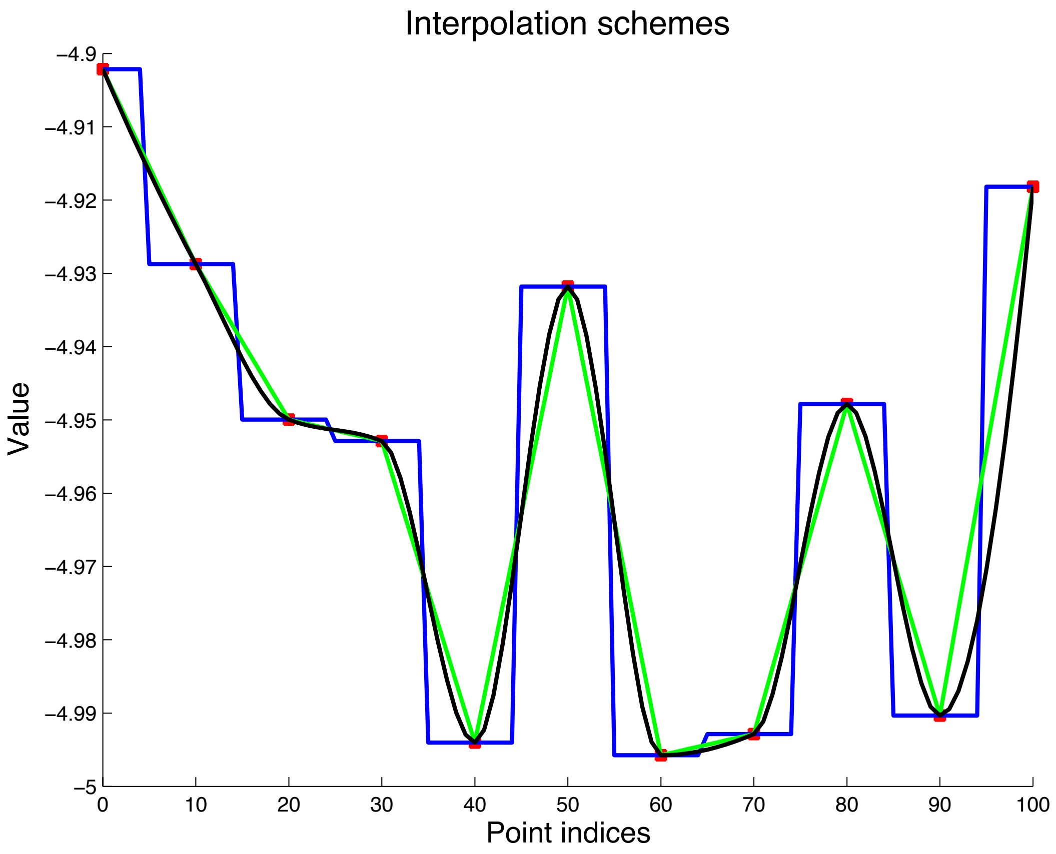
- Classical approaches pose difficult optimisation problems
  - High dimensionality
  - Strongly non-linear problem
  - Strongly non-convex energy function with many local minima
    - Shares many features of deep learning!

From discrete samples to a continuous problem

- Digital images are typically a collection of samples on a regular grid of voxels
- Spatial transformations cannot be accurately represented by exact (discrete) voxel matches
  - Need to be a continuous representation
- Image similarity measure typically rely on continuous integrals
- Interpolation and resampling used to “work-around” this conundrum
- For deep learning-based approaches, it is important to make sure the steps are differentiable

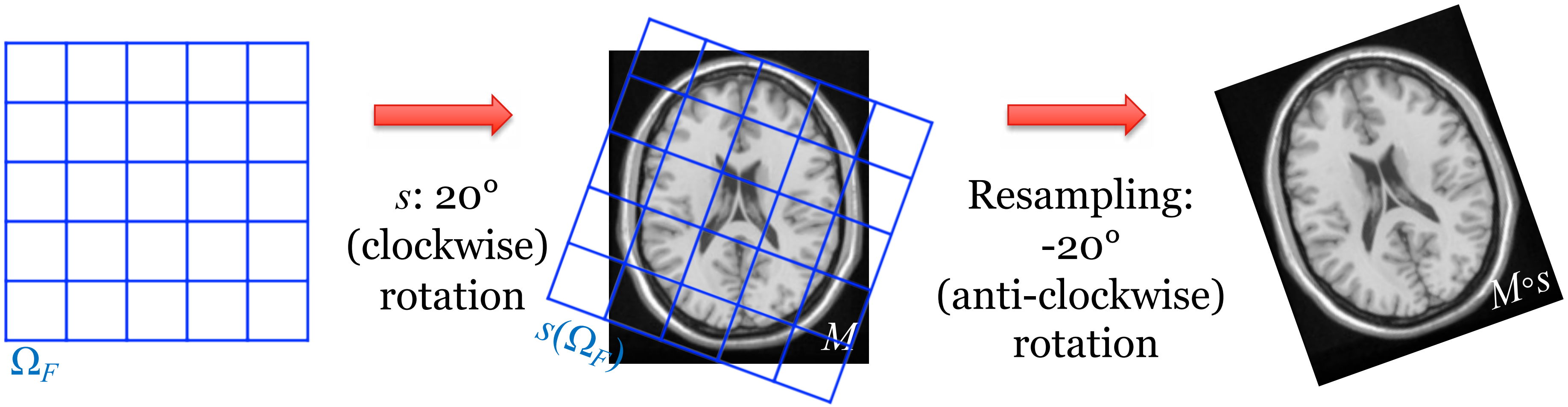
Interpolation and resampling

- For a voxel position $x \in \Omega_F$, $s(x)$ does not in general fall on a voxel position in Ω_M
- What does $M \circ s(x) = M(s(x))$ mean?
  - For Nyquist–Shannon sampling theorem band-limited continuous function can be exactly recovered from a set of discrete samples by using a *sinc* kernel
  - In practice, due to the sinc computational complexity and the related artefacts (e.g. ringing), nearest neighbour, linear or cubic interpolation is used



