Computational Registration of Biomedical Data towards More Effective Image Analysis

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Introduction: Matching and Registration of Images
Image Matching

Image matching is the process of establishing correspondences between objects in images

Original images and contours

Some of the correspondences found

Image Registration

Image registration is the **process of searching for the best transformation that change one image in relation to another image** in order to correlated features assume similar locations in a common space.

*Template (or fixed) image*

*Source (or moving) image*

*Overlapped images before and after the registration*

Image Registration

Applications

- Facilitate image-based diagnosis
  - Fusion of images from different imaging modalities (CT/PET, MRI/CT, SPECT/CT, MRI/PET, …)
  - Follow-up of pathologies
- Support surgical interventions (more efficient localization of lesions, find alignments between devices and patients, etc.)
- Optimization of radio-therapeutic treatments
- Automatic recognition of organs/tissues (e.g. support complex tasks of image segmentation and identification)
- Building of Atlas (with well-known cases used for comparison)
- Simplify posterior statistical analysis (e.g. SPM, Z-scores, etc.)
- …
Image Registration

In the last years, considerable research has been done concerning biomedical data registration. The **methodologies can be classified based on** different criteria:

- **Data dimensionality:** 2D/2D, 2D/3D, 3D/3D, 2D/3D+Time
- **Features used:** extrinsic (using features external to the patient) or intrinsic (using information from the patient; e.g. pixel intensity values, relevant points, contours, regions, skeletons, surfaces, …)
- **Interaction:** manual, semiautomatic or automatic
- ...
Image Registration

(Cont.)

- **Transformation type:** rigid, similarity, affine, projective, curved
- **Transformation domain:** local or global
- **Modalities involved:** same modality (CT/CT, MRI/MRI, PET/PET, …), different modalities (CT/MRI, MRI-T1/MRI-T2, PET/CT, …) or patient/model (e.g. between a patient and an atlas or between a patient and a device)
- **Subjects:** registration of images from the same subject or from different subjects, or images of a subject with images in an atlas
- **Organs/tissues involved:** brain, liver, etc.
- ...

Image Registration

In the registration of image data, similarity measures based on pixel intensity values are commonly used; e.g.:

- Cross-Correlation (CC) and related measures

\[ CC_{fg} = \sum_i f(i)g(i) \]

- Sum of Squared Differences (SSD) and correlated measures, like the Mean Squared Error (MSE)

\[ SSD_{fg} = \sum_i (f(i) - g(i))^2 \quad \text{MSE}_{fg} = \frac{1}{N} \sum_i (f(i) - g(i))^2 \]

- Mutual Information (MI) and derived measures

\[ MI = H(f) + H(g) - H(f, g) \]

where \( H(f) \) and \( H(g) \) are the Shannon’s entropy of \( f \) and \( g \) images, and \( H(f, g) \) the Shannon’s entropy of the joint histogram of \( f \) and \( g \)
Image Registration

In the last years, we have been developing methods for biomedical image data matching and registration based on different techniques and applied them in several applications

– **Techniques**
  - Based on features (points, contours) extracted from the images and based on the intensity of the pixels (or voxels)
  - By computing the optimal registration transformation directly or iteratively
  - By using different transformation models

– **Data**
  - Images from the same patient and from different patients
  - Images from the same or different modalities
  - Registration of 2D and 3D images, and of 2D image sequences
Methods: Spatial Registration of 2D and 3D images
Registration **based on Contours Matching**

1. Extract the contours
2. Assemble the matching cost matrix
3. Search for the optimal matching
4. Compute the geometric transformation
5. Register the moving image

**Fixed image**

**Moving image**

**Registered moving image**

The cost matrix is built based on geometric or physical principles.

The matching is found based on the minimization of the sum of the costs associated to the possible correspondences.

To search for the best matching is used an optimization assignment algorithm based on the Hungarian method, simplex method, graphs or dynamic programming.


Registration based on Direct Maximization of the Cross-Correlation (CC)

Assumption: The higher the cross-correlation between the pixel intensity values of the two images, the better the registration.

Cross-correlation between $I_0$ and $I_1$ in function of a shift $a$:

$$CC_{I_0I_1}(a) = \int I_0(x)I_1(x - a)dx$$

It can be written as a convolution:

$$CC_{I_0I_1}(a) = \int I_0(x)\bar{I}_1(a - x)dx = \{I_0 \ast \bar{I}_1\}(a)$$

And from the convolution Theorem, one have:

$$\mathcal{F}\{I_0 \ast \bar{I}_1\} = \mathcal{F}\{I_0\}\mathcal{F}\{\bar{I}_1\}$$

Thus, computing the product of the Fourier transform of $I_0$ and $\bar{I}_1$ and then its inverse Fourier transform, the cross-correlation can be obtained for all shifts.

(* represents the convolution operation and $\mathcal{F}$ the Fourier transform)
The scaling and rotation are obtained from the spectrum images after their conversion to the log-polar coordinate system.

The fundament of this methodology is to search for the geometric transformation involved using the shift, scaling and rotation properties of the Fourier transform.

