Medical Image Analysis: An Introduction

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- Registration
- Classification

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

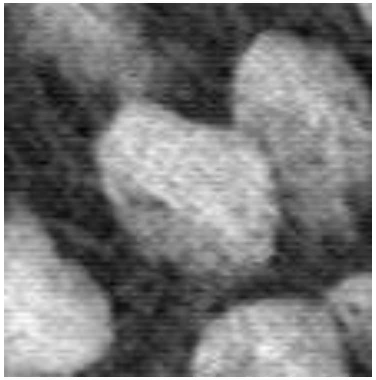
- Diagnosis
- Follow up on treatments
- Comparing different treatments/patients/drugs
- On-line imaging for active intervention
- Predicting development
- etc

Image analysis problems

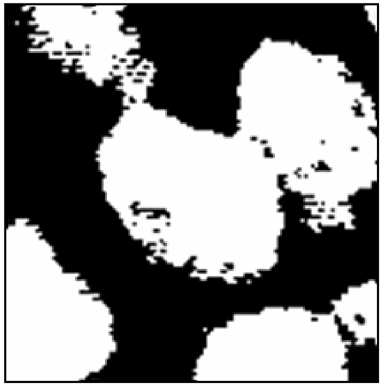
- Segmentation – delineating different organs
- Classification – determining e.g. types of leukocytes
- Registration – comparing different modalities/patients
- Reconstruction – making 3D-measurments
- Measuring flow – e.g. inside aorta
- Reconstructing flow fields – e.g. inside the heart
- Building shape priors effeciently
- 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 $\mathbf{v}(s)=[x(s),y(s)]$ that minimizes

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

- Examples of external energies

$$E_{\mathrm{ext}} = -|\nabla I(x,y)|^2$$

$$E_{\mathrm{ext}} = -|\nabla G_\sigma(x,y) * I(x,y)|^2$$

Solution

- The Euler-Lagrange equations gives:

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

- Dynamic snake – Active contour

$$\mathbf{v}_t(s,t) = \alpha \mathbf{v}''(s,t) - \beta \mathbf{v}^{(4)}(s,t) - \nabla E_{\text{ext}}(\mathbf{v}(s,t))$$

Numeric solution

- Discretising

$$\delta\left(x_k^n - x_k^{n-1}\right) = \frac{\alpha}{h^2}\left(x_{k+1}^n - 2x_k^n + x_{k-1}^n\right) -$$

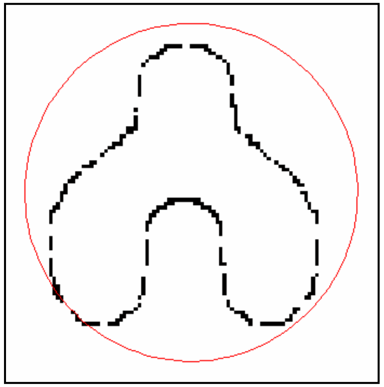
$$-\frac{\beta}{h^4}\left(x_{k+2}^n - 4x_{k+1}^n + 6x_k^n - 4x_{k-1}^n + x_{k-2}^n\right) - f_x\left(x_k^n, y_k^n\right)$$

- Linear system of equations

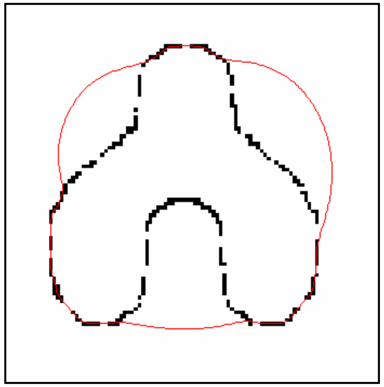
$$\left(\mathbf{A} + \delta\mathbf{I}\right)\mathbf{x}^n = \mathbf{x}^{n-1} - \mathbf{f}_{\mathbf{x}}\left(\mathbf{x}^{n-1}, \mathbf{y}^{n-1}\right)$$

- Re-sampling

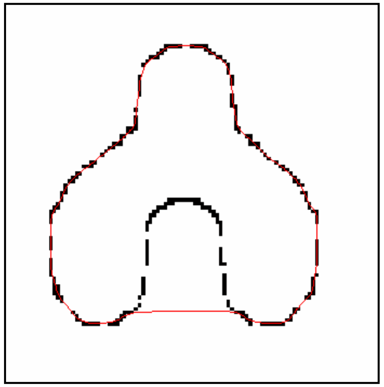
An Example



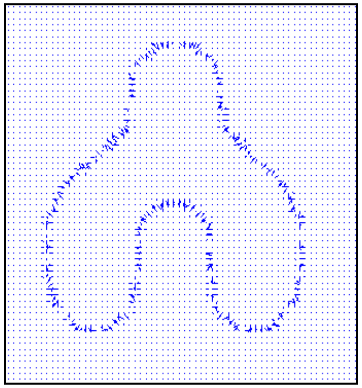
Initialization



200 iterations



700 iterations



Gradient field

GVF Field

- Definition: **g**(*x,y*)=[*u(x,y),v(x,y)*], that minimizes

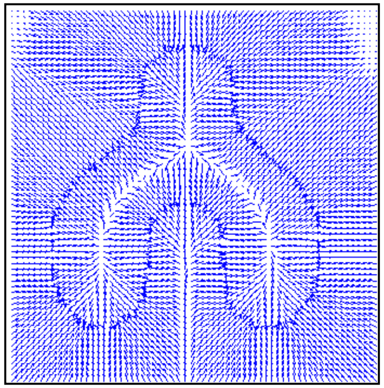
$$\varepsilon = \iint \mu \left(u_x^{\;2} + u_y^{\;2} + v_x^{\;2} + v_y^{\;2}\right) + \left|\nabla f\right|^2 \left|\mathbf{g} - \nabla f\right|^2 dxdy$$

- Calculus of variations and the introduction of a time variabel gives

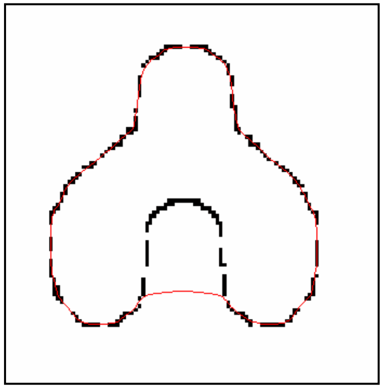
$$u_t\left(x,y,t\right) = \mu \nabla^2 u\left(x,y,t\right) - b\left(x,y\right) u\left(x,y,t\right) + c^1(x,y)$$