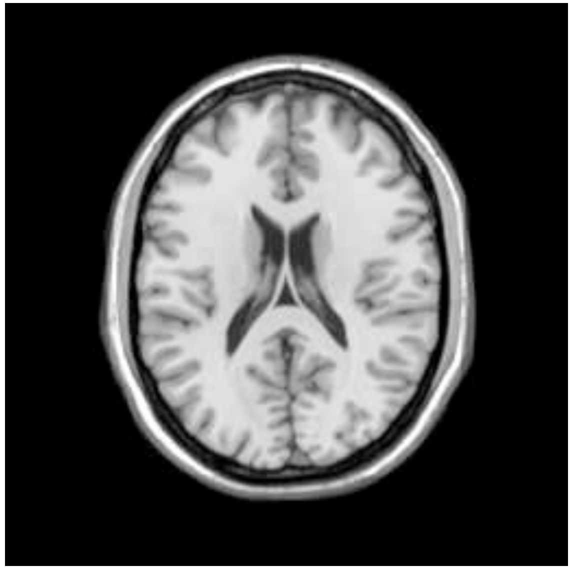
Interpolation and resampling (2)

Talk about direction of transform

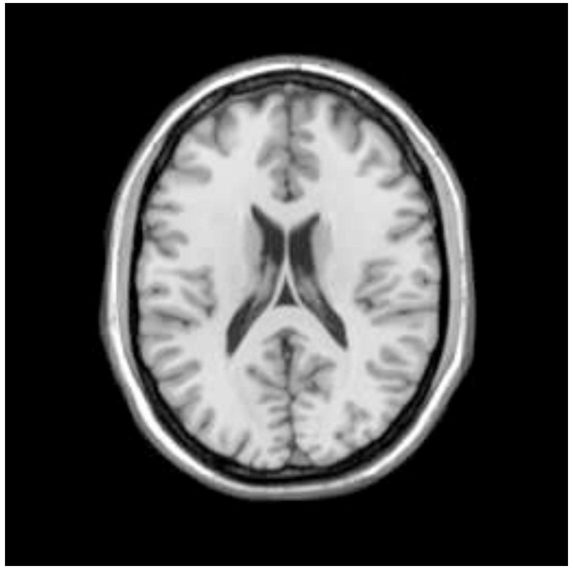


Impact of the interpolation strategy

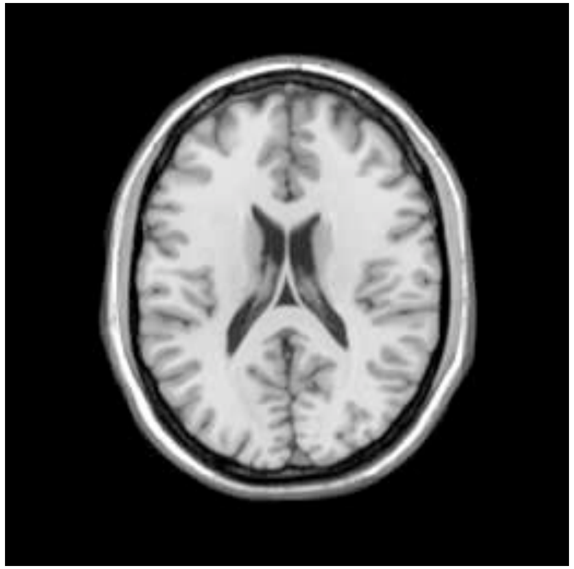
- Resampling many times with a small rotation
  - Avoid resampling many times! Linear interpolation is fine if used once



