

# Medical Image Analysis

## Lecture 08

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### Image Registration II

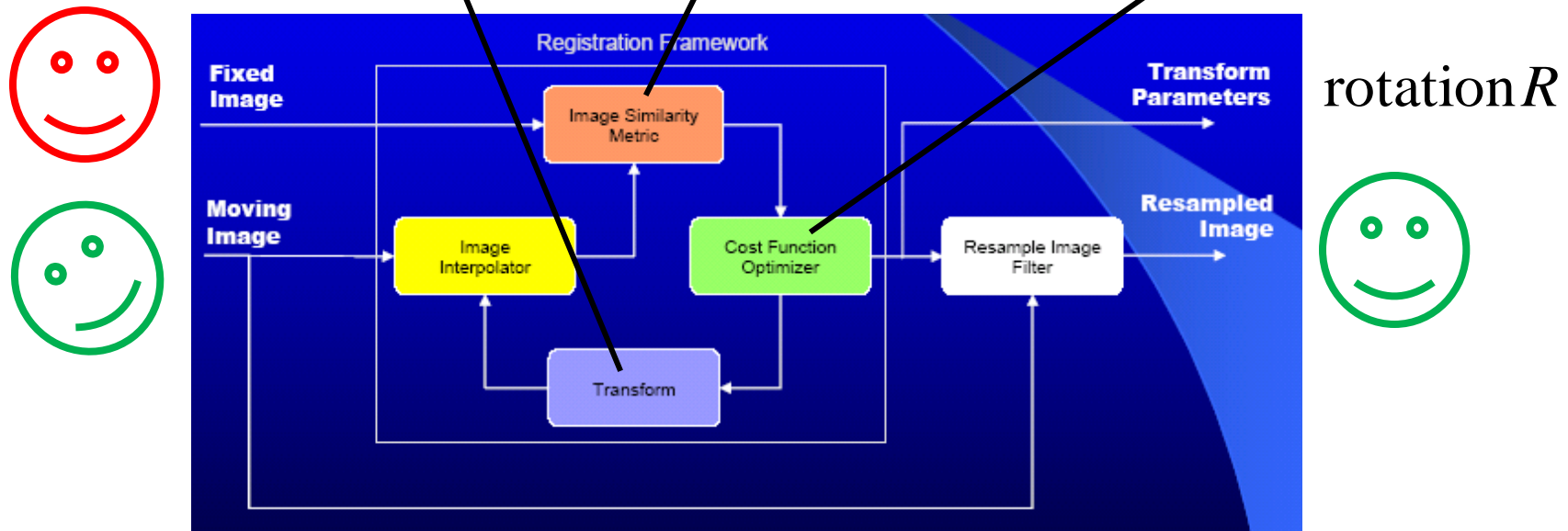
# Overview - Image Registration

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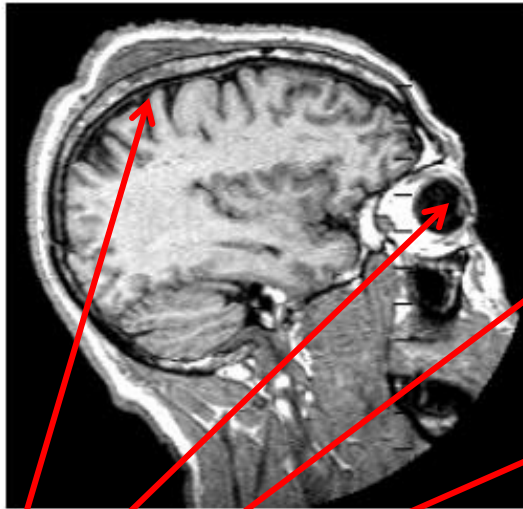
- What is it?
- Motivation
- Formal Definition & Categorization
- Rigid Registration Methods
  - Feature Based: Procrustes Alignment
  - Surface Based: Iterative Closest Point
  - Intensity Based

# Definition of Image Registration

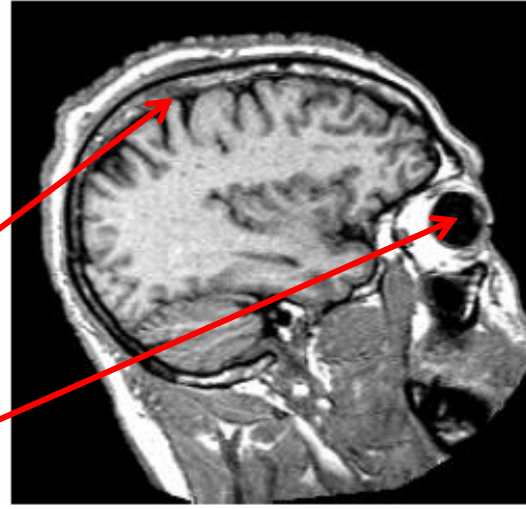
- Find a **mapping**  $h(x)$  aligning an image („moving“) with a second image („fixed“) such that a defined **similarity measure** is **maximized**.



# Registration - Features vs. Voxels

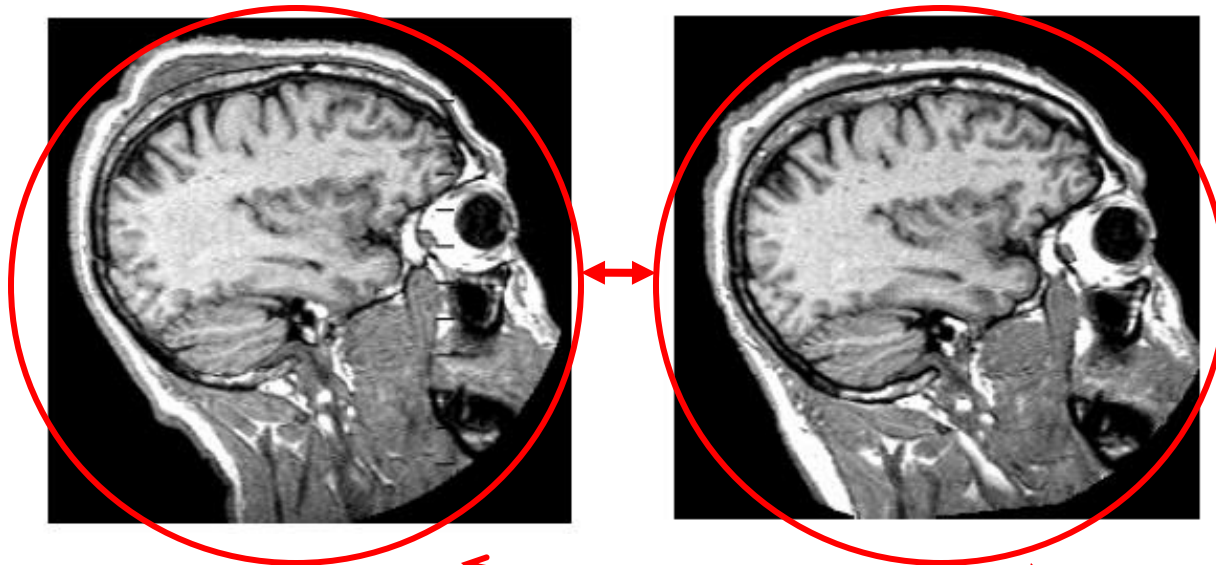


Feature Based Approach



Voxel Based Approach

# Registration - Features vs. Voxels



Feature Based Approach

Voxel Based Approach

# Registration based on voxel similarity

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- Registration based on **geometrical features**
  - requires the extraction of points, lines or surfaces
  - is affected by feature localization
- Registration based on **voxel similarity measures**
  - uses some measure derived directly from the intensity of the image voxels
  - assumes some form of relationship between the image intensities of both images if in registration
  - does not require any feature extraction

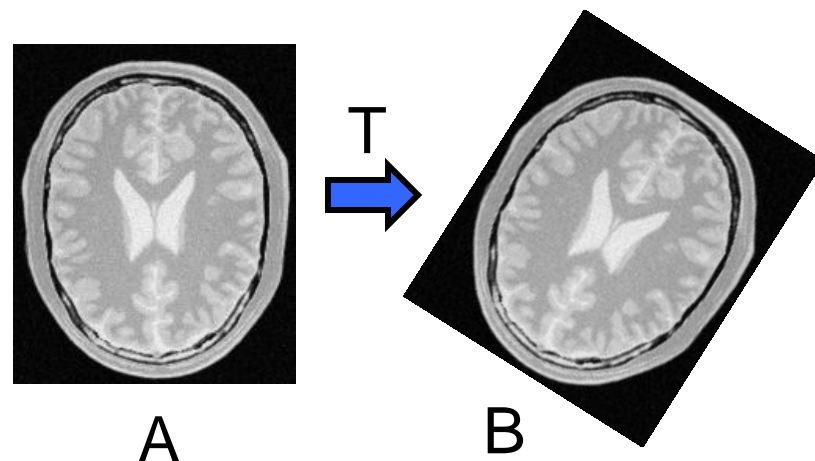
# Registration based on voxel similarity

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- Registration based on **geometric features** is independent of the modalities from which the features have been derived, if features are visible
- Registration based on **voxel similarity measures** must distinguish between
  - Single-modality registration:
    - CT-CT, MR-MR, PET-PET, etc
  - Multi-modality registration
    - MR-CT, MR-PET, CT-PET, etc

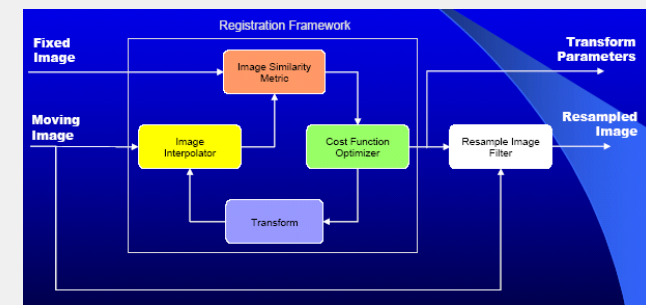
# Registration based on voxel similarity

- Optimal transformation  $T$  is determined iteratively by **minimizing** a voxel-based **dissimilarity measure**  $C$ .
- Voxel-dissimilarity measure  $C$  is a function of
  - image  $A$ 
    - target, reference, fixed
  - image  $B$ 
    - source, moving
  - transformation  $T$ 
    - rigid, affine, nonlinear

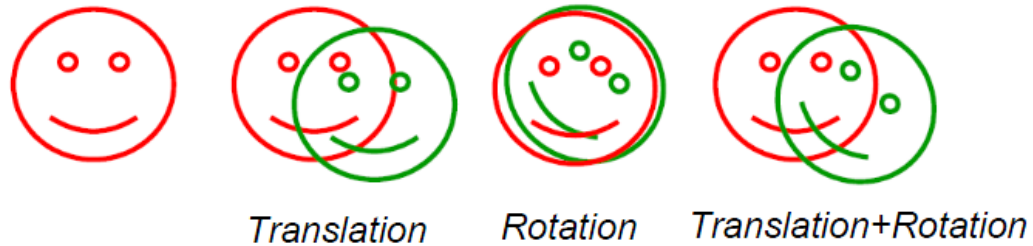




# Transformations



## Rigid

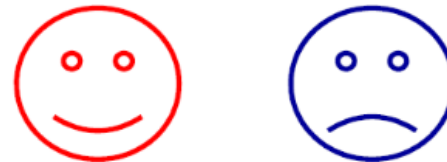


## Affine & Projective



## Non-rigid

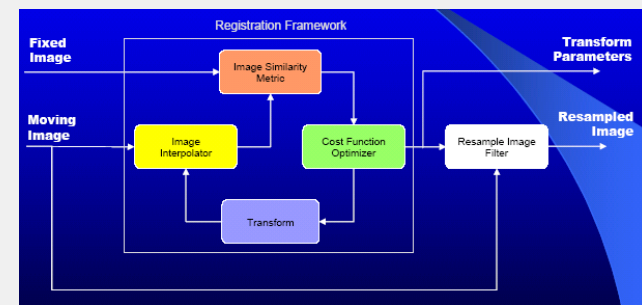
- Elastic
- Splines
- Fluid
- ...



e.g.

$$T_{rigid}(x, y, z) = \begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = \begin{pmatrix} r_{11} & r_{12} & r_{13} & t_x \\ r_{21} & r_{22} & r_{23} & t_y \\ r_{31} & r_{32} & r_{33} & t_z \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}$$

# Similarity Metrics

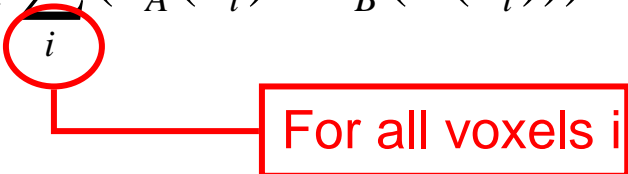


- Used to measure the similarity between two images
- Depends on the type of images to register
- **Similarity assumptions:**
  - Identity: Single-modality, only differ by Gaussian noise
  - Linear: Single-modality, differ by constant intensity
  - Information Theoretic / Probabilistic:  
Multi-modality, intensity changing, related by some statistical or functional relationship

# Single-modal image registration

- Sum of Squared Differences (SSD)

$$C(x; T) = \frac{1}{N} \sum_i (I_A(x_i) - I_B(T(x_i)))^2$$

For all voxels  $i$

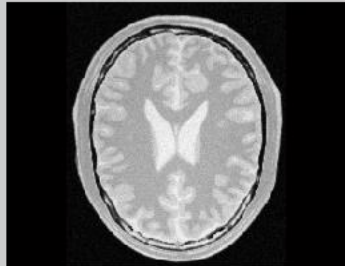
- assumes an *identity* relationship between image intensities in both images
- optimal measure if the difference between both images is Gaussian noise
- sensitive to outliers -> use Sum of Absolute Differences (SAD)!