- Generalized diffusion equations

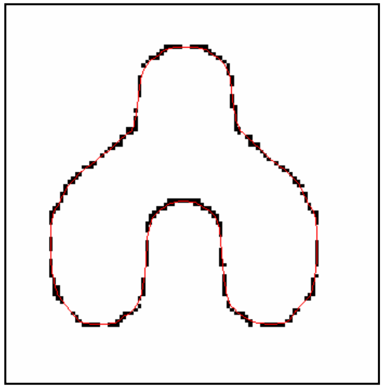
The Example again



GVF-field

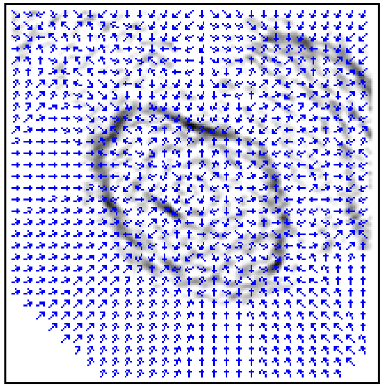


50 iterations

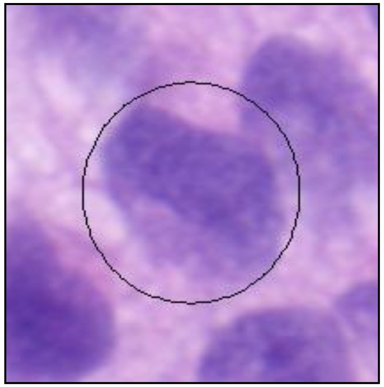


160 iterations

GVF-field and snake



GVF-field



Initialization

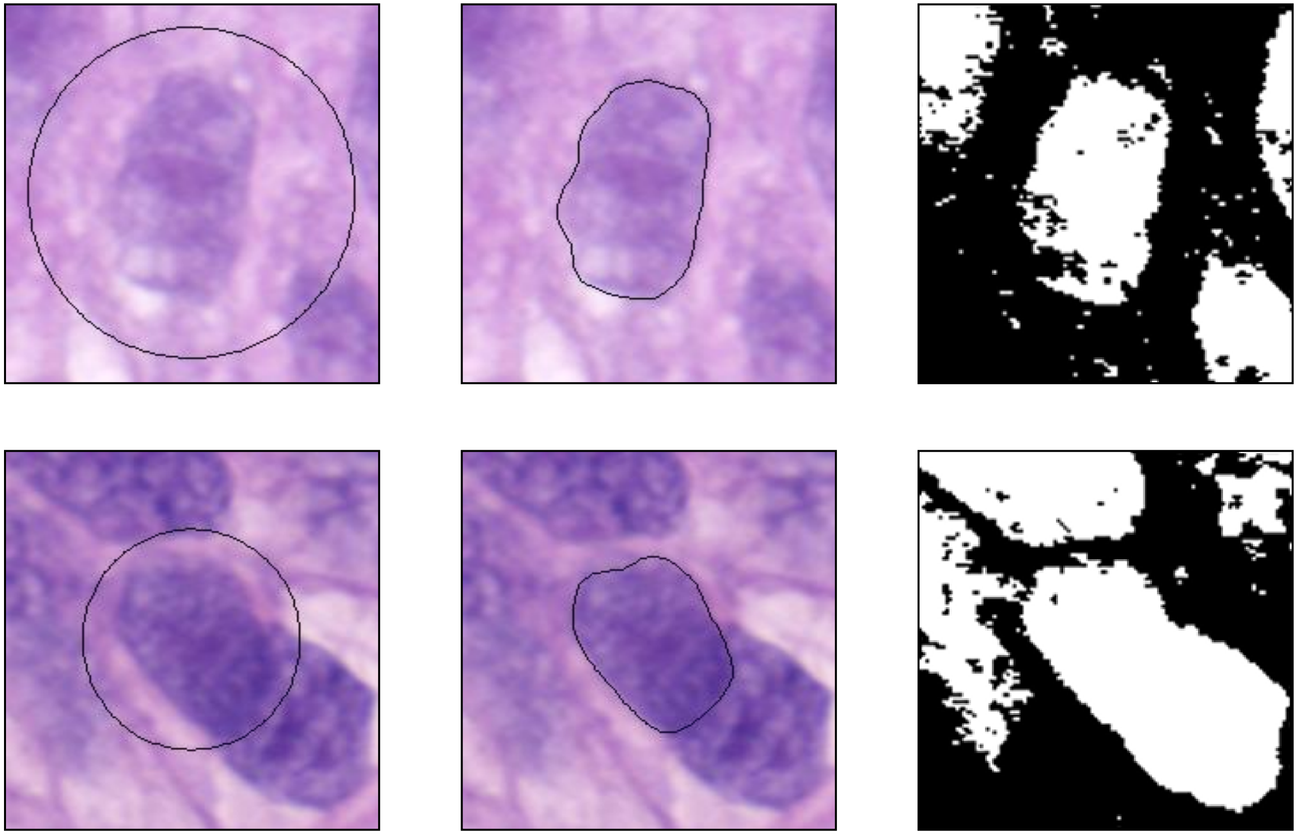
Result

Alfa and Beta

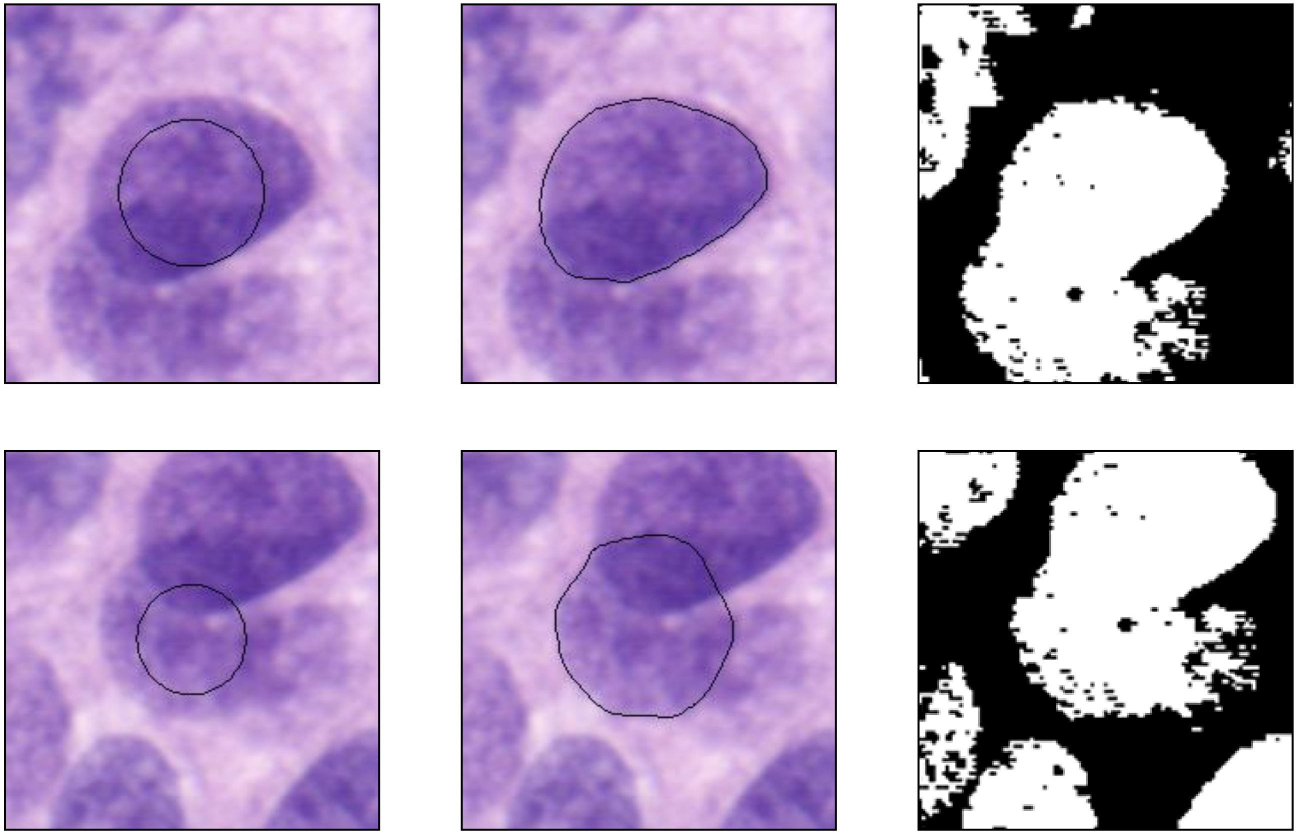
Initialization $\alpha = 10, \beta = 3$ $\alpha = 2, \beta = 3$

Initialization $\alpha = 1, \beta = 1$ $\alpha = 2, \beta = 3$

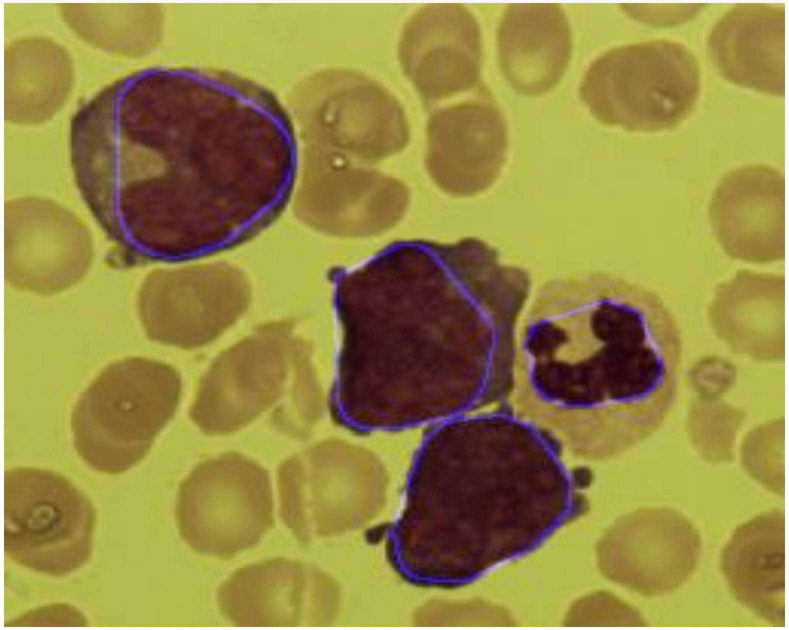
Results, initialisering from the outside

