Medical Image Analysis: An Introduction

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What is medical image analysis?

Medical image analysis is the science of solving/analyzing medical problems based on different imaging modalities and digital image analysis techniques.
Different Image Modalities

- Geometric
- X-ray: 2D and 3D
- MR-Images: 2D, 3D, 4D, etc
- Tomographic methods
- Microscopic images
  - Standard (requires staining)
  - HMC (Huffman modulated contrast)
- SPECT (Radioactive isotopes)
- Ultrasound
- Different artificially created images (bulls-eye for hearts)
Medical problems

• Diagnosis
• Follow up on treatments
• Comparing different treatments/patients/drugs
• On-line imaging for active intervention
• Predicting development
• etc
Image analysis problems

- Segmentation – delineating different organs
- Classification – determining e.g. types of leukocytes
- Registration – comparing different modalities/patients
- Reconstruction – making 3D-measurements
- Measuring flow – e.g. inside aorta
- Reconstructing flow fields – e.g. inside the heart
- Building shape priors efficiently
- Visualizing results
- etc
Segmentation - Thresholding

• Thresholding

Gray-scale image

Thresholded image
Segmentation – Active contours

- Define a moving contour
- Driven by external and internal forces
Active contours – Snakes

- Find \( v(s) = [x(s), y(s)] \) that minimizes

\[
E[v(s)] = \int_S \frac{1}{2} \left( \alpha |v'(s)|^2 + \beta |v''(s)|^2 \right) + E_{\text{ext}}(v(s)) \, ds
\]

- Examples of external energies

\[
E_{\text{ext}} = - |\nabla I(x, y)|^2
\]

\[
E_{\text{ext}} = - |\nabla G_\sigma(x, y) \ast I(x, y)|^2
\]
Solution

• The Euler-Lagrange equations gives:

\[ \alpha v''(s) - \beta v^{(4)}(s) - \nabla E_{\text{ext}}(v(s)) = 0 \]

• Dynamic snake – Active contour

\[ v_t(s, t) = \alpha v''(s, t) - \beta v^{(4)}(s, t) - \nabla E_{\text{ext}}(v(s, t)) \]
Numeric solution

- Discretising
  \[ \delta x^n_k - x^{n-1}_k = \frac{\alpha}{h^2} x^n_{k+1} - 2x^n_k + x^n_{k-1} - \frac{\beta}{h^4} x^n_{k+2} - 4x^n_{k+1} + 6x^n_k - 4x^n_{k-1} + x^n_{k-2} - f_x x^n_k, y^n_k \]

- Linear system of equations
  \[ A + \delta I \ x^n = x^{n-1} - f_x \ x^{n-1}, y^{n-1} \]

- Re-sampling
An Example

Initialization

200 iterations

700 iterations

Gradient field
GVF Field

• Definition: $g(x,y) = [u(x,y), v(x,y)]$, that minimizes

$$
\varepsilon = \iint \mu \left( u_x^2 + u_y^2 + v_x^2 + v_y^2 + |\nabla f|^2 \right) |g - \nabla f|^2 \, dx \, dy
$$

• Calculus of variations and the introduction of a time variable gives

$$
u_t \ x, y, t = \mu \nabla^2 u \ x, y, t - b \ x, y u \ x, y, t + c^1(x, y)
$$

• Generalized diffusion equations
The Example again

GVF-field

50 iterations

160 iterations
GVF-field and snake

GVF-field  Initialization  Result
Alfa and Beta

Initialization

α = 10, β = 3

α = 2, β = 3

Initialization

α = 1, β = 1

α = 2, β = 3
Results, initialising from the outside
Results, initialization from the inside
Segmenting white blood cells
Contour evolution

L: Local properties
G: Global properties
I: Independent properties

F: Speed function

F = F(L, G, I)
The speed function $F$

- Depends on image intensities
- Depends on image derivatives
- Depends on local curvature
- Depends on a global flow fields
- etc

The speed function has to be carefully selected and adapted to the application!!
Segmentation – Fast Marching Methods

Assume $F>0$ (i.e. the contour only moves outwards)

Define the contour at time $T$ is defined as the collection of points with arrival time $= T$

Start from $distance = rate \times time$ in one dimension:

$$dx=F \, dT \Rightarrow 1=F \, T'(x)$$

In several dimensions the arrival time is calculated from the speed function using the Eikonal equation

$$|r_T|F=1 \quad T=0 \text{ at initial location}$$
Practical Aspects

1. Start with initial contour *(known points)*
2. Compute T for all neighbours to the contour *(trial points)*
3. Add the point in *trial* with the smallest T to *known*
4. Update T for all neighbours not in *known* and add to *trial*
5. Repeat 3-4 until all points are in *known*