# Sum of Squared Differences (SSD)

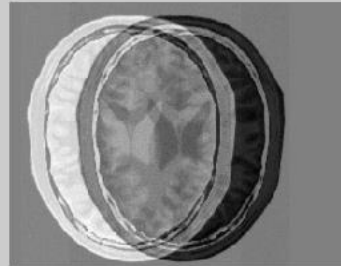
Matlab!

intensity registration test

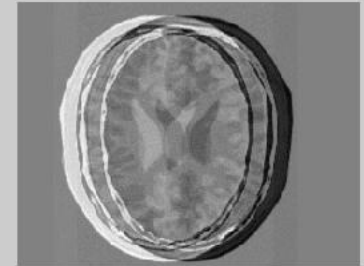
Input Image



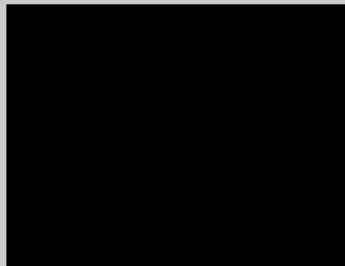
Difference after translation -40



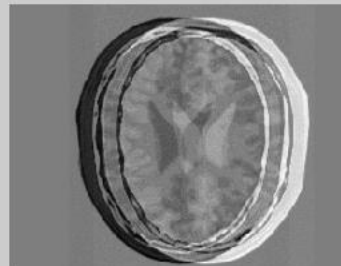
Difference after translation -20



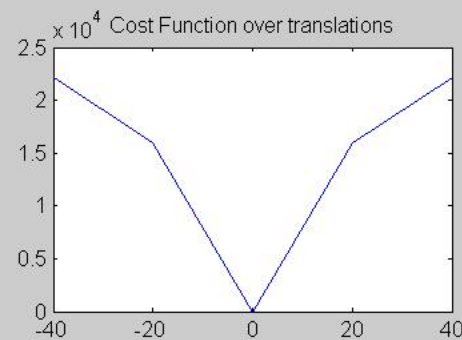
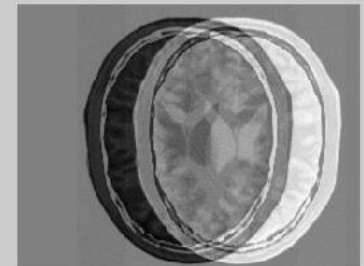
Difference after translation 0



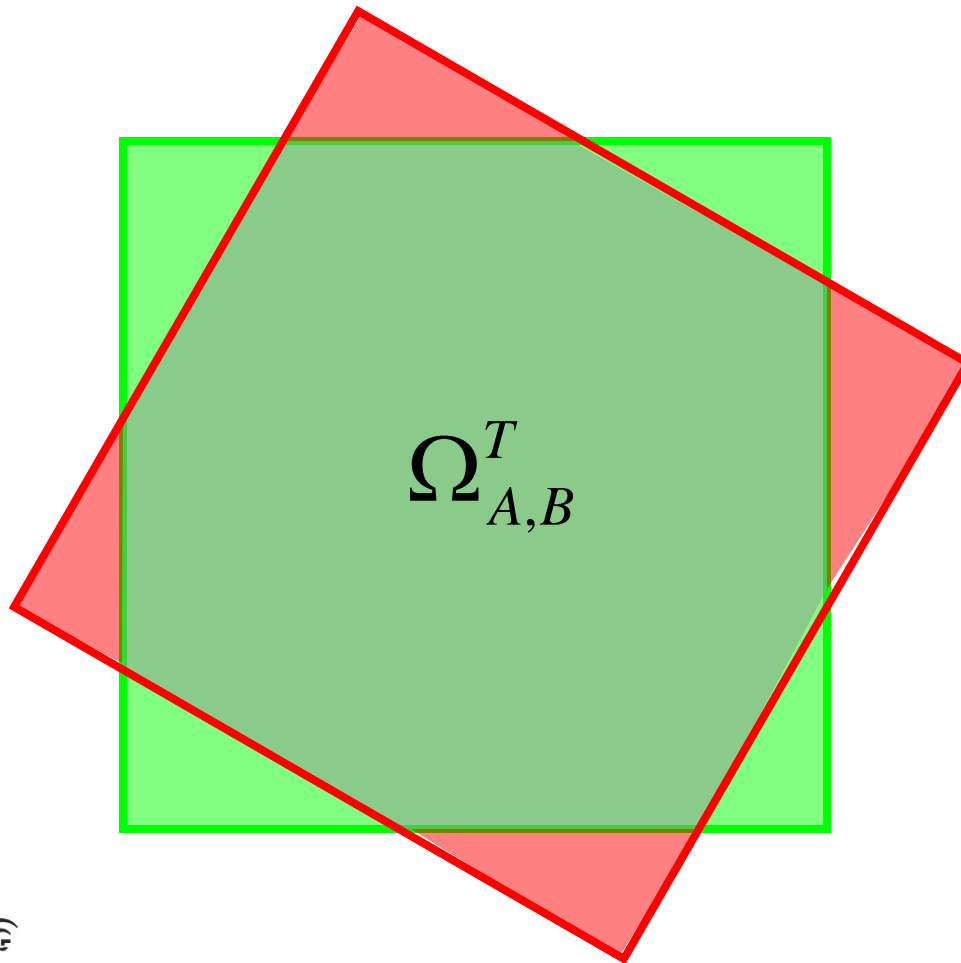
Difference after translation 20



Difference after translation 40



# Image overlap



$\Omega_A$

Image A only

$\Omega_B^T$

Image B<sup>T</sup> only



Overlap between  
image A and B<sup>T</sup>

# Single-modal image registration

- Normalized Cross Correlation (CC)

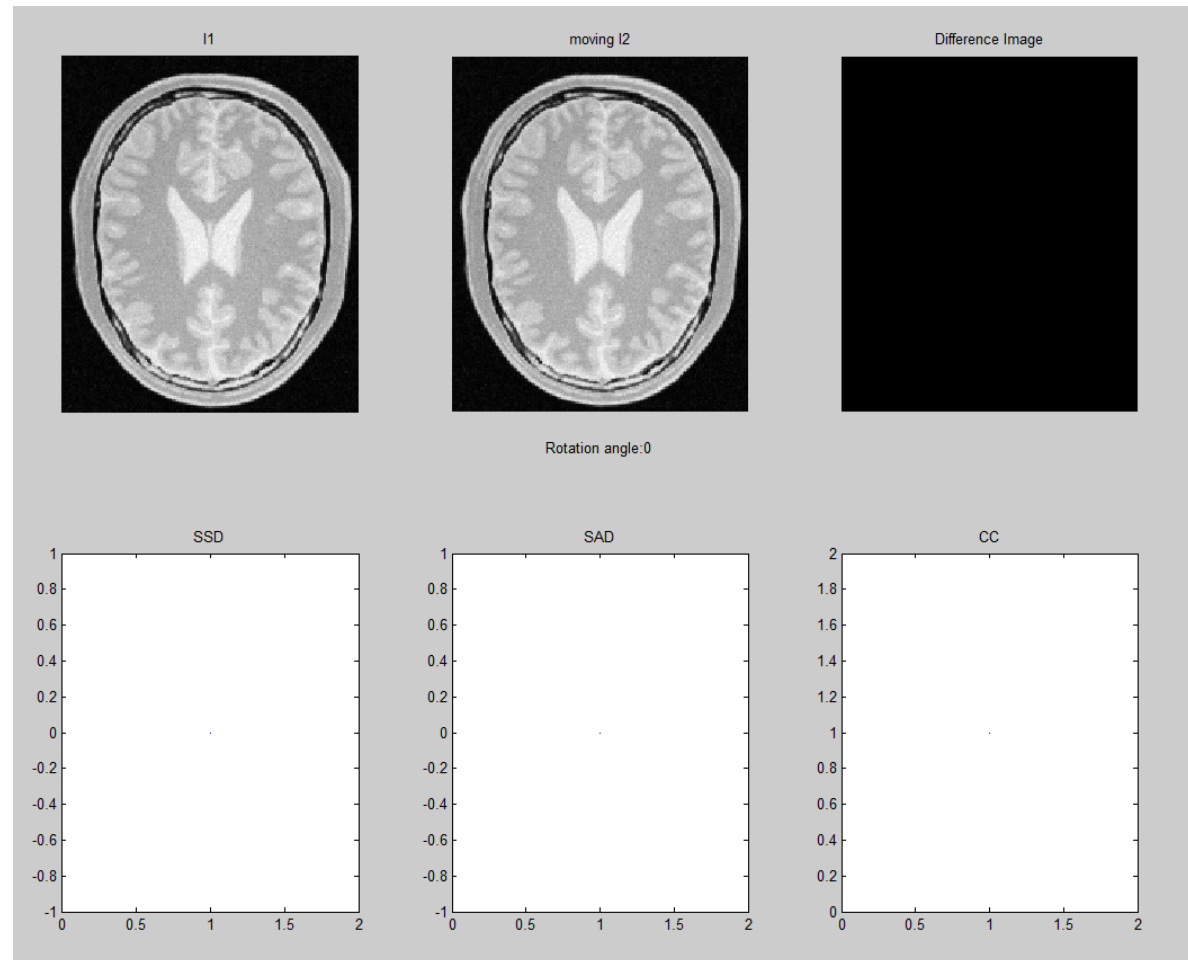
$$CC(x; T) = \frac{\sum [(I_A(x) - \mu_A)(I_B(T(x)) - \mu_B)]}{\sqrt{\sum (I_A(x) - \mu_A)^2 \sum (I_B(T(x)) - \mu_B)^2}}$$

- $\mu_A$  average intensity in image A
- $\mu_B$  average intensity in image B
- assumes a *linear* relationship between image intensities ( $I_B = a * I_A + b$ )
- useful if images have different intensity windows

# Metrics

Matlab!

SimilarityMetrics  
Movie



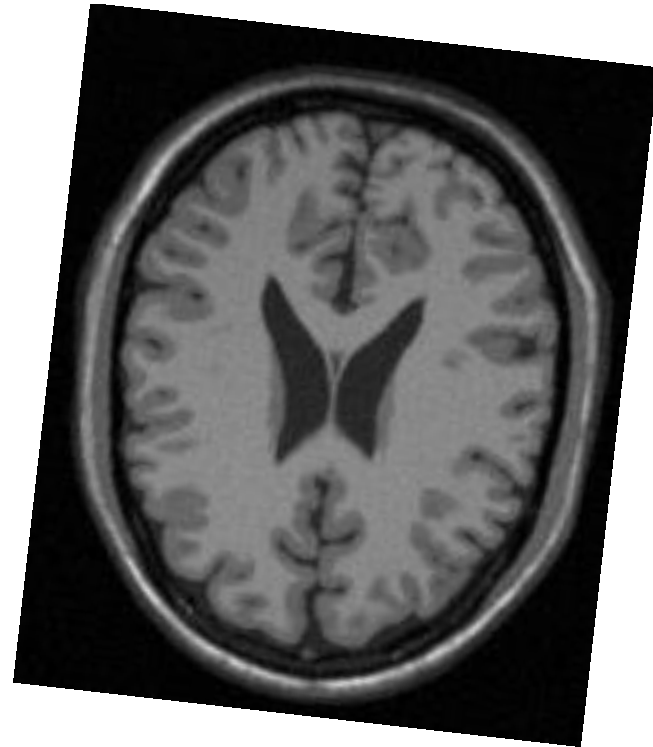
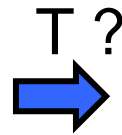
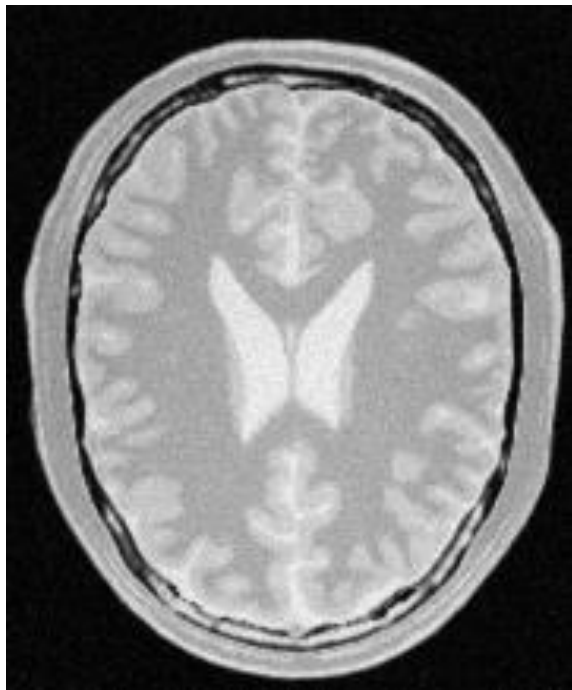
# Registration basis: Image intensity

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- Single-modal image registration
  - Image intensities are related by some simple function
    - identity: Use SSD or SAD
    - linear: Use CC
- Multi-modal image registration
  - Image intensities are related by some unknown function or statistical relationship
  - Relationship between intensities is not known a-priori
  - Relationship between intensities can be viewed by inspecting a 2D histogram or co-occurrence matrix

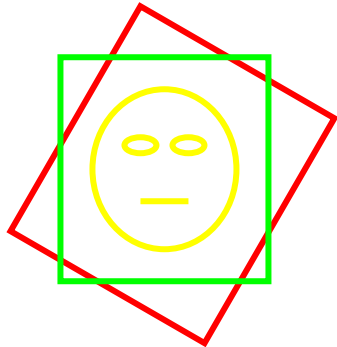


# Multi-modality image registration

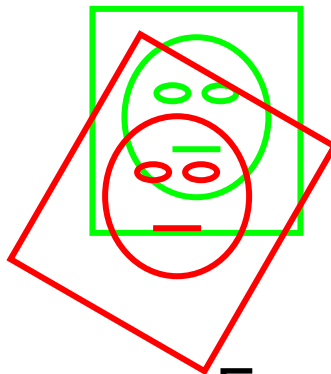


# Multi-modality image registration

- Information theoretic point of view
- Look at two images combined



Two eyes,  
a mouth



Four eyes,  
two mouthes

Same as *reducing  
amount of information  
in combined image!*

- Registration tries to **maximize** the amount of **shared information** in two images!