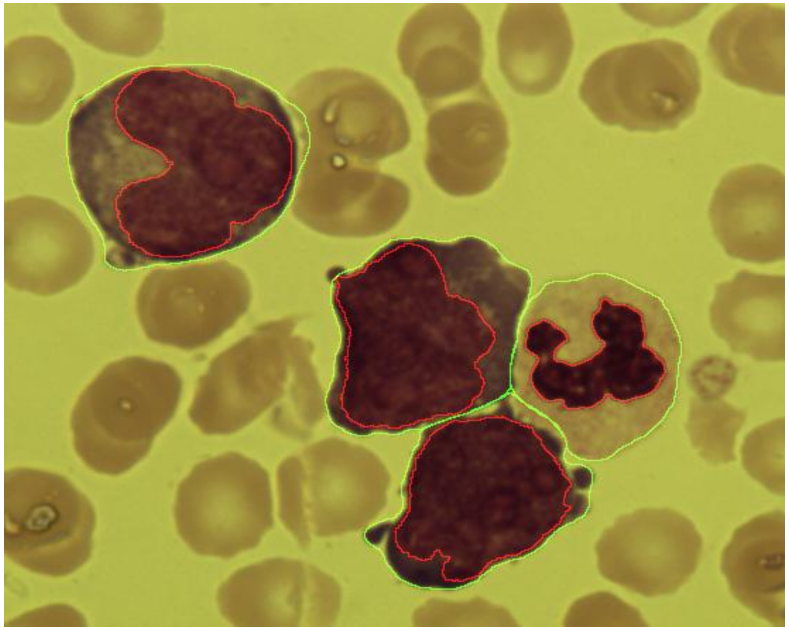


Results, initialization from the inside

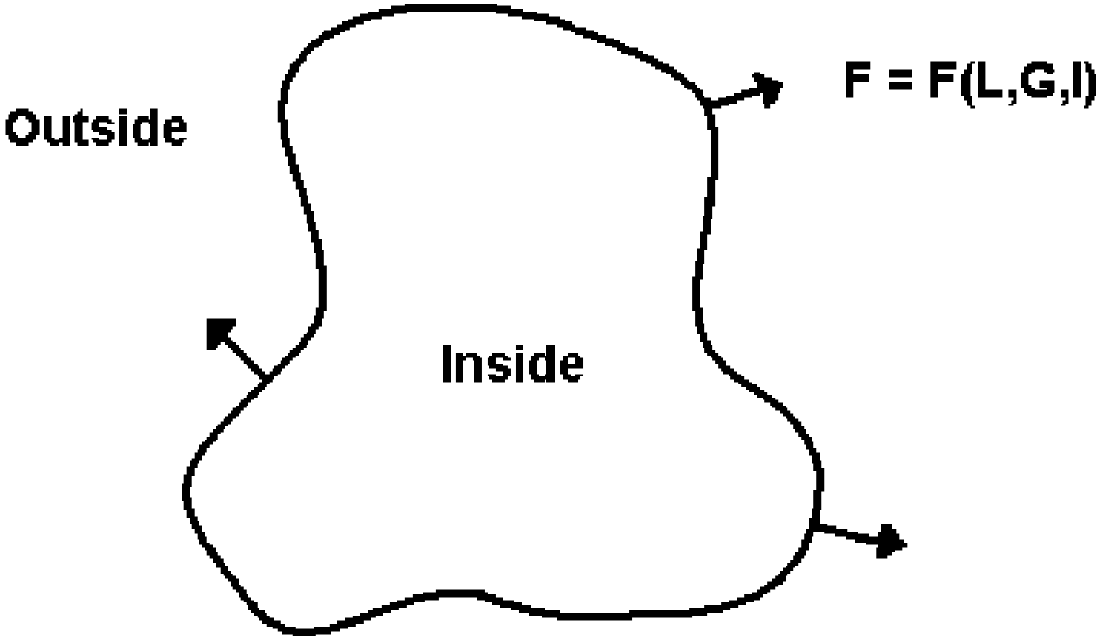


Segmenting white blood cells





Contour evolution



L: Local properties

G: Global properties

I: Independent properties

F: Speed function

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 * time* in one dimension:

dx=F dT => 1=F T´(x)

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

|r T|F=1 T=0 at intial location

Practical Aspects

1. Start with inital 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 Ψ, i.e. $\Psi(\mathbf{x}(t),t)=c$ (usually $c=0$), $\mathbf{x}(t)=(x(t),y(t))$, with

$$\Psi(\mathbf{x}(t))<0 \quad \text{inside } \partial S$$

$$\Psi(\mathbf{x}(t))=0 \quad \text{on } \partial S$$

$$\Psi(\mathbf{x}(t))>0 \quad \text{outside } \partial S$$

Differentiate with respect to t:

$$\Psi_t + \mathrm{r}\Psi(\mathbf{x}(t),t) \text{ ¢ } \mathbf{x}'(t) = 0$$

The fundamental equation of motion.

Level Set Methods (ctd.)

The outward unit normal of the level set is given by

$$\mathbf{n} = \nabla\Phi / |\nabla\Phi|$$

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

$$F = \mathbf{x}'(t) \cdot \mathbf{n}$$

Now

$$\Phi_t + \nabla\Phi(\mathbf{x}(t),t) \cdot \mathbf{x}'(t) = 0$$

can be written as

$$\Phi + F\,|\nabla\Phi| = 0$$

The level-set equation.

Practical Aspects

- Φ needs only to be known close to the level-set
- Φ is usually shosen as a signed distance function

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

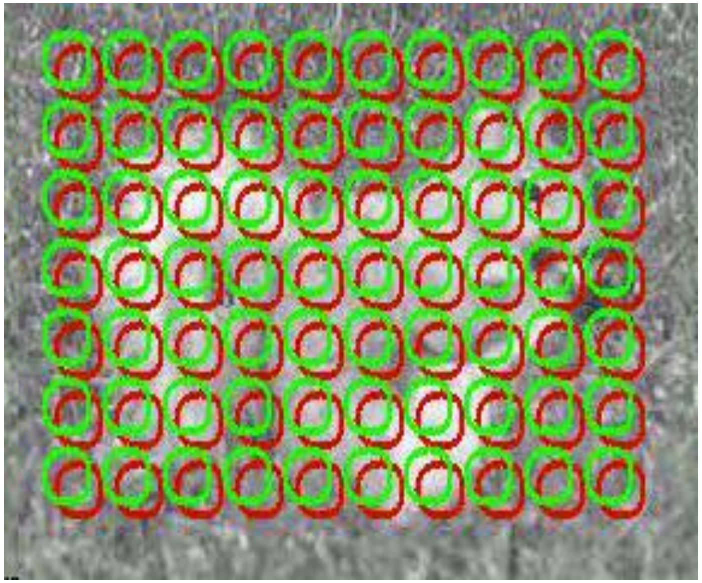
- Φ can be constructed using distance transform or fast marching

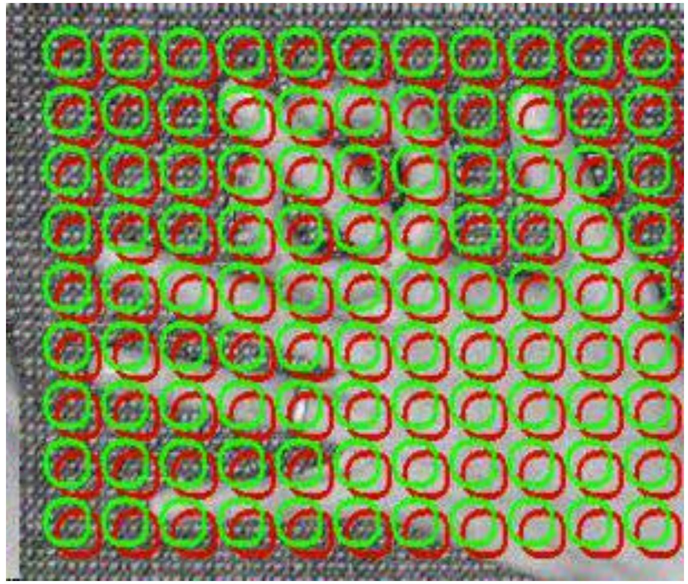
$$\Phi_\tau + \mathrm{sign}(\Phi_0 (|r\Phi| - 1)) = 0$$

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

- narrow band algorithm (update Φ in each step)
- numerical scheme: fixed grid, multigrid