Using nearest-neighbor interpolation



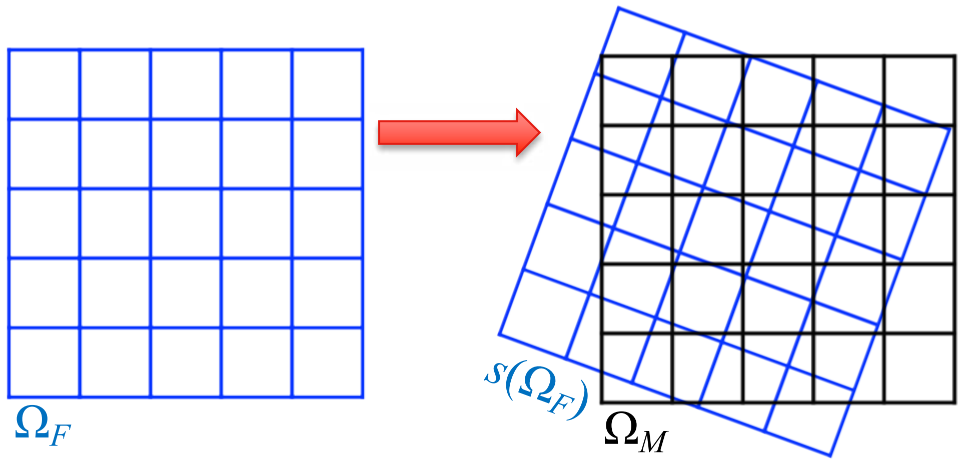
Using linear interpolation



Using cubic interpolation

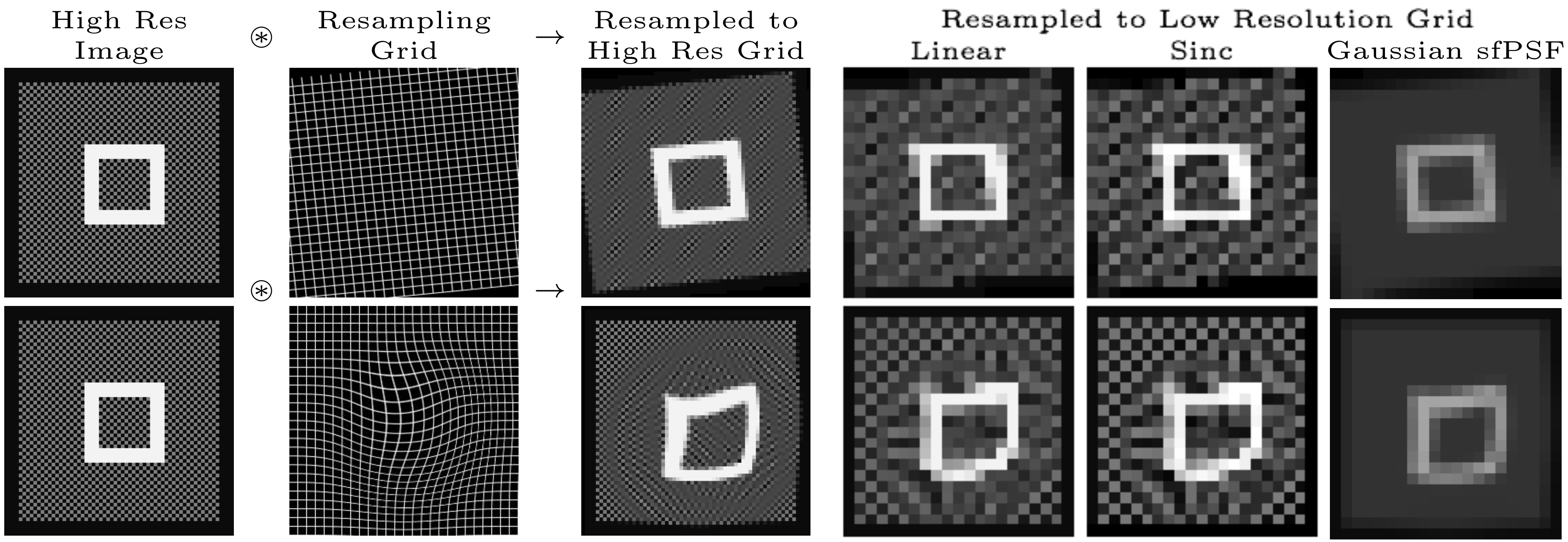
Basic registration walk-through (1)

- $s(x) = \mathrm{S}\cdot x$
  - May use homogeneous coordinates
- $\mathrm{Sim}(F, M \circ s) = \int |F(x) - M(\mathrm{S}\cdot x)|^2 \, \mathrm{d}x$
- $\mathrm{Reg}(s) = 0$
- Where do we take the integral on?
  - $x \in \Omega_F$
  - $s(x) \in \Omega_M$
- $\Omega_s = \Omega_F \cap s^{-1}(\Omega_M)$



Basic registration walk-through (2)

- How to compute the integral?
  - $\int_{\Omega s} |F(x) - M(\mathrm{S} \cdot x)|^2 \, \mathrm{d}x \approx \sum_{x \in \Omega s} |F(x) - M(\mathrm{S} \cdot x)|^2$
  - $\mathrm{Sim}(F, M \circ s) \triangleq \sum_{x \in \Omega s} |F(x) - M(\mathrm{S} \cdot x)|^2$
  - Didn't we introduce aliasing? See Cardoso et al. MICCAI'15



Basic registration walk-through (3)

- $\mathrm{Sim}(F, M \circ s) \triangleq \sum_{x \in \Omega_S} |F(x) - M(\mathrm{S} \cdot x)|^2$
- How to optimise it?
  - We probably need the gradient of Sim (or half of it…)
    - Use the chain rule
  - $\nabla \mathrm{Sim}(\mathrm{S}) = -\sum_{x \in \Omega_S} (F(x) - M(\mathrm{S} \cdot x)) \cdot (\nabla M)(\mathrm{S} \cdot x)^{\mathrm{T}} \cdot (x^{\mathrm{T}} \otimes \mathrm{Id}_{\mathrm{N}})$
  - Didn't we miss the fact that Ω_s depends on S?
    - Let's neglect this…
  - Also, what is ∇M? Does it need to be compatible with the interpolation strategy? How do we evaluate it at non-grid points?

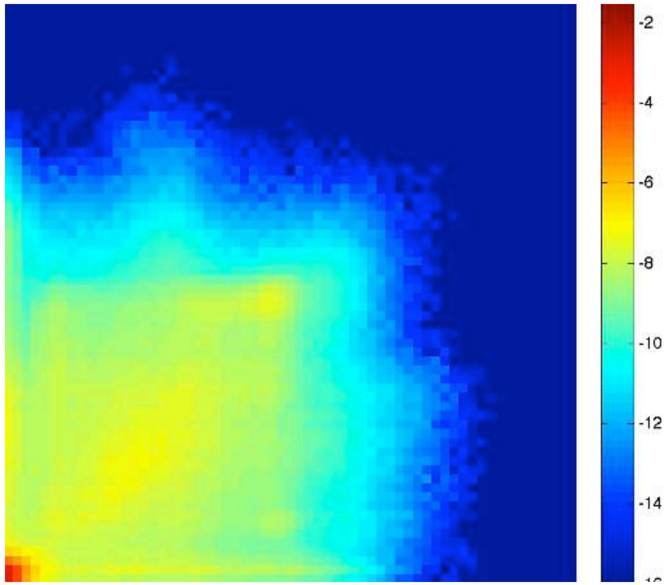
Basic registration walk-through (4)

- We can now do a gradient descent
  - $S_{n+1} = S_n + \lambda \nabla Sim(S_n)$
  - We need a rule for the step length. Ad-hoc? Line search?
  - We only get first order convergence. Can we get better?
- Newton-Raphson (using the Hessian) could be an option
  - How do we get a stable estimate of the Hessian of the cost function?
  - Can this scale for deformable registration?

