## Image registration

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2010-2013

### Image registration



### Image registration



# (Biomedical) applications

... of image registration

- Comparing images
  - Different times
  - Different methods
  - Different subjects
- Analyzing sequences
  - Motion estimation
  - Segmentation

Qualitative and quantitative information.

## Other applications of image registration

- video stabilization
- video compression
- image mosaicking
- stereo matching
- structure from motion

Motion analysis example

### ▶ heart ultrasound sequence (2C,4C)

```
mplayer -fs -loop 10
```

### Registration example



EPI MRI



anatomical MRI

### Image alignment



before

### Image alignment



### Correspondence function



#### Reference image

Test image

## Correspondence function



Reference image

Test image

$$\mathbf{g}([x \ y]^T) = [x' \ y']^T$$



 $0\ \%$  deformation









 $100\ \%$  deformation











 $100\ \%$  deformation

## Classification of registration methods

- ► Feature space intermediate data extracted from image
- Search space representation of the deformation
- Similarity metric measuring the dissimilarity
- Search strategy how to find the minimum
- User interaction level

### Registration methods – Feature space



### Registration methods - Search space

- Local
  - Variational
  - PDE
- Semi-local
  - ► (Quad)tree
  - B-splines
  - Wavelets
- Global
  - linear
  - polynomial
  - harmonic
- RBF, krigging
- Image dependent models (e.g. adaptive quadtrees)

## Similarity metrics

### Data term for pixel based criteria

- ► *l*<sub>2</sub> norm (SSD)
- ► *l*<sub>1</sub> norm
- correlation, normalized correlation
- mutual information, normalized mutual information

### Other data terms

- image interpolation important
- feature-based methods distance
- template-based methods windowed pixel-based criteria
- transform-based methods norm in the transform domain
- preprocessing filtering, histogram equalization,...

### Regularization

- Norm  $(I_p)$  of the derivatives
- Implicit regularization (constrained model)
- Smoothing

## Search strategy

- Direct solution
- Exhaustive search
- Dynamic programming
- PDE evolution
- Multidimensional optimisation
  - gradient descent
  - Newton-like methods, exact/estimated Hessian, Marquardt-Levenberg, conjugated gradients, BFGS, ....
- Multiresolution

### User interaction level

- Manual
- Automatic
- Semi-automatic

# Manual registration





### Landmark identification

### Manual registration





- Landmark identification
- Landmark interpolation

## Variational reconstruction



#### Find a function

### Variational reconstruction



### Find a function

### Variational reconstruction

### Find a function



### Rank functions



. . .



### Rank functions





Variational criterion $J: (\mathbb{R}^m \to \mathbb{R}^n) \to \mathbb{R}^+_0$ 

. . .

$$J(\mathbf{f}) \ge 0$$
# Variational reconstruction

Find the best function satisfying the constraints.



$$J(f) = \left\| \frac{\partial^M f}{\partial x^M} \right\|^2$$



reference



test



alpha=0.5

 $\int \|\nabla^{0.5} g(\mathbf{x})\|^2 \mathrm{d}\mathbf{x}$ 



alpha=0.9

 $\int \|\nabla^{0.9} g(\mathbf{x})\|^2 \mathrm{d}\mathbf{x}$ 



 $\int \|\nabla^{1.3}g(\mathbf{x})\|^2 \mathrm{d}\mathbf{x}$ 



 $\int \|\nabla^{2.5} g(\mathbf{x})\|^2 \mathrm{d}\mathbf{x}$ 

# Landmark interpolation (2)

#### Constraints

Hard constraints

$$\mathbf{g}(\mathbf{x}_i) = \begin{bmatrix} g_x(\mathbf{x}_i) \\ g_y(\mathbf{x}_i) \end{bmatrix} = \mathbf{z}_i = (x'_i, y'_i) \text{ for all } i \in \{1, \dots, N\}$$

Soft constraints

$$\sum_{i=1}^{N} \left\| \mathbf{g}(\mathbf{x}_i) - \mathbf{z}_i \right\|^2 \leq \varepsilon$$

#### Properties

- invariance to scale, shifts, rotations
- representability of linear transforms

# Thin-plate splines

Minimize an energy

$$J(g) = \int \left(\frac{\partial^2 g}{\partial x^2}\right)^2 + 2\left(\frac{\partial^2 g}{\partial x \partial y}\right)^2 + \left(\frac{\partial^2 g}{\partial y^2}\right)^2 dxdy$$
$$J(g) = J(g_x) + J(g_y)$$

under constraints

$$g(x_i, y_i) = z_i$$

# Thin-plate splines

Minimize an energy

$$J(g) = \int \left(\frac{\partial^2 g}{\partial x^2}\right)^2 + 2\left(\frac{\partial^2 g}{\partial x \partial y}\right)^2 + \left(\frac{\partial^2 g}{\partial y^2}\right)^2 dxdy$$
$$J(g) = J(g_x) + J(g_y)$$

under constraints

$$g(x_i, y_i) = z_i$$

▶ Solution (for *g*<sub>*x*</sub> only)

$$g_{\mathbf{x}}(x,y) = \sum_{i=1}^{N} \lambda_i \varrho(\|\mathbf{x} - \mathbf{x}_i\|) + a_0 x + a_1 y + a_2$$
  
with  $\|\mathbf{x} - \mathbf{x}_i\| = \sqrt{(x - x_i)^2 + (y - y_i)^2} = r$   
where  $\varrho(r)$  is a radial basis function and  $\varrho(r) = r^2 \log r$ 

