Medical Image Analysis

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First Medical Image

Roentgen, 1895

Development of Computed Tomography
Characteristics of medical images (1)

Intensity values are related to physical tissue characteristics which in turn may relate to a physiological phenomenon.

Main Imaging Modalities

- MRI
  - Density and structure of Protons
- CT-Scanner
  - Density of X-Ray absorption
- Ultrasound
  - Variations of Acoustic Impedance
- Scintigraphy
  - Density of injected isotopes

Common Structure of 3-D Images

- Voxel Representation
  \[ M(i,j,k) = I(x,y,z) \]
- \( I(x,y,z) \) measures physical properties of a volume element centered around \((x,y,z)\).
Magnetic Resonance Imagery (MRI)

I(x,y,z) measures a function of the density and structure of protons
Millimeter Resolution
16 millions of points

CT-scan (Scanner)

Size: 512 x 512 x 128
Resolution: 0.5 x 0.5 x 1 mm

Other 3-D Modalities

- Functional MRI (fMRI), DT MRI
- Interventional MRI (iMRI)
- MR Angiographies (MRA)
- Spectroscopic MRI
- US Angiographies, Perfusion US,
- Magneto-EncephaloGraphies (MEG)
- Electro-EncephaloGraphies (EEG)
Visual Examination
• Difficult task, mainly qualitative

Digital Image Analysis
• To improve diagnosis
  • quantitative and objective measurements
  • Fusion and comparison of images, patients

• To improve therapy
  • planning before
  • control during
  • evaluation after

Intensive Use of Medical Imaging

 DIAGNOSIS

 Patient

 Pre-operative

 Post-operative

 CT
 MRI
 US
 NM

 SIMULATION

 Virtual Patient

 THERAPY

 Patient

 Pre-operative

 Post-operative

 US
 X-Ray
 Video
 iMRI

 robot
## Digital Image Analysis: Classes of Generic Problems

1. Enhancement  
2. Visualization  
3. Segmentation  
4. Compression  
5. Registration  
6. Statistics  
7. Morphometry  
8. Motion  
9. Simulation  
10. Robotics, ...

### Segmentation

#### 1. Introduction

Isolate a Region of Interest in a Medical Image
### Segmentation Task
- Large number of available algorithms
- Possible classifications:
  - Generic vs task-oriented
  - Bottom-up vs Top-down approaches
  - Boundary vs Region approaches
  - Explicit vs Implicit A priori knowledge
- Validation

### No Universal Segmentation Algorithm
- A segmentation algorithm has a limited range of application
- Example: deformable models

#### Diagram:
- High Contrast vs Low Contrast
- Non typical Shape vs Typical Shape

### Bottom-up Approach
- Medical Image
- Feature Extraction
- Feature Grouping
- Region/Boundary Extraction
### Region vs Boundary Methods

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<th>Image</th>
<th>Region-based segmentation</th>
<th>Boundary-based segmentation</th>
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### Computational vs Explicit

**A priori knowledge**
- A priori knowledge about the structure to segment is the key to enhance robustness
- Computational knowledge: statistical analysis

**Explicit knowledge**
- Explicit knowledge: expert system
  - Define rules of delineation from expert
  - Translate predicate into high/low level image processing
  - Combine rules in a probabilistic framework

**Training**

- Statistical classifier
  - Neural Networks
  - Principal Component Analysis
  - ….
Validation of Segmentation Algorithm

- **Intrinsic Validation**: comparison against
  - Observation of Physical Phantoms
    - Difficult and expensive to build
    - May not be representative of real data
  - Simulated images (MNI Brain Atlas, …)
    - Difficult to simulate artefacts
  - Segmentation of experts
    - Large inter and intra variability of segmentation across experts
    - May not be representation of population variability

How to judge segmentations of the peripheral zone?