# How do we measure information?

- Given:
  - a set of distinct symbols  $\{v_1, v_2, \dots, v_n\}$
  - **events** of randomly drawing a symbol  $v$  from this set
  - a probability distribution **p** over the set
- Measure of information:
  - Metaphor: measure the „degree of surprise“ of a random event
  - How much information do we gain, after a certain  $v$  has been drawn from the set?

# How do we measure information?

$$\{v_1, v_2, \dots, v_n\}$$

- Drawing  $v_i$  from the set is done with probability  $p_i$
- A highly improbable event surprises us, while an almost certain event gains us not much information!
- -> Measure of information (gain) depends on  $p$ !
- Define measure of information  $h$ :
  - For **two unrelated events**  $x, y$  the information gain from observing both is  $h(x, y) = h(x) + h(y)$

# How do we measure information?

$$\{v_1, v_2, \dots, v_n\}$$

- Two unrelated events  $x, y$  also are **statistically independent**!  $p(x, y) = p(x) * p(y)$
- The only possible definition for  $h$  using  $p$  is:  
 $h(x) = -\log_2 p(x)$
- Example: coin flip  $\{v_1: \text{head}, v_2: \text{tails}\}$ 
  - $p(x=v_1) = p(x=v_2) = 0.5$
  - $h(x=v_1) = -\log_2 p(x) = -\log_2 0.5 = 1$
  - $h(x=v_2) = 1$

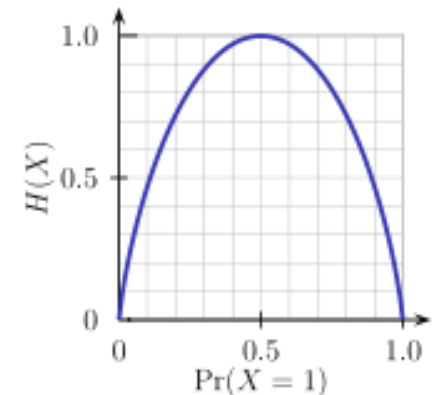


# Measuring information

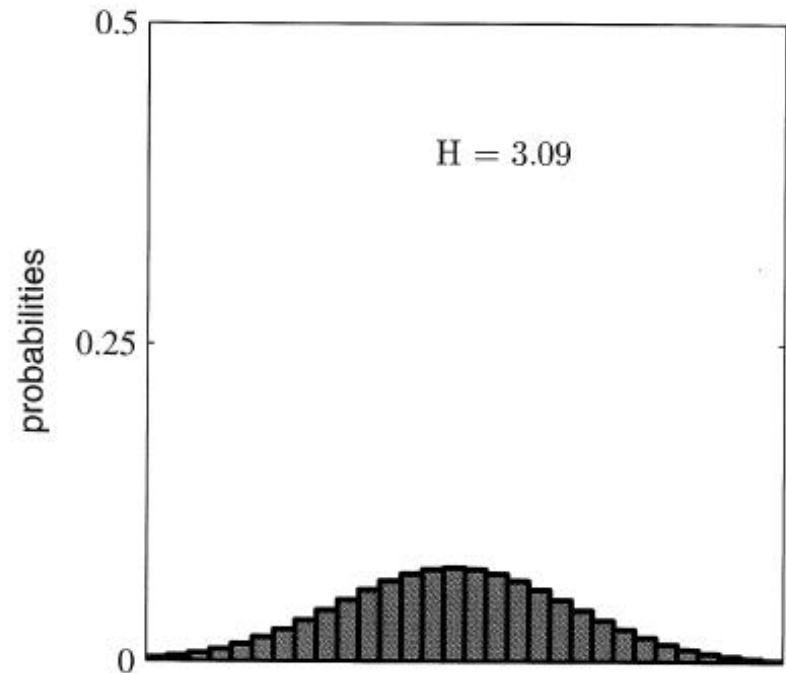
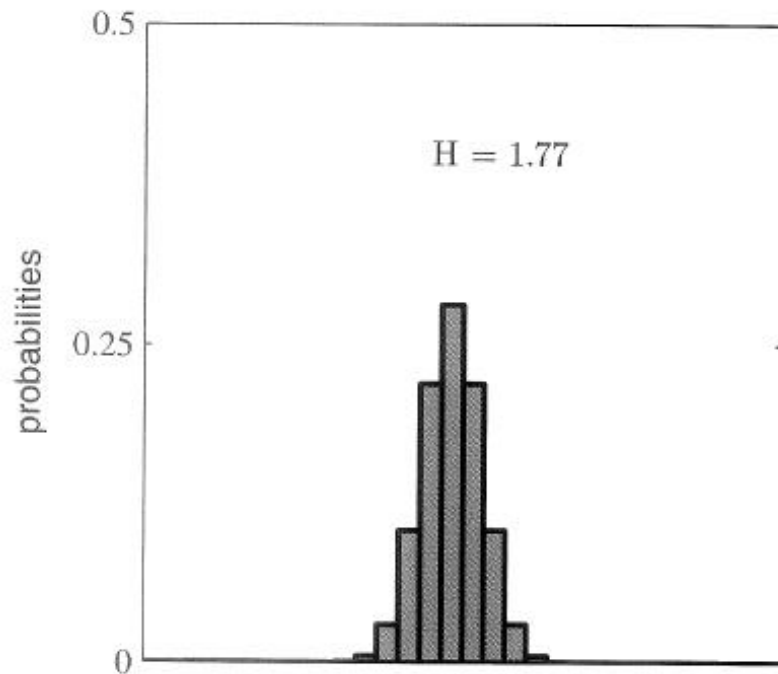
- Now suppose we want to transmit value of random variable  $x$  over a communication channel:
  - **Average** amount of information transmitted is the **expectation of  $h$**  with respect to  $p$

$$H(X) = \sum_x p(x)(-\log_2 p(x)) \quad \text{Quantity known as entropy!}$$

- Back to coin flip:  
 $H(x) = 0.5 * h(x=v_1) + 0.5 * h(x=v_2) = 1$  **bit**
- What happens with **non-equal probabilities**?
- „Unfair Coin“:  $p(x=v_1) = 0.3$ ,  $p(x=v_2) = 0.7$   
 $H(x) = 0.3 * -\log_2(0.3) + 0.7 * -\log_2(0.7) = 0.88$  bit



# Distributions and Entropy

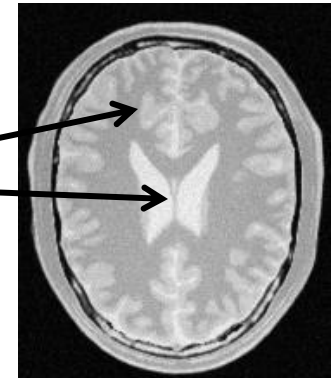


Q: How does a prob. distribution have to look like for  $H=0$ ?  
How for  $H=\max$ ?

# Images as probability distributions

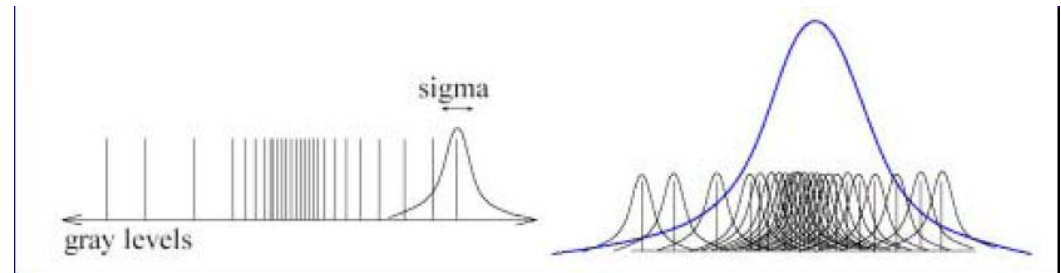
- Images can be viewed as (pixel-wise) grey level probability distributions

- marginal probability  $p(a)$  of any pixel having intensity  $a$



- Probability distribution of an image can be estimated using **histograms**

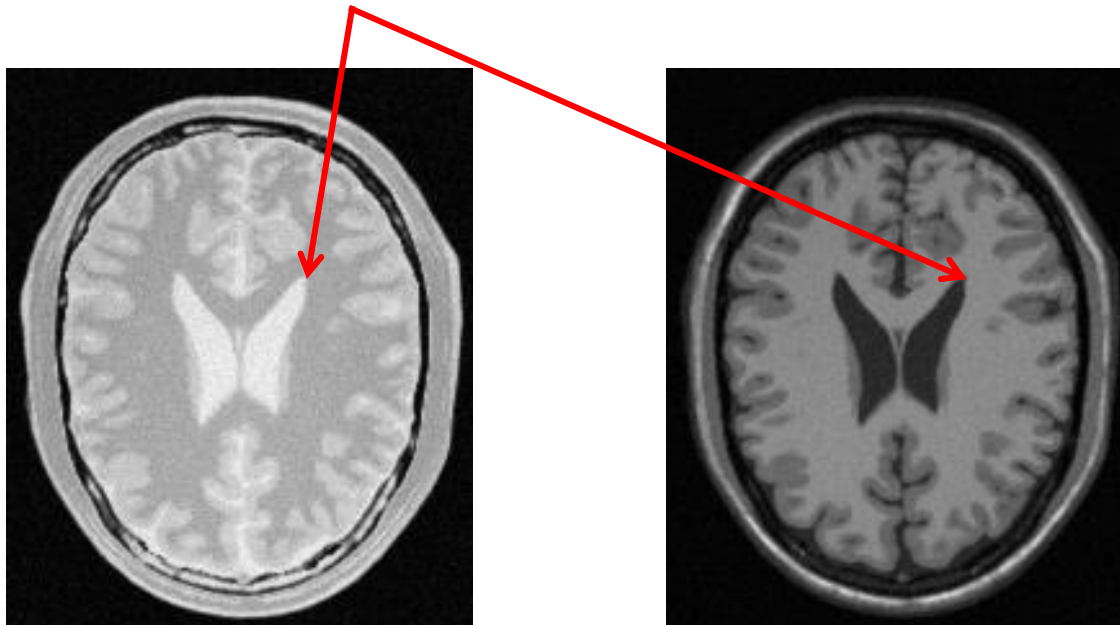
- Requires binning!
- 32 to 256 bins
- May be refined by Parzen Windowing





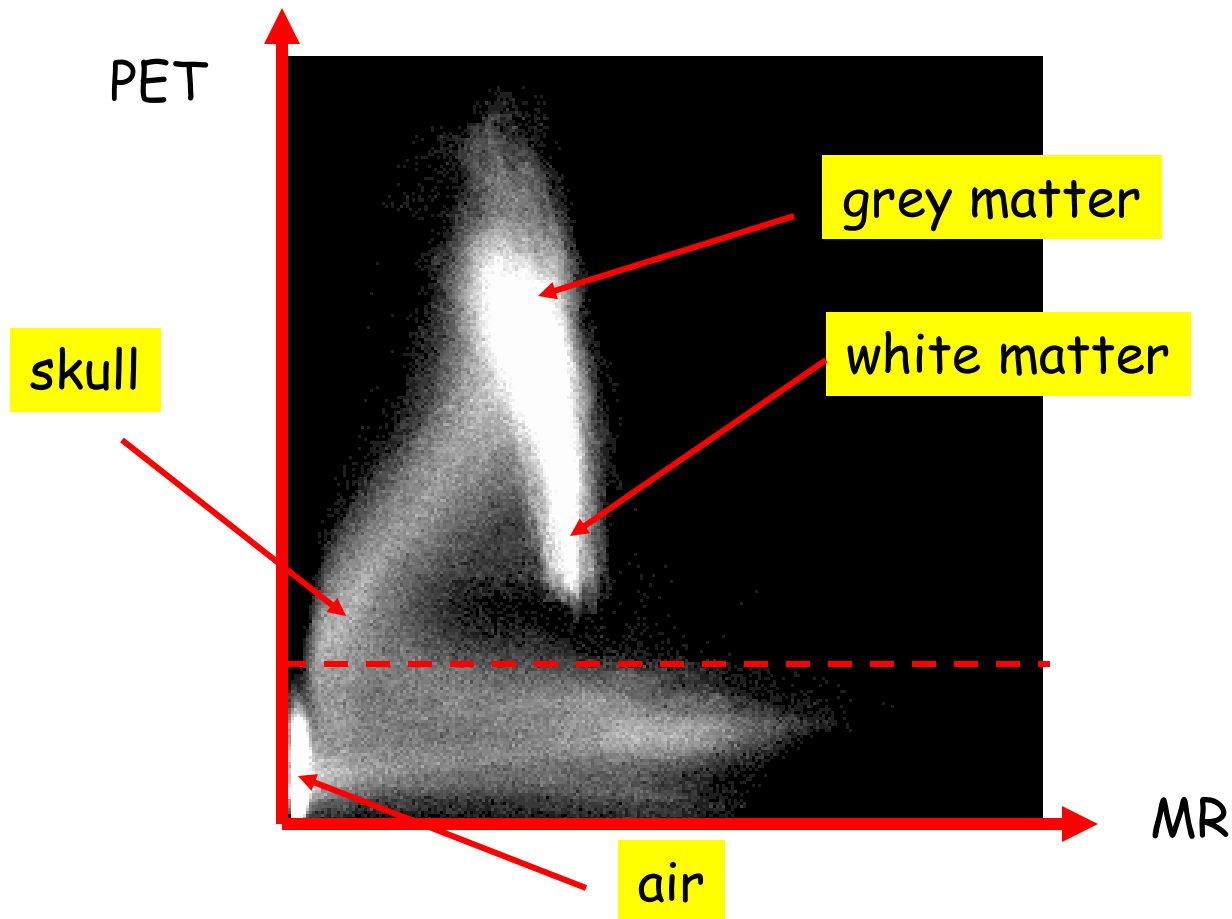
# Images as probability distributions

- Joint probability  $p(a, b)$  of a pixel having intensity **a** in one image and intensity **b** in another image (corresponding locations!)