## Thin-plate spline calculations

$$g_{x}(x,y) = \sum_{i=1}^{N} \lambda_{x,i} \varrho(\|\mathbf{x} - \mathbf{x}_{i}\|) + a_{0}x + a_{1}y + a_{2}$$
$$g_{y}(x,y) = \sum_{i=1}^{N} \lambda_{y,i} \varrho(\|\mathbf{x} - \mathbf{x}_{i}\|) + a_{3}x + a_{4}y + a_{5}$$

We have the data constraints:

$$g_x(x_i, y_i) = x'_i$$
  $g_y(x_i, y_i) = y'_i$ 

and the orthogonality constraints

$$\sum_{i} \lambda_{x,i} = 0 \qquad \sum_{i} \lambda_{y,i} = 0$$
$$\sum_{i} \lambda_{x,i} x_{i} = 0 \qquad \sum_{i} \lambda_{y,i} x_{i} = 0$$
$$\sum_{i} \lambda_{x,i} y_{i} = 0 \qquad \sum_{i} \lambda_{y,i} y_{i} = 0$$

# Thin-plate spline calculations (2)

Matrix form (for  $g_x$  only)

$$\underbrace{\begin{bmatrix} \mathsf{A} & \mathsf{Q} \\ \mathsf{Q}^{\mathsf{T}} & \mathsf{0} \end{bmatrix}}_{\mathsf{B}} \begin{bmatrix} \boldsymbol{\lambda} \\ \mathbf{a} \end{bmatrix} = \begin{bmatrix} \mathbf{s} \\ \mathbf{0} \end{bmatrix}$$

with

$$\lambda = [\lambda_1 \dots \lambda_N]$$
$$\mathbf{a} = [a_0 \ a_1 \ a_2]^T$$
$$\mathbf{s} = [x'_1 \ x'_2 \dots x'_N]^T$$
$$(\mathsf{A})_{i,j} = \varrho(\|\mathbf{x}_i - \mathbf{x}_j\|)$$
$$(Q)_{i,:} = [x_i \ y_i \ 1]$$

# Thin-plate spline approximation

Matrix form (for  $g_x$  only)

$$\underbrace{\begin{bmatrix} \mathsf{A} + \gamma^{-1} I & \mathsf{Q} \\ \mathsf{Q}^T & \mathsf{0} \end{bmatrix}}_{\mathsf{B}} \begin{bmatrix} \boldsymbol{\lambda} \\ \mathbf{a} \end{bmatrix} = \begin{bmatrix} \mathbf{s} \\ \mathbf{0} \end{bmatrix}$$

 $\gamma$  is a regularization weight and a Lagrange coefficient corresponding to the allowed error  $\varepsilon.$ 

Assume that the transformation  $\mathbf{g}$  is parameterized by a small number of parameters  $\boldsymbol{\theta}$ .

Minimize the landmark registration error:

$$oldsymbol{ heta}^* = rg\min_{oldsymbol{ heta}} \sum_i \lVert \mathbf{g}(\mathbf{x}_i) - \mathbf{z}_i 
Vert^2$$

In simple cases, closed form solution is available, otherwise minimize iteratively.

$$\mathbf{x}^{(1)} = (x_1^{(1)}, y_1^{(1)}, x_2^{(1)}, y_2^{(1)}, \dots, x_N^{(1)}, y_N^{(1)})^T$$
$$\mathbf{x}^{(2)} = (x_1^{(2)}, y_1^{(2)}, x_2^{(2)}, y_2^{(2)}, \dots, x_N^{(2)}, y_N^{(2)})^T$$

Find a transformation (rotation, translation, scaling) of  $\mathbf{x}^{(2)}$ 

$$\mathcal{T}(\mathbf{x}^{(2)}) = s R \begin{bmatrix} x_i^{(2)} \\ y_i^{(2)} \end{bmatrix} + \begin{bmatrix} t_x \\ t_y \end{bmatrix} = \begin{bmatrix} x_i^{(2)} s \cos \theta - y_i^{(2)} s \sin \theta \\ x_i^{(2)} s \sin \theta + y_i^{(2)} s \cos \theta \end{bmatrix} + \begin{bmatrix} t_x \\ t_y \end{bmatrix}$$

such that a sum of squared distances is minimized

$$E = \sum_{i=1}^{M} w_i \left\| s \begin{bmatrix} \cos \theta & -\sin \theta \\ \sin \theta & \cos \theta \end{bmatrix} \begin{bmatrix} x_i^{(2)} \\ y_i^{(2)} \end{bmatrix} + \begin{bmatrix} t_x \\ t_y \end{bmatrix} - \begin{bmatrix} x_i^{(1)} \\ y_i^{(1)} \end{bmatrix} \right\|^2$$

$$E = \sum_{i=1}^{M} w_i \left\| s \begin{bmatrix} \cos \theta & -\sin \theta \\ \sin \theta & \cos \theta \end{bmatrix} \begin{bmatrix} x_i^{(2)} \\ y_i^{(2)} \end{bmatrix} + \begin{bmatrix} t_x \\ t_y \end{bmatrix} - \begin{bmatrix} x_i^{(1)} \\ y_i^{(1)} \end{bmatrix} \right\|^2$$

