technische universiteit eindhoven

Biomedical Image Analysis: Rapid Prototyping with *Mathematica*

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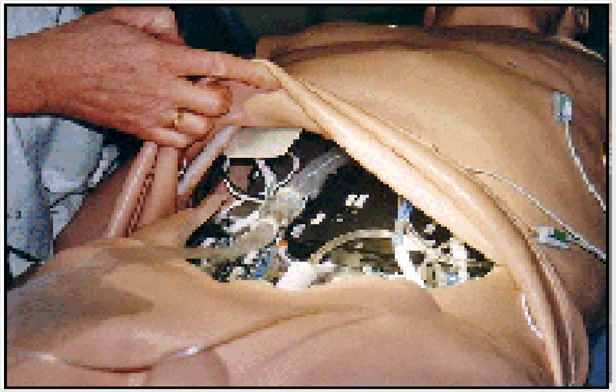
TU/e Biomedical Engineering



Goal:

- *learn the functioning of the human body*
- *learn mathematical models and computer simulations*
- *critical analysis of measurement methods*
- *design of new materials and techniques*

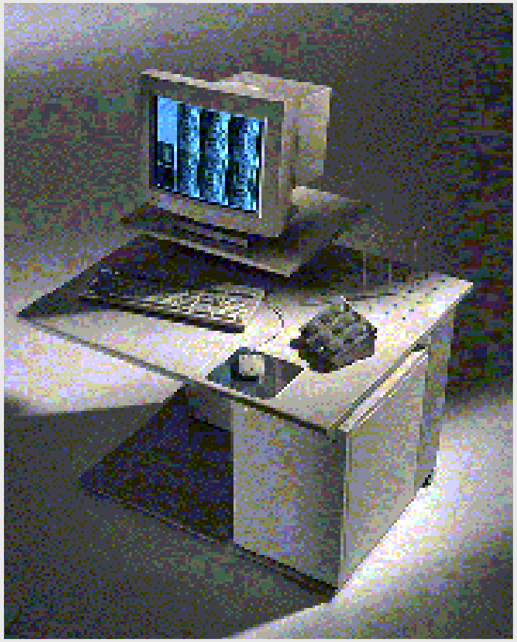
Started in Sept. 1997
- 3 yr Bachelor, 2 yr MSc
- 400 students
- 75 staff

3 Master tracks:

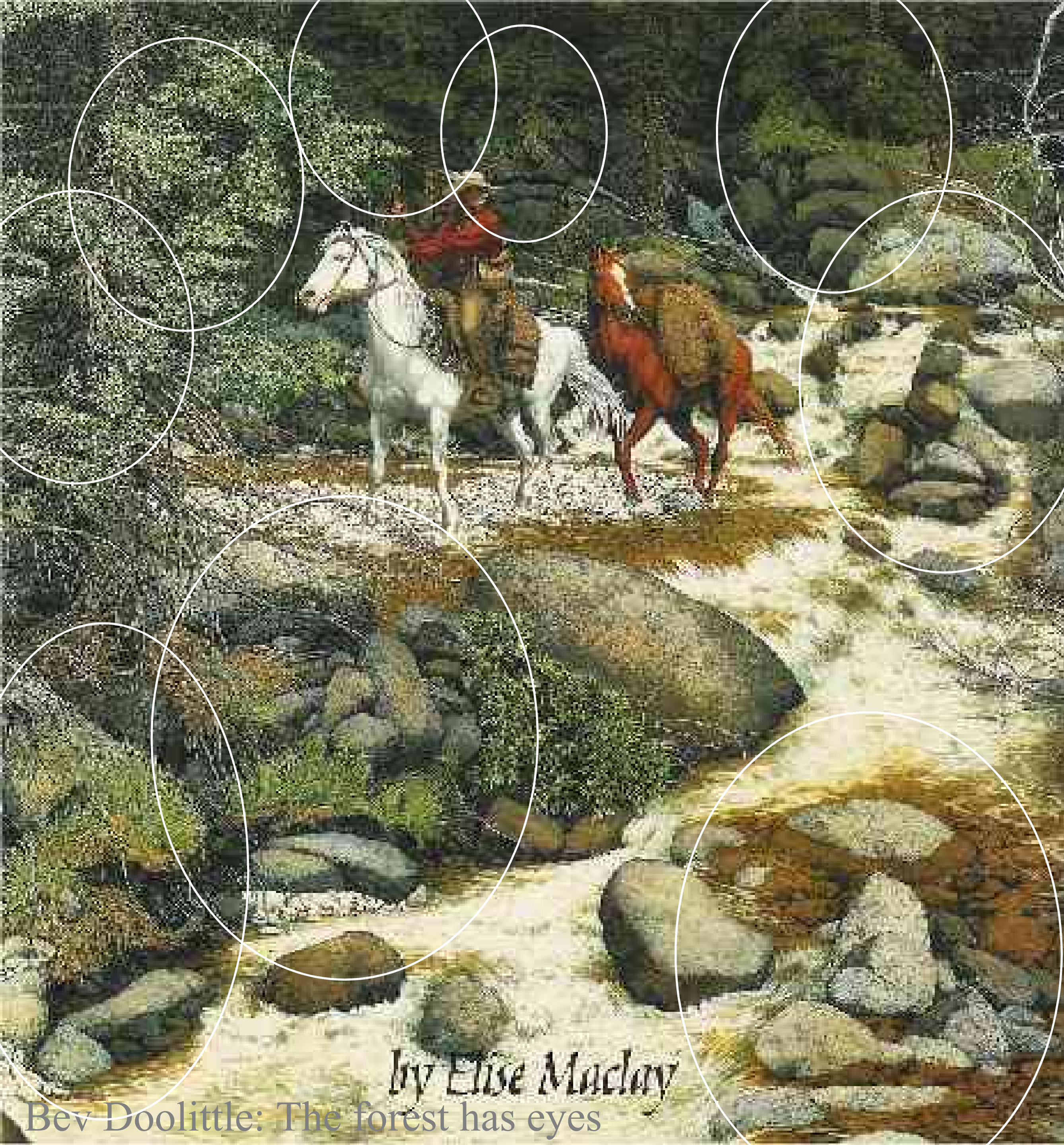
- **Biomedical Imaging and Informatics**
- Biomechanics and Tissue Engineering
- Molecular Engineering

Image analysis

The extraction of
the essential information
from all available data
and present this
in optimal format



- Our focus: the **design of computer algorithms** that answer questions on images
- Clinical validation

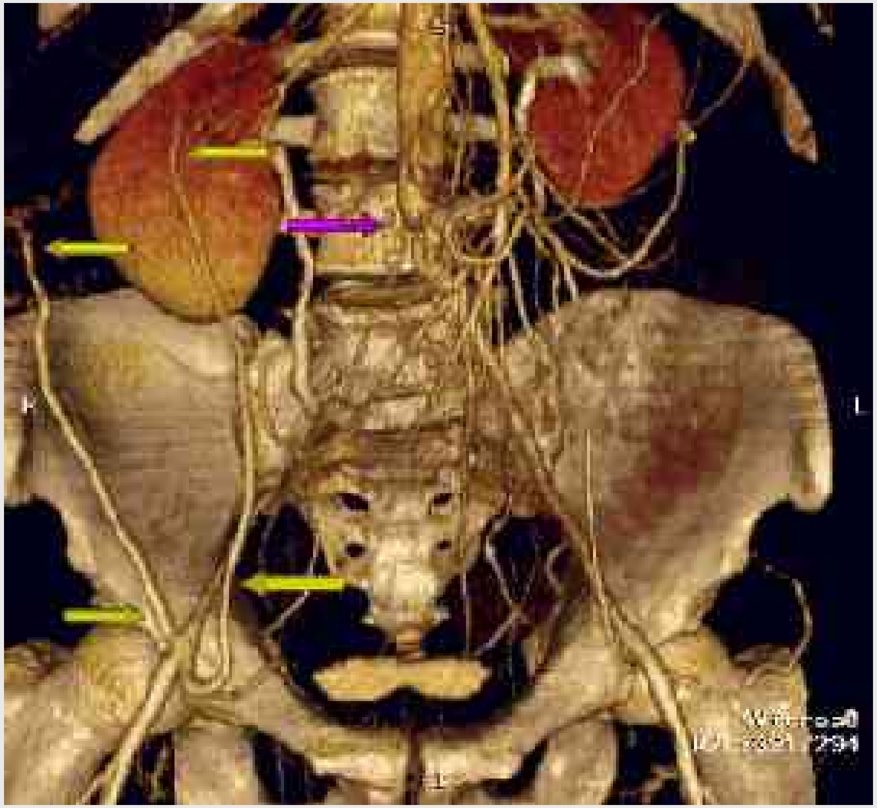


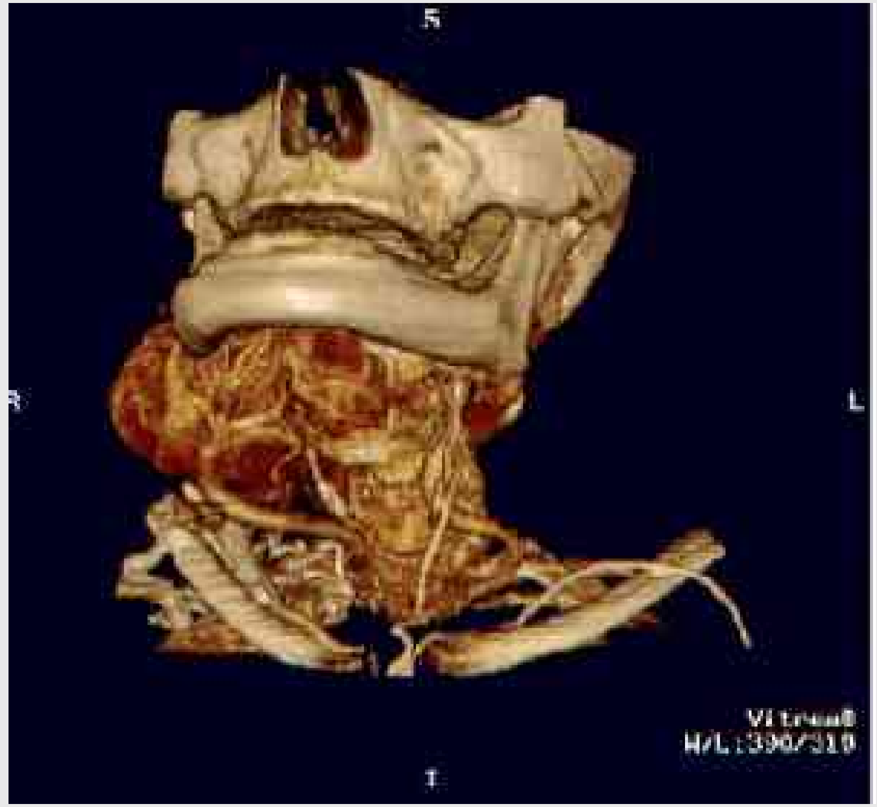
Χομπυτερ–Αιδεδ Διαγνοσισ

The challenge

How do we do it?