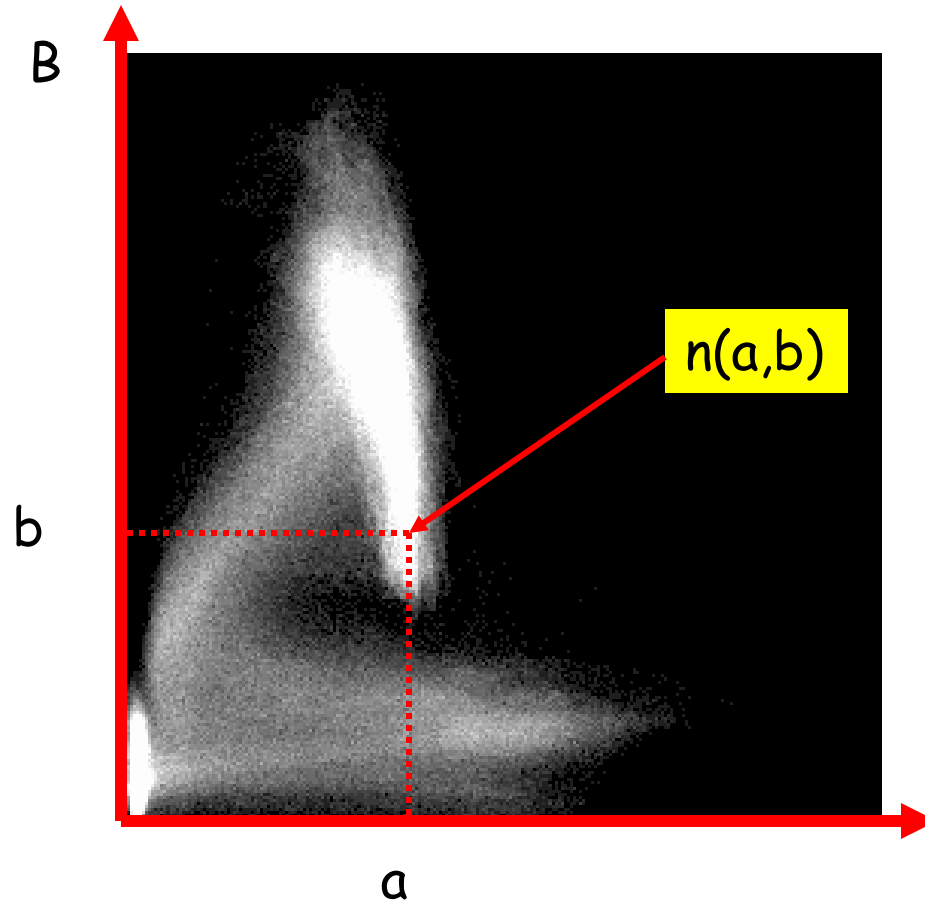


Joint Histogram

# 2D Joint Histograms



# 2D Joint Histograms



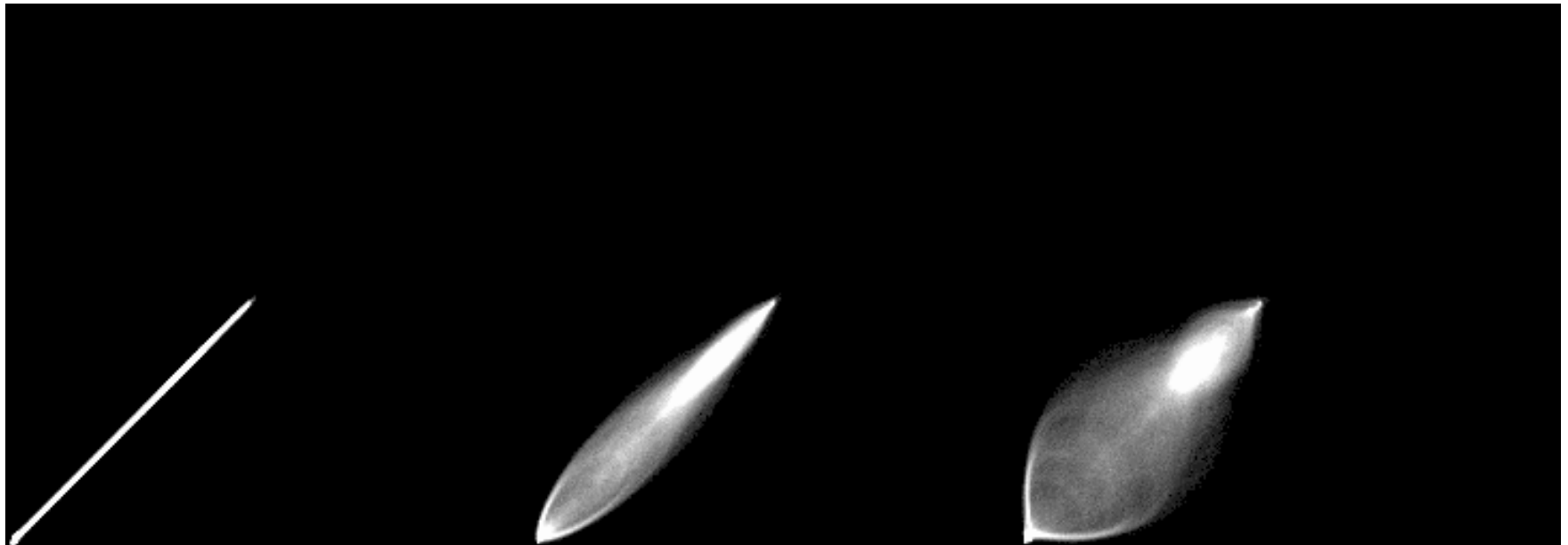
How often does it occur that intensities  $a$  and  $b$  are located at the same location in the two images?

$A \rightarrow n(a,b)$

# 2D Joint Histograms

MR/MR

→  
Histograms for increasing joint entropy



registered

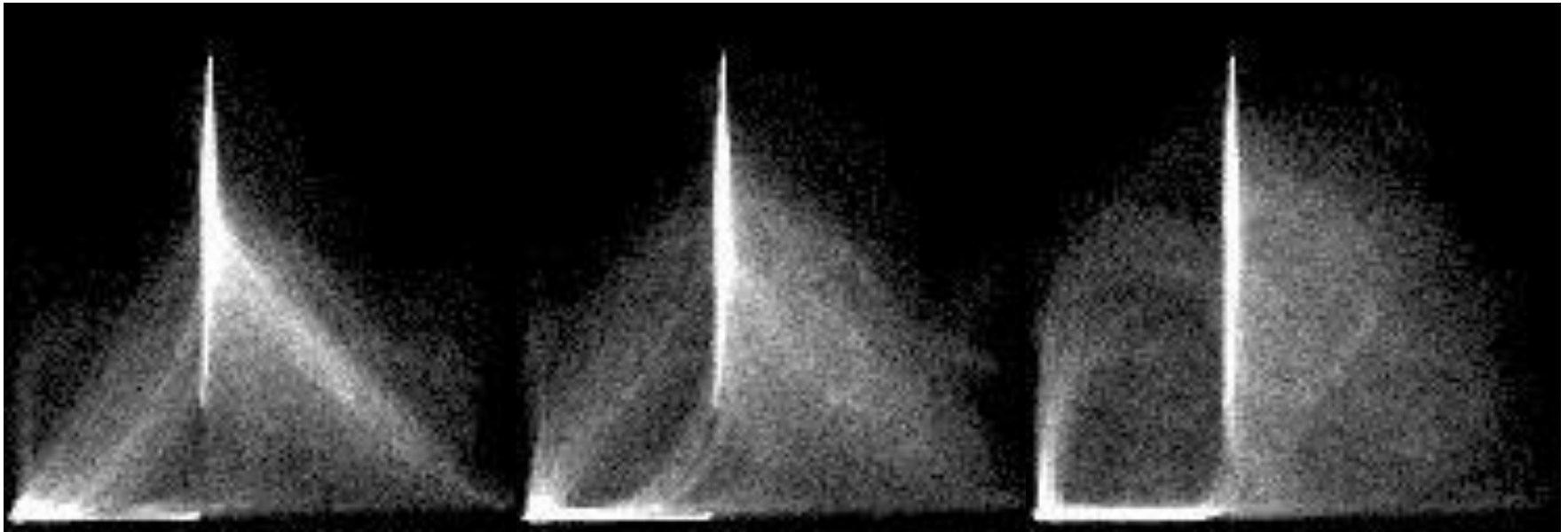
misregistered by 2mm

misregistered by 5mm

# 2D Joint Histograms

MR/CT

→  
Histograms for increasing joint entropy



registered

misregistered by 2mm

misregistered by 5mm

# 2D Joint Histograms

MR/PET

→  
Histograms for increasing joint entropy



registered

misregistered by 2mm

misregistered by 5mm

# Images as probability distributions

- Frequency of corresponding intensity pairs can be interpreted in terms of probabilities

$$p(a,b) = \frac{n(a,b)}{N}$$

is the joint probability of a voxel having greyvalue  $a$  in the first image and greyvalue  $b$  in the second image

$$p(a) = \sum_b p(a,b)$$

is the marginal probability of a voxel in the first image having greyvalue  $a$

$$p(b) = \sum_a p(a,b)$$

is the marginal probability of a voxel in the second image having greyvalue  $b$

# Voxel similarity based on information theory

- Entropy (Shannon-Wiener)

$$H(A) = - \sum_a p(a) \log_2 p(a)$$

describes the average amount of information in image A.

- The **information content of an image is maximal** (in the information theoretic sense) if all intensities have equal probability.
- The **information content of an image is minimal** (in the information theoretic sense) if one intensity  $a$  has a probability of one, i.e.  $p(a) = 1$ .



# Voxel similarity based on information theory

- Joint Entropy (Hill et al., 1994)

$$H(A, B) = - \sum_a \sum_b p(a, b) \log_2 p(a, b)$$

describes the average amount of information in the combined images A and B.

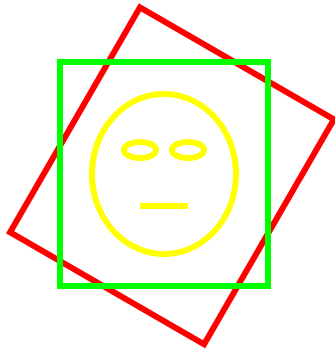
- If A and B are totally unrelated, the joint entropy will be the sum of the entropies of A and B
- If A and B are related, the joint entropy will be smaller, i.e.

$$H(A, B) \leq H(A) + H(B)$$

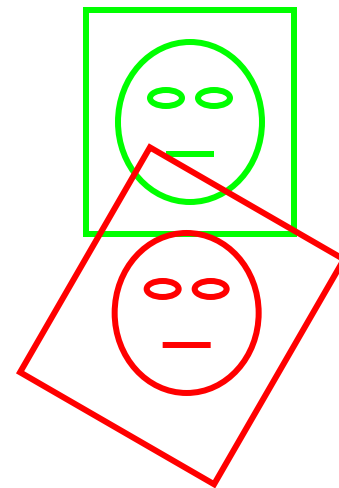
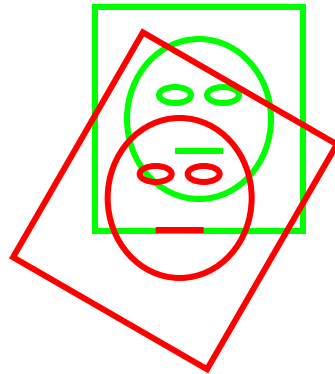
- Registration can be achieved by **minimizing** the **joint entropy** between both images