 $\text{Minimize } E(\theta, s, t_x, t_y) \text{ as } \min_{\theta} \min_{s, t_x, t_y} E_{\theta}(s, t_x, t_y)$ 

• Inner minimization wrt  $s, t_x, t_y$ 

$$rac{\partial E}{\partial t_x} = 0 \;, \qquad rac{\partial E}{\partial t_y} = 0 \;, \qquad rac{\partial E}{\partial s} = 0 \;,$$

**•** Inner minimization wrt  $s, t_x, t_y$ 

$$rac{\partial E}{\partial t_x} = 0 \;, \qquad rac{\partial E}{\partial t_y} = 0 \;, \qquad rac{\partial E}{\partial s} = 0 \;,$$

leads to linear equations:

$$s \sum_{i=1}^{M} w_i q(y_i, -x_i, \theta) - N t_x = -\sum_{i=1}^{M} w_i x'_i$$
  

$$s \sum_{i=1}^{M} w_i q(-x_i, -y_i, \theta) - N t_y = -\sum_{i=1}^{M} w_i y'_i$$

$$s \sum_{i=1}^{M} w_i^2 \left( q^2(y_i, -x_i, \theta) + q^2(x_i, y_i, \theta) \right) - t_x \sum_{i=1}^{M} w_i q(y_i, -x_i, \theta) \\ - t_y \sum_{i=1}^{M} w_i q(-x_i, -y_i, \theta) \\ = - \sum_{i=1}^{M} w_i x_i' q(y_i, -x_i, \theta) + \sum_{i=1}^{M} w_i y_i' q(x_i, -y_i, \theta)$$

where  $q(a, b, \theta) = a \sin \theta + b \cos \theta$ .

- Inner minimization wrt  $s, t_x, t_y$
- Outer minimization wrt θ One dimensional functional minimization, e.g. Brent's routine or golden section search. (Alternatively, Horn's absolute orientation method can be used.)

# Automatic landmark registration

#### Feature point detection

► Harris corner detector (smoothed derivatives → local structure matrix → eigenvalues → corner response function)

#### Feature point matching

- Template correlation
- ► Invariant descriptors, e.g. Scale Invariant Feature Transform (gradient direction → rotation invariance, scale-space image → scale invariance, 4 × 4 8-bin histograms of orientations and magnitudes in a neighborhood, normalization → 128-element descriptor)
- Outlier pruning
  - RANdom Sampling And Consensus
- Landmark fitting (interpolation)

Medical applications of landmark registration

# Overview

- Point- and surface based registration
  - Image-to-image registration
  - Image-to-physical space registration
- · Image guided surgery (IGS) applications
  - Pre-operative imaging
    - · Can be slow
  - Intra-operative imaging
    - · Must be fast
  - Tracking of surgical instruments and alignment of pre/intraoperative data with physical space of patient lying on operating table
    - · Must be near real-time and very accurate



Amputation at St. Thomas' Hospital 1775 (source: The Old Operating Theatre Museum, St. Thomas' Street, London SE1 9RT)









Registration of pre-operative CT and MRI to intra-operative scene









Augmented Reality

## **Registration Chain for IGS**



# Generic Feature-Based Registration Procedure

1. Distortion correction and camera calibration for each modality

while *dissimilarity* > 0 and *improvement* do

- 2. Feature extraction
- 3. Feature pairing
- 4. Similarity formulation and outlier removal
- 5. Dissimilarity reduction (optimization)

Great differences in each step depending on images and task!

### **Point-Based Registration**

- Orthogonal Procrustes problem:
  - Named after a robber in Greek mythology, who would offer travellers the opportunity to stay the night in a perfectly fitting bed.
  - Unfortunately, it was the guest who was altered to fit the bed, rather than the bed to fit the guest!
  - Short visitors were stretched to fit, and tall visitors had parts of their body cut off so that they would fit, with invariably fatal results.

The hero Theseus stopped this unpleasant practice by subjecting Procrustes to his own method.



## **Point-Based Registration**

- Orthogonal Procrustes problem:
  - "Procrustes" became the criticism for the practice of unjustifiably forcing data to look like they fit another set.
  - Now Procrustes statistics has lost is negative associations and is used in shape analysis.
  - The Procrustes problem is an optimal fitting problem of least square type.

### Point-based registration

- · Optimal fitting problem of least square type:
  - Closed-form solution for rigid case. Non-rigid registration requires iterative solution
  - Given two sets of *N* corresponding points {x<sub>i</sub>} and {y<sub>i</sub>}, find the rigid-body transformation (rotation matrix **R** and translation vector **t**) that minimizes the mean squared distance between the points:

$$\frac{1}{N}\sum_{i=1}^{N} |R\mathbf{x}_{i} + \mathbf{t} - \mathbf{y}_{i}|^{2}$$

## Point-based registration

- Centre points: - Compute mean: - Centre wrt mean:  $\mathbf{x}_i = \sum_{i=1}^N \mathbf{x}_i$   $\mathbf{y}_i = \sum_{i=1}^N \mathbf{y}_i$  $\mathbf{y}_i = \mathbf{y}_i - \mathbf{y}$
- Determine rotation matrix R via singular value decomposition (SVD) of correlation matrix H:

$$\begin{split} \mathbf{H} &= \sum_{i=1}^{N} \widetilde{\mathbf{x}}_{i} \widetilde{\mathbf{y}}_{i}^{T} & \\ \mathbf{H} &= U \mathbf{A} \mathbf{V}^{T}, \mathbf{U}^{T} \mathbf{U} = \mathbf{V}^{T} \mathbf{V} = \mathbf{I} & \mathbf{R} = \mathbf{V} \mathbf{D} \mathbf{U}^{T}, \mathbf{D} = diag(\mathbf{1}, \mathbf{1}, \det(\mathbf{V} \mathbf{U}^{T})) \end{split}$$