Advanced volume visualization; needs enhancement, segmentation, recognition, validation





Computer Vision techniques:

Image matching

Enhancement

Shape analysis

Motion analysis

Geometric corrections

Colour analysis

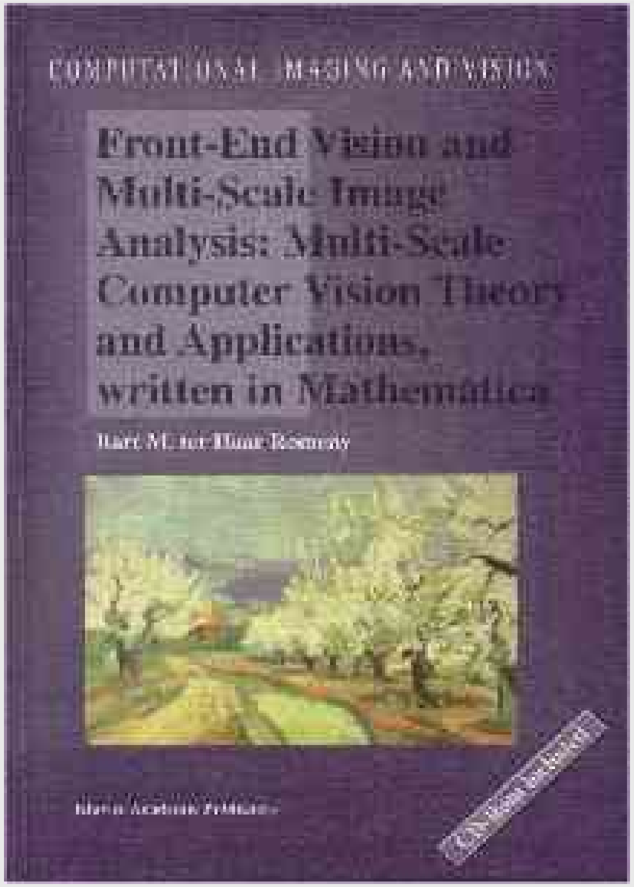
Detection and classification

Texture analysis

Segmentation

Multi-Scale Image Analysis

Biologically inspired computer vision
→ **bio-mimicking**



- National MSc/PhD course
- Conference series

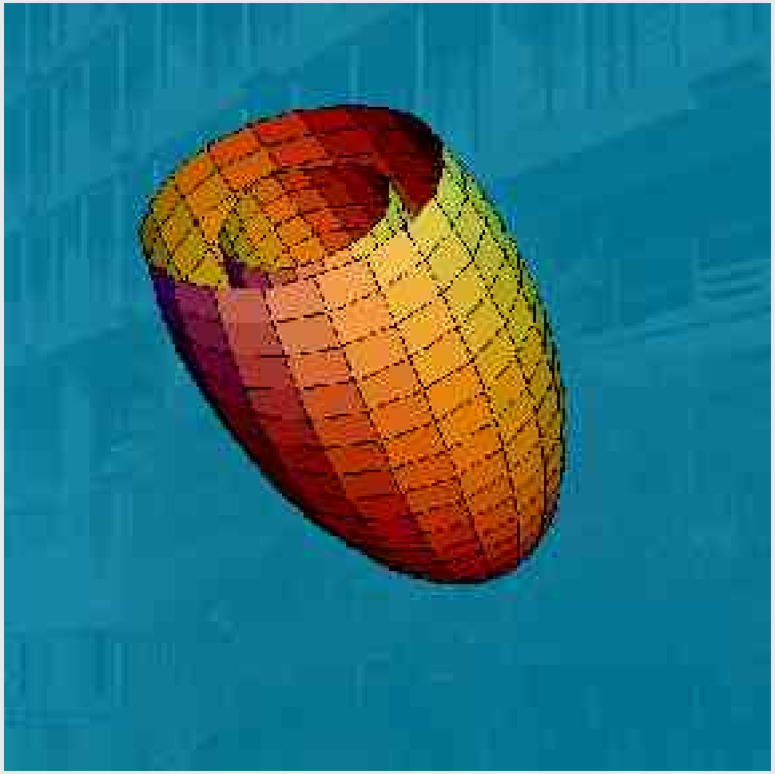
The development language: *Mathematica*

Mathematica is a high level computer algebra environment by Wolfram Inc.

- Ideal for student use for algorithm prototyping
- Full *symbolic* functionality, complete
- Fast *numerical* functionality
- A steep learning curve, training < 1 week
- Interpreter, typically very short code
- Integration of code and text in ‘notebook’
- Write mathematics as usual (symbols, operators, Greek
- Functional programming & pattern matching
- Platform independent
- Version 5 faster than Matlab

“Here is a paper: read it, implement it, and understand it”

T. Arts, W. Hunter, A. Douglas, A. Muijtjens, and R. Reneman, "Description of the deformation of the left ventricle by a kinematic model", J. Biomechanics, 25(10), 1992.



Ventricular heart motion:
- Prolate ellipsoid
- Rotation, scale, shear
- Matrix operations - transforms
- Done in 1 day

A. Suinesiaputra, TU/e - BME

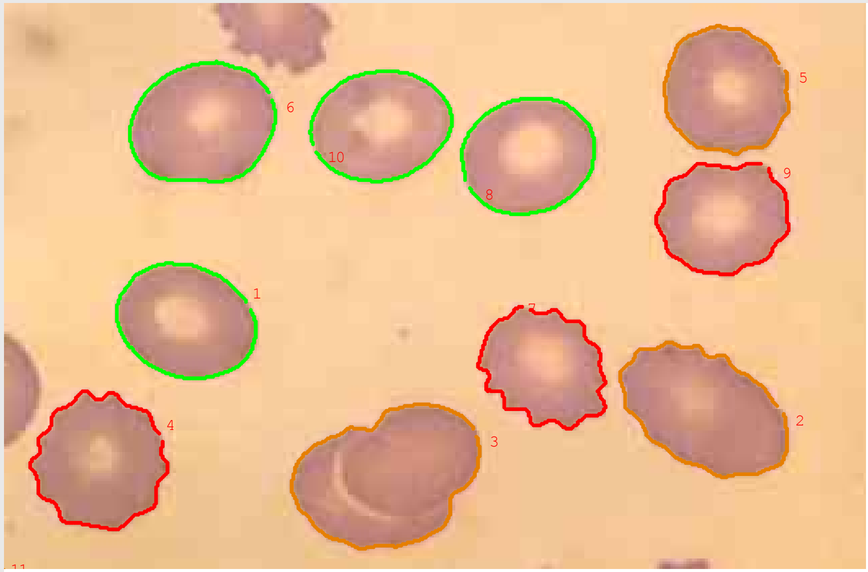
TU/e: strong emphasis on problem-driven projects

Examples BMT student projects :

• 6-week	• 10-weeks	• 3-months
• 50% time	• 50% time	• 50% time
• 2nd year	• 3rd year	• 4th year

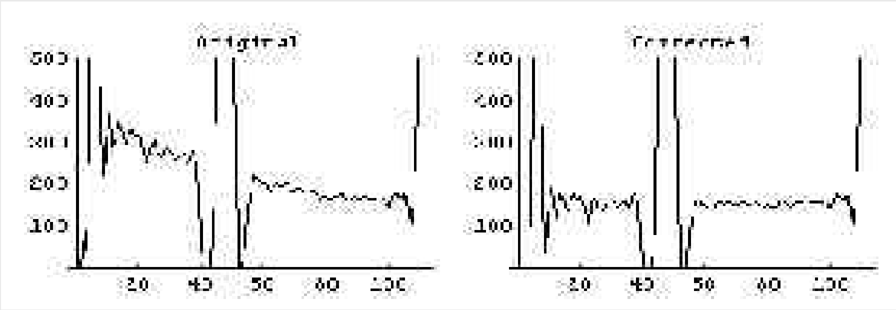
2^{nd} year: 10 groups of 8 students: Image Analysis for Pathology

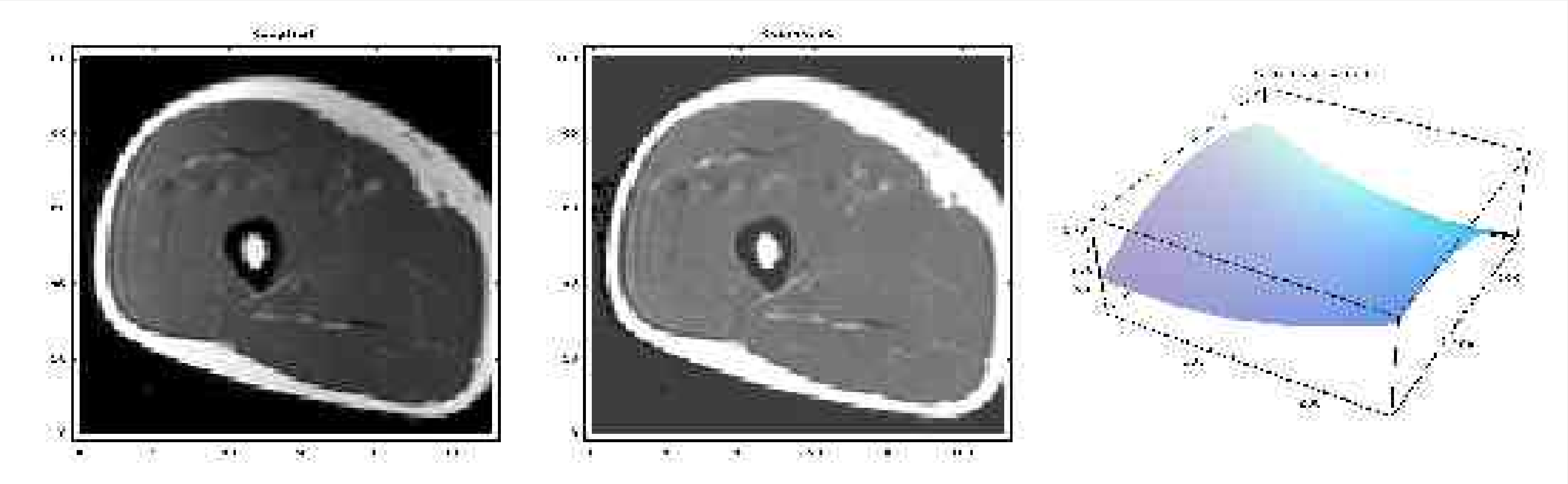
- Task: Find the deviating cells
- “Invent” the method yourself
- Brainstorm sessions
- Competitive
- *Mathematica*: first encounter
- Successfully finished in
  6 weeks half-time



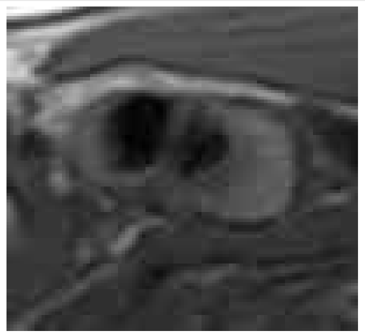
Automatic background correction by entropy minimization

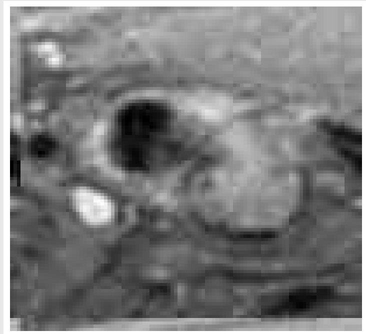
Method: subtract a polynomial surface
$a x + b y + c x y + d x^2 + e y^2$,
gradient descent multivariable coefficient optimization for minimum entropy (p Log p) of the histogram.