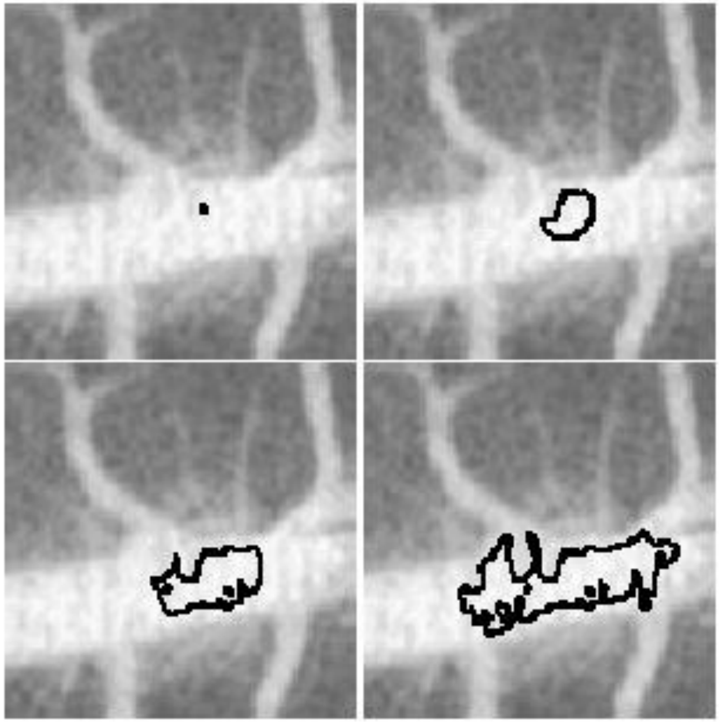
Level-set example





Observe that level sets can easily change topology!

Experiments



Experiments

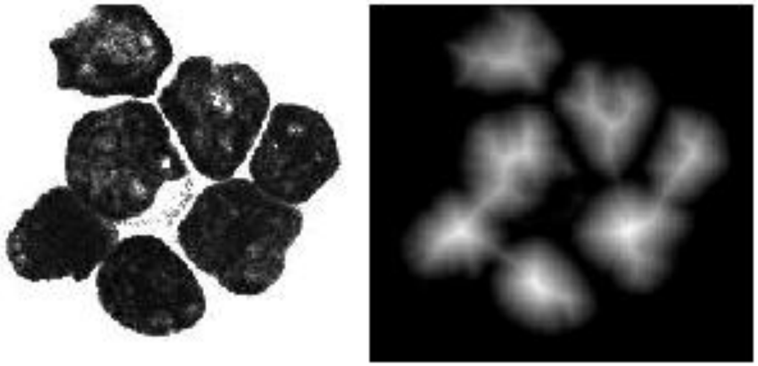


Figure 3. The speed function F_{nuc} in CZ and the resulting $T(x)$ landscape.

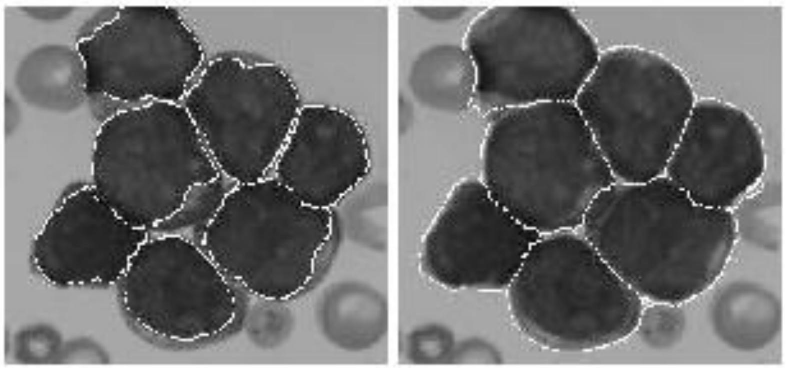
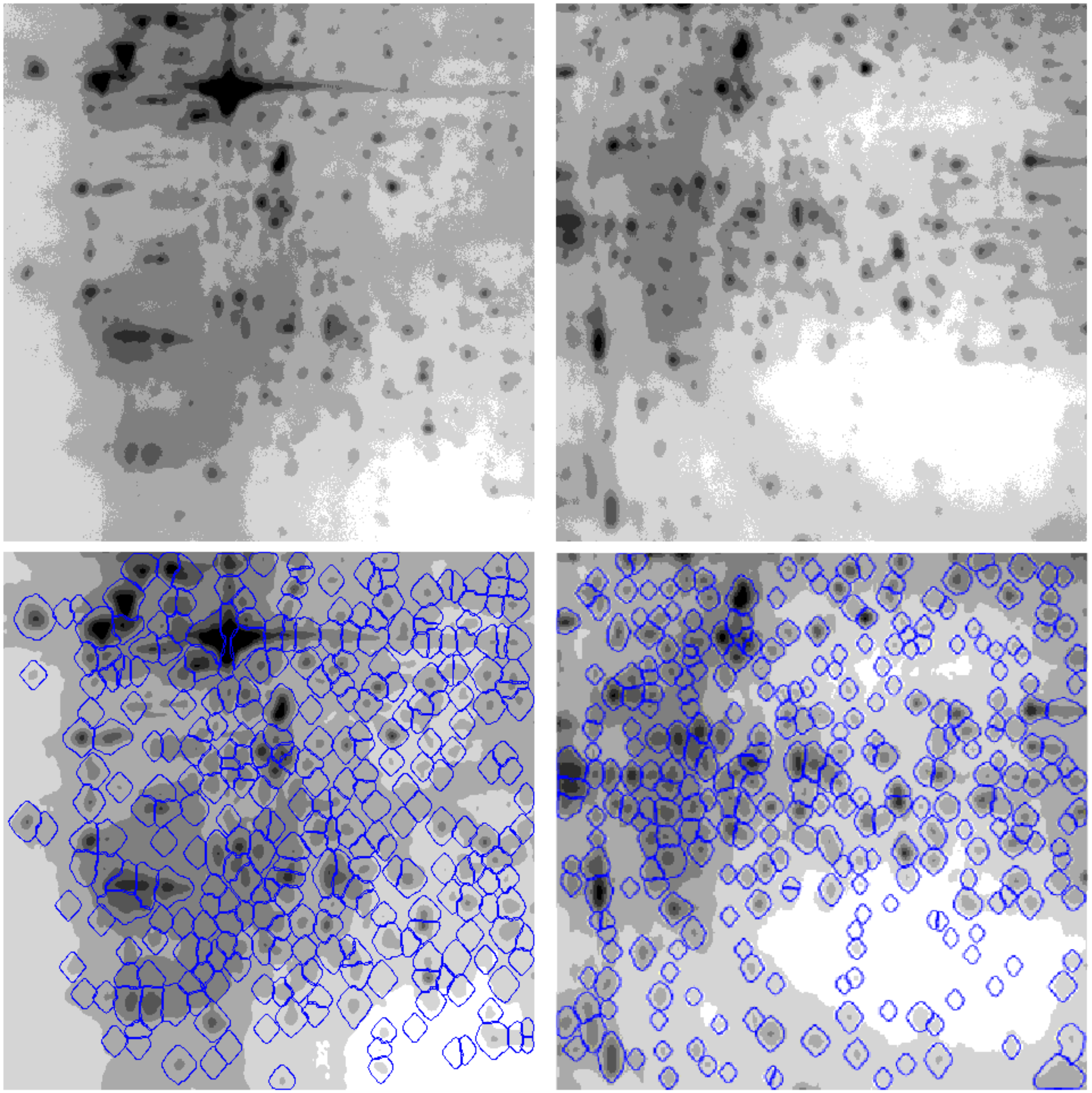
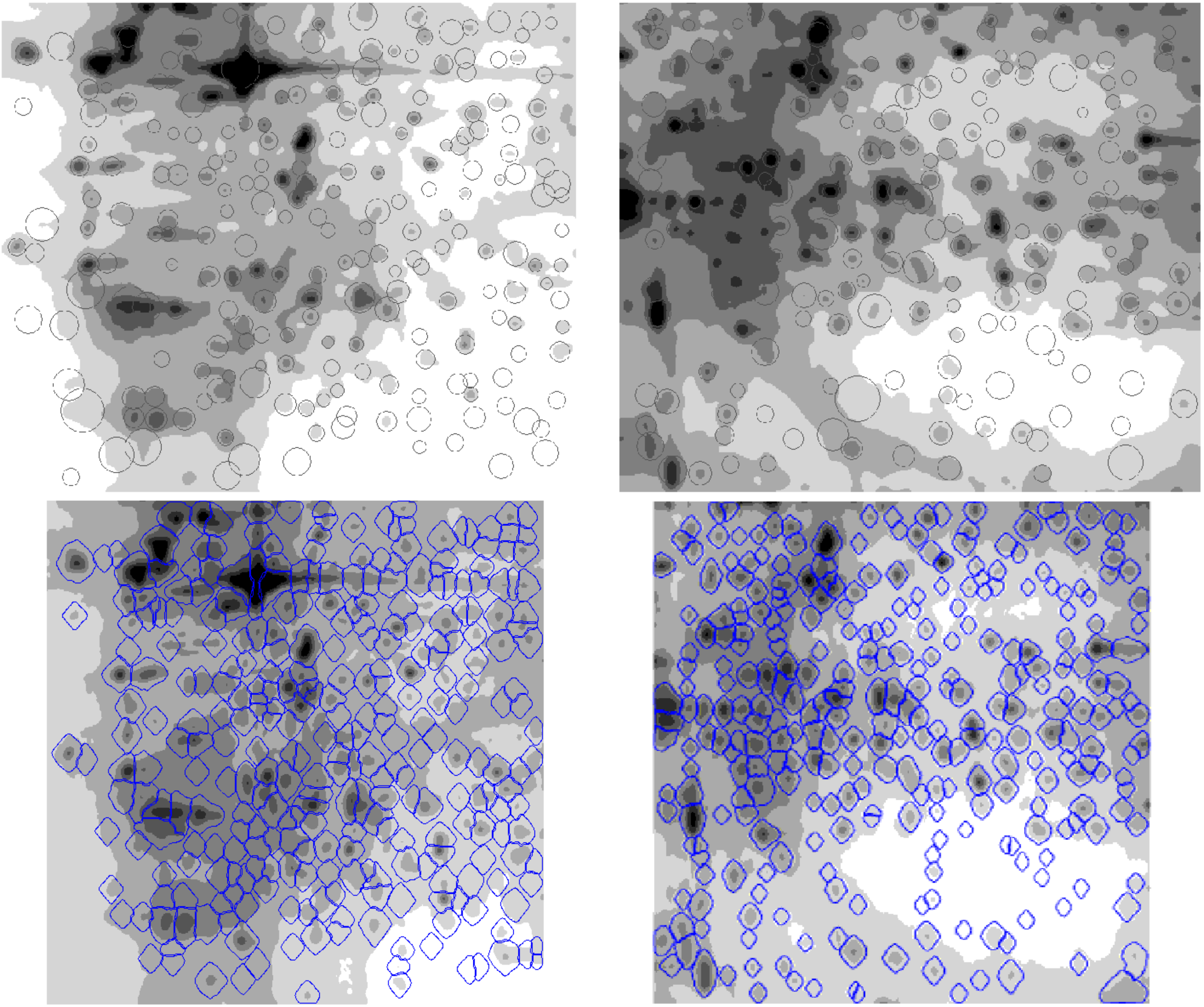