- Linear complexity
- Use a heap and a heap sort
Level Set Methods

Model the contour as the level set to a 3D-function $\Psi$, i.e.
$\Psi(x(t),t)=c$ (usually $c=0$), $x(t)=(x(t),y(t))$, with

$\Psi(x(t))<0$ inside $\partial S$

$\Psi(x(t))=0$ on $\partial S$

$\Psi(x(t))>0$ outside $\partial S$

Differentiate with respect to $t$:

$\Psi_t + r\Psi(x(t),t) \phi x'(t) = 0$

*The fundamental equation of motion.*
The outward unit normal of the level set is given by

\[ \mathbf{n} = \mathbf{r} \Phi / |\mathbf{r} \Phi | \]

Assume that F is normal to the level set, i.e.

\[ F = \mathbf{x}^{\prime}(t) \cdot \mathbf{n} \]

Now

\[ \Phi_t + r \Phi(x(t), t) \cdot \mathbf{x}^{\prime}(t) = 0 \]

can be written as

\[ \Phi + F |\mathbf{r} \Phi | = 0 \]

*The level-set equation.*
Practical Aspects

• $\Phi$ needs only to be known close to the level-set
• $\Phi$ is usually chosen as a signed distance function

$$\phi(x) = \begin{cases} -d(x, \Gamma) & \text{inside } \Gamma \\ d(x, \Gamma) & \text{outside } \Gamma \end{cases}$$

• $\Phi$ can be constructed using distance transform or fast marching

$$\Phi_\tau + \text{sign}(\Phi_0) (|r\Phi| - 1)) = 0$$

$$\Phi(\tau=0) = \Phi_0$$

• narrow band algorithm (update $\Phi$ in each step)
• numerical scheme: fixed grid, multigrid
Level-set example

Observe that level sets can easily change topology!
Experiments
Experiments

Figure 3. The speed function $F_{\text{nuc}}$ in $\Omega$ and the resulting $T(x)$ landscape.

Figure 4. The final nucleus (left) and cytoplasm outlines (right).
Example: Segmented 2D-gel image
Another example
Variational methods

1. Define the “best” segmentation of an image as the local minima to an energy functional

\[ E(\Omega) = \int_{\Omega} f(\Omega) dx \, , \]

2. Write down the Euler-Lagrange equations, giving

\[ dE(\Omega) = 0 \]

3. Introduce a “dummy” variable \( t \) (time) and solve

\[ \Phi_t = dE(\Phi) \]

Where \( \Phi \) is a level set function corresponding to \( \Omega \)
The Classical Chan-Vese Model

- Divide the image $I(x)$ into two subsets $D_0$, $D_1$ such that the following segmentation functional is minimized:

$$J(\Gamma, \mu) = \frac{1}{2} \int_{D_0} |I(x) - \mu_0|^2 \, dx + \frac{1}{2} \int_{D_1} |I(x) - \mu_1|^2 \, dx + \alpha \int_\Gamma ds$$

where $\mu_0$ and $\mu_1$ are constant image intensities on $D_0$ and $D_1$

- If the subsets are fixed, then the optimal parameter values are given by

$$\mu_i^* = \mu_i^*(D_i) = \int_{D_i} I(x) \, dx / \int_{D_i} dx, \quad (i = 0, 1)$$

- This model may be sensitive to noise and outliers!!
The Reduced Functional

• Define the \textit{reduced functional}:  
  \[ \hat{J}(\Gamma) = J(\Gamma, \mu^*(\Gamma)) \]

• The solution is found by gradient descent:
  \[
  \nabla \hat{J}(\Gamma) = V_1(I(x) - \mu_1^*) - V_0(I(x) - \mu_0^*) + \alpha \kappa \\
  \frac{\partial \phi}{\partial t}(x, t) = -\nabla \hat{J}(\phi(x, t)) \mid \nabla \phi(x, t), \hspace{1cm} \phi(x, 0) = \phi_0(x)
  \]
Variational methods

Minimize a functional of the following form (Chan-Vese)

\[ E(c_1, c_2, \Gamma) = \int_{\text{int}(\Gamma)} |I(x) - c_1|^2 \, dx + \]
\[ + \int_{\text{ext}(\Gamma)} |I(x) - c_2|^2 \, dx + \]
\[ + \nu(\Gamma) , \]

where \( c_1 \) and \( c_2 \) denote the constant image intensities inside and outside the curve respectively and the last term denote a measure on the curve.
HMC-images of human embryos
Variational formulation

The outer circumference:

$$J(\gamma) = \iint_{\Omega} |I(x) - w \cdot \frac{x - x_0}{|x - x_0|}|^2 dx + \iint_{\Omega^c} |I(x)|^2 dx$$