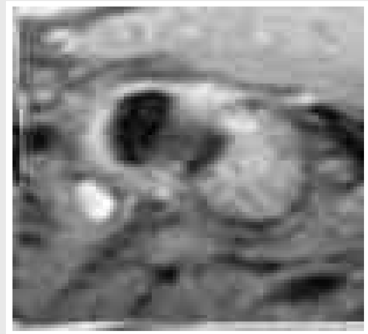




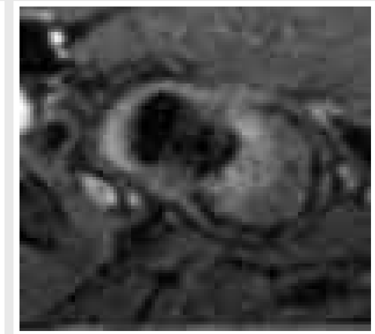
Atherosclerotic plaque classification from multi-spectral data

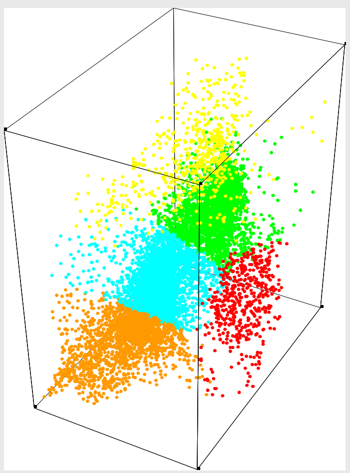

T1 weighted TFE


T1 weighted TSE

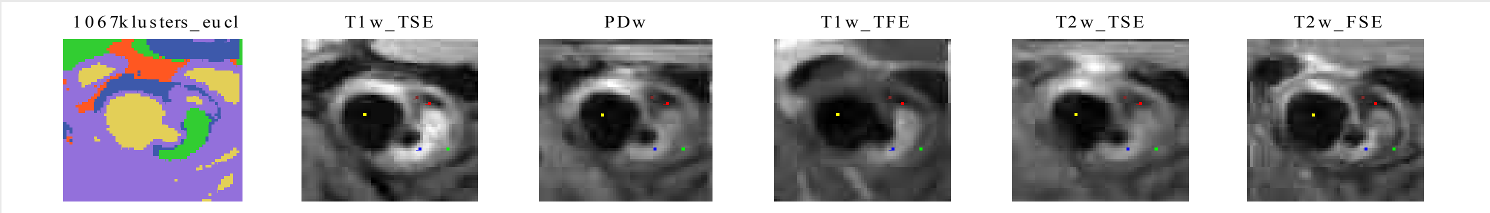

proton density weighted


T2 weighted FSE


T2 weighted TSE



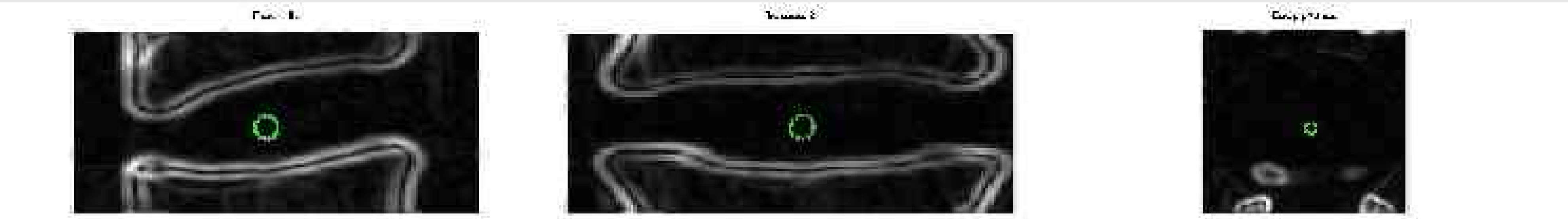
- Cluster analysis in 5-dimensional space



J. Wijnen, TU/e - BMT

Examples of student projects with Mathematica:

- Active contours: intervertebral disk design (with TNO Industry)



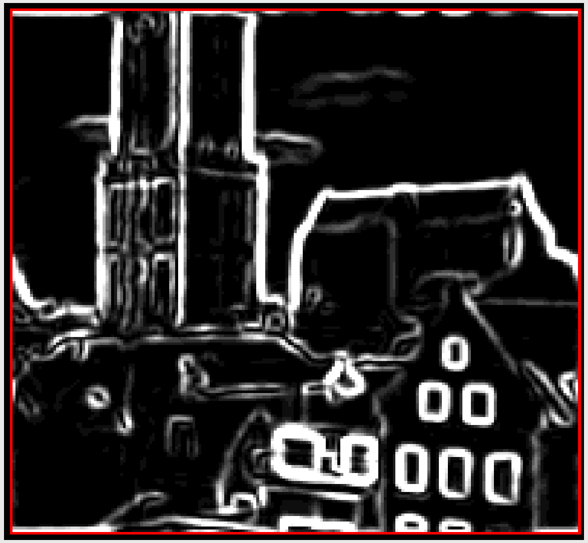
STL model for automated disk manufacture

E. Bennink, TU/e - BME

Differential geometry on images

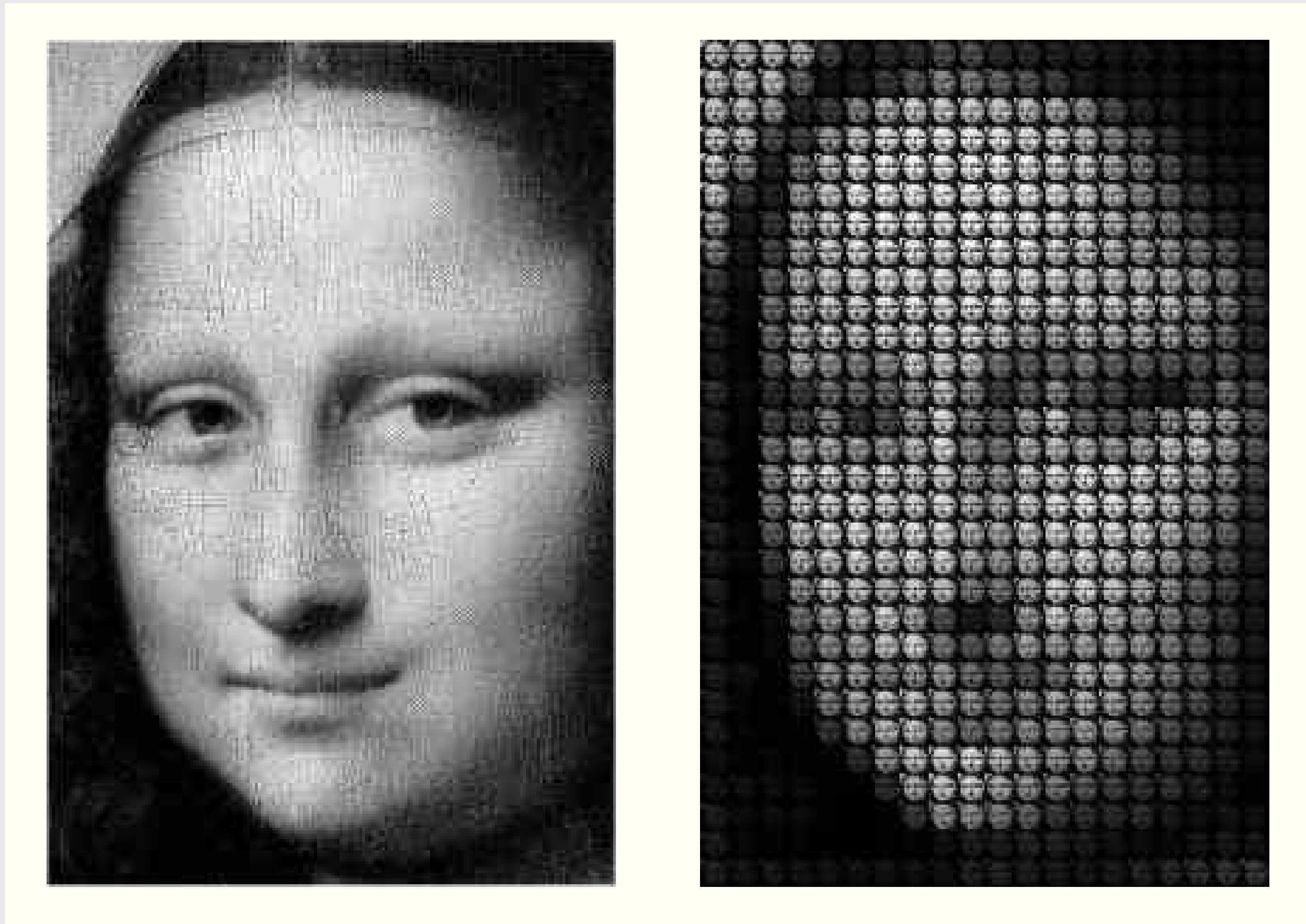
original

Gradient (scale 1 pixel)