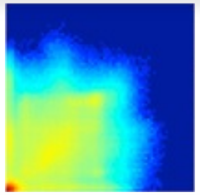
Measures of image similarity – Examples

- Sum of squared differences (SSD) for identical intensities + Gaussian noise
- Normalised Cross-correlation (NCC) for affine relationships
  - Illumination differences, small contrast changes
  - Local version (LNCC) provides good versatility
- Joint entropy, the dispersion in the joint image histogram and (normalised) mutual information for non-parametric statistical relationship between intensities
  - Multimodal registration

Joint histogram

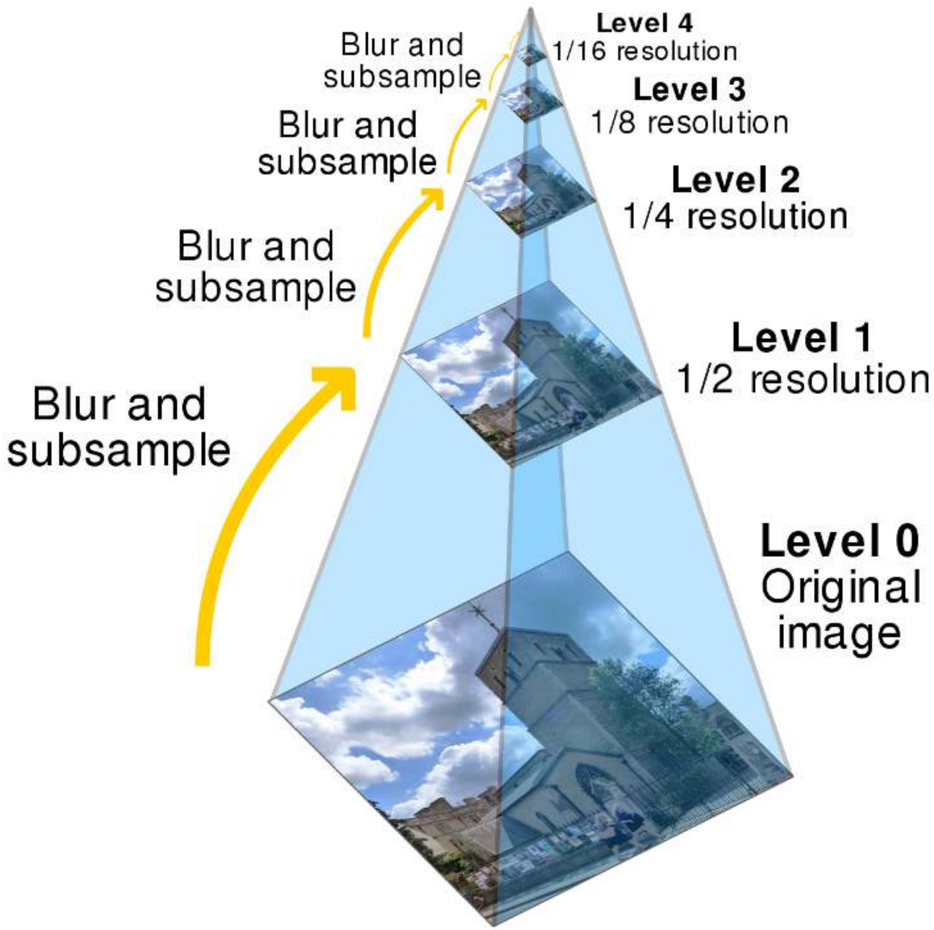


Initial joint histogram