• Determine translation vector:  $t = \overline{y} - R\overline{x}$ 

# Point-based registration



## Points for Registration

- Anatomic landmarks
- · Skin-affixed markers
- · Bone-implanted markers
- · Advantages of markers
  - Fiducial is independent of anatomy
  - Automatic algorithms for locating fiducial markers can take advantage of marker's shape and size in order to accurately and robustly compute the fiducial point

## "Bummer of a birthmark, Hal!"


### **Skin-Affixed Markers**

- Advantage: non-invasive
- · Disadvantage: can move due to mobility of skin



### **Bone-Implanted Markers**



### **Bone-Implanted Markers**



# **Registration Error Measures**

- Fiducial localization error (FLE)
  - Error of localizing fiducials
- Fiducial registration error (FRE)
  - Distance between points (fiducials) used for registration
  - Minimum value of cost function
- Target registration error (TRE)
  - Distance between points (targets) not used for registration
  - This is the clinically relevant error



### Point-Based Registration Error: Theory

- Expected value of FRE and TRE has been estimated using perturbation theory
- FRE = f(FLE, N)
- TRE = f(FLE, N, shape of fiducial configuration, target position)

### Point-Based Registration Error: Theory

$$\left< \text{FRE}^2 \right> = \frac{N-2}{N} \left< \text{FLE}^2 \right>$$

$$\left\langle \text{TRE}^{2}(\mathbf{r})\right\rangle = \frac{\left\langle \text{FLE}^{2}\right\rangle}{N} \left\{1 + \frac{1}{3}\sum_{k=1}^{3}\frac{d_{k}^{2}}{f_{k}^{2}}\right\}$$

# Characteristics of TRE

- TRE proportional to FLE
- TRE inversely proportional to N<sup>1/2</sup>
- TRE depends on target position r
- TRE has its minimum value at fiducial configuration centroid (translational component)
- TRE increases as the distance of the target point from the principal axes increases
- Iso-error TRE contours are ellipsoidal



# Guidelines for Fiducial Marker Placement in Cranial IGS

- · Use as many markers as feasible
- Place markers so that the centroid of their configuration is near the regions that are most critical during surgery
- Distribute the markers as far apart as is possible
- Avoid linear, or almost linear, fiducial configurations
- Avoid placing markers on mobile areas of the scalp

### **Design of Optically Tracked Probes**



# Optical Tracking of Instruments: Point-based Registration



# Automatic rigid registration

- Look for rigid (euclidean or affine) transformation
- To compensate different position, scale
- ... or to simplify a more complicated problem

# Registration based on voxel similarity

- Registration based on geometrical features requires
  - the extraction of points, lines or surfaces
  - registration error is affected by localization errors during the feature extraction stage
- Registration based on voxel similarity measures
  - uses some measure derived from the intensity of the voxels directly
  - assumes that there is a relationship between the image intensities of both images if the images are registered
  - does not require any feature extraction, thus registration error is not affected by any localization errors

# Registration as minimization



# Registration based on voxel similarity

- Optimal transformation **T** is determined iteratively by maximizing a voxel-based similarity measure *C*.
- Voxel-similarity measure C is a function of
  - image A (target or reference image)
  - image B (source image)
  - transformation T

### **Registration algorithm**



## Registration based on voxel similarity

- Registration based on geometric features is independent of the modalities from which the features have been derived
- Registration based on voxel similarity measures features must make a distinction between
  - monomodality registration:
    - CT-CT, MR-MR, PET-PET, etc
  - multimodality registration
    - MR-CT, MR-PET, CT-PET, etc

• Sums of Squared Differences (SSD)

$$C = \frac{1}{N} \sum_{i} (I_{A}(\mathbf{p}_{i}) - I_{B}(\mathbf{T}(\mathbf{p}_{i})))^{2}$$
  
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

- Robust statistics can be used to reduce the influence of outliers on the registration
- Sum of absolute differences (SAD)

$$C = \frac{1}{N} \sum_{i} \left| I_A(\mathbf{p}_i) - I_B(\mathbf{T}(\mathbf{p}_i)) \right|$$

- assumes an identity relationship between image intensities
- less sensitive to outliers

Correlation

$$C = \frac{1}{N} \sum_{i} I_A(\mathbf{p}_i) \cdot I_B(\mathbf{T}(\mathbf{p}_i))$$

- assumes a linear relationship between image intensities
- sensitive to large intensity values
- useful if images have been acquired with different intensity windowing

Normalized Cross Correlation (CC)

$$C = \frac{\sum (I_{A}(\mathbf{p}) - \mu_{A}) (I_{B}(\mathbf{T}(\mathbf{p})) - \mu_{B})}{\sqrt{\left(\sum (I_{A}(\mathbf{p}) - \mu_{A})^{2}\right) \left(\sum (I_{B}(\mathbf{T}(\mathbf{p})) - \mu_{B})^{2}\right)}}$$