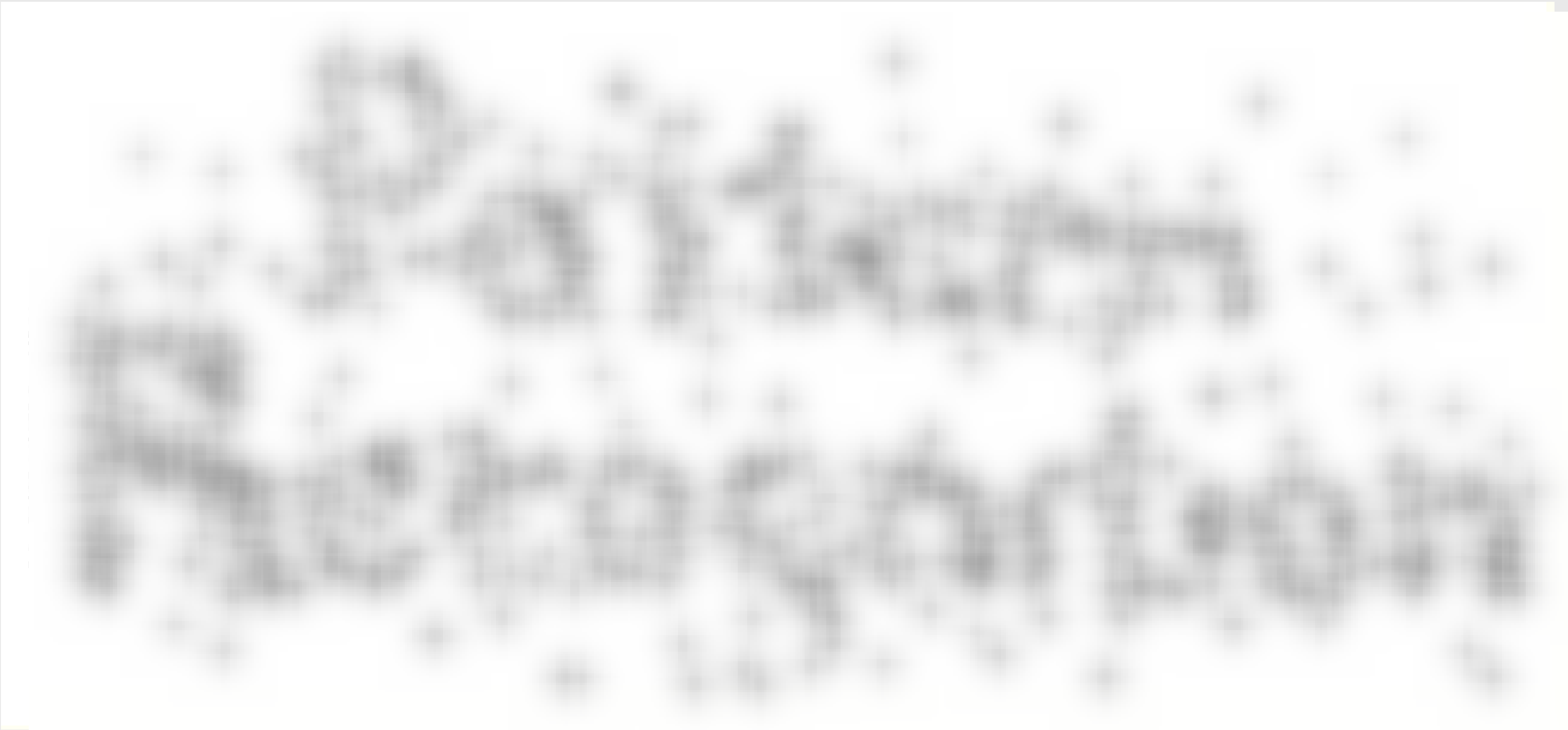


Gradient (scale 4 pixels)

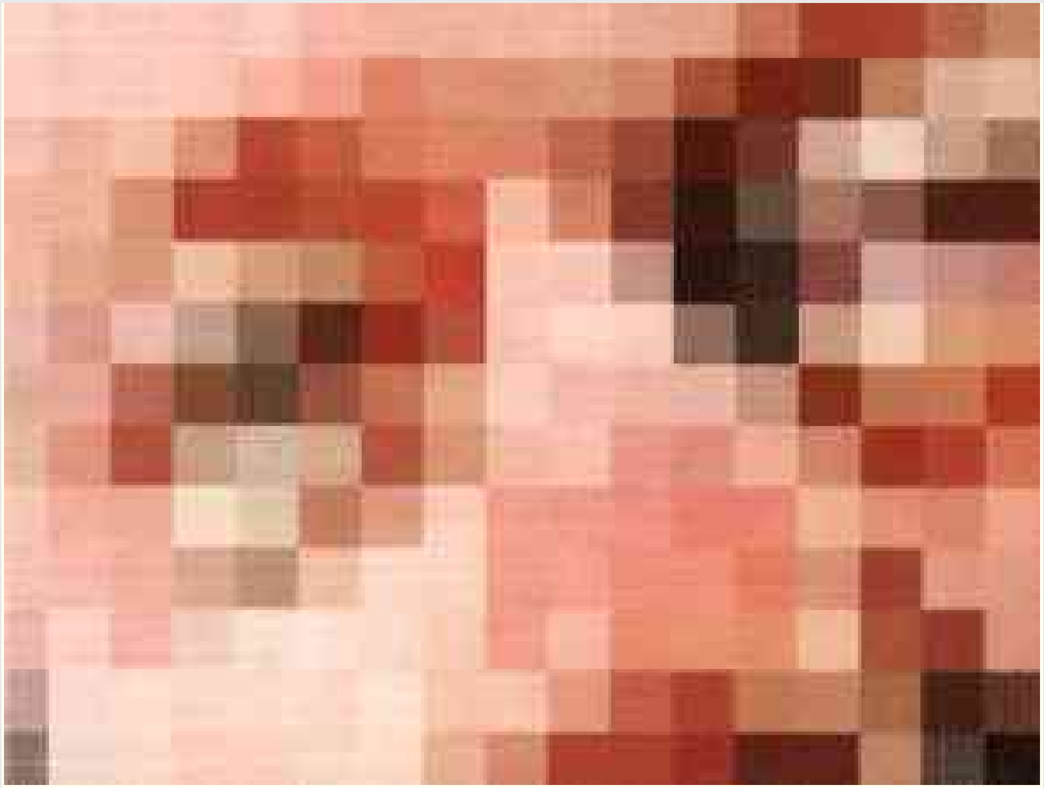
Image structure comes at multiple scales.
Scale induces an image hierarchy.

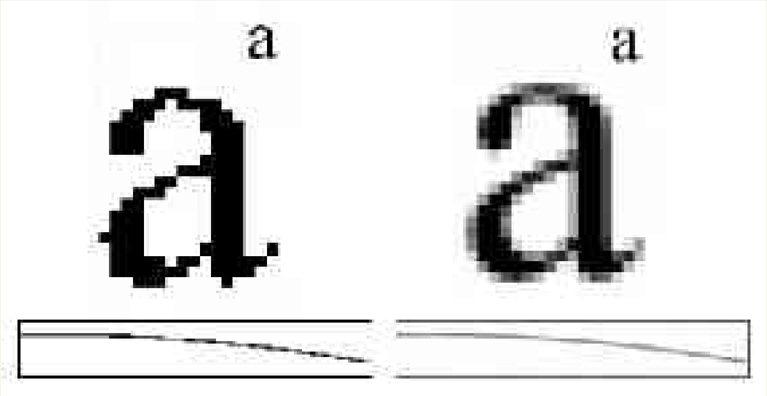


We blur by looking



Scale is embedded in the *task*: do you want the leaves or the tree?





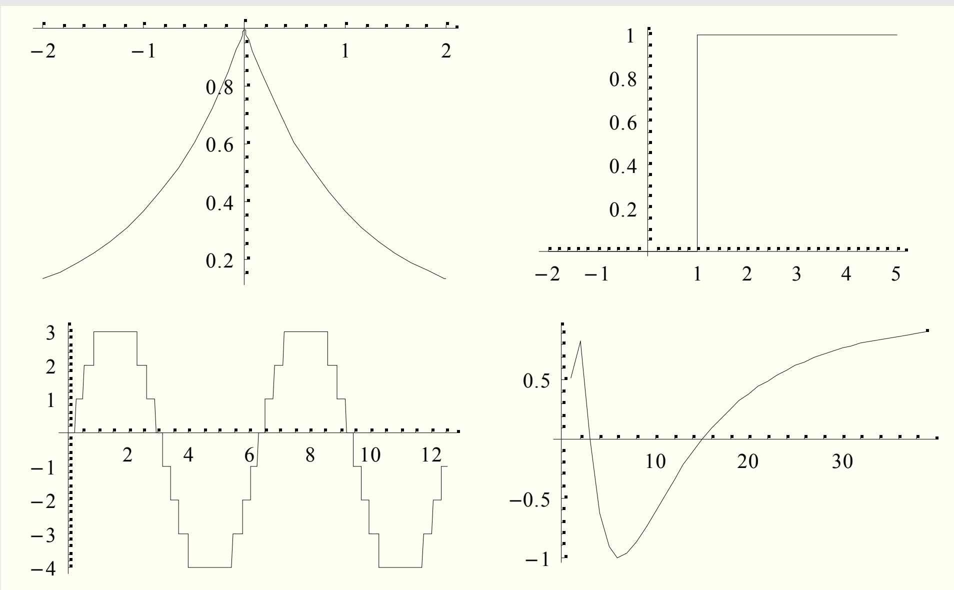
Aliasing,
partial volume effect

‘Spurious resolution’: artefact due to the wrong aperture

What is the best aperture?

Regularization is the technique to make data behave well when an operator is applied to them. A small variation of the input data should lead to small change in the output data.

Differentiation is a notorious function with 'bad behavior'.



Some functions that can not be differentiated.

- smoothing the data, convolution with some extended kernel, like a 'running average filter' or the Gaussian;
- interpolation, by a polynomial (multidimensional) function;
- energy minimization, of a cost function under constraints
- fitting a function to the data (e.g. splines). The cubic splines are named so because they fit to third order;
- graduated convexity [Blake1987];
- deformable templates ('snakes') [McInerney1996];
- thin plates splines [Bookstein1989];
- Tikhonov regularization.