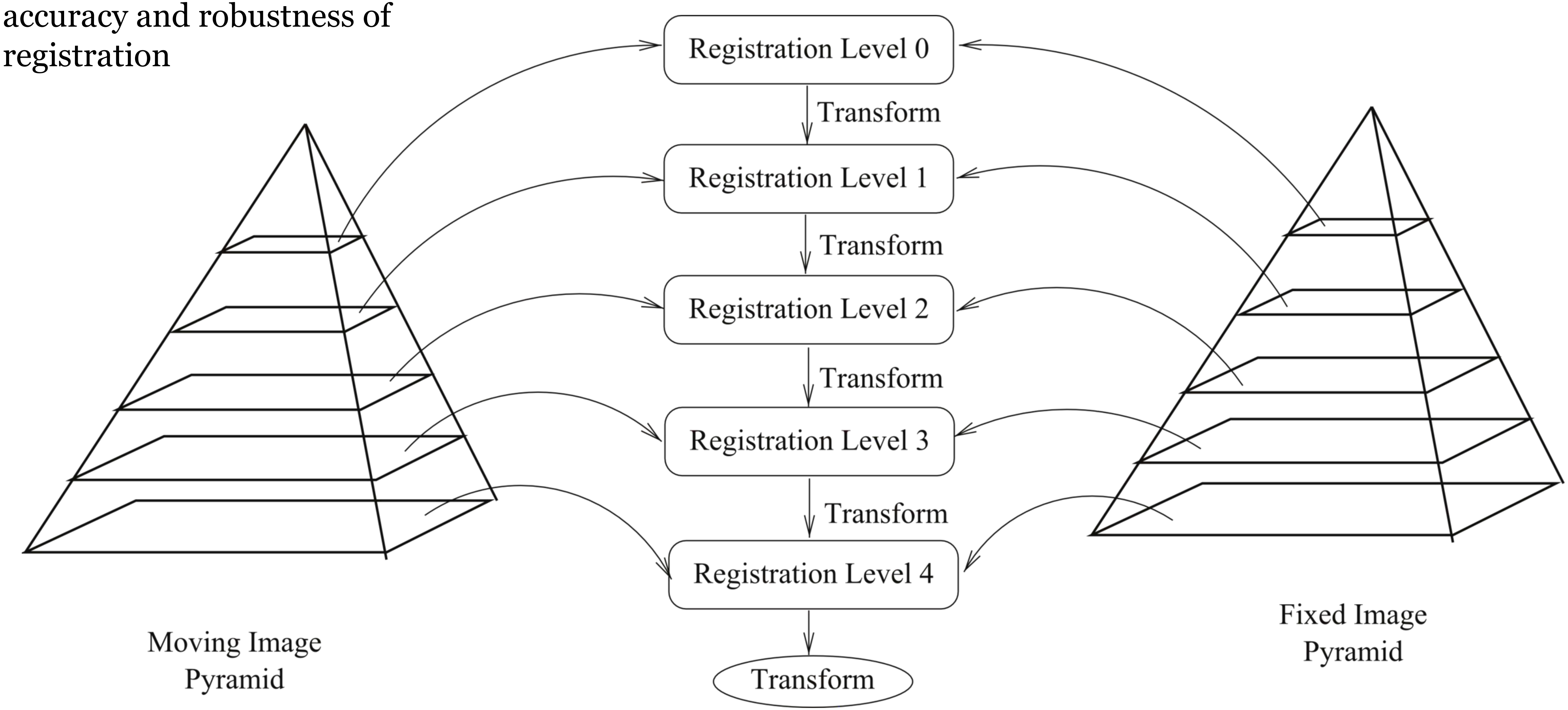
Spatial multiresolution pyramids

- Multiscale representation of images
  - Capture large-scale information efficiently on small images
  - Propagate to finer grained levels and refine
- Simple downsampling /subsampling would introduce aliasing
- Apply a low-pass first and then downsample
  - Gaussian smoothing + downsampling by a factor 2 is the most classical approach



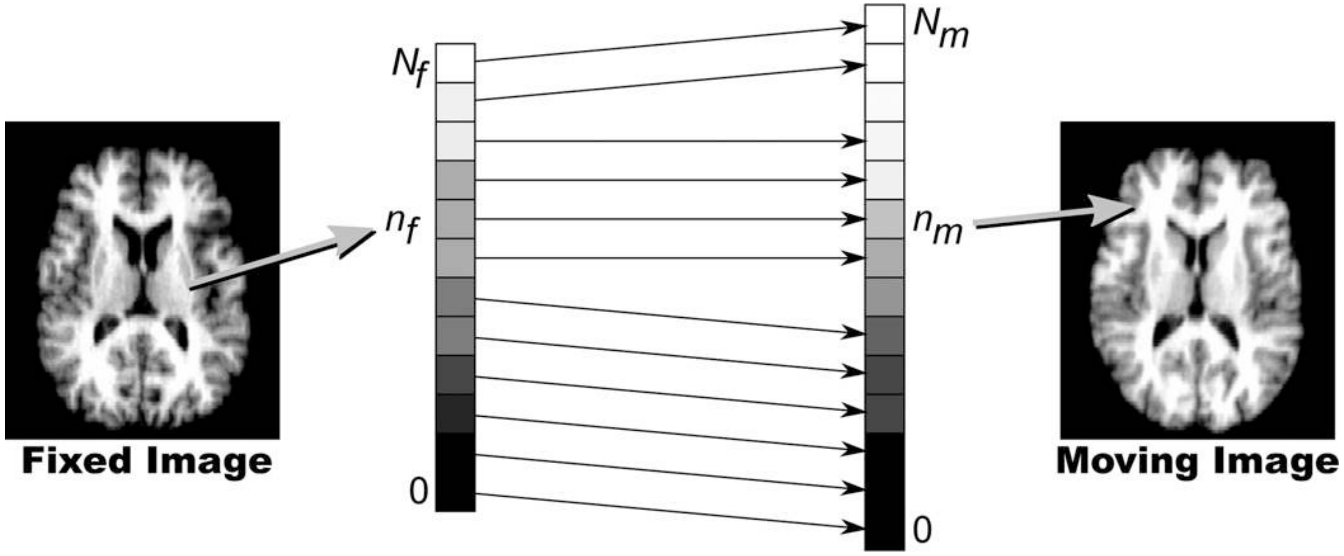
Gaussian pyramids for image registration

Often improves speed, accuracy and robustness of registration



Do we need all this sophistication?