- $\mu_{A}$  average intensity in image A
- $-\mu_{B}$  average intensity in image B
- assumes a linear relationship between image intensities
- useful if images have been acquired with different intensity windowing

• Ratio of Image Uniformity (RIU, Woods et al. 1992)

$$R(\mathbf{p}) = \frac{I_{A}(\mathbf{p})}{I_{B}(\mathbf{T}(\mathbf{p}))} \qquad \overline{R} = \frac{1}{N} \sum R(\mathbf{p})$$
$$RIU = \frac{\sqrt{\frac{1}{N} \sum \left(R(\mathbf{p}) - \overline{R}\right)^{2}}}{\overline{R}}$$

aims to maximize the uniformity of the ratio between intensities in image A and B which is measured in form of their standard deviation

# Registration basis: Image intensity

- Mono-modal image registration
  - Image intensities are related by some simple function
    - · identity: Use SSD or SAD
    - · linear: Use CC or RIU
- 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

- Intensity remapping (van den Elsen et al. 1993)
  - specific to MR-CT registration
  - CT intensities are remapped so that
    - · soft tissue is bright
    - · bone and air are dark
    - · CT looks like MR
  - use correlation
- Gradient correlation (van den Elsen et al. 1993)
  - extract features like gradients, ridges or creases
  - use correlation

• Partitioned Image Uniformity (PIU, Woods et al. 1993)

$$PIU_{B} = \sum_{a} \frac{n_{a}}{N} \frac{\sigma_{B}(a)}{\mu_{B}(a)}$$
 or  $PIU_{A} = \sum_{b} \frac{n_{b}}{N} \frac{\sigma_{A}(b)}{\mu_{A}(b)}$ 

- $PIU_B$  measures the sum of the normalized standard deviation of voxel values in image B for each intensity level in image A
- PIU<sub>A</sub> measures the sum of the normalized standard deviation of voxel values in image A for each intensity level in image B

Partitioned Image Uniformity (PIU)

$$PIU_{B} = \sum_{a} \frac{n_{a}}{N} \frac{\sigma_{B}(a)}{\mu_{B}(a)}$$

 $\boldsymbol{N}$  is the total number of voxels

 $n_a$  is the total number of voxels with intensity a

$$\mu_{s}(a) = \frac{1}{n_{s}} \sum_{a} h(a,b)$$

is the average intensity in image B

corresponding to intensity a image A

$$\sigma_{s}(a) = \frac{1}{n_{s}} \sum_{s} \left( h(a,b) - \mu(a) \right)^{2}$$

is the standard deviation in image B corresponding to intensity *a* image A

or

Correlation Ratio (CR, Roche et al. 1998)

$$CR_{B} = \frac{1}{\sigma_{B}^{2}} \sum_{a} \frac{n_{a}}{N} \sigma_{B}(a)$$

$$CR_{A} = \frac{1}{\sigma_{A}^{2}} \sum_{b} \frac{n_{b}}{N} \sigma_{A}(b)$$

$$\sigma_{B} = \frac{1}{N} \sum_{a} \sum_{b} \left( h(a,b) - \mu_{B} \right)^{2}$$

is the standard deviation in image B

$$\sigma_{\scriptscriptstyle B}(a) = \frac{1}{n_{\scriptscriptstyle \sigma}} \sum_{a} \left( h(a,b) - \mu(a) \right)^2$$

is the standard deviation in image B corresponding to intensity *a* in image A

### Images as probability distributions

- Images can be viewed as probability distributions p(a)
  - marginal probability p(a) of a pixel having intensity a
  - joint probability p(a, b) of a pixel having intensity a in one image and intensity b in another image
- Probability distribution of an image can be estimated using
  - parzen windowing
  - histograms
- Histograms require "binning"
  - usually use 32 to 256 bins per image

# Registration based on voxel similarity: Problems



СТ

MR

#### MR/MR



registered misregistered by 2mm misregistered by 5mm







registered



misregistered by 2mm



misregistered by 5mm





registered



misregistered by 2mm



misregistered by 5mm





а
#### Images as probability distributions

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

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

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

• Entropy (Shannon-Wiener)

$$H(A) = -\sum_{a} p(a) \log p(a)$$

describes the 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.

• Joint Entropy (Hill et al., 1994)

$$H(A,B) = -\sum_{a} \sum_{b} p(a,b) \log p(a,b)$$

describes the amount of information in the combined images A and B.  $\ensuremath{\mathsf{B}}$ 

- 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.

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

Registration can be achieved my minimizing the joint entropy between both images

Interpretation of Joint Entropy



· Joint Entropy is highly sensitive to the overlap of the two images

• Mutual Information (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.