The formal mathematical method to solve the problems of ill-posed differentiation was given by Laurent Schwartz (1950):

A *regular tempered distribution* associated with an image is defined by the action of a *smooth test function* on the image.

$$T_L = \int_{-\infty}^{\infty} L(x)\, \phi(x)\, dx$$

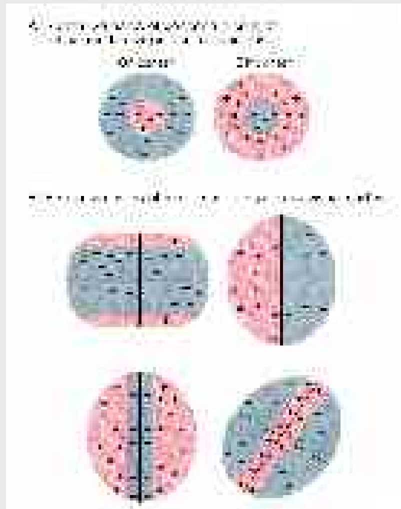
The derivative is:

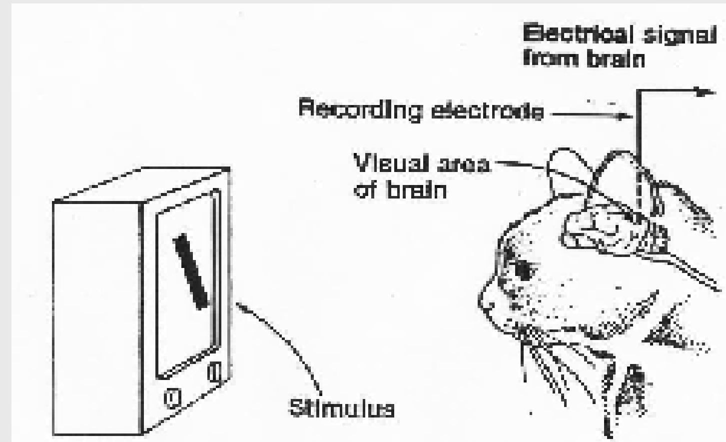
$$\partial_{i_1 \ldots i_n} T_L = (-1)^n \int_{-\infty}^{\infty} L(x)\; \partial_{i_1 \ldots i_n} \phi(x)\; dx$$

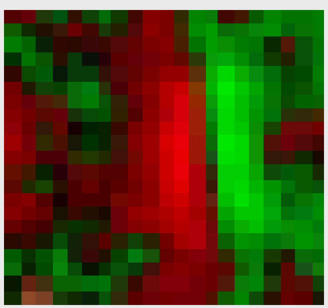
Laurent Schwartz (1915 -)

Fields Medal 1950 for his work on the theory of distributions.
Schwartz has received a long list of prizes, medals and honours in addition to the Fields Medal. He received prizes from the Paris Academy of Sciences in 1955, 1964 and 1972. In 1972 he was elected a member of the Academy. He has been awarded honorary doctorates from many universities including Humboldt (1960), Brussels (1962), Lund (1981), Tel-Aviv (1981), Montreal (1985) and Athens (1993).

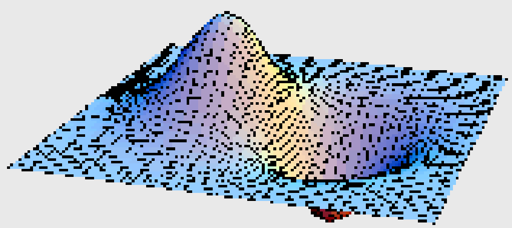
Simple cell sensitivity profiles in V1







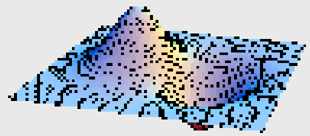
Model:
several orders
Gaussian
derivatives

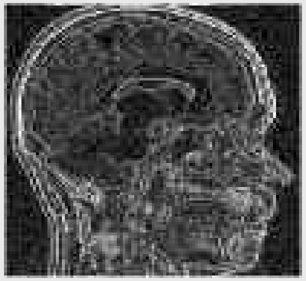


Receptive fields measure
spatio-temporal structure

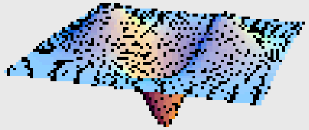
differential geometry

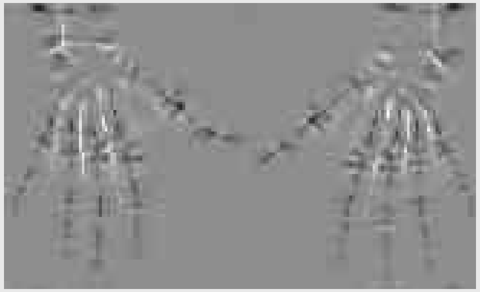
The front-end measures changes in place and time: **derivatives**



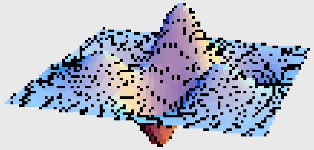


1st order
(edges_





2nd order
(ridges,
curvature)

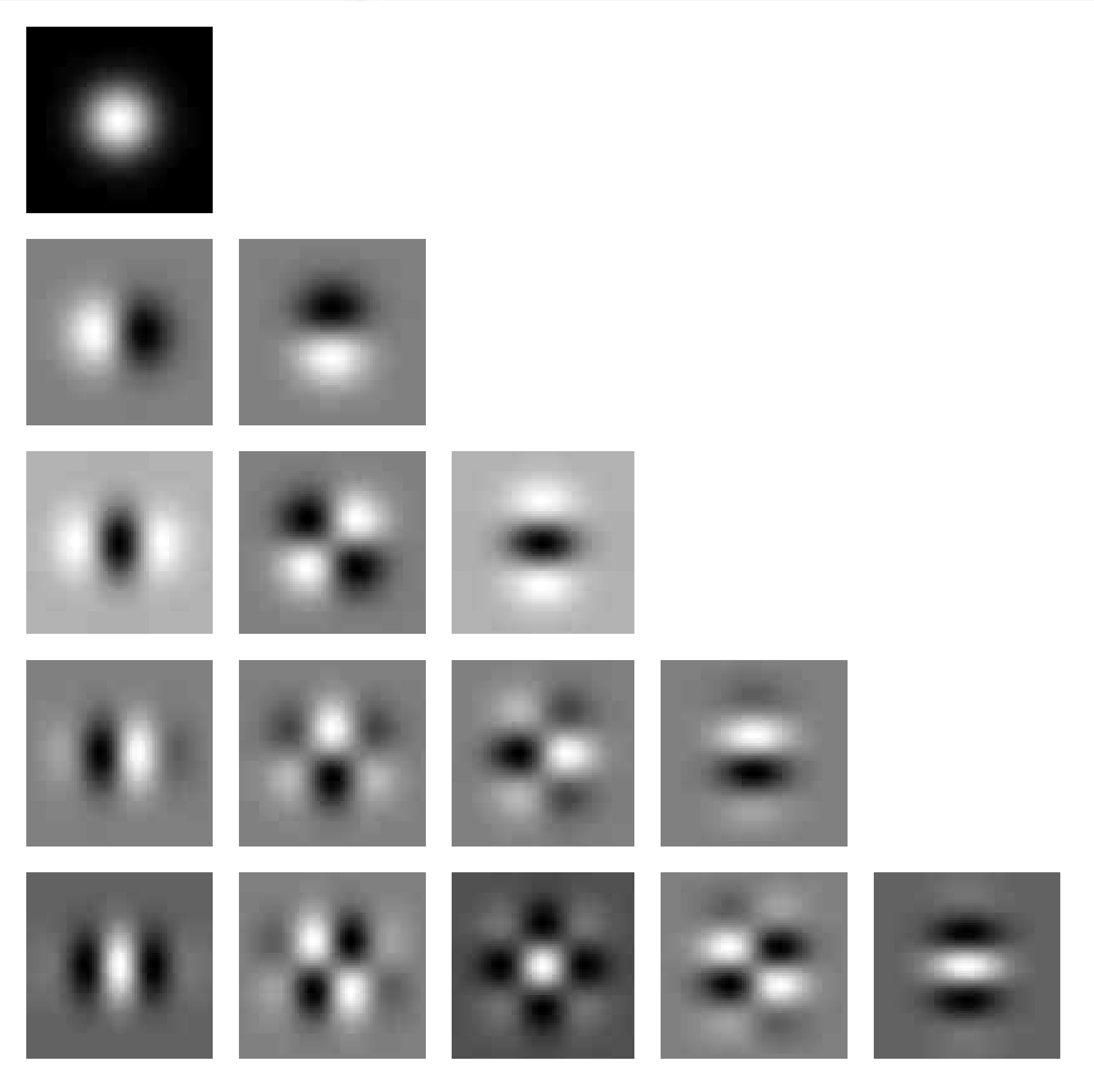


3rd order
(T-junctions)

Rotation *invariant*
T-junction detection:

$$\frac{1}{(L_x^2+L_y^2)^3}\Big(-L_{xxy}L_y^5+L_y^4\left(2L_{xy}^2-L_x(L_{xxx}-2L_{xyy})+L_{xx}L_{yy}\right)+$$
$$L_x^4\left(2L_{xy}^2-L_xL_{xxy}+L_{xx}L_{yy}\right)+L_x^2L_y^2\left(3L_{xx}^2-8L_{xy}^2+L_x(-L_{xxx}+L_{xyy})-4L_{xx}L_{yy}+3L_{yy}^2\right)+$$
$$L_xL_y^3\left(6L_{xy}(L_{xx}-L_{yy})+L_x(L_{xxy}-L_{yyy})\right)+L_x^3L_y\left(6L_{xy}(-L_{xx}+L_{yy})+L_x(2L_{xxy}-L_{yyy})\right)\Big)$$

Mathematics	$\Leftrightarrow$	Smooth test function
Computer vision	$\Leftrightarrow$	Kernel, filter
Biological vision	$\Leftrightarrow$	Receptive field