0.5T MR of prostate

Peripheral zone and segmentations

Validation of Segmentation Algorithm (2)

- **Extrinsic Validation**: comparison against other segmentation algorithms
  - Only possibility when no ground truth exists (Inter-patient registration of images) or when it not available
  - Estimate consistency, repeatability and size of convergence basin
Two Segmentation Methods

Focus on 2 segmentation methods:

- **Bottom-up**: Thresholding/Classification
- **Top-down**: 3D and 4D deformable models

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<th>Thresholding Classification</th>
<th>Deformable Models</th>
<th>Markov/MRF/RF</th>
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<td>Intensity Information</td>
<td>New</td>
<td>Improved</td>
<td>Old</td>
</tr>
<tr>
<td>Boundary/Region</td>
<td>Region</td>
<td>Boundary</td>
<td>Region</td>
</tr>
</tbody>
</table>

Segmentation

2. **Thresholding and Classification**

- **Basic idea**: A structure is uniquely characterized by its intensity values in the image.
- **Basic thresholding algorithm**:
  - Thresholding between two grey-levels (windowing)
  - Mathematical morphology operations [Serra82]
  - Erosion and Dilation
  - Closure and Opening
  - Connected components extraction

Valid for highly contrasted structures.
Thresholding Example (1)

Interactive thresholding

Abdominal CT scan Image

Thresholded Image

Thresholding Example (2)

After mathematical morphology operations

Isosurface

Isosurfacing (Marching Cube) + decimation algorithm

Thresholding + mathematical morphology + connected components
Limitation of thresholding

Thresholding:
- Choice of threshold can be computed from grey-level histogram
- Does not assume any spatial correlation of voxel intensity
- Does not take into account the effect of **partial volume effect** (PVE)

Use of classification methods

Classification Method

- It is often not valid to consider that a voxel belongs to a single tissue type.
- It is therefore reasonable to estimate that each voxel has a probability $p_k(x)$ of belonging to a tissue class $k$ ($1\leq k \leq K$)

$$\sum_{k=1}^{K} p_k(x) = 1$$

CT scan image of the Liver with 3 tissue classes

Classification Method (2)

- Various classification methods:
  - Fuzzy c-means
    - General classification approach
    - Non parametric
  - EM Algorithm
    - Parametric approach (mixture of Gaussians)
    - Can take into account bias field
  - Curve fitting
    - Use a hierarchical approach
    - Non-linear optimization
Brain Tissue Classification
• Typical application: use MR cerebral image

Optimisation (3)
• Use the EM algorithm [Dempster77, Wells94]:
  Expectation-Maximisation

Stage 1: classification
\[ p_i(s) = \frac{\phi_i(I(s))}{\sum \phi_j(I(s))} \]
Stage 2: Distribution Estimation

\[ \mu_k = \frac{\sum p_k(x) f(x)}{\sum p_k(x)} \]

\[ \sigma_k^2 = \frac{\sum p_k(x)(f(x) - \mu_k)^2}{\sum p_k(x)} \]

Initialisation issue

Use a computed digital atlas with \( p_k(x) \)

Affine registration between the image and atlas to initialize \( p_k(x) \)

Fuzzy C-means (Exemple)
Deformable model

- Snake / active contours
- Minimisation of a two/three terms energy:

\[ E(v(s)) = \int E_{\text{in}}(v(s)) + E_{\text{in}}(v(s)) + E_{\text{con}}(v(s)) ds \]

- \( E_{\text{in}} \): internal energy (regularisation)
- \( E_{\text{in}}(v(s)) \): \( \norm{\nabla I - \mathbf{v}(s)}^2 \)
- \( E_{\text{con}} \): external energy (regularisation)
- \( E_{\text{con}}(v(s)) \): \( \norm{\mathbf{v}_c(s)}^2 \)
Deformable Model Segmentation

- A deformable model is a container of prior knowledge about the **Shape** and **Appearance** of anatomical structures in medical images.
- Two levels of prior knowledge:

<table>
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<tr>
<th>Weak Prior</th>
<th>Strong Prior</th>
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<tbody>
<tr>
<td><strong>Shape</strong></td>
<td><strong>Appearance</strong></td>
</tr>
<tr>
<td>C1 or C2 continuity constraint \ Initiation with generic shape (sphere, ...).</td>
<td>Shape continuity constraint \ Initiation with mean shape</td>
</tr>
<tr>
<td><strong>Appearance</strong></td>
<td>Use gradient, edge or region information</td>
</tr>
</tbody>
</table>

Weak prior deformable model

- Valid for highly contrasted structures
- May require user interaction

Segmentation: endocranium

CT scan image, Bony structures

Time of convergence: 13.8 s

- model: 1169 cm³
- mold: 1150 cm³
Strong prior deformable model

- Valid a given structure and a given image modality
- More robust except with abnormal shapes