Figure 4. The final nucleus (left) and cytoplasm outlines (right).

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

$$E(\Omega) = \int_\Omega f(\Omega)dx \quad ,$$

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 Φ is a level set function corresponding to Ω

The Classical Chan-Vese Model

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

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

  where μ_0 and μ_1 are constant image intensities on D_0 and D_1

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

$$\mu_i^* = \mu_i^*(D_i) = \int_{D_i} I(\mathbf{x}) \, d\mathbf{x} \Big/ \int_{D_i} d\mathbf{x}, \qquad (i = 0, 1)$$

- This model may be sensitive to noise and outliers!!

The Reduced Functional

- Define the ***reduced functional***:

$$\hat{J}(\Gamma) = J(\Gamma, \boldsymbol{\mu}^*(\Gamma))$$

- The solution is found by gradient descent:

$$\nabla \hat{J}(\Gamma) = V_1(I(\mathbf{x}) - \mu_1^*) - V_0(I(\mathbf{x}) - \mu_0^*) + \alpha\kappa$$

$$\frac{\partial \phi}{\partial t}(\mathbf{x}, t) = -\nabla \hat{J}(\phi(\mathbf{x}, t))|\nabla \phi(\mathbf{x}, t)|, \qquad \phi(\mathbf{x}, 0) = \phi_0(\mathbf{x})$$

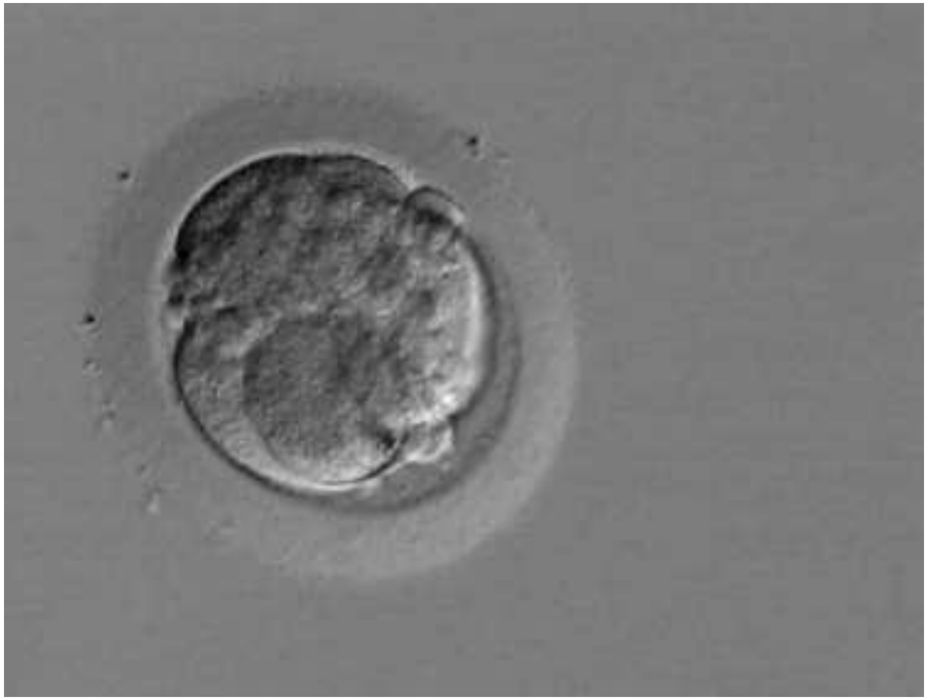
Variational methods

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

$$
\begin{aligned}
E(c_1, c_2, \Gamma) = \int_{\mathrm{int}(\Gamma)} & |I(x) - c_1|^2 \, dx + \\
+ \int_{\mathrm{ext}(\Gamma)} & |I(x) - c_2|^2 \, dx + \\
+ \, \nu(\Gamma) & \quad ,
\end{aligned}
$$

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:

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

w: direction along which the intensity varies most

x_0: the centroid of γ

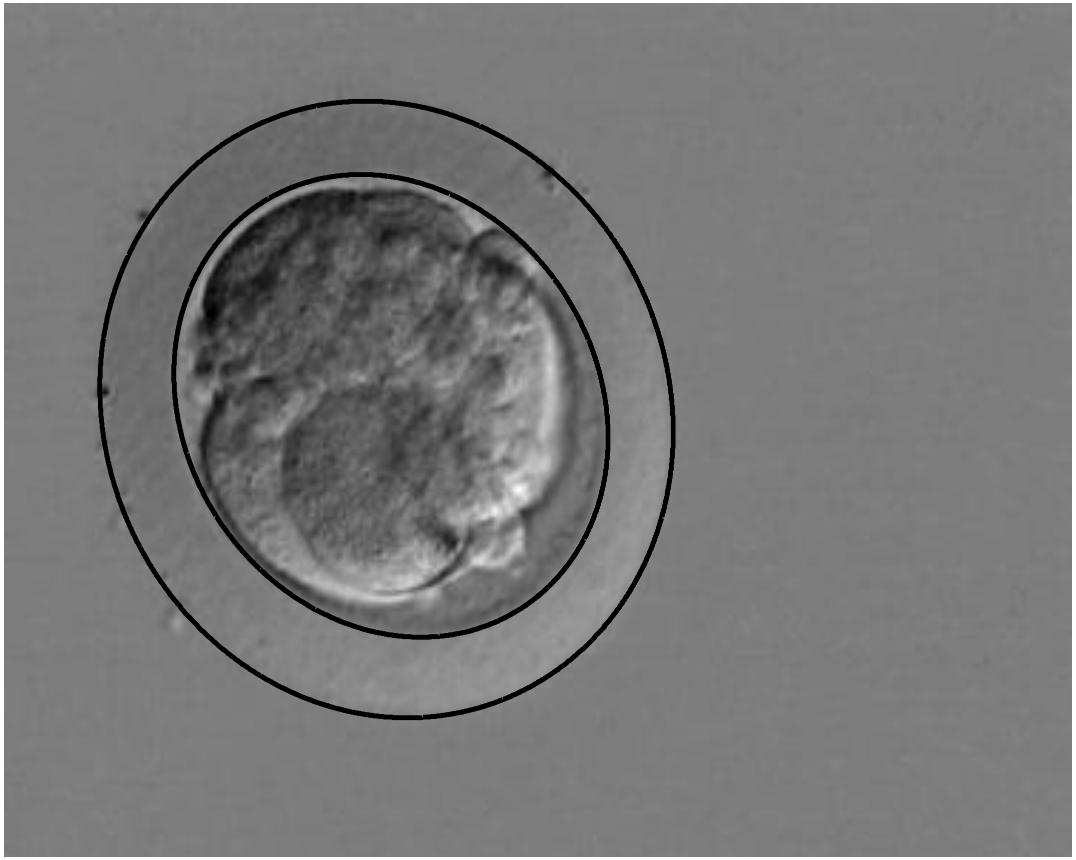
The inner circumference:

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

μ: avarage over the zona

σ: 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”:

Manual classification

Goal

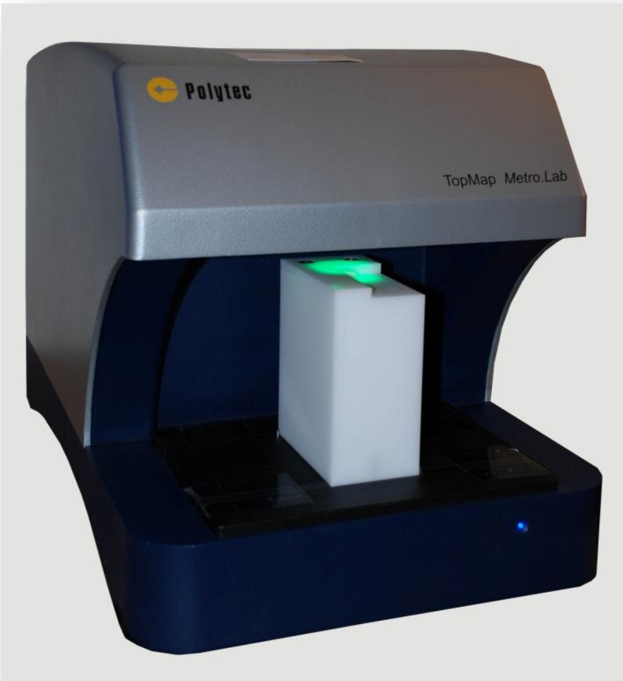
- Develop a method for automatic classification of chewing gums.

- Method: Analys the shape of the chewing gums based on measurements.

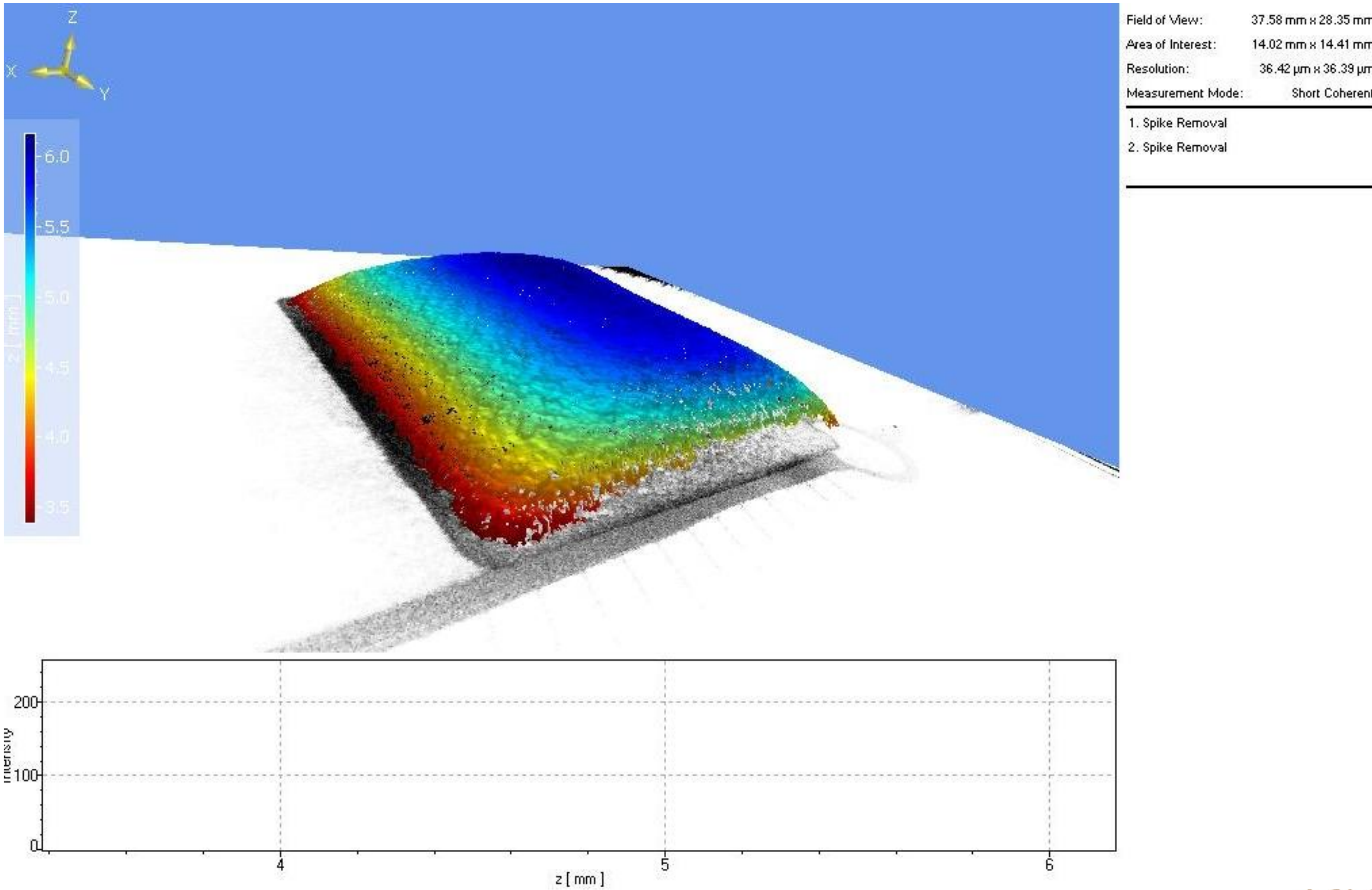
Proposed method

- Measurment system: TMS-100
- Construction of fixture
- Development of algorithm for shape analysis
- Statistical validation

Measurment machine and fixture



Measurments



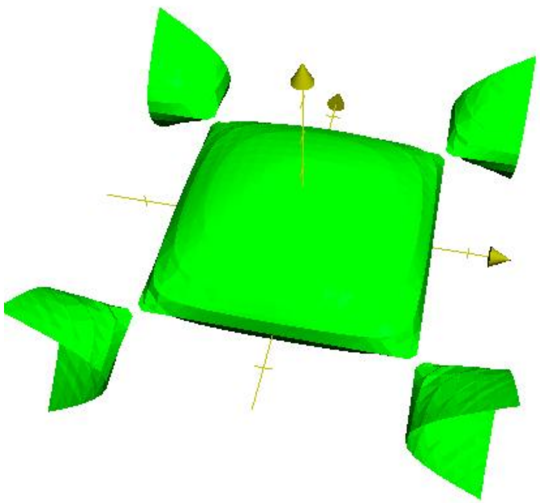
Algorithm

- Model the shape of the chewing gum mathematically
- Fit a geometrical model to the measurments
- Develop a suitable quality measure

X	Y	Z
.	.	.
.	.	.
19.847	6.769	1.3326874
19.883	6.769	1.3829173
19.920	6.769	1.2791595
19.956	6.769	1.2594673
19.993	6.769	1.1855045
20.029	6.769	1.1687934
20.320	6.769	1.2254806
20.357	6.769	1.2330464
20.612	6.769	1.0770782
20.685	6.769	1.1264039
20.721	6.769	1.0626094
20.757	6.769	1.1141516
.	.	.
.	.	.