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

$$I(A,B) = -\sum_{a} \sum_{b} p(a,b) \log \frac{p(a,b)}{p(a)p(b)}$$

• Venn diagram:



Communication model:



- Mutual Information is still 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

### Evaluation of voxel-similarity measures



#### Optimization of voxel-similarity measures

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

#### Optimization of voxel-similarity measures



### Optimisation of voxel-similarity measures



### Multi-resolution optimization

• Capture range can be increased by using multiscale techniques:



### Multi-resolution optimization

 Registration can be accelerated by using multiresolution techniques:



### Optimization of voxel-similarity measures



ITK (Insight Registration and segmentation toolbox)

# Automatic elastic B-spline registration

- Look for elastic (non-linear) transformation
- Smooth deformation wanted
- Semi-local model with many parameters

# (Uniform) splines

~

# (Uniform) splines



- Piecewise polynomial of degree n
- Continuous  $(n-1)^{\text{th}}$  derivative
- ► (Uniform) knots

# Non-uniform splines (1D)

- Polynomial in each interval
- Continuous derivatives
- Boundary conditions (natural)
- $\blacktriangleright$   $\longrightarrow$  band system of linear equations
- Example: cubic splines

# Uniform B-splines

Haar	$\beta_0$
linear	$\beta_1$
quadratic	$\beta_2$
cubic	$\beta_3$



# Uniform B-splines

Haar $\beta_0$ linear $\beta_1$ quadratic $\beta_2$ cubic $\beta_3$ 



- Generation:  $\beta_{n+1} = \beta_n * \beta_0$
- Basis for splines:  $s(x) = \sum_{i} c_i \beta(x-i)$

# Practical B-splines

Separability > speed

- B-spline transform (finding coefficients) fast through IIR filtering
- Interpolation fast (small support)
- Extension to n-D by Cartesian product. Separability.

### Software

Splines Matlab, Numerical Recipes, ...

**B**-splines Unser, Thevenaz, bigwww.epfl.ch

## B-spline image interpolation

$$f(x,y) = \sum_{i,j} c_{ij}\beta_n(x-i)\beta_n(x-j)$$

- B-spline interpolation is global, while P0,P1,P2,P3... are local
- Pixels on a regular grid 
   B-spline coefficients can be
   precalculated (IIR filtr)
- Evaluation  $\beta_3$  as fast as for P3, better quality.
- Boundary conditions (zero, periodic, mirror)
- Higher orders lead to Gibbs artifacts (ringing).

# Spline based warping



- Approximation properties > precision
- ► Short support → speed
- Scalability
- Representability of linear transforms

$$\mathbf{g}(\mathbf{x}) = \mathbf{x} + \sum_{\mathbf{i} \in \mathbb{Z}^2} \mathbf{c}(\mathbf{i}) \, \beta(\mathbf{x}/\mathbf{h} + \mathbf{d} - \mathbf{i})$$

# Evaluating the difference



# Evaluating the difference



# Evaluating the difference



 $E = (1/N) \sum_{\mathbf{i}} \left( f_t^c(\mathbf{g}(\mathbf{i})) - f_r(\mathbf{i}) \right)^2$ 

#### 32 imes 32



#### 64 imes 64



#### $128\times128$



#### $256\times256$



## Multiresolution algorithm



video of the registration

xanim -Ss2

## Applications

► EPI distortion



Before

(with Arto Nirkko)

# Applications

► EPI distortion



After
- EPI distortion
- MRI atlas



Atlas

- EPI distortion
- MRI atlas



Aligned

- EPI distortion
- MRI atlas
- CT alignment







Before

- EPI distortion
- MRI atlas
- ► CT alignment









- EPI distortion
- MRI atlas
- CT alignment
- SPECT atlas



(with University Hospital in Geneva)

- EPI distortion
- MRI atlas
- CT alignment
- SPECT atlas
- Ultrasound



velocity

(with Mara J. Ledesma-Carbayo)

- EPI distortion
- MRI atlas
- CT alignment
- SPECT atlas
- Ultrasound
- MRI heart sequence





- EPI distortion
- MRI atlas
- CT alignment
- SPECT atlas
- Ultrasound
- MRI heart sequence
- MRI perfusion



#### Validation of registration

- Before an image registration can enter clinical practice, it must undergo thorough validation
  - Technical validation
    - Speed, robustness, accuracy, reliability,...
  - Clinical validation
    - Usefulness, improved clinical diagnosis and patient management in health care
  - FDA approval, incorporation into commercial system
    - · Liability

## Validation of rigid registration

- Robustness:
  - Measurement precision
- Consistency:
  - Circular (invertible) transformations
- · Visual assessment:
  - subtraction images, overlays, landmarks
- · Gold standard:
  - Implanted/attached markers, landmarks
- Simulation of a ground truth:
  - misregistration followed by motion recovery

#### Robustness

- Robustness can be measured as the discrepancy of registration transformations if different starting estimates are given or the images are perturbed:
  - Misregistration of an image by a known amount, e.g. by upto
     +-30mm or +- 30 degrees
  - Adding noise, inhomogeneity
- Deviation from identity transformation which forms the ground truth
  - Individual deviations of DOFs (tx,ty,tz,rx,ry,rz,...)
  - Target registration error (TRE) at landmarks or within volume overlap

- Involves registration of an image triple, A to B, B to C, and C to A
- Ideally, the resulting transformations form a circular registration:

 $\mathbf{T}_{AB} \mathbf{T}_{BC} \mathbf{T}_{CA} (\mathbf{x}) = \mathbf{I}(\mathbf{x}) = \mathbf{x}$ 

- This can be tested as for robustness via individual transformation parameters or via TRE
- Consistency is not a measure for registration accuracy!

· Can individual registrations be composed ?





Scan-Rescan Consistency



• Forward-reverse registration consistency.