Registration based on Direct Minimization of the Sum of Squared Differences (SSD)

Assumption: The lower the sum of the squared differences between the pixel intensity values of the two images, the better registered the images

Sum of squared differences between $I_0$ and $I_1$ in function of a shift $a$:

$$SSD_{I_0I_1}(a) = \int (I_0(x) - I_1(x - a))^2 \, dx$$

This equation can be written as:

$$SSD_{I_0I_1}(a) = \int I_0^2(x) \, dx + \int I_1^2(x - a) \, dx - 2\int I_0(x)I_1(x - a) \, dx$$

The first two terms can be directly evaluated, and the third term can be transformed into a convolution and then efficiently evaluated using the Fourier transform.

The algorithm implemented is quite similar to the Cross-Correlation based algorithm; the main difference is the similarity measure used.

Registration **based on the Phase Correlation Technique**

This technique is basically based on the shift property of the Fourier transform:

If \( I_1(x) = I_0(x - x_0) \)

then \( \mathcal{F}\{I_1(x)\}(u) = e^{-2i\pi u x_0} \mathcal{F}\{I_0(x)\}(u) \)

To estimate the shift between the input images, the inverse of the Fourier transform of the cross-power is computed:

Cross-power:

\[
\frac{\mathcal{F}\{I_0\} \mathcal{F}^*\{I_1\}}{|\mathcal{F}\{I_0\} \mathcal{F}^*\{I_1\}|} = e^{2i\pi u x_0} \]  

(the * represents the complex conjugate)

The algorithm implemented is also similar to the cross-correlation based algorithm

Registration **based on Iterative Optimization**

**Fundaments:** This methodology is based on the iterative search for the parameters of the transformation that optimizes a similarity measure between the input images.

The optimization algorithm stops when a similarity criterion is achieved.

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Registration based on Iterative Optimization

To speedup the computational process, the multi-resolution strategy is frequently used.
Registration using Iterative Optimization and a curved transformation based on B-splines

- Fixed image
- Moving image
- Pre-registration using a rigid transformation
- New pre-registration using an affine transformation
- Coarse registration based on B-splines
- Fine registration based on B-splines
- Registered moving image
Registration using Iterative Optimization and a curved transformation based on B-splines

The registration based on B-splines is of the \textit{free-form deformation type}: The deformation is locally defined based on the localization associated to the grid knots; if the localization of a knot changes, then all pixels under its influence are moved accordingly to the B-spline type.
Methods: Spatio & Temporal Registration
Spatio & Temporal registration of image sequences

**Fixed sequence**
- Compute the similarity measure
- Optimizer

**Moving sequence**
- Apply the spatio & temporal transformation
- Build the spatio & temporal transformation

**Registration optimization**
- Build the temporal representative images
- Search for the transformation that register the temporal representative images
- Estimate the linear temporal registration

**Pre-registration**
- Build the temporal representative images

Applications and Results: Plantar Pressure Images
Applications in Plantar Pressure Images Studies

A computational solution, device independent, has been developed to assist studies based on the registration of plantar pressure images:

- Foot segmentation
- Foot classification: left/right, high arched, flat, normal, …
- Foot axis computation
- Footprint indices computation
- Posterior statistical analysis

Registration **based on Contours Matching**

**Example 1**

I - Contours extraction and matching

*Fixed image and contour (optical plantar pressure device)*

*Moving image and contour (optical plantar pressure device)*

*Matching established*
Registration based on Contours Matching

Example 1 (cont.)

Registration: 2D, monomodal, intrasubject

Processing time: 0.125 s (AMD Turion64, 2.0 GHz, 1.0 GB of RAM)

Images dimensions: 160x288 pixels
Registration based on Direct Maximization of the CC

Examples 2 & 3

Image acquisition device: Footscan
Registration: 2D, monomodal, intrasubject (on the top) and intersubject (on the bottom)
Processing time: 0.04 s (AMD Turion64, 2.0 GHz, 1.0 GB of RAM)
Images dimensions: 45x63 pixels

Using a rigid transformation
Using a similarity transformation
Spatio & Temporal registration of Plantar Pressure Image Sequences

Example 1

| Device: EMED (25 fps, resolution: 2 pixels/cm², images dimensions: 32x55x13; 32x55x18) |
| Registration: rigid (spatial), polynomial (temporal); similarity measure: MSE |
| Processing time: 4 s - AMD Turion64, 2.0 GHz, 1.0 GB of RAM |

<table>
<thead>
<tr>
<th>Fixed sequence</th>
<th>Moving sequence</th>
<th>Overlapped sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before the registration</td>
<td>After the registration</td>
<td></td>
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</table>
Spatio & Temporal registration of Plantar Pressure Image Sequences

Example 2

- Fixed sequence
- Moving sequence
- Registered moving sequence using a polynomial temporal transf. of 1st degree
- Registered moving sequence using a polynomial temporal transf. of 4th degree
Applications and Results: Medical Images
Registration based on Contours Matching