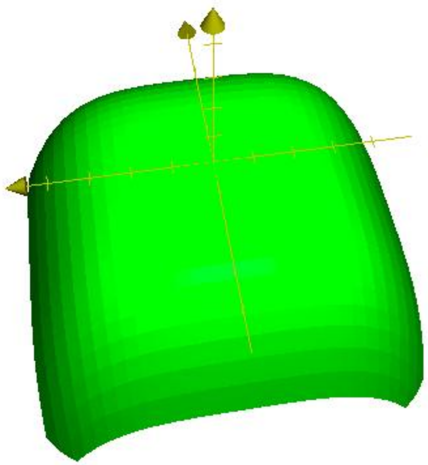
Chewing gum-model 1

$$k_3 z^2 + k_2 y^2 + k_1 x^2 - k_4 x^2 y^2 = R^2$$



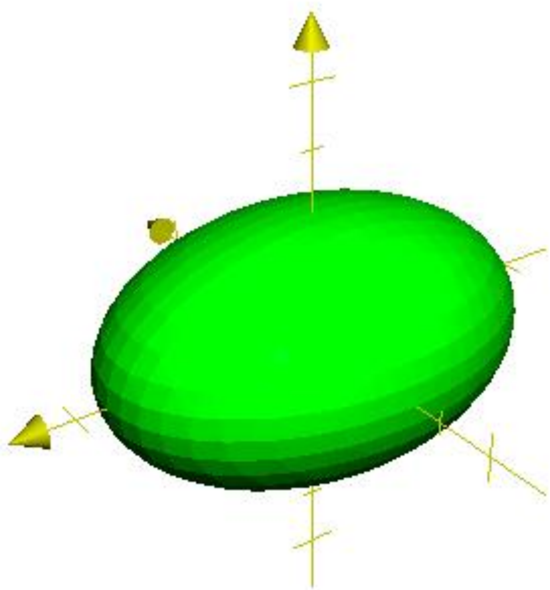
Chewing gum-model 2

$$k_5(z - z_0) = k_1(x - x_0)^4 + k_2(y - y_0)^4 + k_3(x - x_0)^2 + k_4(y - y_0)^2$$



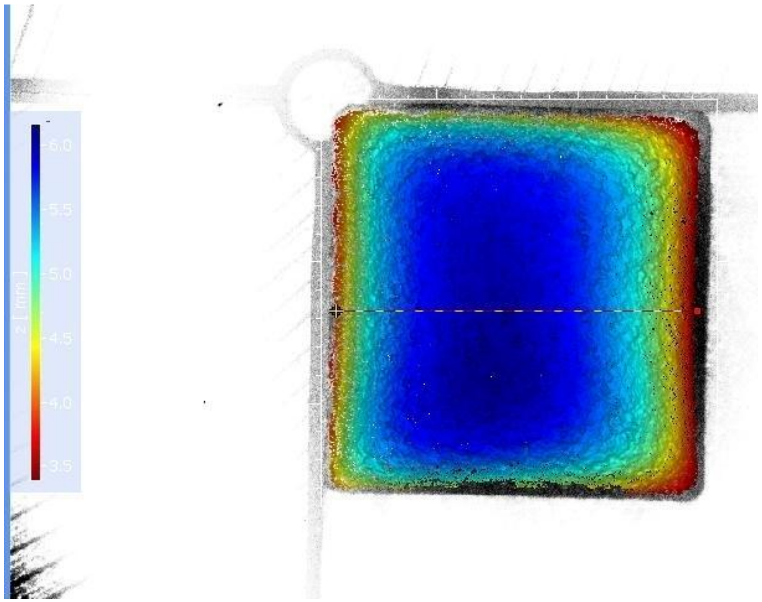
Ellipsoidal model

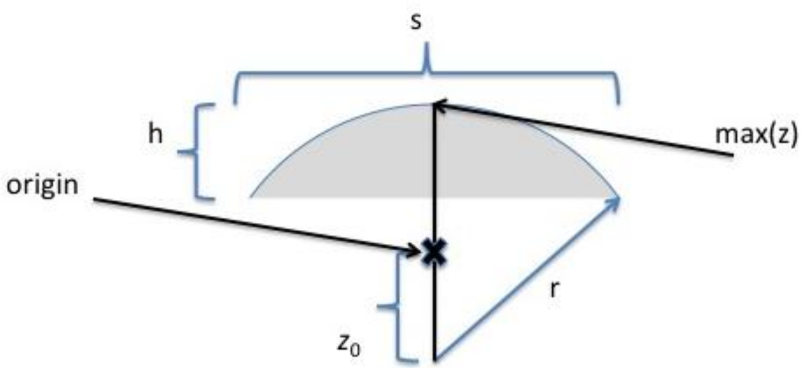
$$k_3(z-z_0)^2 + k_2(y-y_0)^2 + k_1(x-x_0)^2 - R^2 = 0$$



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 measurment gives a linear constraint on the surface parameters. Collecting all these equatioins 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