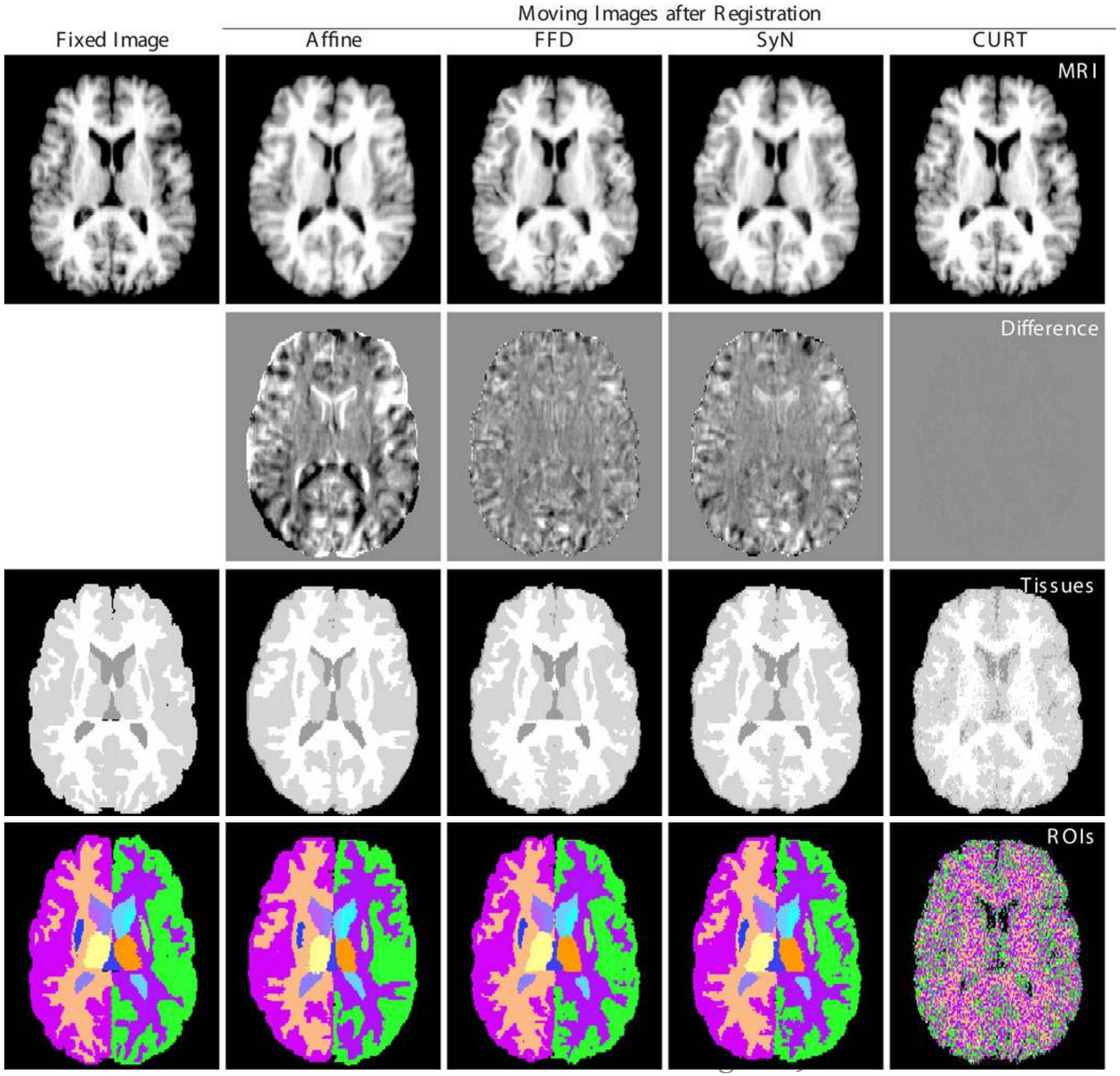
- Let's look at a very simple deformable registration algorithm: CURT
  - Rohlfing IEEE TMI 2012 Feb; 31(2)



$$n_m = \lfloor N_m \frac{n_f}{N_f} \rfloor$$

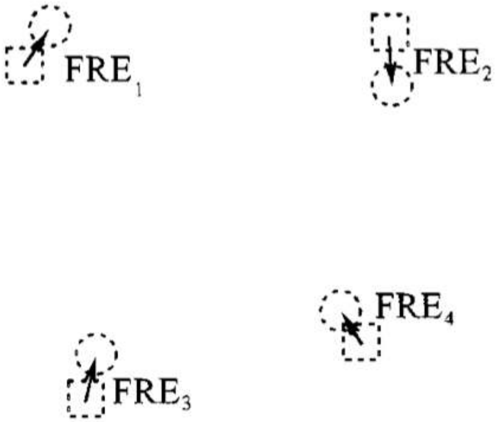
CURT

- From the paper
  - *“We introduce a new non-rigid registration algorithm based on a closed-form solution to maximizing the Rank Correlation criterion. The new algorithm produces more accurate registrations than two state-of-the-art methods as judged by image similarity and tissue overlap scores. It is also two to three orders of magnitude faster, requires no affine pre-registration, and has no tunable parameters.”*

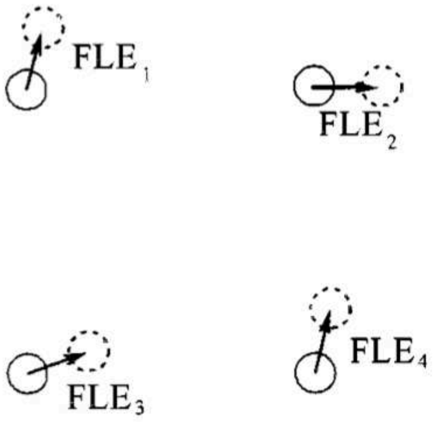


CURT: Completely Useless Registration Tool

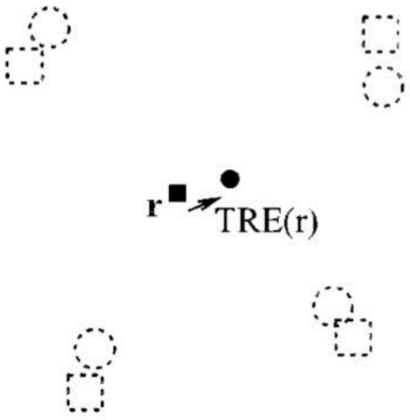
Important definitions for validation (see Fitzpatrick & West, 2001)



Fiducial Registration Error (FRE): root- mean square distance between corresponding fiducial points after registration