Example 1

Registration: 2D, monomodal, intrasubject

Processing time: 0.5 s (AMD Turion64, 2.0 GHz, 1.0 GB of RAM)

Images dimensions: 217x140 pixels

Registration based on the matching of the Corpus Callosum contours
Registration based on Direct Maximization of the CC

Example 2

Registration: 2D, monomodal, intrasubject
Processing time: 2.1 s (AMD Turion64, 2.0 GHz, 1.0 GB of RAM)
Images dimensions: 221x257 pixels
Registration based on Iterative Optimization

Example 3

Fixed image (MRI - T1)

Moving image (MRI - proton density)

Overlapped images before the registration

Overlapped images after the registration

Sum of the images after the registration

Difference of the images after the registration

Registration: 2D, multimodal, intrasubject (without pre-registration)

Similarity measure: MI

Processing time: 5.4 s (AMD Turion64, 2.0 GHz, 1.0 GB of RAM)

Images dimensions: 221x257 pixels
Registration based on Iterative Optimization

Example 4

Registration: 2D, multimodal, intrasubject (without pre-registration)

Similarity measure: MI

Processing time: 4.6 s (AMD Turion64, 2.0 GHz, 1.0 GB of RAM)

Images dimensions: 246x234 pixels
Registration based on Iterative Optimization

Example 5

Registration: 2D, monomodal, intrasubject (without pre-registration)

Similarity measure: MSE computed only in the ROI defined

Processing time: 1.6 s - AMD Turion64, 2.0 GHz, 1.0 GB of RAM

Images dimensions: 230x216 pixels
Registration based on Iterative Optimization

Example 6 – 3D

“Checkerboard” of the images before the registration (CT/MRI-PD, brain)

The “checkerboard” image is built by interchanging square patches of both images and preserving their original spatial position in the fixed (F) and moving (M) images.
Registration based on Iterative Optimization

Example 6 – 3D

*Checkerboard of the images after the registration (CT/MRI-PD, brain)*

Registration: 3D, multimodal, intrasubject; Similarity measure: MI
Registration using Iterative Optimization and a curved transformation based on B-splines

Example 7 – 3D

Checkerboard of the images (CT, thorax, Δt: 8.5 months) before the registration
Registration using Iterative Optimization and a curved transformation based on B-splines

Example 7 – 3D

Checkerboard of the images (CT, thorax, Δt: 8.5 months) after a rigid registration
Registration using Iterative Optimization and a curved transformation based on B-splines

Example 7 – 3D

Checkerboard of the images (CT, thorax, Δt: 8.5 months) after a cubic B-spline registration
Registration using Iterative Optimization and a curved transformation based on B-splines

Example 8 – 3D

*Checkerboard of the images (CT, brain) before the registration*
Registration **using Iterative Optimization and a curved transformation based on B-splines**

**Example 8 – 3D**

*Checkerboard of the images (CT, brain) after an affine registration*

Registration: 3D, monomodal, intersubject; Similarity measure: MI
Registration using Iterative Optimization and a curved transformation based on B-splines

Example 8 – 3D

*Checkerboard of the images (CT, brain) after a cubic B-spline registration*

Registration: 3D, monomodal, intersubject; Similarity measure: MI
DaTSCAN SPECT images are used to assist the diagnosis of the Parkinson’s disease and to distinguish it from other degenerative diseases. The solution developed is able to:

- Segment the relevant areas and perform dimensional analysis
- Quantify the binding potential of the basal ganglia
- Automatic computation of statistical data regarding a reference population
- Provide statistical analysis and comparisons relatively to the reference values of a population

**Applications in DaTSCAN SPECT image studies**

**Normal**

**Alzheimer**

**Idiopathic Parkinsonism**

**Essential tremor**
Applications in DaTSCAN SPECT image studies

Example

The 3D volume images are automatically registered

Mean slice from the population used as reference

Corresponding slice of a patient

Difference of intensities

Z-scores mapping over the slice

(The blue rectangles represent the 3D ROIs used to compute the binding potentials, which are based on the counts inside the ROIs. On the z-score mapping image, the red color means high z-score values)
Applications in DaTSCAN SPECT image studies

Example

3D basal ganglia shape reconstruction and quantification

Basal ganglia from a mean image of a normal population

Basal ganglia from a patient with idiopathic Parkinson’s disease

Basal ganglia from a patient with vascular Parkinson’s disease
Applications in SPECT/CT registration and fusion

Example

Three slices (coronal, sagittal and axial) after registration and identification of the lesion

3D visualization after fusion CT/SPECT (the lesion identified in the SPECT images is indicated)
Conclusions
Conclusions

- Hard efforts have been done by the Computational Vision community to develop methods more robust and efficient to register image data.
- The Biomedical area has been one of the major promoters for such efforts; particularly, due to the requirements in terms of low computational times, robustness and of complexity of the structures involved.
- We have been developing several methods that have been applied successfully.
- However, several difficulties still to be overcome and better addressed; such as, severe non-rigidity, complex spatio & temporal behaviors, high differences between the data to be registered (e.g. from very dissimilar image sources), etc.
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