#### Visual assessment

- View image pair before and after registration
  - Subtraction mode (single-modal images)
  - Overlay mode
    - · Iso-contour, colour
    - · Chess-board, morphing
    - · Horizontal or vertical "shutters"
  - At interesting anatomical positions
- Image reslicing using intensity interpolation
  - Nearest-neighbour, trilinear, b-spline, sinc
  - Blurring artefacts vs computational complexity
- Only a qualitative validation tool!

#### Visual Assessment : Subtraction





de=3°





#### Visual Assessment



## Visual Assessment (cont'd)



## Visual Assessment (cont'd)



## Visual Assessment (cont'd)



#### Automatic dense PDE-based registration

- Look for elastic (non-linear) transformation
- General motion (vector) field is sought
- Criteria formulated in the continuous domain
- Regularization to impose smoothness

## Some facts about cervical cancer

- Cervical cancer is the second most common cancer among women worldwide
- ► Nearly 380,000 new cases are diagonosed yearly
- ▶ When detected early, cervical neoplasia is nearly 100% curable
- Papanicolau test (Pap Smear) and Colposcopy are the most widespread tests for cancer screening



# Diagnosis: Colposcopy

- Colposcopy visually inspects inspects the cervix area at low magnification
- The application of acetic-acid will temporally alter the appearence of cancerous tissue
- Colposcopists must subjectively asses appearence changes in small areas over prolonged periods of time





We represent correspondence function H as a dense vector field

$$H([x,y]) = [x',y']$$







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**Deformation Field** 



### Registration as optimization

► Correspondence function *H* and vector field **h** are related by:

$$H([i,j]) = [i,j] + \mathbf{h}(i,j) \tag{1}$$

The problem is then formulated as the minimization of a criterion J with respect to vector field h:

$$\mathbf{h}^* = \arg\min_{\mathbf{h}} (J(\mathbf{f} \circ \mathbf{h}, \mathbf{g}, \mathbf{h}))$$
(2)

where  $\mathbf{h}^*$  is the optimal solution,  $\mathbf{f}$  and  $\mathbf{g}$  are the images to be registered and J is a cost function measuring the dissimilarity between the images and the likelihood of the transformation.

Cost function J is divided into a data and a regularization term multiplied by a proportionality constant:

$$J(\mathbf{f}, \mathbf{g}, \mathbf{h}) = J_D(\mathbf{f} \circ \mathbf{h}, \mathbf{g}) + \alpha J_R(\mathbf{h})$$
(3)

## Similarity criteria

The data term J<sub>D</sub> is the sum of squared differences (SSD) between the template image g and the moving image f deformed by h:

$$J_D(\mathbf{f} \circ \mathbf{h}, \mathbf{g}) = \int_{(x,y) \subset \Omega} (\mathbf{f}(\mathbf{h}(x,y) + [x,y]) - \mathbf{g}(x,y))^2 \, \mathrm{d}x \, \mathrm{d}y$$
(4)

Discretized version:

$$J_D(\mathbf{f} \circ \mathbf{h}, \mathbf{g}) = \sum_{(i,j) \subset \Omega} (\mathbf{f}(\mathbf{h}(i,j) + [i,j]) - \mathbf{g}(i,j))^2 \qquad (5)$$

## Regularization

- Regularization term penalizes un-smooth deformations and makes the optimization of J a well-posed problem
- Regularization criterion J<sub>R</sub> is chosen so its gradient coincides with the linearized 2D elasticity operator describing equilibrium in an elastic material.

$$\nabla J_{R}(\mathbf{h}) = \xi \Delta \mathbf{h} + (1 - \xi) \nabla (\nabla \cdot \mathbf{h})$$
(6)

$$J_{R}(\mathbf{h}) = \frac{1}{2} \int_{(x,y)\subset\Omega} \left[ \xi \left(\partial_{x} h_{x}\right)^{2} + (1-\xi) \left( \left(\partial_{x} h_{x}\right)^{2} + \partial_{x} h_{x} \cdot \partial_{y} h_{y} \right) \right] \\ + \left[ \xi \left(\partial_{y} h_{y}\right)^{2} + (1-\xi) \left( \left(\partial_{y} h_{y}\right)^{2} + \partial_{x} h_{x} \cdot \partial_{y} h_{y} \right) \right] \right]$$

## Gradient descent optimization

On every iteration:

Calculate the new deformation field

$$\mathbf{h}' = \mathbf{h}_i - \lambda(\nabla J(\mathbf{f}, \mathbf{g}, \mathbf{h}_i))$$
(8)

If the step is succesful, then the step is accepted and the step size is increased

$$\lambda \leftarrow 2\lambda, \mathbf{h}_{i+1} \leftarrow \mathbf{h}', J_{i+1} \leftarrow J' \tag{9}$$

Otherwise the step size is reduced

$$\lambda \leftarrow \lambda / 10 \tag{10}$$

▶ We iterate until convergence (given by a suitable threshold).