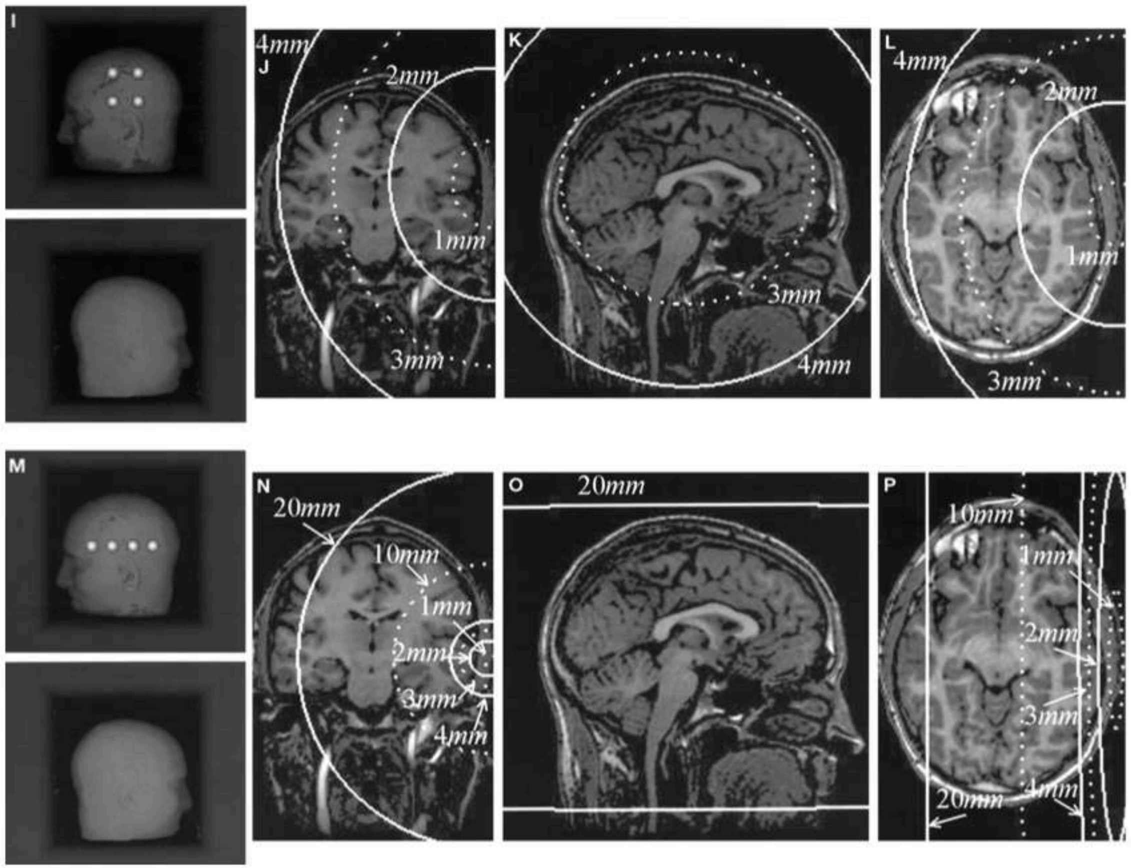
Fiducial Localisation Error (FLE): the error in locating the fiducial points



Target Registration Error (TRE): the distance between corresponding points other than the fiducial points after registration

This is what really matters!

TRE increases as the distance of the target from the fiducial centroid



FRE is not a reliable indicator of registration accuracy (!!)

- FRE is independent of fiducial configuration
- FRE is independent of bias errors (e.g., MRI gradient, digitizer camera malalignment, bent handheld probe)

- TRE has an approximate $N^{-1/2}$ dependence

$$\langle \mathrm{TRE}^2(\boldsymbol{r}) \rangle \approx \frac{\langle \mathrm{FLE}^2 \rangle}{N} \left(1 + \frac{1}{3} \sum_{k=1}^{3} \frac{d_k^2}{f_k^2} \right)$$

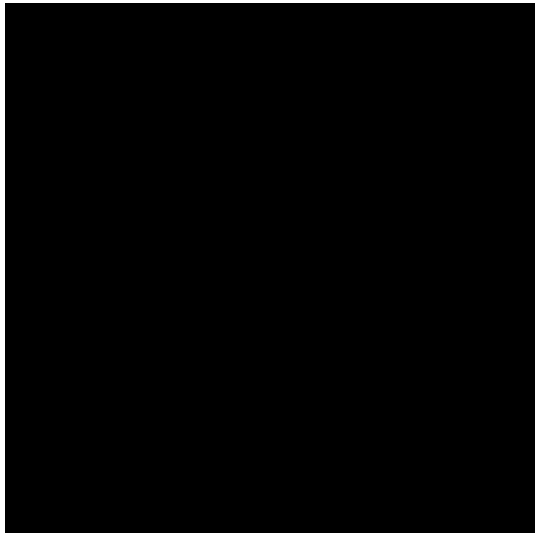
$\langle FRE^2 \rangle$ - Mean square fiducial registration error

N - Number of fiducials

d_k^2 - Distance (squared) between target point and fiducial configuration principle axis k.

f_k^2 - RMS (squared) between fiducial points and fiducial configuration principle axis k.