$w$: direction along which the intensity varies most

$x_0$: the centroid of $\gamma$

The inner circumference:

$$J(\gamma) = \iint_{\Omega} |I(x) - w \cdot \frac{x - x_0}{|x - x_0|} - \mu| - 2\sigma dx$$

$\mu$: average over the zona

$\sigma$: standard deviation of model error
Segmentation of the Zona Pellucida
Segmentation – Continuous graph cuts

• The Chan-Vese functional can be formulated in terms of the characteristic function, $u$, for the internal subset
• The functional is non-convex, since $u$ is a set function
• If $u$ is relaxed to a soft set-function with values in $[0,1]$, then the Chan-Vese functional is convex in $u$
• Chen and Esidouglo showed that the given a solution to the convex relaxation, a solution to the original problem can be obtained by arbitrarily thresholding $u$
• Continuous graph cuts
A modeling example:

Analysis of the 3D-shape of chewing gums
Problem

Chewing gums sometimes stick together during processing. This is assumed to happen when the chewing gums are "flat":

![Image of chewing gum](image.png)
Manual classification

Konvexitetskategorier, 1-5:
Goal

• Develop a method for automatic classification of chewing gums.

• Method: Analys the shape of the chewing gums based on measurements.
Proposed method

- Measurement system: TMS-100
- Construction of fixture
- Development of algorithm for shape analysis
- Statistical validation
Measurement machine and fixture
Measurements

Field of View: 37.58 mm x 26.25 mm
Area of Interest: 14.42 mm x 14.41 mm
Resolution: 0.62 µm x 0.62 µm
Measurement Mode: Short Coherence

1. Spike Removal
2. Spike Removal
Algorithm

- Model the shape of the chewing gum mathematically

- Fit a geometrical model to the measurements

- Develop a suitable quality measure

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Chewing gum-model 1

\[ k_3 z^2 + k_2 y^2 + k_1 x^2 - k_4 x^2 y^2 = R^2 \]
Chewing gum-model 2

\[ k_5(z - z_0) = k_1(x - x_0)^4 + k_2(y - y_0)^4 + k_3(x - x_0)^2 + k_4(y - y_0)^2 \]
Ellipsoidal model

\[ k_3(z - z_0)^2 + k_2(y - y_0)^2 + k_1(x - x_0)^2 - R^2 = 0 \]
Pre-conditioning

- Eliminate $x_0$ & $y_0$ by changing the coordinate system
The new coordinate system

\[ x_{ny} = x - \frac{1}{n} \sum_{n} x \]

\[ y_{ny} = y - \frac{1}{n} \sum_{n} y \]

Implies that

\[ k_3(z - z_0)^2 + k_2(y - y_0)^2 + k_1(x - x_0)^2 - R^2 = 0 \]

changes to

\[ k_3(z - z_0)^2 + k_2 y_{ny}^2 + k_1 x_{ny}^2 - R^2 = 0 \]
Fitting

Each measurement gives a linear constraint on the surface parameters. Collecting all these equations give:

\[ A\bar{x} = 0 \]

Require

\[ ||\bar{x}|| = 1 \]

The least squares solution is given from the singular value decomposition:

\[ A = USV^H \]
Forming the equations

Assume \( k_1 = k_3 \)

Gives

\[
k_1(z - z_0)^2 + k_2 y_n^2 + k_1 x_n^2 - R^2 = 0
\]

Form the system of eq:s \( A\bar{x} = 0 \)

with

\[
A = \begin{pmatrix}
z^2 + x^2 & -2z & y^2 & 1
\end{pmatrix}
\]

\[
\bar{x} = \begin{pmatrix}
k_1 & k_1z & k_2 & k_1z_0 - R^2
\end{pmatrix}^T
\]
Fitting: chewing gum model vs ellipsoidal
A two-step procedure

The ellipsoidens equation was

$$k_1(z - z_0)^2 + k_2y_{ny}^2 + k_1x_{ny}^2 - R = 0$$

$z_0$ is fixed from this solution in order to estimate

$$k_1, k_2, k_3 & R$$

in

$$k_3(z - z_0)^2 + k_2y_{ny}^2 + k_1x_{ny}^2 - R = 0$$
Quality measure

- Use the volume of the ellipsoid
- Take into account all the radii
- A flatter chewing gum gives a higher volume
Adding extra skew terms

\[ k_1(z - z_0)^2 + k_2 y_{ny}^2 + k_1 x_{ny}^2 + k_4 xz + k_5 yz + k_6 xy - R^2 = 0 \]
Skewing
Volume variation for different classes