# Voxel similarity based on information theory

- Interpretation of Joint Entropy



low joint entropy

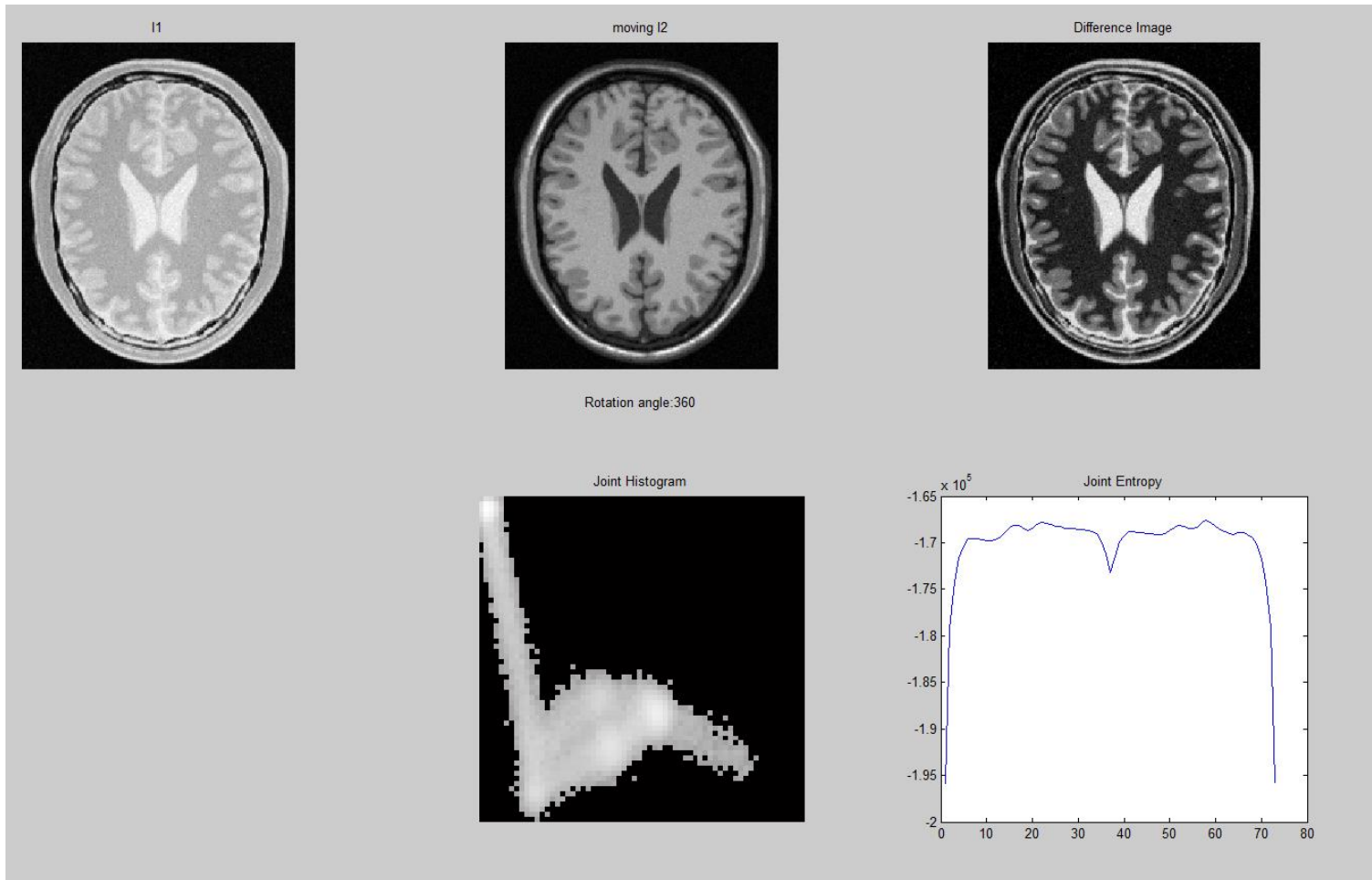


high joint entropy

# Joint Entropy Metric

Matlab!

joint\_histogram\_  
movie



# Voxel similarity based on information theory

- Joint Entropy is highly sensitive to the overlap of the two images
- **Mutual Information** (MI, Viola et al., 1995 and Collignon et al., 1995)

$$I(A, B) = H(A) + H(B) - H(A, B)$$

describes **how well one image can be explained by another image** (i.e. the reduction of uncertainty about A when knowing B).

- Mutual Information can be expressed in terms of marginal and joint probability distributions:

$$I(A, B) = \sum_a \sum_b p(a, b) \log_2 \frac{p(a, b)}{p(a) p(b)}$$

# Voxel similarity based on information theory

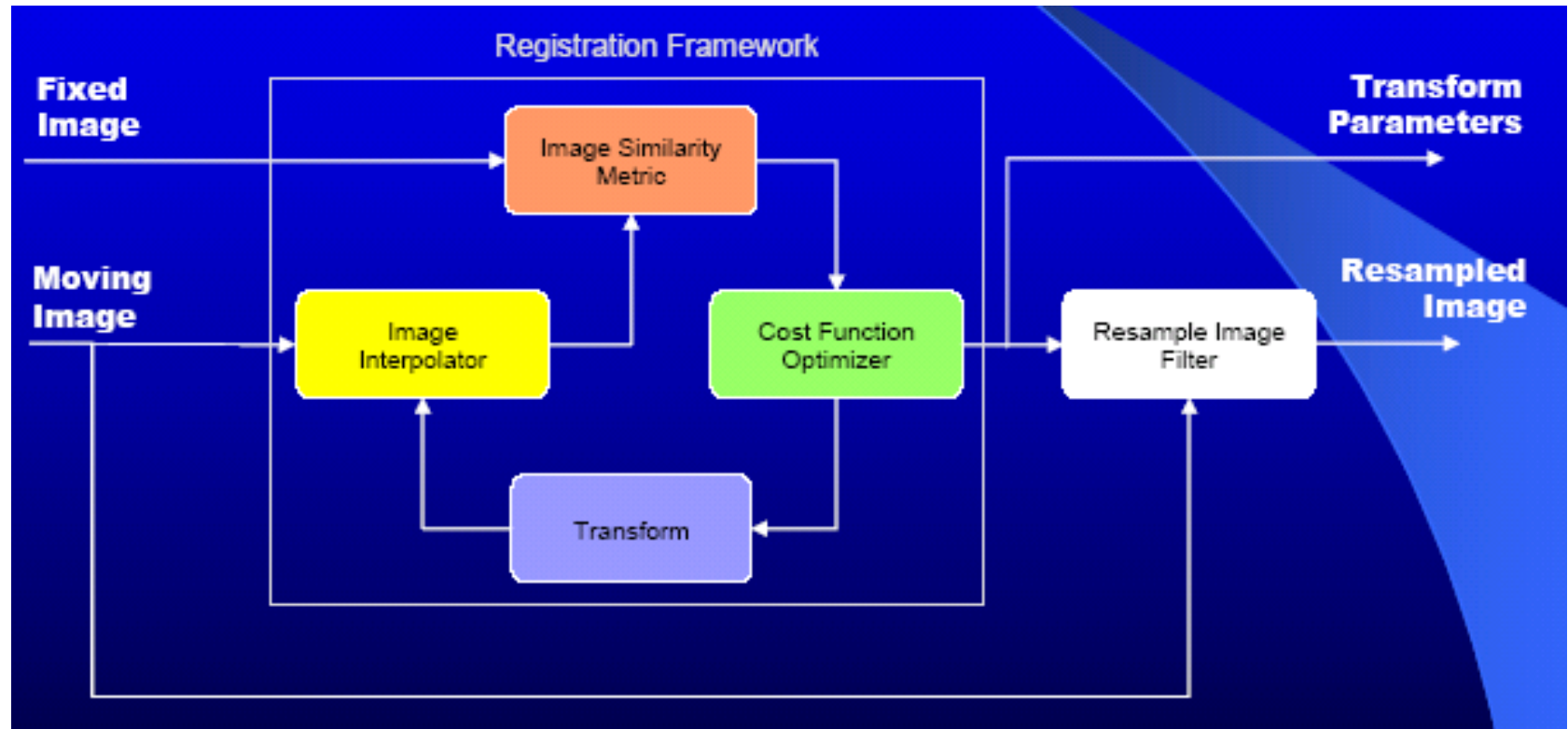
- Mutual Information is still to a certain degree sensitive to the overlap of the two images
- Normalized Mutual Information (Studholme et al, 1999)

$$I(A, B) = \frac{H(A) + H(B)}{H(A, B)}$$

can be shown to be independent of the amount of overlap between images.

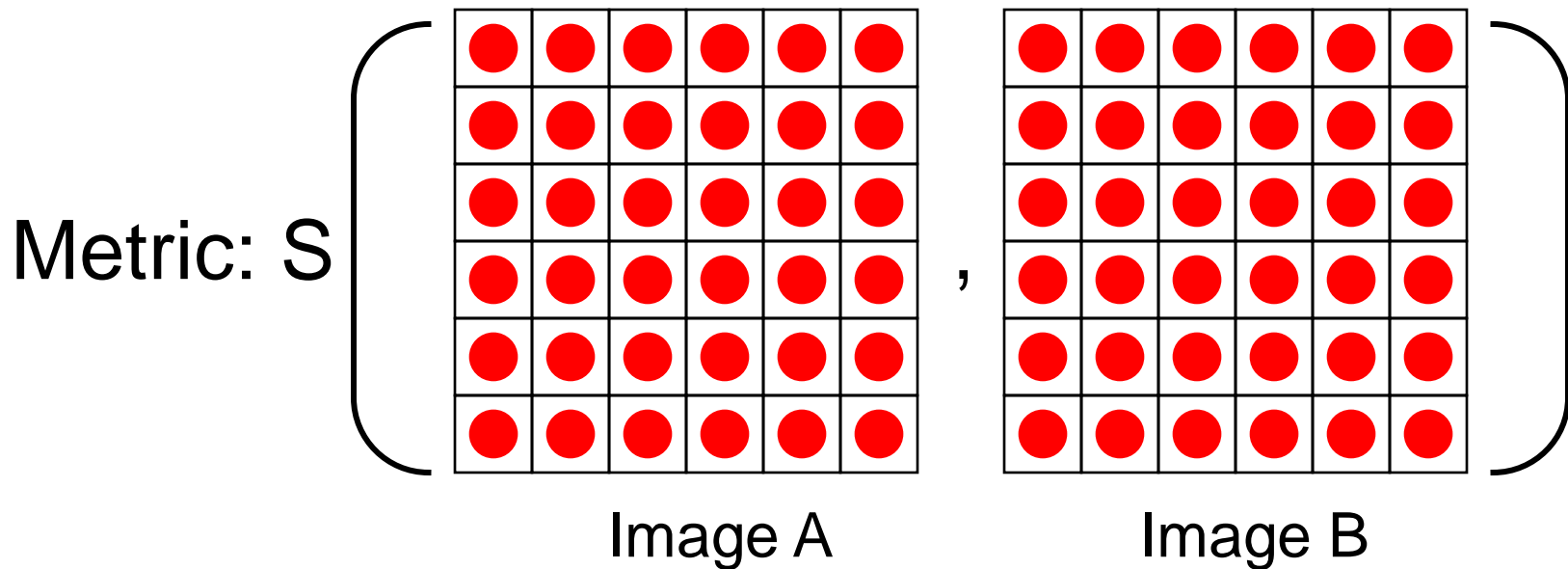
- Registration can be achieved by **maximizing** (Normalized) Mutual Information between both images (i.e. a similarity measure)

# Registration in practice



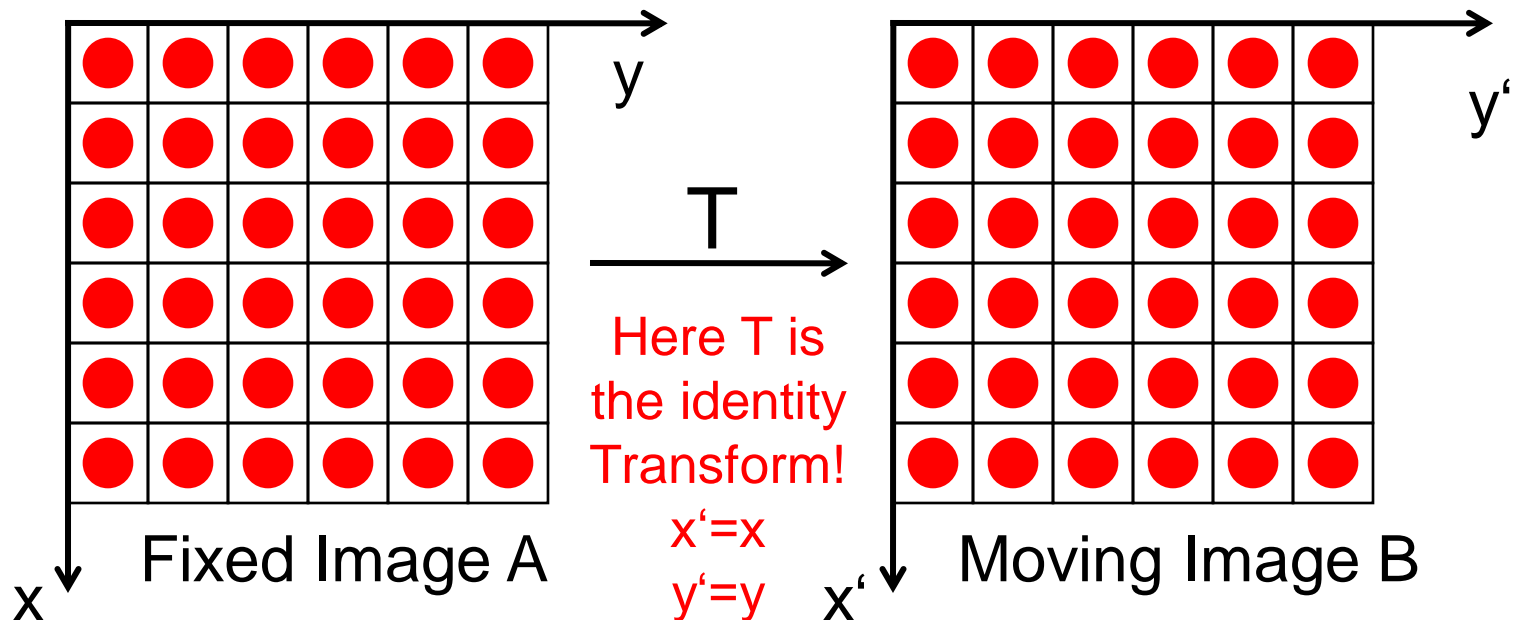
# Registration Comparing Images

- (Dis-)Similarity Metric (S) computation needs discrete representations of two images