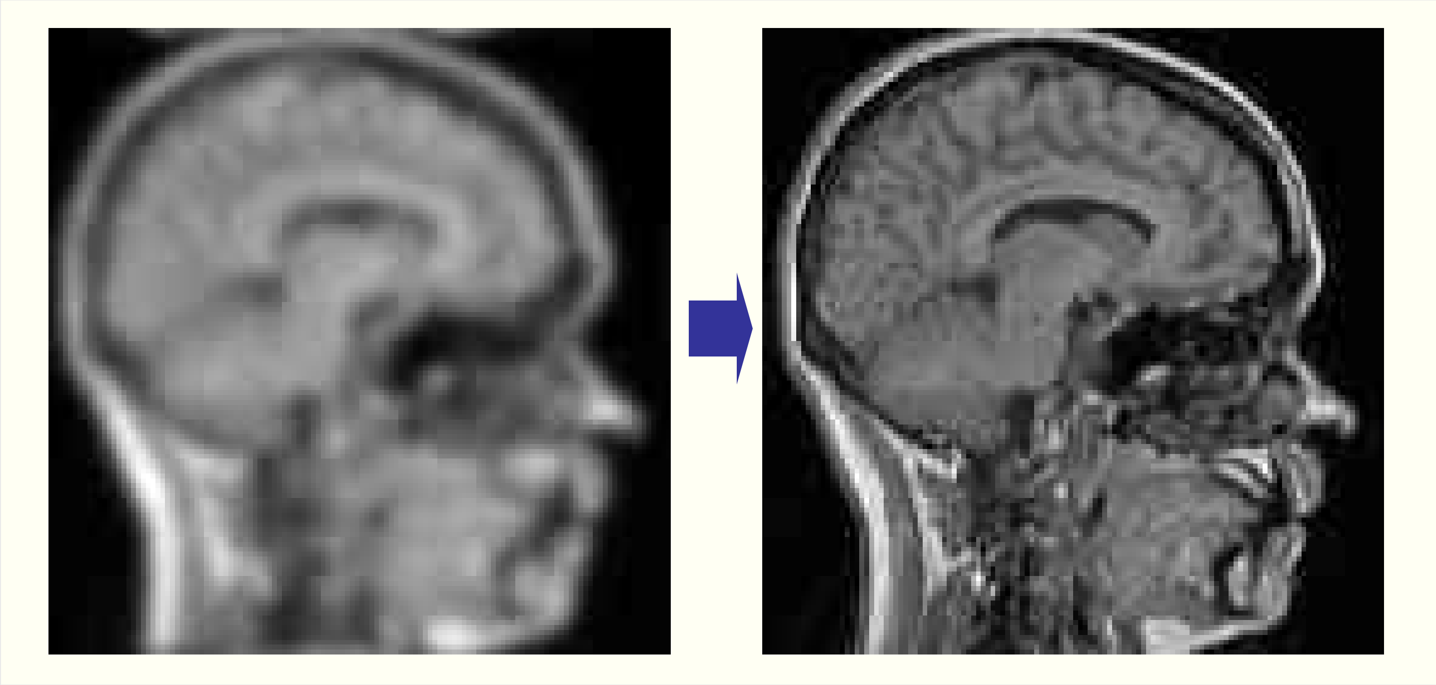


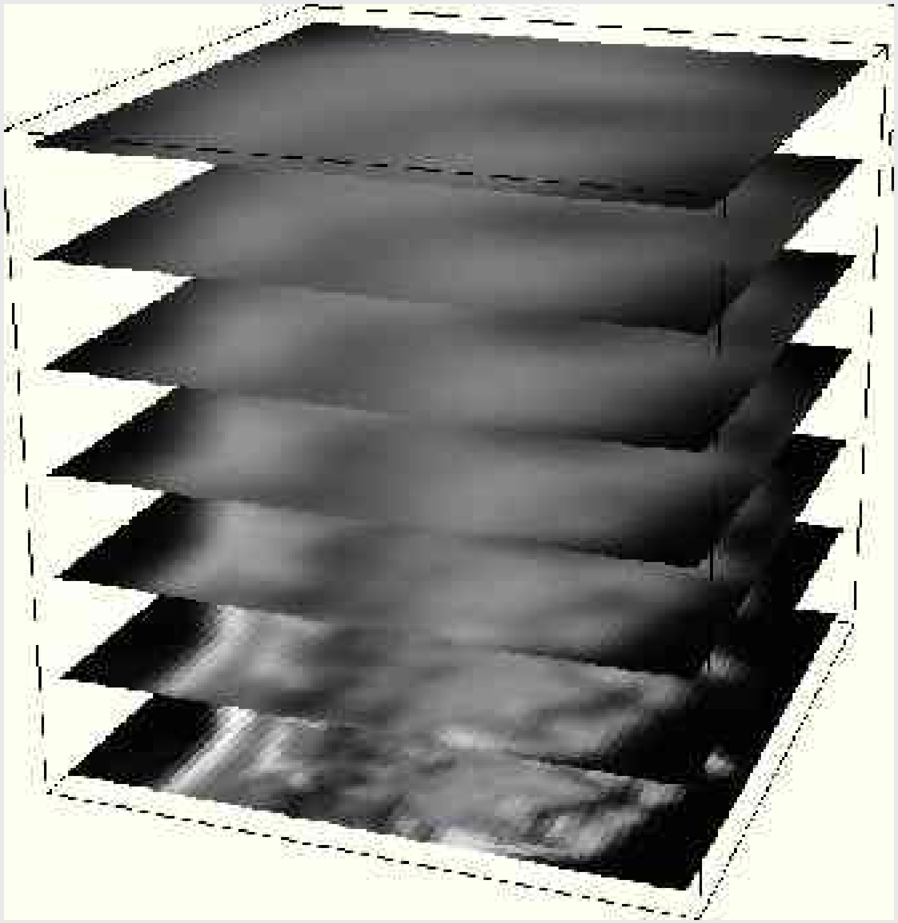
Gaussian derivative profiles up to 4th order

Differentiation becomes integration: ListConvolve

Examples

Deblurring with a multi-scale approach



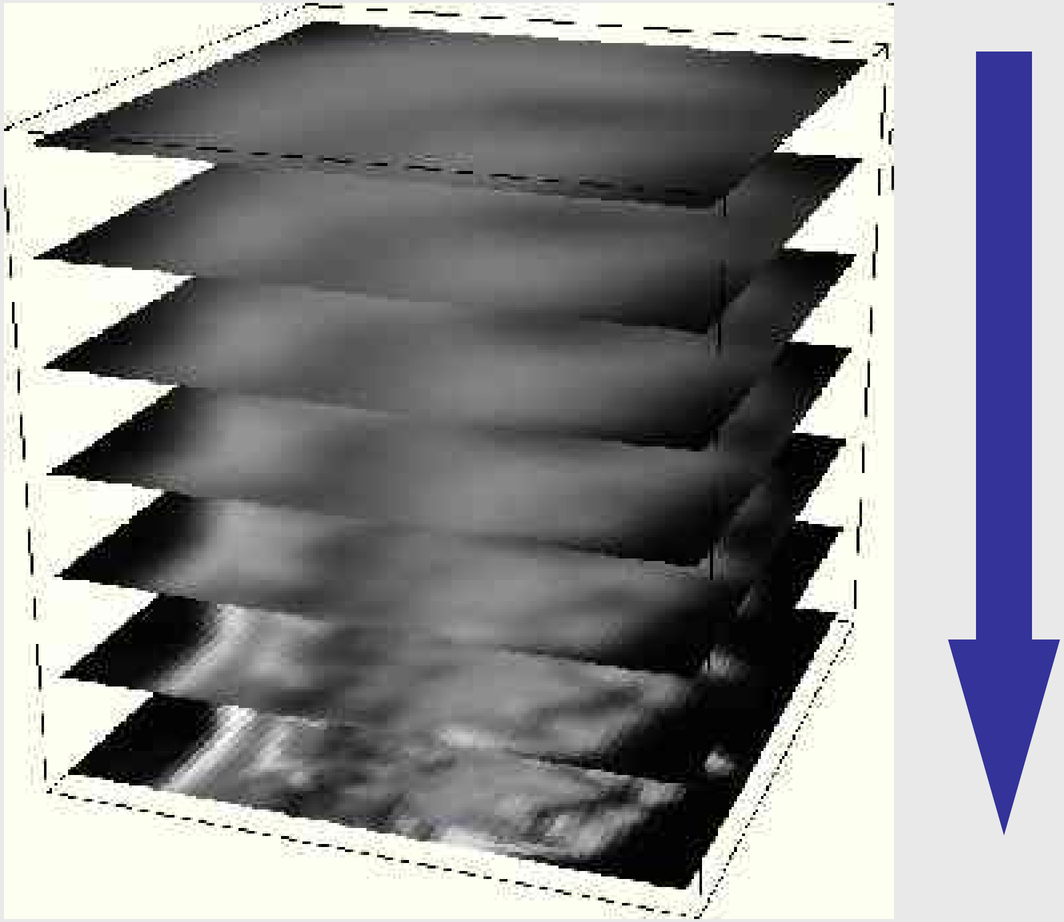


Blurring is described by the diffusion equation:

Diffusion of the intensity over time/scale

Can we inverse the diffusion equation?

Can we inverse the diffusion equation?



We can construct a Taylor expansion of the scale-space in any direction, including the negative scale direction.

Taylor expansion ‘downwards’:

$$L(x, y, s - \delta\mathrm{s}) = L - \frac{\partial L}{\partial s}\,\delta\mathrm{s} + \frac{1}{2!}\,\frac{\partial^2 L}{\partial s^2}\,\delta\mathrm{s}^2 - \frac{1}{3!}\,\frac{\partial^3 L}{\partial s^3}\,\delta\mathrm{s}^3 + O(\delta\mathrm{s})^4$$

The derivatives with respect to s (scale) can be expressed in spatial derivatives due to the diffusion equation

$$\frac{\partial L}{\partial t} = \frac{\partial^2 L}{\partial x^2} + \frac{\partial^2 L}{\partial y^2}$$

$$
\begin{aligned}
& L(x, y, s - \delta s) = \\
& \quad L - \left(\frac{\partial^2 L}{\partial x^2} + \frac{\partial^2 L}{\partial y^2} \right) \delta s + \\
& \quad \frac{1}{2!} \left(\frac{\partial^4 L}{\partial x^4} + 2\, \frac{\partial^4 L}{\partial x^2\, \partial L^2} + \frac{\partial^4 L}{\partial y^4} \right) \delta s^2 - O(\delta s)^3
\end{aligned}
$$

It is well-known that subtraction of the Laplacian sharpens the image. It is the first order approximation of the deblurring process.