$$k_1(z - z_0)^2 + k_2 y_{ny}^2 + k_1 x_{ny}^2 - R^2 = 0$$

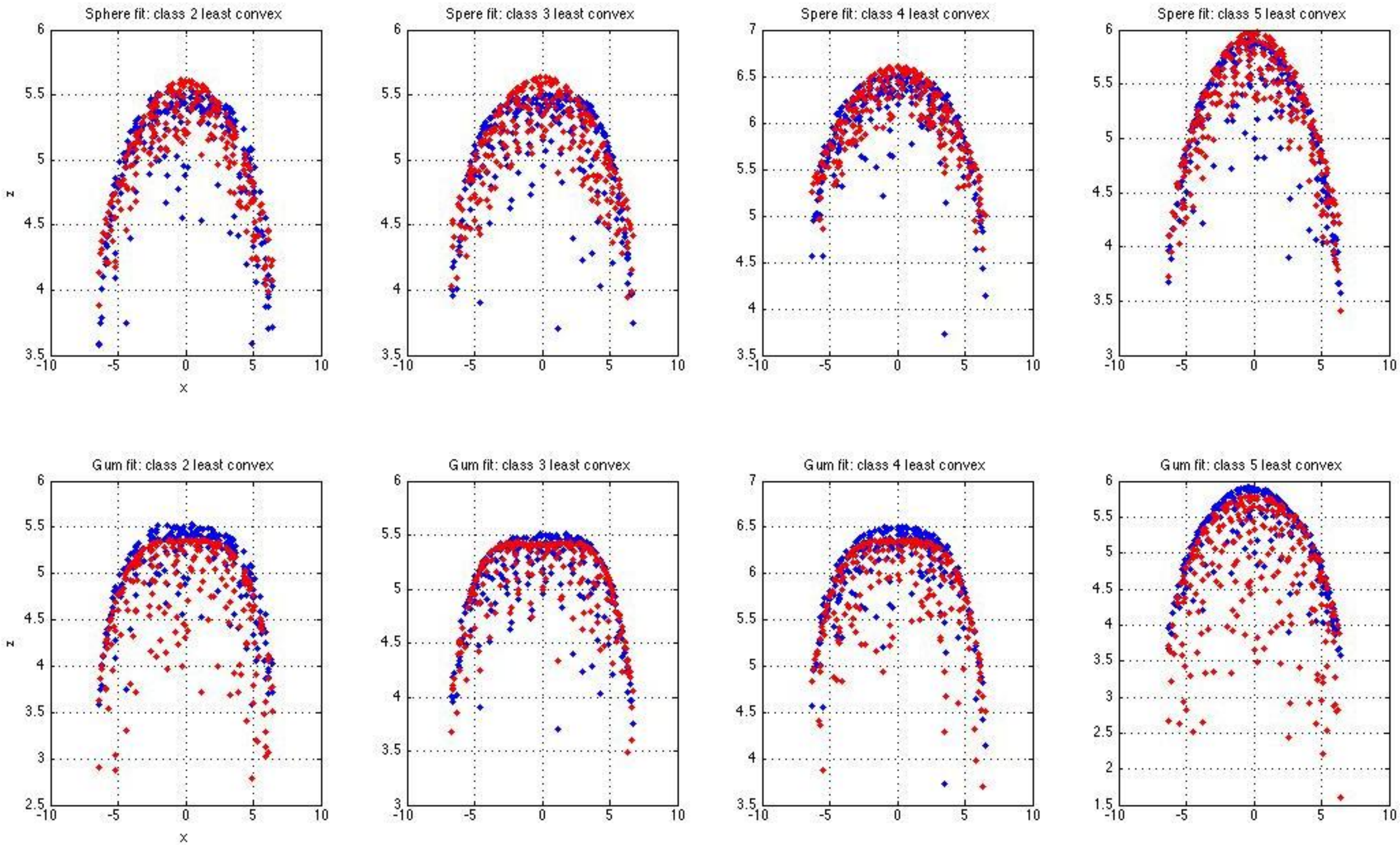
Form the system of eq:s $A\bar{x} = 0$

with

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

$$\bar{x} = \begin{pmatrix} k_1 & k_1 z & k_2 & k_1 z_0 - R^2 \end{pmatrix}^T$$

Fitting: chewing gum model vs ellipsoidal



A two-step procedure

The ellipsoidens equation was

$$k_1(z - z_0)^2 + k_2 y_{ny}^2 + k_1 x_{ny}^2 - R = 0$$

z_0 is fixed from this solution in order to estimate

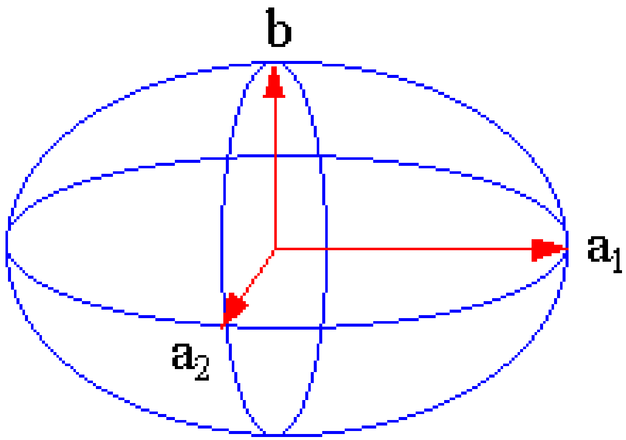
$$k_1, k_2, k_3 \ \& \ R$$

in

$$k_3(z - z_0)^2 + k_2 y_{ny}^2 + k_1 x_{ny}^2 - R = 0$$

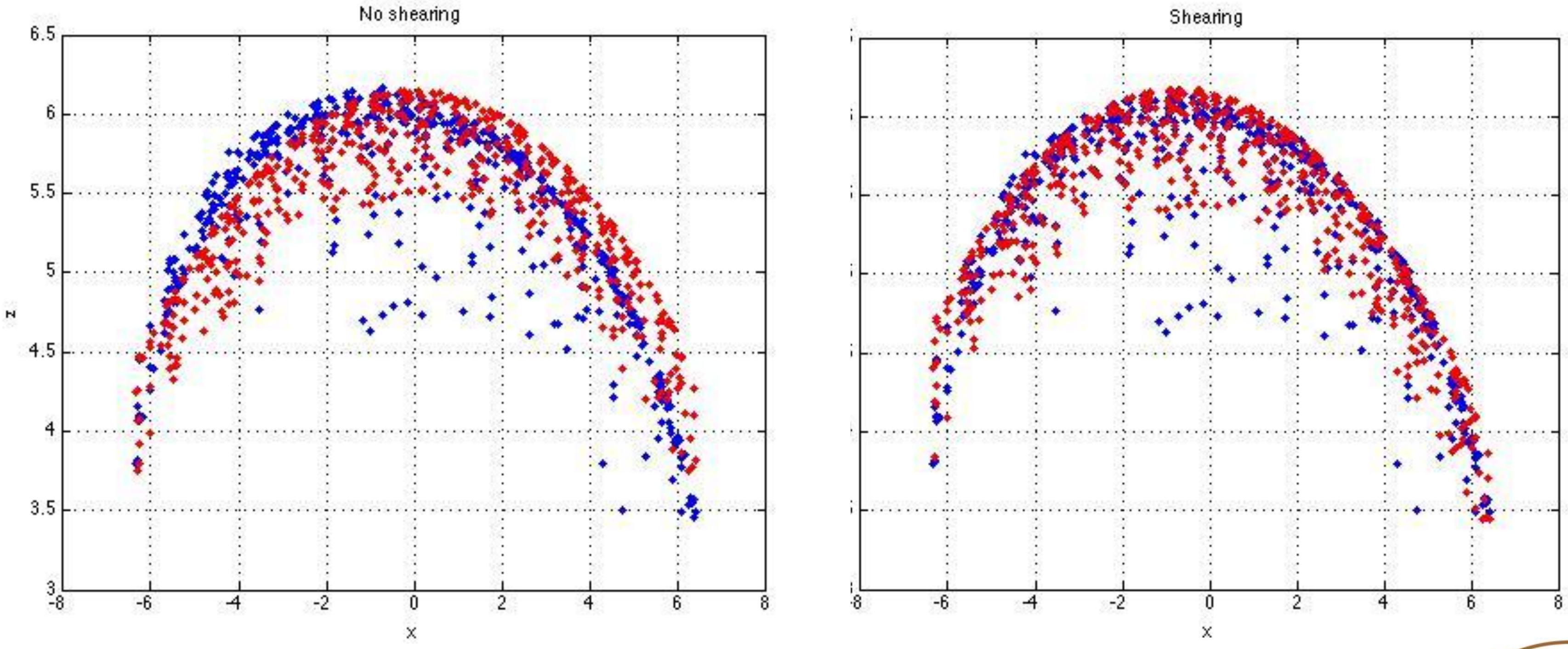
Quality measure

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

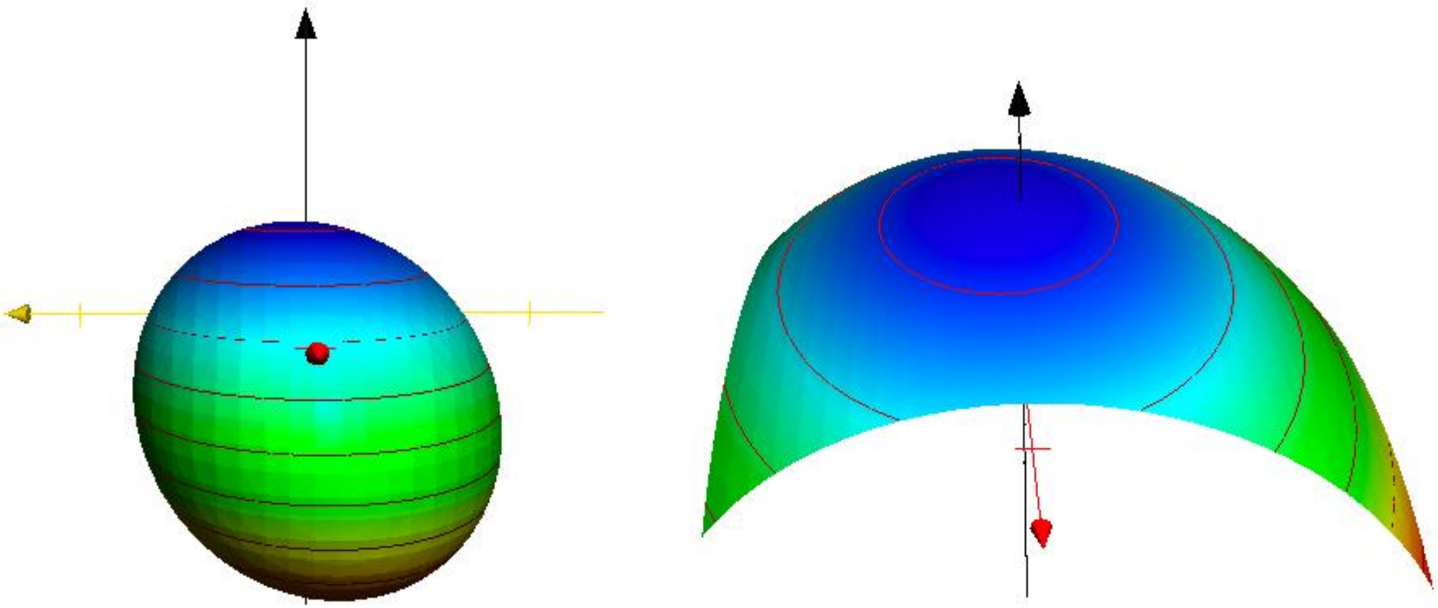


Adding extra skew terms

$$k_1(z - z_0)^2 + k_2 y_{ny}^2 + k_1 x_{ny}^2 + k_4 xz + k_5 yz + k_6 xy - R^2 = 0$$



Skewing



Volume variation for different classes