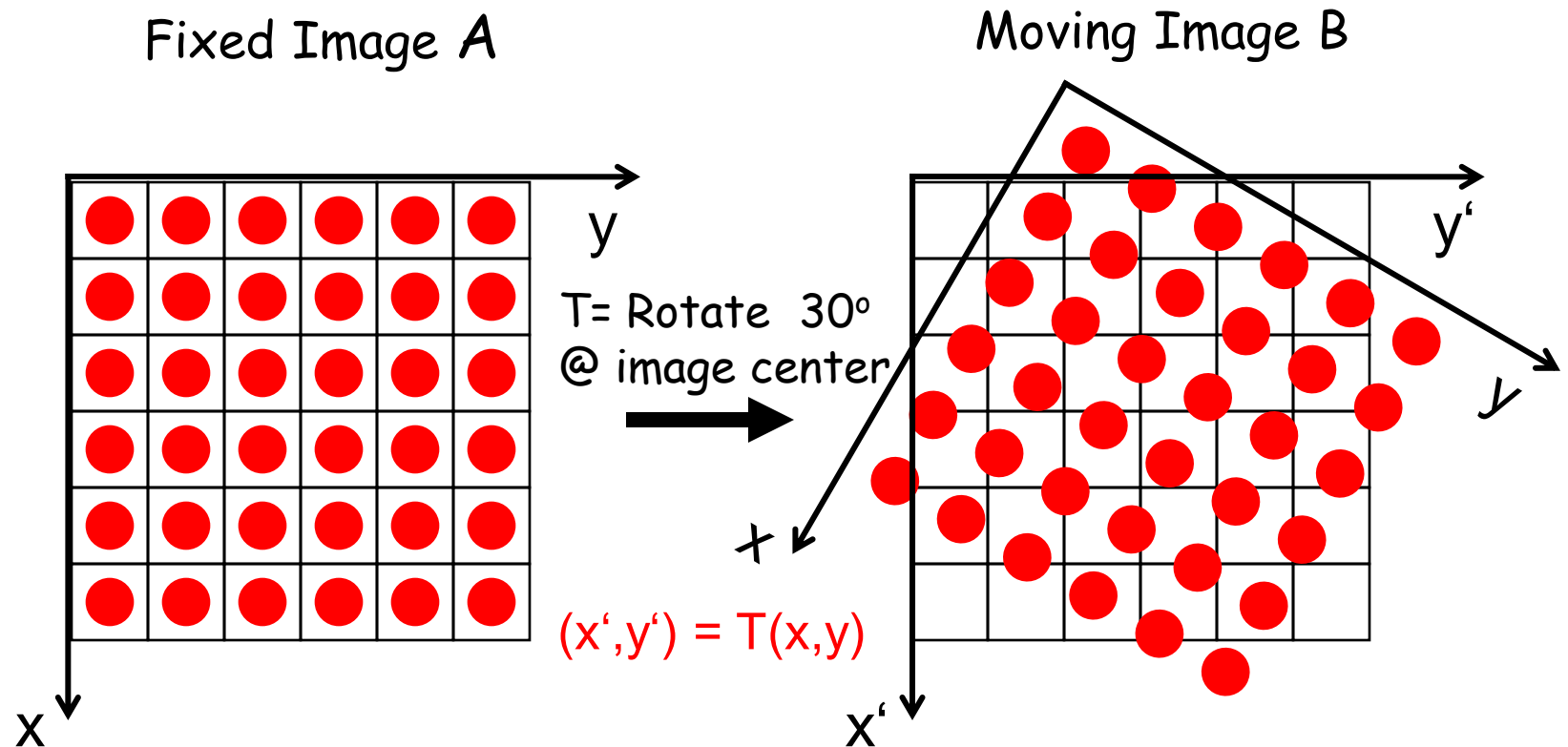
# Registration Transformation

- Relation of the two coordinate systems depends on transformation  $T$



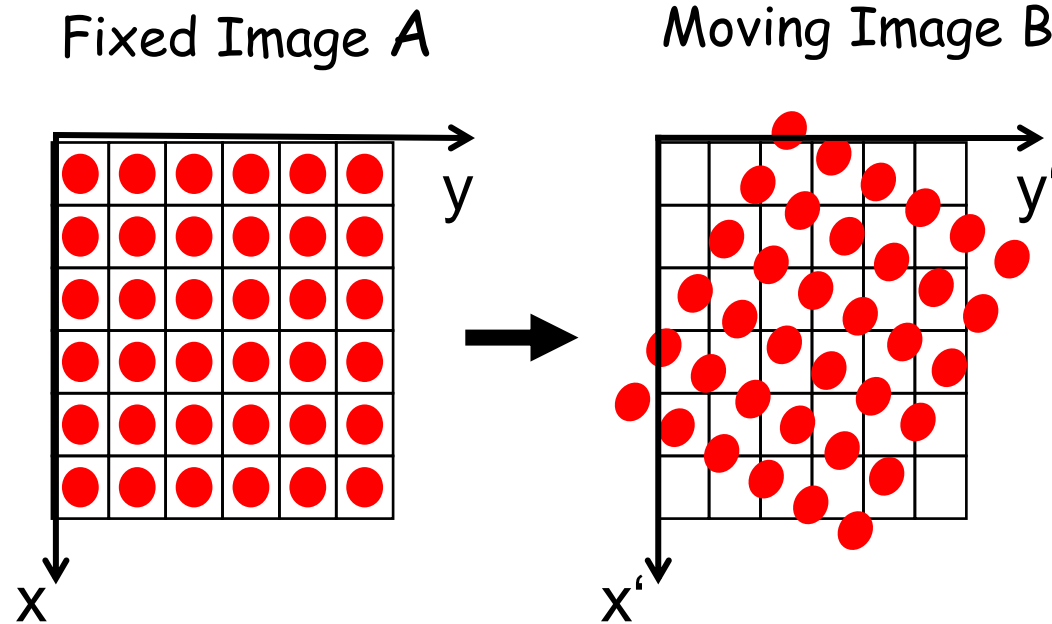


# Forward transformation



- Coordinate system of image A mapped onto image B

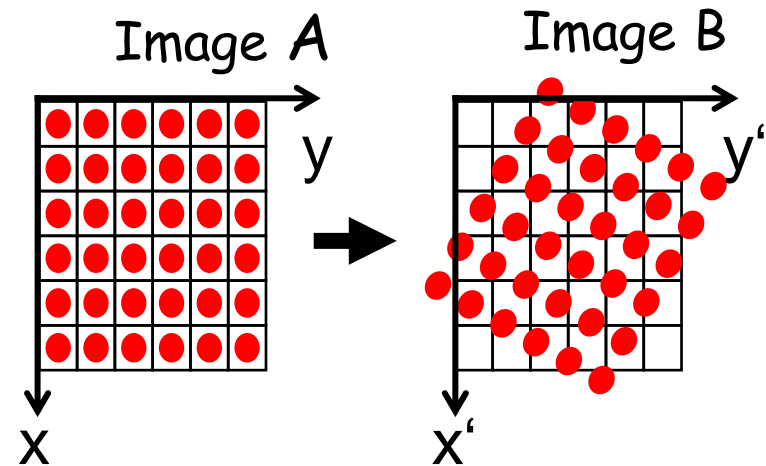
# How to calculate Forward transform?



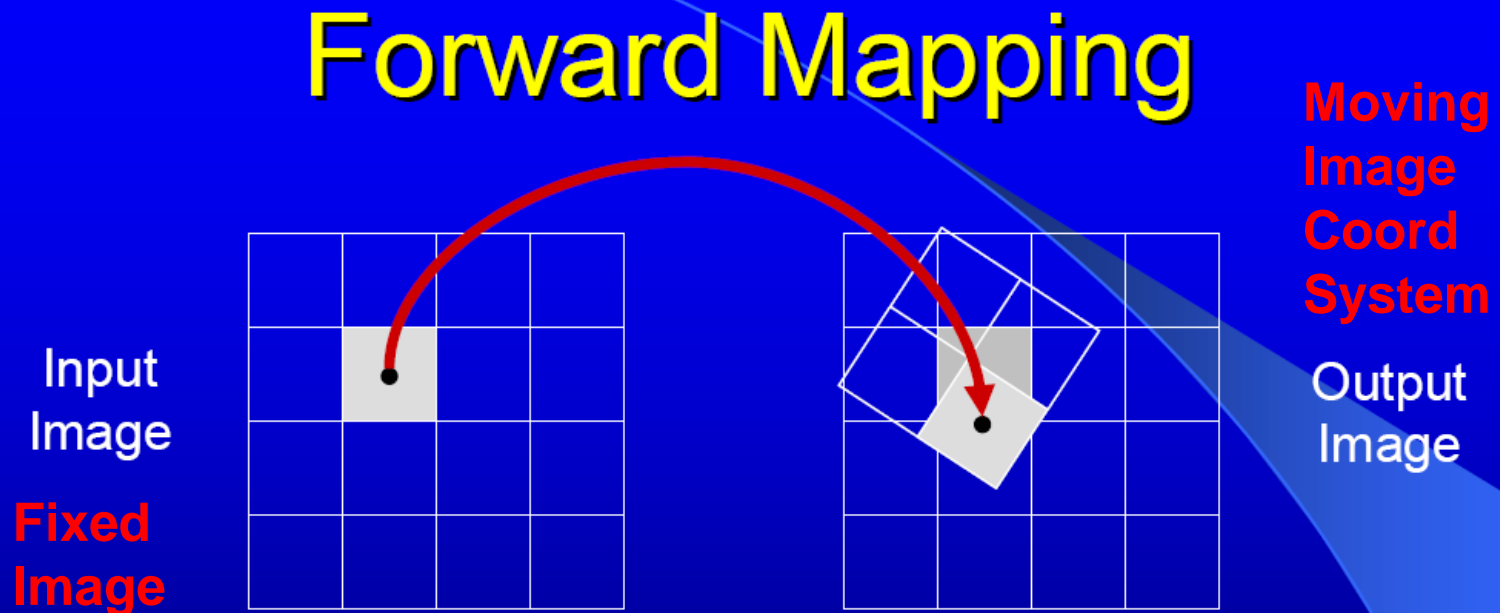
- Forwards Mapping
- Inverse Mapping

# How to calculate Forward transform?

- Forwards Mapping
  - Generate output image of same size as image B
  - Go over voxels of A, transform coordinate using T and **put the intensity of voxel from A** into transformed location in output
  - **Compare** output image and image B **in coordinate frame of image B**



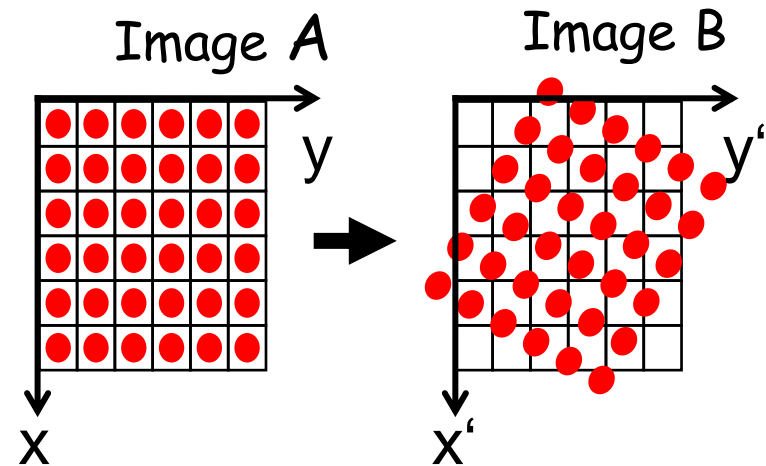
# Problem with Forward Mapping



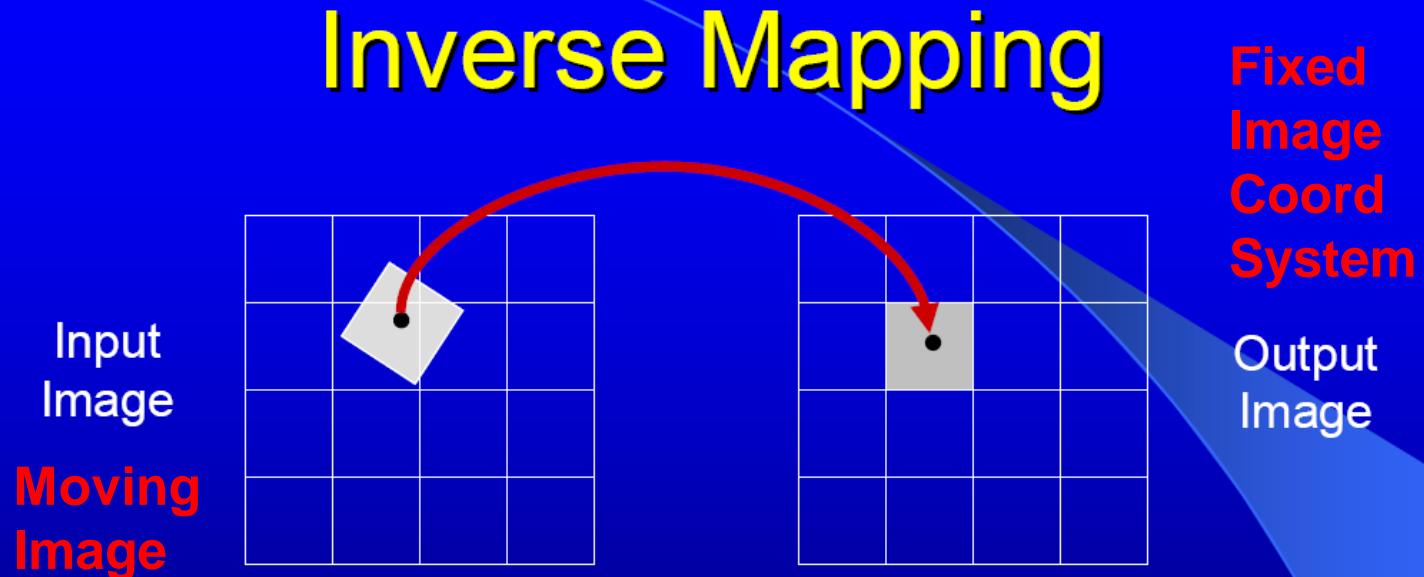
- Input image pixel is mapped onto the output image
- Output pixels with more than one hit: overlap
  - Value must be accumulated from overlapping pixels
- Output pixels with no hits: hole