Segmentation: MRI

Deformed 4D model

Model intersection with image

Deformable Model Geometry (3)

[Montagnat2001]
Deformable models

- Level-sets
  - Curve/Surface $C$ (in $\mathbb{R}^2$/$\mathbb{R}^3$) that corresponds to an iso-level of a surface/hypersurface (in $\mathbb{R}^2$/$\mathbb{R}^4$)
  $$C(t) = \{(x,y) | u(x,y,t) = 0\} \quad u_t + F \nabla u = 0$$
  - Implicit representation

Main difficulties in segmentation algorithms

- Ill-posed problem
  - Boundaries between structures may not be seen on images
  - Strong variability between experts for validation
- Most algorithms are dependent on the acquisition protocol and image modality
- Robustness required in the presence of pathologies

Use of Image Segmentation Software

- Segmentation software is not widely available in current medical practice:
  - Diagnosis (low demand):
    - Currently almost no quantitative analysis in performed even in oncology
  - Therapy planning (high demand)
    - Bottleneck stage in radiotherapy or surgery planning
Perspectives (1)

- Current trends in medical imaging
  - Number of image modalities is exploding
  - Image resolution is increasing
  - Image quality is improving
  - IT is invading hospitals (PACS)
  - More patients less doctors

Perspectives (2)

- Applications of segmentation:
  - Diagnosis
    - demand for very fast and automated algorithms with degree of confidence
  - Planning - Prediction - Prevention
    - demand for accurate but potentially not fully automated algorithms combined with high quality meshing
  - Clinical Research
    - demand for automated and accurate algorithm for use with large database (grid computing)

Perspectives (3)

- Segmentation techniques is more and more split between:
  - Registration techniques:
    - registration with a anatomical/physical/physiological model
    - registration with a set of images (data fusion)
  - Low-level techniques:
    - anisotropic filtering, watershed, mathematical morphology

Need to define a unifying framework
Registration

1. Introduction

- A central problem

- Survey by Maintz and Viergever in Medical Image Analysis journal (MedIA) (300 references)

[vol 2, No 1, pages 1-36, 1998]

Objective of Registration

- Find the best geometric transformation \( T \) which superimposes homologous points between two 3-D images

\[ x' = T(x) \]
Main Applications

- Temporal Evolution
- Fusion of multimodal images
- Inter-patients comparaison
- Atlas Superposition

Temporal Evolution

- Precise comparison of images of a given patient, taken at different times.
- One must suppress the apparent motion of the patient.

Fusion of Multimodal Images

- IRM
- TEP
- TDM
- US
- Visible Man
- anatomical
Atlas Superposition

Classes of Problems

- Mono- or multimodal images
- Intra- or Inter-patients
- Rigid or Deformable

Classes of Problems vs. Applications

- Temporal Evolution
- Fusion multimodal images
- Inter-patients comparison
- Atlas Superposition
  - Intra Patient: Rigid or Non-Rigid
  - Inter Patients: Non-Rigid
Classes of Solutions

- Geometric Registration (or feature-based)

- Iconic Registration (or intensity-based)

Registration

2. Geometric Approaches

Principle of Geometric (Feature-Based) Approaches

- Extract geometric landmarks

- Find correspondences and best transformation $T$
Temporal Evolution (To Start!)

- Rigid, Mono-patient, Monomodal

Choosing a Class of Transformations

- In the case of brain images of the same patient, one can restrict the geometric transformation to the group of rigid transformations (3-D displacements)

- Combination of Rotation and Translation (6 parameters)

Issues

- Not a one to one mapping between images (occlusions)

- For an accurate solution, one must find explicitly correspondences (matches) between images

- High computational complexity
Artificial Landmarks

- Stereotactic Frame
  - Invasive
  - External markers
  - Brain motion
  - Limited period

Anatomical Landmarks

- Search for geometric invariants to characterize a limited number of singular points and lines on anatomical surfaces

- Generalization of edges and vertices on differentiable surfaces (Monga-Ayache-Sander, Thirion)

Crest Lines and Extremal Points

- Defined from differential properties of the anatomical surfaces;

- Correspond to extremal values of one or two principal curvatures
Stage 1: Anatomical Surfaces

- Iso-surfaces defined by an implicit equation
- Zero-crossings of the Laplacian of the intensity

\[ f(x, y, z) = I \]
\[ \nabla^2 f(x, y, z) = 0 \]