# Other implementation details

- Multi-resolution was used
- ROI masks were automatically generated
- Images were rigidly pre-registred
- Green color channel only

#### Experiments

- Algorithm tested with 45 image pairs
- Images taken before and 60 seconds after acetic-acid application
- Cross-polarization filters used to reduce the glint
- Uncompressed 1125x750 pixel 16-bit images were used
#### Template







#### Unregistered Checkerboard



#### Unregistered Difference



# **Deformation Field** Registered

#### Unregistered Checkerboard



#### Registered Checkerboard



#### Unregistered Difference



#### **Registered Difference**



# Insufficient Regularization



Video cervix registration

# Surface-Based Registration

- · Surface-based registration:
  - Generally aligns a large number of points
  - 3D correspondence of anatomy or pathology is often not known or unavailable
  - The 3D boundary of an object is an intuitive and easily characterized geometrical feature that can be used for registration
  - Surface-based methods involve determining corresponding surfaces in different images and/or physical space and finding transformation that best aligns these surfaces

# Surfaces

- Skin surface (air-tissue interface)
- Bone surface (tissue-bone interface)
- Representations
  - Point set (collection of points on the surface)
  - Faceted surface, e.g., triangle set approximating surface
  - Implicit surface
  - Parametric surface, e.g., B-spline surface

# Surface Feature Extraction

#### Images

- Isointensity contour extraction (Marching Cubes)
- Deformable models
- · Physical space
  - Laser range finders
  - Stereo video systems (photogrammetry)
  - Localizers
    - · Articulated mechanical
    - Magnetic
    - · Active and passive optical
  - Tracked ultrasound for bone surface

# Marching Cubes: Example



# Marching Cubes: Example



Skin surface



Bone surface

## Surface-Based Registration

Given a set of N surface points {x<sub>i</sub>} and a surface Y, find the rigid-body transformation (rotation matrix **R** and translation vector **t**) that minimizes the mean squared distance between the points and the surface:

$$d(T) = \frac{1}{N} \sum_{j=1}^{N} |T(\mathbf{x}_j) - \mathbf{y}_j|^2$$
$$\mathbf{y}_j = C(T(\mathbf{x}_j), Y)$$

where  $y_j$  denotes the closest (rather than corresponding) point on Y.

## Surface-Based Registration Iterative Closest Point (ICP)

- [Besl & McKay, PAMI 1992]
- To register data shape X to model shape Y, decompose X into point set {x<sub>i</sub>}, then
  - Compute closest points  $\{y_i\}$  on Y
  - Register points  $\{x_i\}$  to points  $\{y_i\}$
  - Apply resulting transformation to points {x<sub>i</sub>}
  - Repeat until convergence

# Surface-Based Registration





# Point-to-Surface Distance

- The calculation of point-to-surface distance is computationally intensive
- Special data structures
  - Octree
  - k-d binary search tree
- Distance transforms
  - Assignment to each voxel v of the distance between v and the closest feature voxel
  - If feature voxels are surface voxels, then DT provides method for precomputing and storing point-to-surface distance

# Quadtrees/Octrees

	°
	 c o

## 3D/3D CT-to-Physical Registration









## Image-Physical Registration Accuracy

- Stereotactic frame systems (~ 1-2 mm)
- · Point-based registration
  - External anatomic landmarks (~ 2-4 mm)
  - Skin-affixed markers (~ 2-4 mm)
  - Bone-implanted markers (~ 1 mm)
- · Surface-based registration
  - Skin surface (~ 2-5 mm)
  - Bone surface (~ 1 mm)

# 2D-3D registration – Example: Image-guided cardiac interventions



# 2D-3D registration – Example: XMR System

- XMR = X-Ray + MR in same room
- Common sliding patient table
- Provides path to MRguided intervention



# 2D-3D registration – Example: Image-Guided Cardiac Interventions

- Registration by optical tracking
- · X-ray table & c-arm are tracked by Optotrak
- · Sliding patient table is tracked by MR system



# 2D-3D registration – Example: Image-Guided Cardiac Interventions



x-ray

MR rendering

x-ray + MR rendering

> Rhode et al. IEEE TMI 2003

# 2D-3D registration

- So far we have assumed that registration for IGS is based either on
  - points
  - surfaces

which are identified in the pre-operative image and intra-operative scene

- Registration for IGS can also involve registration of pre-operative image to intra-operative images
  - ultrasound
  - video
  - fluoroscopy

# Perspective Transformations

- Subset of projective transformations
- · Describe image formation for many modalities
  - Photography (pinhole camera) including video
  - X-ray projection
  - Microscopy
  - Endoscopy

### 2D-3D registration



by the registration

### 2D-3D registration

$$\mathbf{T}_{projective}(x, y, z) = \begin{pmatrix} x' \\ y' \\ 1 \end{pmatrix} = T_{intrinsic} \cdot T_{extrinsic} \cdot \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}$$

Simplest form of projection:

$$T_{inviscie} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{z} & 0 \end{pmatrix}$$

can be extended to take more physical properties of the imaging into account, e.g. focal length, primary point, distortion, etc

# **3D-3D Registration**



# 2D-3D Registration



# 2D-3D Registration Via Digitally Reconstructed Radiograph (DRR)



L. Lemieux et al. Med. Phys. Volume 21, Issue 11, pp. 1749-1760, 1994

# 2D-3D Registration of Bone Fluoroscopy to CT via DRR Construction


## 2D-3D registration using photo-consistency





Clarkson et al., IEEE PAMI 2001

### 2D-3D registration using photo-consistency



#### Clarkson et al., IEEE PAMI 2001

## 2D-3D registration using photo-consistency



#### Clarkson et al., IEEE PAMI 2001

#### Contour/Surface Projection



# Registration conclusions

- Many different approaches
- Many different applications
- Very frequent in medical imaging
- ... but also video processing, 3D reconstruction...
- Trade-off between robustness, speed and generality
- A priori knowledge always usefull, sometimes essential