# How to calculate Forward transform?

- Inverse Mapping
  - Generate output image of same size as image A
  - Go over voxels of image A, transform coordinate using  $T$ , **interpolate the intensity of voxel from B** and put the interpolated value into same coordinate of output image
  - **Compare** output image and image A in coordinate **frame of image A**



# Backwards (Inverse) Mapping



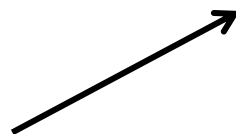
- Output pixels are mapped back onto the input image
- Scheme avoids any holes and overlaps in the output image because all pixels are scanned sequentially
- Output pixel value must be interpolated from a neighborhood in the input image

# Registration in practice – Summary so far

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- Calculate (dis-)similarity metric in fixed image coordinate frame!
- Registration frameworks use **inverse mapping** to interpolate moving image
- Transforms map points from fixed image space to moving image space (**forward transform**)

$$\mathbf{x}' = T(\mathbf{x})$$

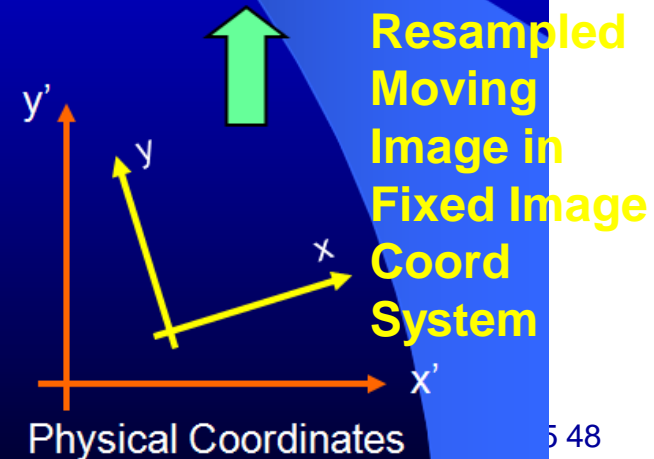
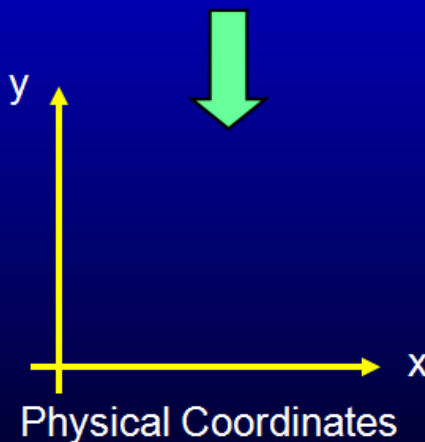
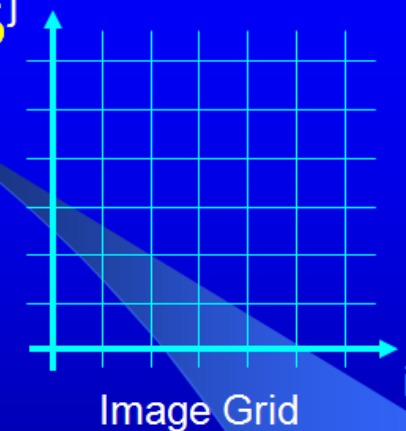
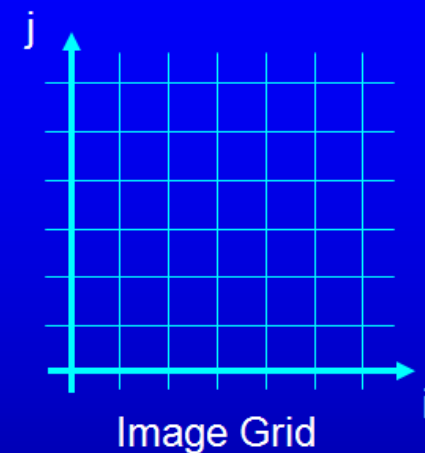


Point in moving image space

Point in fixed image space

# Registration in practice

## Coordinate System Conversions





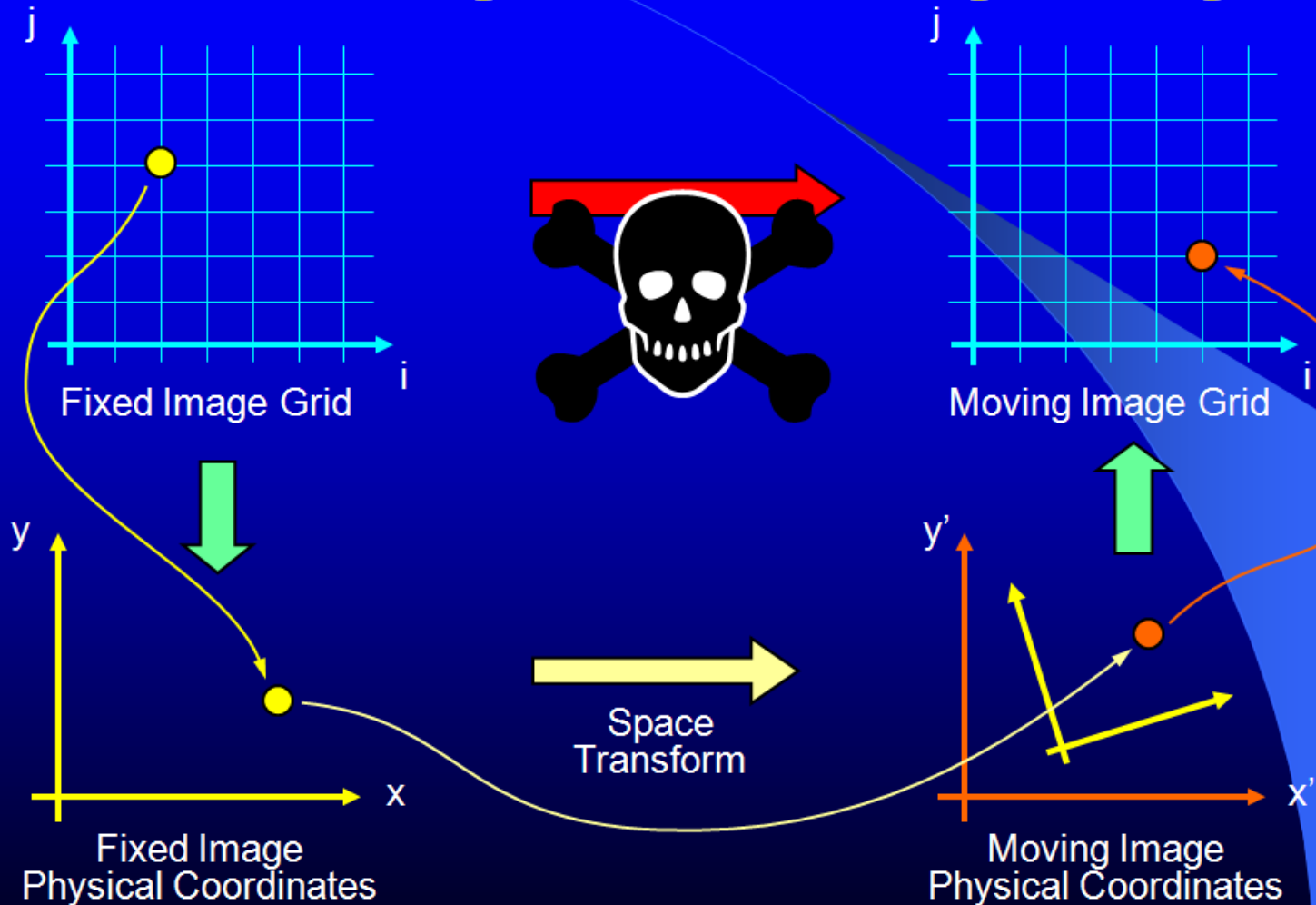
# Registration in practice

*I will not register images in pixel space*  
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*I will not register images in pixel space*



# Registration in practice

## Fixed Image & Moving Image



# Registration in practice

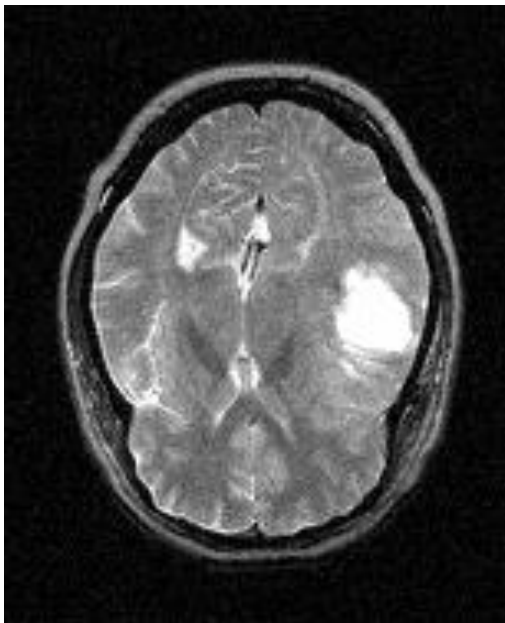
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- In principle the denomination of **fixed** & **moving** image is arbitrary
- In practice the **moving** image is the one that will be **resampled into** the **fixed** image coordinate system

# Registration in practice

## Quiz #1

MRI-T2



256 x 256 pixels

PET



128 x 128 pixels

Images from the same patient



Moving Image ?

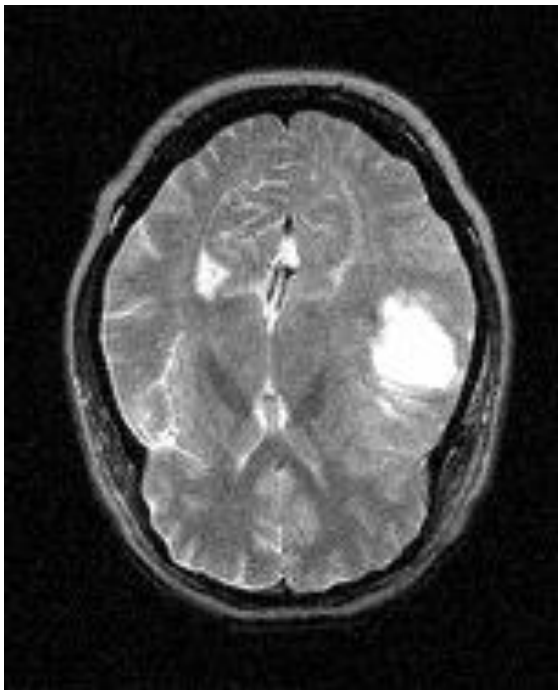
Fixed Image ?



Reason: Resample  
higher resolution image!

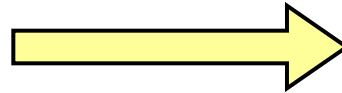
# Registration in practice

MRI-T2



256 x 256 pixels

## Quiz #2



What scale factor ?

- a) 2.0
- b) 1.0
- c) 0.5

PET



128 x 128 pixels

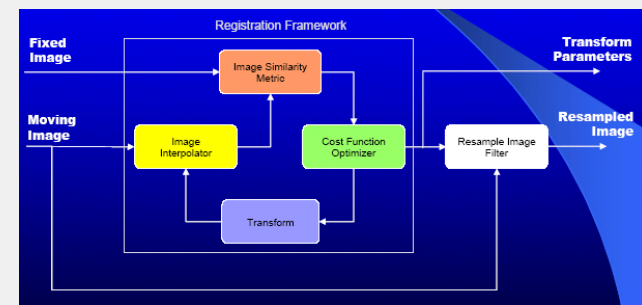
Images provided as part of the project: "Retrospective Image Registration Evaluation",  
NIH, Project No. 8R01EB002124-03, Principal Investigator, J. Michael Fitzpatrick, Vanderbilt University, Nashville, TN.