Considerations remain valid for learning-based image registration



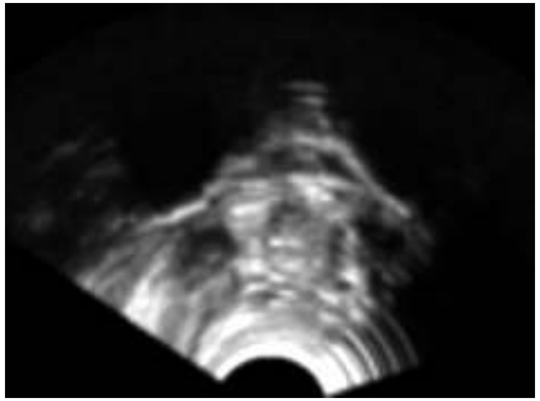
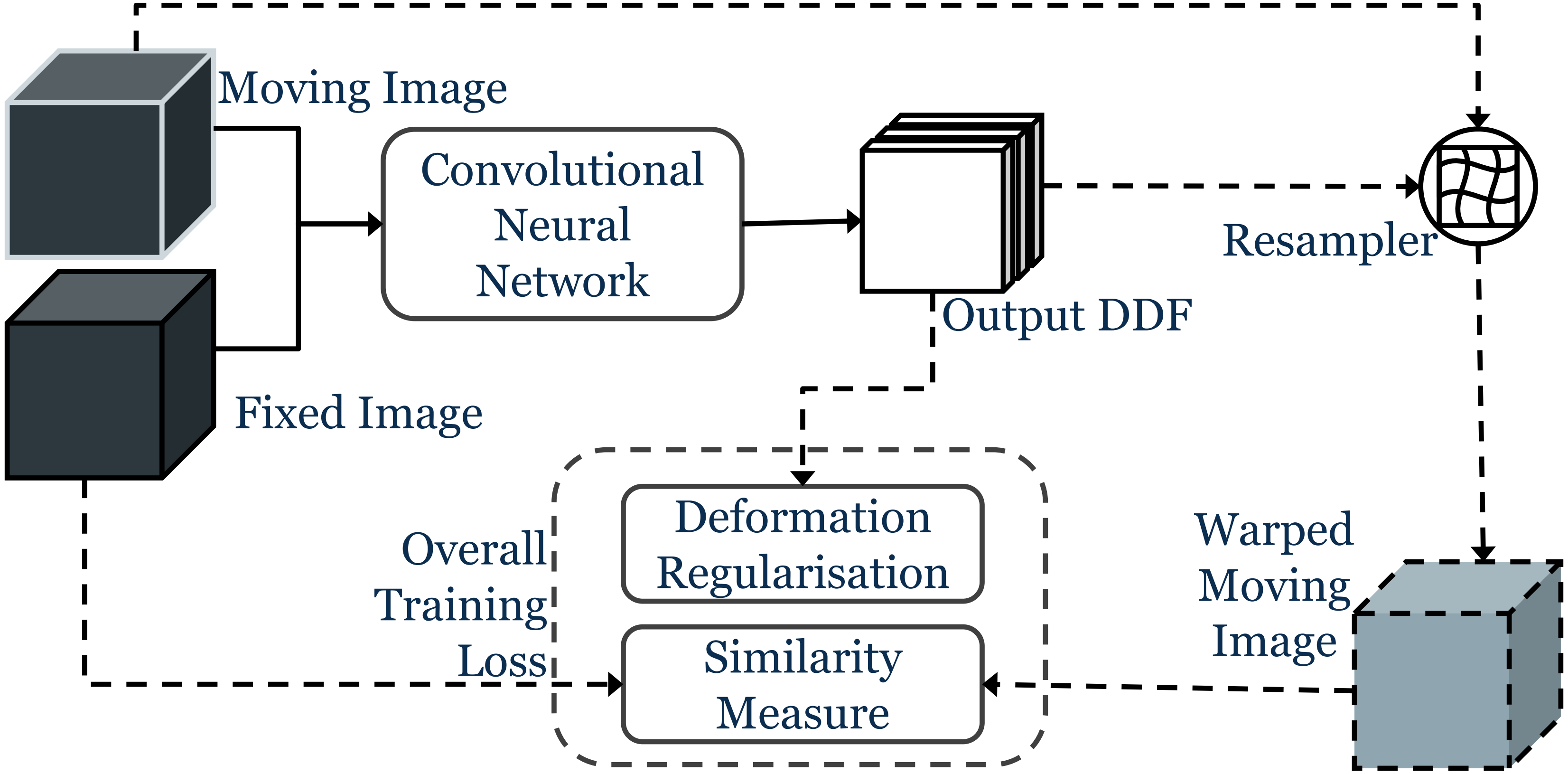


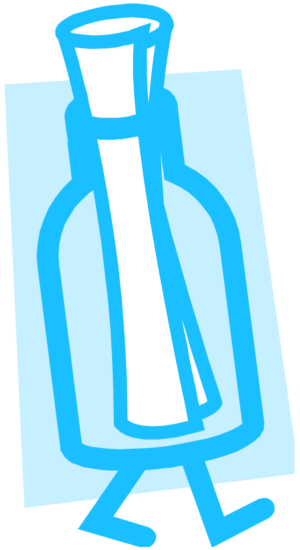
Image-intensity-based similarity measure

e.g. de Vos et al 2017, Yang et al 2017, Cao et al 2017



Take Home Messages

- For good image registration performance
  - Study application constraints
  - Pick most suitable tools w.r.t constraints
  - Understand the numerics involved
- Evaluation is more than important
- There is room for research!



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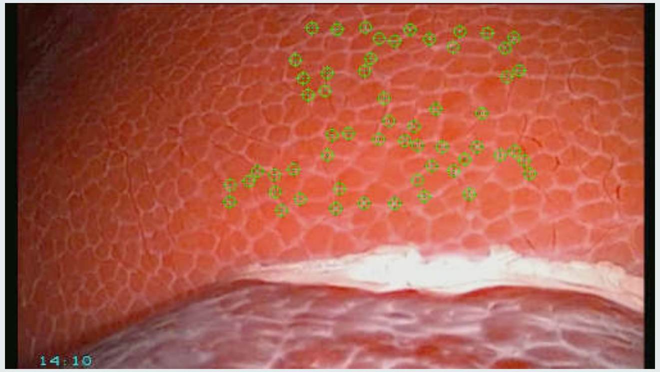

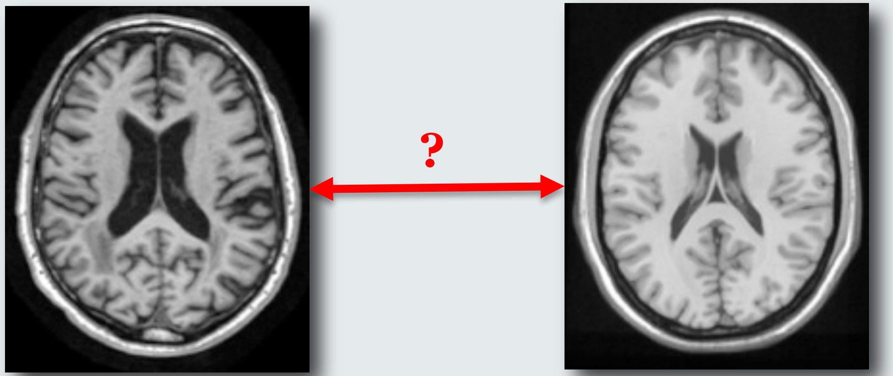

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