Stage 2: Crest Lines

- Maximum principal curvature (in absolute value) must be extremal in the associated principal direction (not defined at umbilics)

\[ c_1 = \nabla k_1, t_1 = 0 \]

Stage 3: Extremal Points

- Second principal curvature is also extremal in the second principal direction.

\[ c_1 = \nabla k_1, t_1 = 0 \]
\[ c_2 = \nabla k_2, t_2 = 0 \]
Skull Crest Lines on Cortex (IRM)

Compact description Invariant by displacement

Rigid Registration

• Geometric Hashing algorithms establish correspondences between homologous points and the best rigid transformation between the 2 images (Rigoutsos-Wolfson, Guéziec-Pennec-Ayache-IEEE Trans. Computers)

• These algorithms use additional invariants computed along crest lines and on the underlying anatomical surface
Geometric Invariants on Crest Lines

- Curvature, Torsion, and angles between Frénet frame and local surface frame

Registration by Geometric Hashing

- The sought transformation is the most represented one
- Robust to occlusions and small local deformations
- Fully automatic, low computational complexity, high accuracy
Application of Rigid Registration to Multiple Sclerosis Evolution

24 3-D images before registration

- Same patient followed during one year

Brigham & Women's Hospital, Harvard Medical School

After Rigid Registration (24 times)

24 3-D images after rigid registration

Thanks to rigid registration, one can follow the temporal evolution in any arbitrary 2-D plane

J.P. Thirion, DCV’98

Geometric Registration of Surfaces

Collaboration Epidaure-Robotvis, Feldmar-Devernay
Augmented Reality (Fiction)

Feldmar-Deverney

Augmented Reality (Real)

• Active Stereovision

Brigham & Women’s Hospital– MIT E. Grimson et al.

Non Rigid Geometric Registration

• Some crest lines are anatomical invariants

Court Cutting et al.
Skull (Scanner)

Average Morphology of Skull

Skull Growth through Aging

30
Geometric Registration

- Can be applied to surface registration in augmented reality problems
- Fuse per-operative images with pre-operative images

Limitations of Geometric Registration

- Previous geometric invariants not valid in general to compare multimodal images, or arbitrary homologous structures between different patients (e.g. brain)
- Problems with low-resolution or noisy images.
- Distribution of geometric invariants might be too sparse to handle local deformations

Registration

3. Iconic Approaches
Principle of **Iconic** (Intensity-Based) Registration

- Use all voxels and their *intensity* to guide the registration process
- Energy minimization between registered images

Energy Minimization

- Energy with **two** components:
  \[
  W(T) = \int \int \int f(J, T) \, dx \, dy \, dz + W_d(T)
  \]
  
  - \( f \): Measure of intensity *similarity* between homologous points;
  - \( W_d \): Measure of *deformation* to insure a regular solution (Tikhonov, linear elasticity, viscous fluid, etc.).
  
Minimization Algorithms

- Non Convex Energy
- Convergence towards a Local Minimum
- Important Stages:
  - Good initialization (rigid registration)
  - Multi-scale analysis
  - Hierarchy of deformations
    - similitude, affine, polynomial, free-form, etc.
Classification of similarity measures

- Assumed relationship
  - Identity
  - Affine
  - Functional

- Adapted measures
  - Sum of Squared Differences \( SSD(I,J) = \sum (I_i - J_i)^2 \)
  - Sum of Absolute Differences
  - Measures based on image difference (Buzug et al, 1997)
  - Correlation Coefficient \( \rho(I,J) = \frac{cov(I,J)}{\sqrt{var(I)var(J)}} \)
  - Woods criterion (Woods et al, 1993)
  - Robust Woods criterion (Nikou et al, 1997)
  - Correlation Ratio (Roche et al, 1998)
  - \( \eta(I,J) = 1 - \frac{var(I-J)}{var(I)} \)
Classification of similarity measures

- Assumed relationship
- Statistical

- Adapted measures
  - Joint Entropy (Hill et al., 94)
  - Mutual Information (Viola & Wells, 1997; Maes et al, 1997)
  - Normalised Mutual Information (Studholme, 1998)

\[ MI(J,I) = H(I) - H(I,J) = \sum_{i,j} p(i,j) \log \frac{p(i,j)}{p(i)p(j)} \]

Measure of Intensity Similarity

- sum of squared differences
- correlation coefficient
- correlation ratio
- mutual information

A common framework?