# Registration in practice

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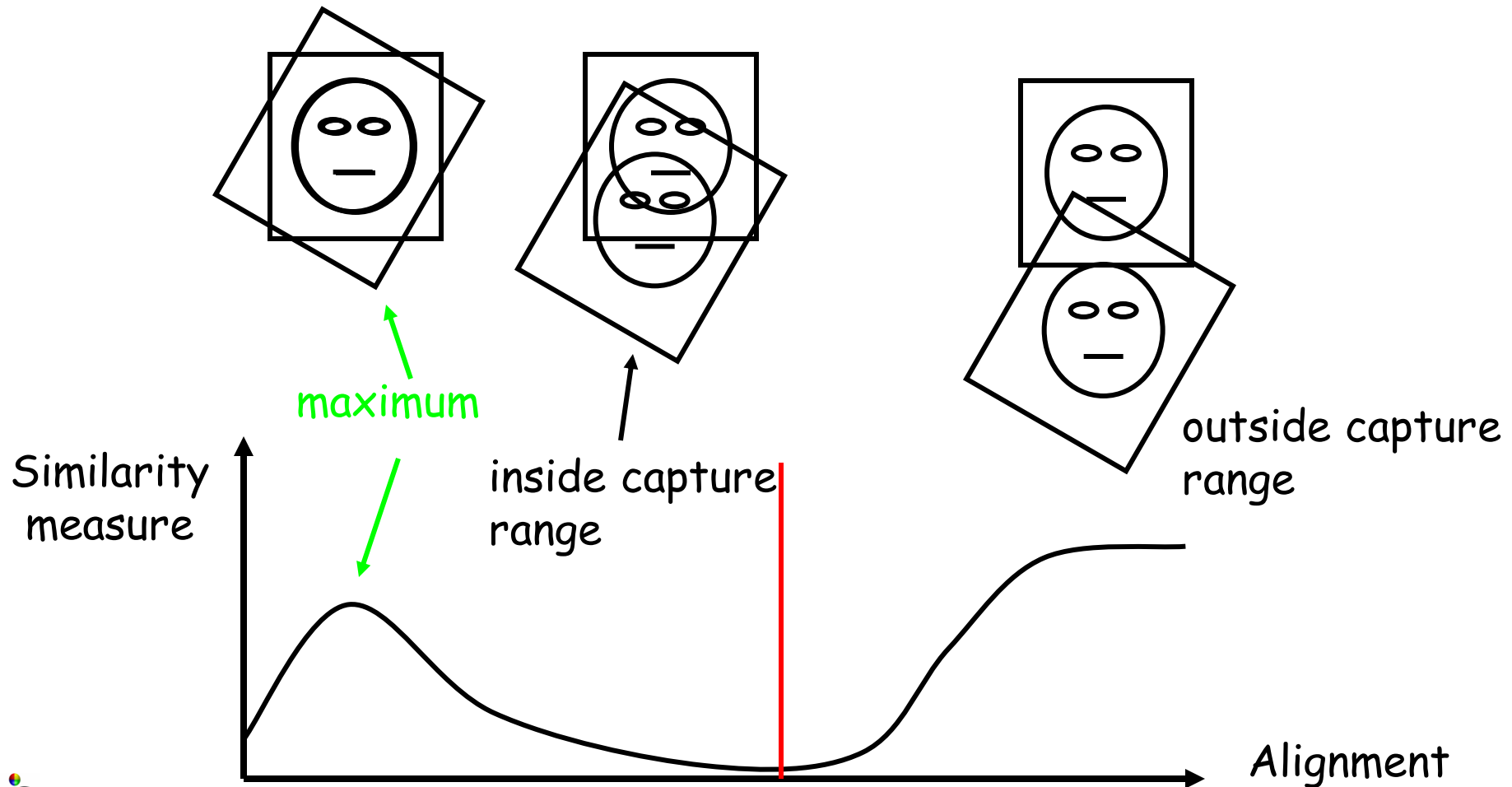


# Optimization



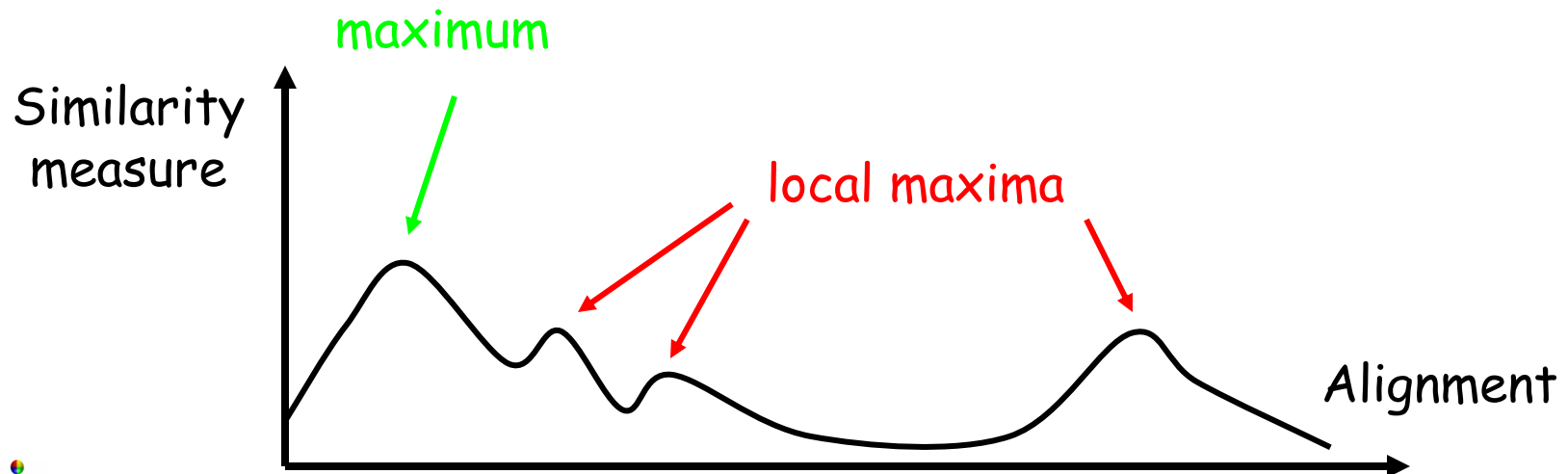
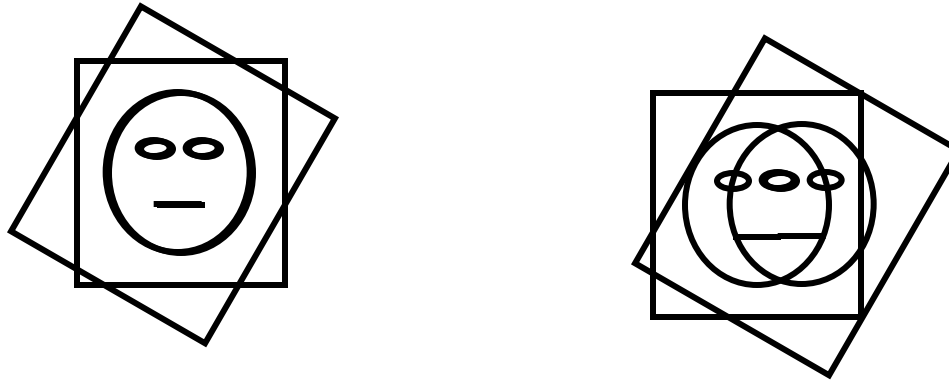
- Optimization of voxel-similarity measures normally requires iterative techniques, i.e.
    - gradient descent
    - Gauss-Newton, Levenberg-Marquardt, BFGS
    - see Numerical Recipes for a description of various optimization schemes
  - Global optimization schemes are not feasible for image registration (exhaustive search, genetic)
  - Local optimization schemes are **much more efficient** but **will get trapped in local optima**
- ⇒ Registration has a limited capture range

# Optimization (Maximization)



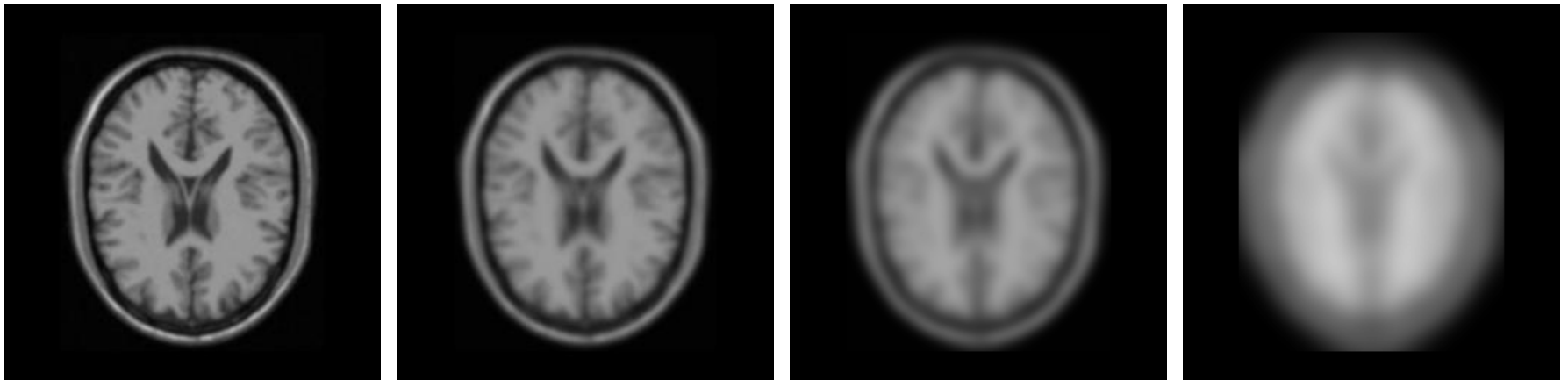


# Optimization



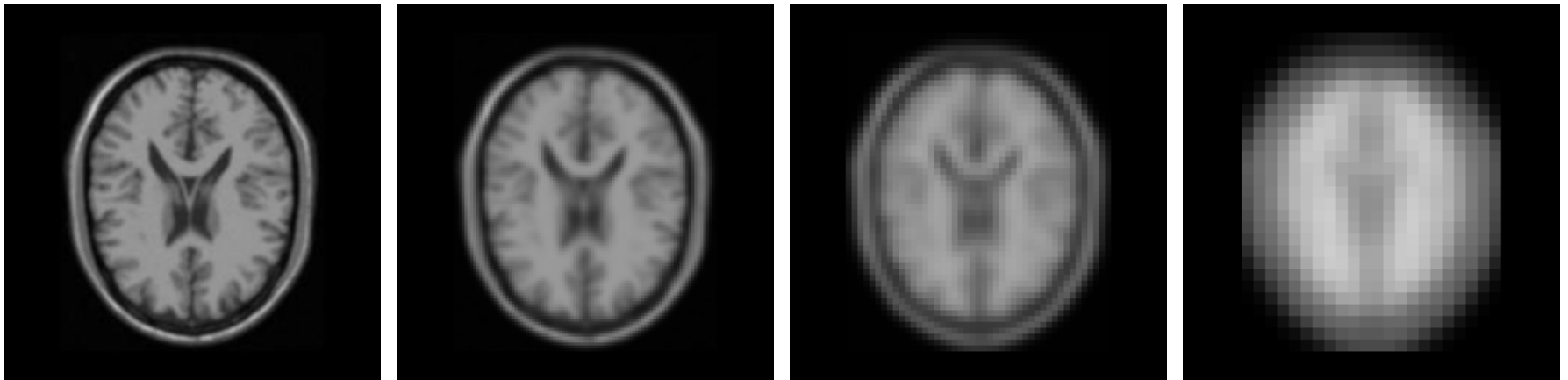
# Multi-resolution optimization

- Capture range can be increased by using multi-scale techniques:



# Multi-resolution optimization

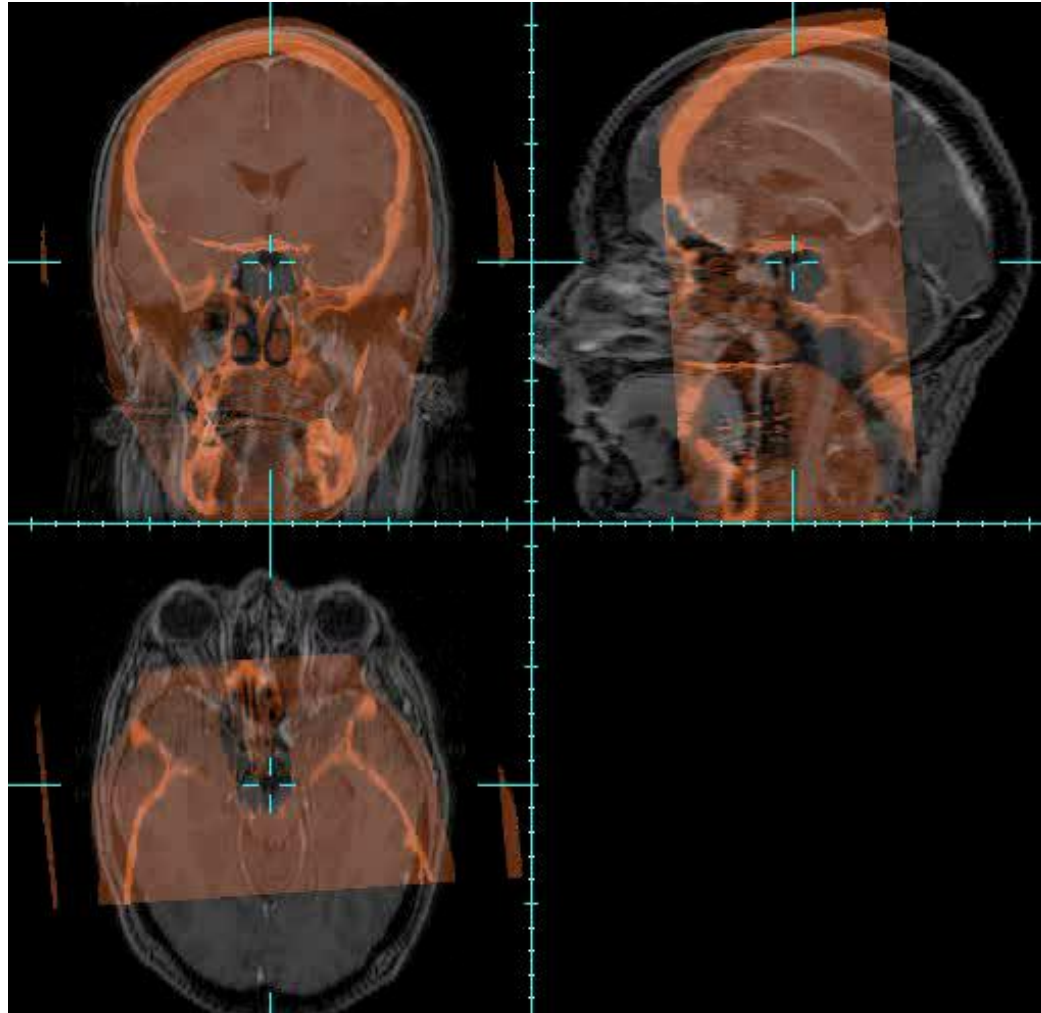
- Registration can be **accelerated** by using **multi-resolution** techniques:



# Optimization of voxel-similarity measures



# Optimization of voxel-similarity measures



# Discussion

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- **Voxel-similarity registration** is a powerful technique for automatic image registration
  - Range of voxel similarity measures exist, whose suitability depends on the imaging modality, the image quality, and the anatomy
- **Information-theoretic methods** are particularly suitable for multi-modal images
  - Joint intensity histograms are used to compute marginal and joint intensity probabilities