Mathematica code:

Replace

```
deblur[im_, order_, σ_] := Module[{expr}, Δ = ∂x,x# + ∂y,y# &;
  expr = Normal[Series[L[x, y, t], {t, 0, order}]] .
    L_^(0,0,1_)[x_, y_, t_] :> Nest[Δ, L[x, y, t], 1];
  expr . L^(n_,m_,0)[x, y, t_] → gD[im, n, m, σ]]
```

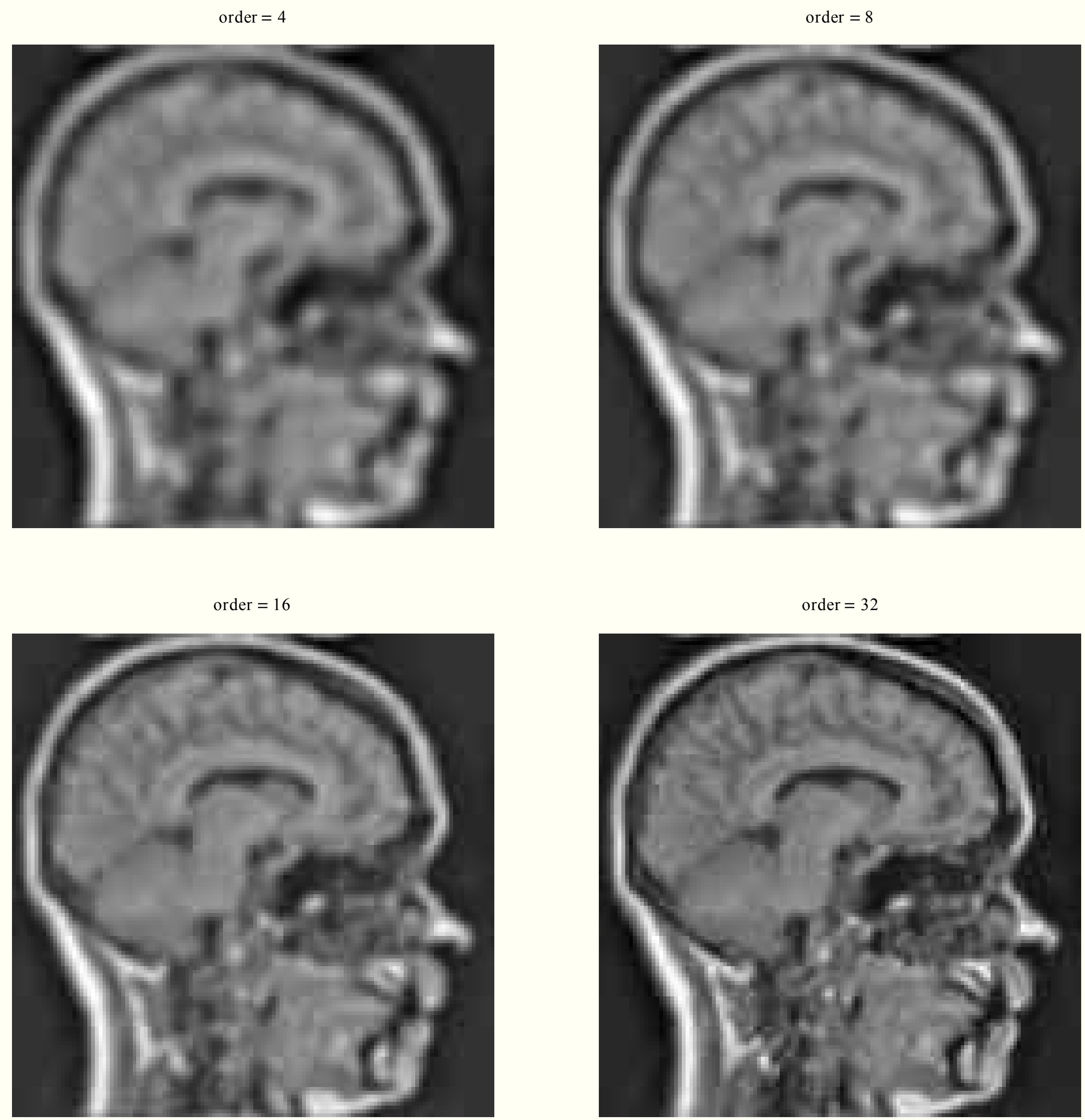
Output:

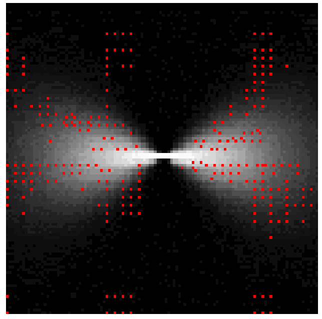
$$\frac{1}{2}\left(-4-\sigma^2\right)(\mathrm{gD}[\mathrm{im}, 0, 2, \sigma]+\mathrm{gD}[\mathrm{im}, 2, 0, \sigma])+\frac{1}{8}\left(-4-\sigma^2\right)^2 (\mathrm{gD}[\mathrm{im}, 0, 4, \sigma]+2\,\mathrm{gD}[\mathrm{im}, 2, 2, \sigma]+\mathrm{gD}[\mathrm{im}, 4, 0, \sigma])+\frac{1}{48}\left(-4-\sigma^2\right)^3 (\mathrm{gD}[\mathrm{im}, 0, 6, \sigma]+3\,\mathrm{gD}[\mathrm{im}, 2, 4, \sigma]+3\,\mathrm{gD}[\mathrm{im}, 4, 2, \sigma]+\mathrm{gD}[\mathrm{im}, 6, 0, \sigma])$$

Deblurring to 4^{th}, 8^{th}, 16^{th} and 32^{nd} order:

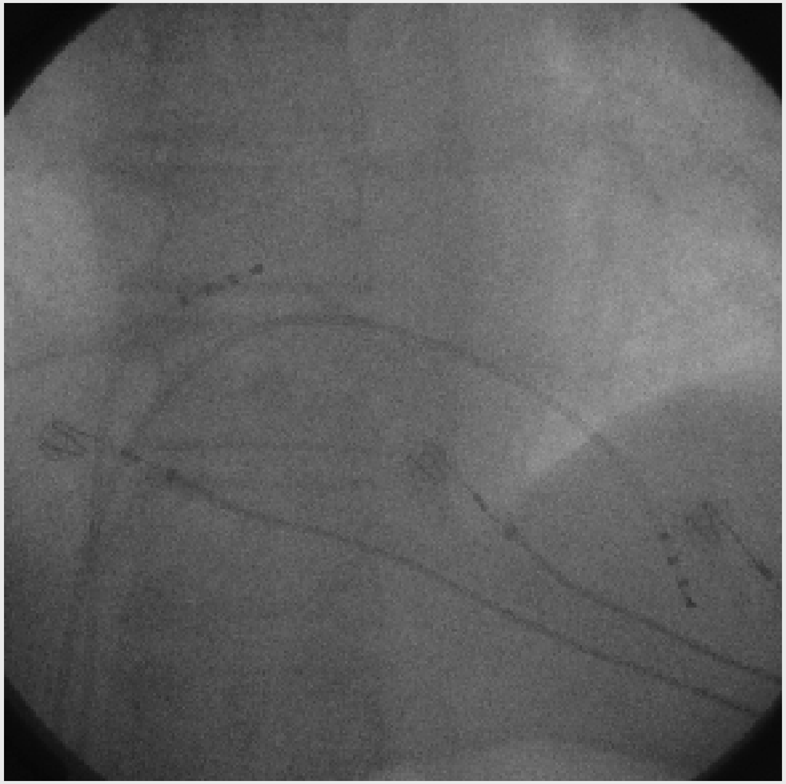
There are 560 derivative terms in the 32^{nd} order expression!
(takes 3 minutes)

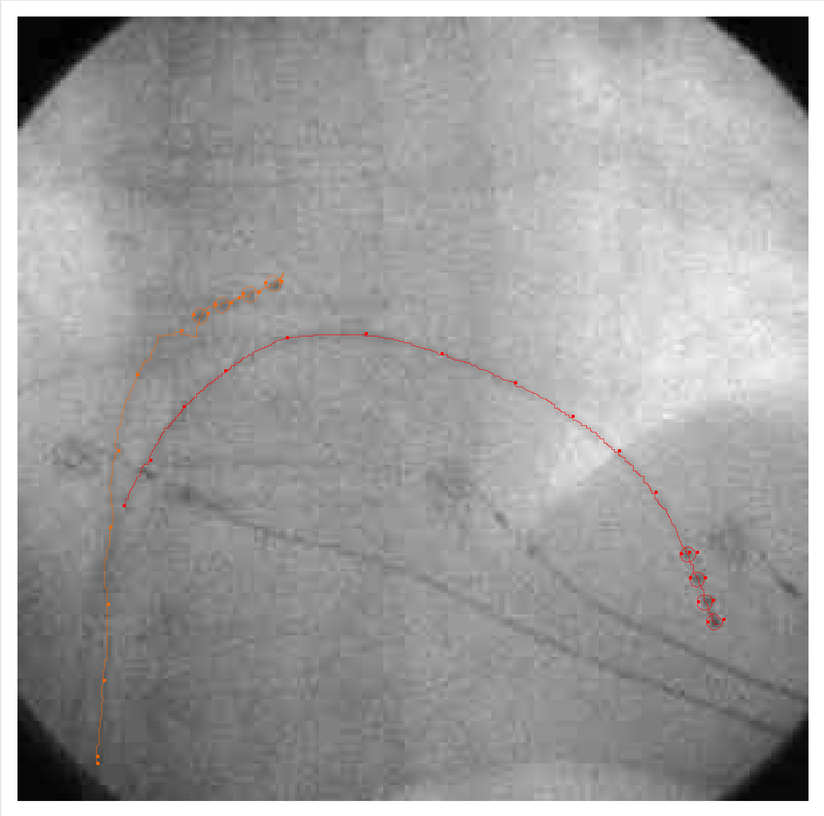
Use:
- Deconvolution in microscopy
- Sharpening MPR
- Removing motion blur





Catheter finding in 1/50 dose fluoroscopy with *context-sensitive* filters





E. Franken, TU/e - BME

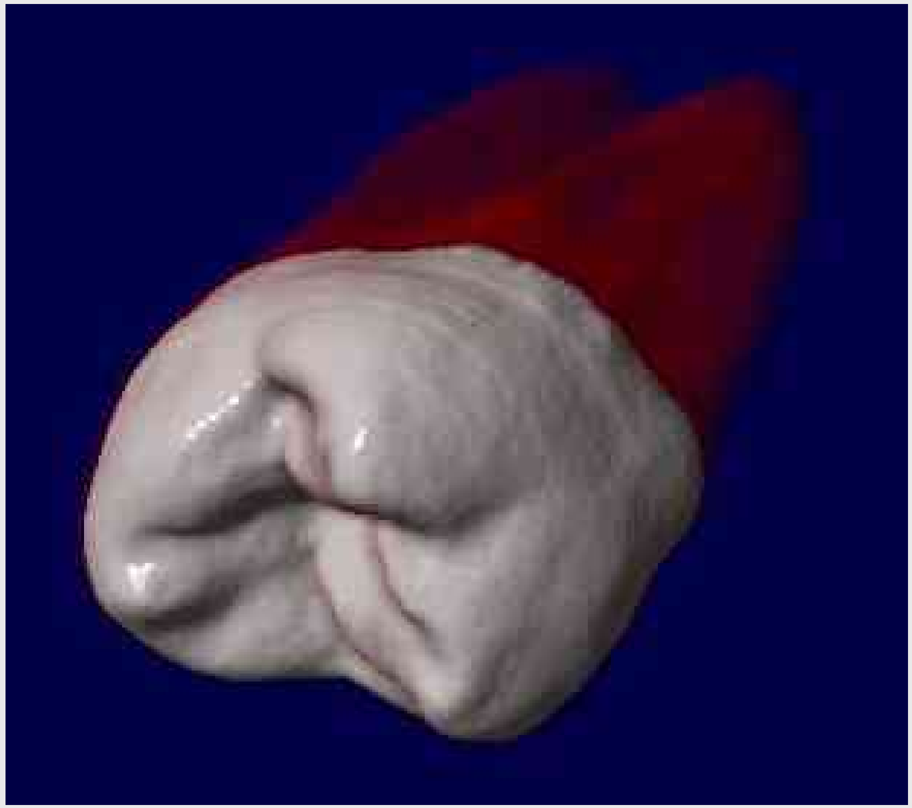
3D Volume Rendering: Shading – Phong illumination