A General Framework

- [Roche-Malandain-Ayache-Prima, MICCAI '99, pp.555-566]
- A Dependence Model between images and a Maximum Likelihood approach
- Following the pioneering work of (Costa et al, 1993), (Viola, 1995), (Leventon & Grimson, 1998), (Bansal et al, 1998)
Choosing the right similarity measure

- Requires a good knowledge of the physics of image formation
- Choosing the model with the lowest number of parameters tends to lead to higher robustness

Experimental Comparison

- Accuracy study
  - CT / MR rigid registration
  - PET / MR rigid registration
- Robustness study
  - Ultrasound / MR rigid registration

Correlation Ratio vs. Mutual information
  - (-) simplistic model (+) more realistic model
  - (-) few parameters (+) many parameters

Some Applications of Iconic Registration

- 1. Detection and Measure of Lesions
- 2. Inter-patient comparisons
- 3. Superposition of an Atlas
- 4. Measure of Asymmetry
- 5. Superposition MRI-Ultrasounds
- 6. Stress-Rest Comparisons
1. Detection and Measure of Multiple Sclerosis Lesions

Deformation Field

Analysis of deformations

- Automatic extraction of regions with an apparent variation of volume (Jacobian operator)
- Segmentation of evolving lesions
- Robust to small errors of rigid registration
Evolution of Lesions (3 times)

Frontal

Sagittal

Digital Microscope

Time 1
Time 2
Time 3

European project Biomorph

Rey-Le Brun-Chanalet -Ayache-Chatel 2000

Axial

Rey-Subsol-Delingette-Ayache IPMI’99

2. Application to inter-patient comparison

Patient 1

Patient 2

Morphometry: average subjects/patients, variations around average
Would Require BOTH Geometric and Iconic Methods

J.P. Thirion, X. Pennec, G. Subsol, A. Guimond,

3. Application to the Superposition of a Brain Atlas

Havard Medical School

Collaboration Pitié-Salpêtrière, Parkinson, S. Ourselin
Centre Antoine Lacassagne.
Radiotherapy (Bondlaar-Malandain)
4. Quantitative Measure of Brain Asymmetry

European Project Biomorph
Prima-Subsid-Thirion-Roberts Miccai '98
Blue: larger than on opposite side
Red: smaller than on opposite side

Roboscope
Image-Guided Manipulator-Assisted Neuro-Endoscopy

Manipulator
Steady Hand Motion Compensation
Active Motion Constraints

Courtesy Brian Davies

QuickTime™ and a Intel Indeo® Video 5.0 decompressor are needed to see this picture.
Multimodal Image Fusion

- Rigid matching tools for MR
- MR / US registration
- US tracking of brain deformations

Typical MR-US Images

Pre-Operative MR Image

Per-Operative US Image

5. MRI-Ultrasound Registration

Roche-Pennec-Ayache-Malandain MICCAI’99
6. Application to 3-D Stress-Rest comparison (Gated Spect)

- Perfusion of cardiac muscle
- Lateral ischemia
- CardioMatch (Focus Imaging)
- Declercq-Feldmar

<table>
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<tr>
<th>Rest</th>
<th>Stress</th>
<th>Rest</th>
<th>Stress</th>
<th>Model</th>
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Conclusion

- Medical Imaging is nearing maturity
- New image modalities across scale and function
- Validation of algorithms sometimes impossible always difficult
- Growing availability of large image databases

On line references and reports http://www-sop.inria.fr/epidaure/
In Vivo Microscopic Confocal Imaging
Source: Mauna Kea Technologies

Reflectance imaging
Fluorescence imaging

Depth of Observation up to 100 microns
Lateral Resolution: 2 – 4 μm
Axial Resolution: 8 – 20 μm

Epithelium

The endoscopy “pill”
Source: Given Imaging

Images obtained when passing through the bowel (Given Imaging System)
Credits

- Medical and Academic Partners
- Gilles Kahn

Conclusion

- Digital Image Processing increases potential use of medical images in medicine, as microscope in 17th century.
- Several connected application domains:
  Pharmacy, biology, neuroscience, paleontology, anthropology, geology, non destructive control, etc.