Full illumination model

$$C_0 = C_a \cdot k_a \cdot$$

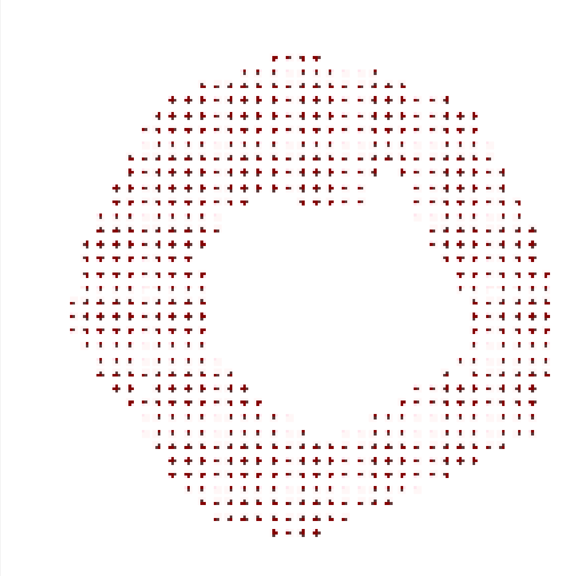
$$k_a \cdot$$

Shading – Shadowfeelers

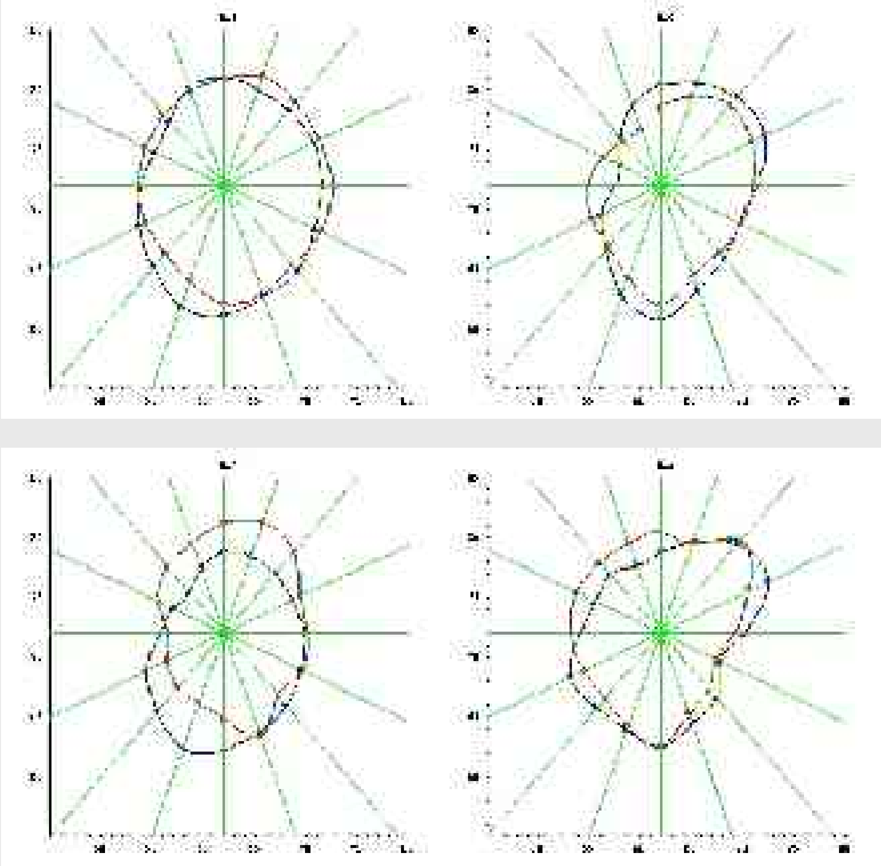


Tooth without shadow
Tooth with shadow

Shape analysis of the infarcted mouse heart



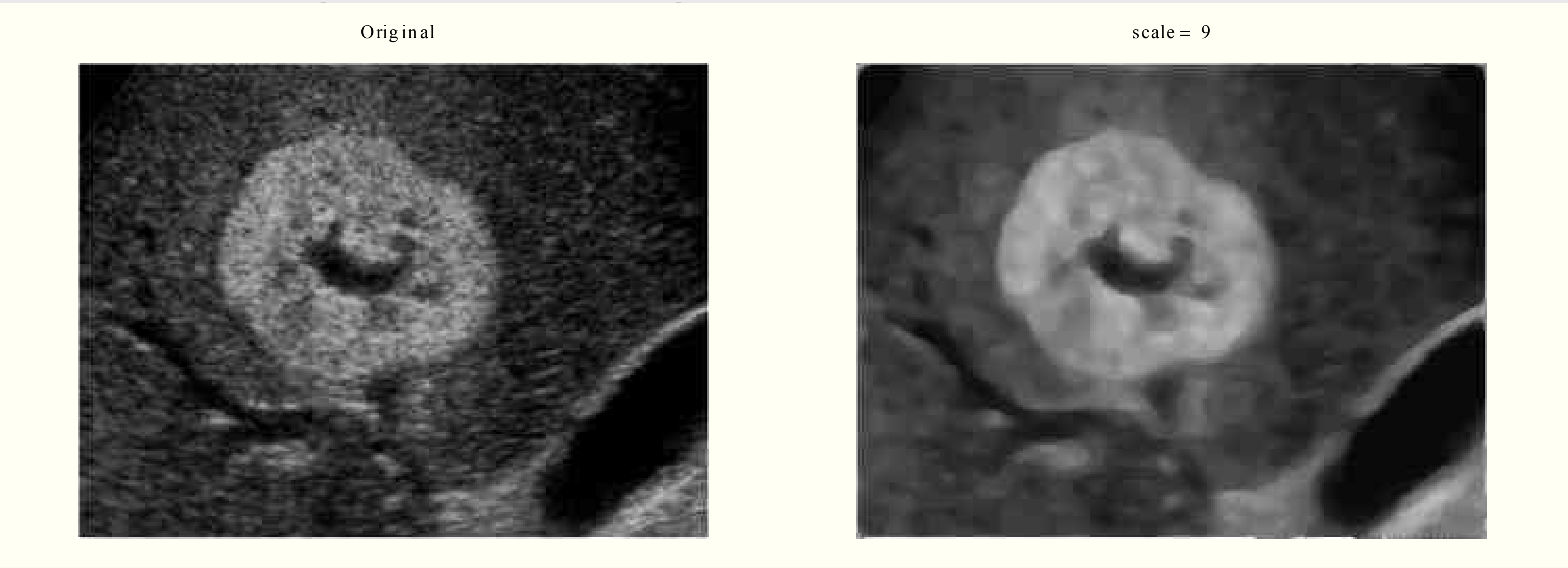
Edwin Heijman, TUE



Stephan Majoor, BMT

Projects successfully build in the MathVisionTools library:

- Image registration by mutual information minimization
- Edge preserving smoothing



Projects successfully built in the MathVisionTools library:

- Image registration by mutual information minimization
- Edge preserving smoothing
- Dense optic flow extraction
- Image recognition by Eigen-images
- Ultrasound multi-scale segmentation
- Vessel enhancement
- Catheter detection in noisy fluoroscopy
- CAD mammography for stellate tumors
- Lung nodule detection
- and many more …

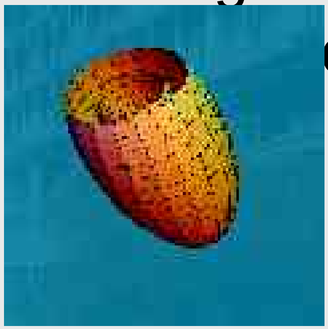
Remote server

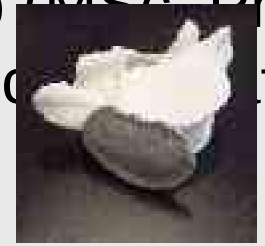
- All 9600 TUE students get a laptop (€ 2000, 50% sponsored)
- Full campus license, on all laptops, home use
- Server with 12 powerful 2.8GHz 2 GB servers
- Accessible from home via VPN
- We slowly expand, next: 64 bit CPU

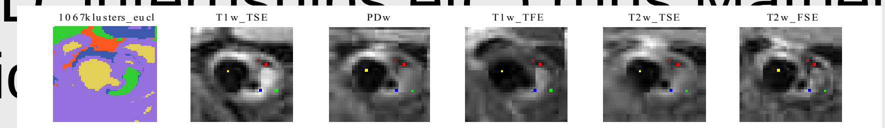
Lecture Saturday, 11:00

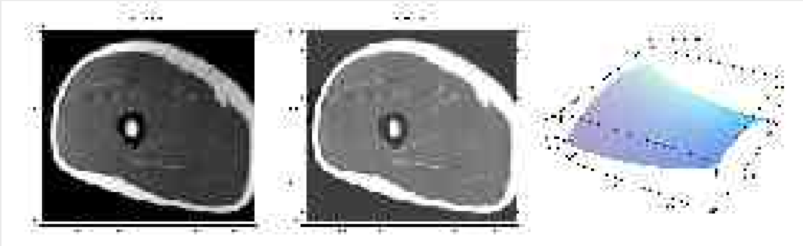
Conclusions:

- *Mathematica* is an ideal environment for algorithm prototyping
- It is fast enough for 2D and 3D and 3D-time image analysis
- Seems 'forgotten' by many after abandoning it some years ago
- Fast development, now faster than Matlab
- In 2.5 years: 35 projects successfully performed
- Full group (MSc, PhD, internships etc.) runs Mathematica



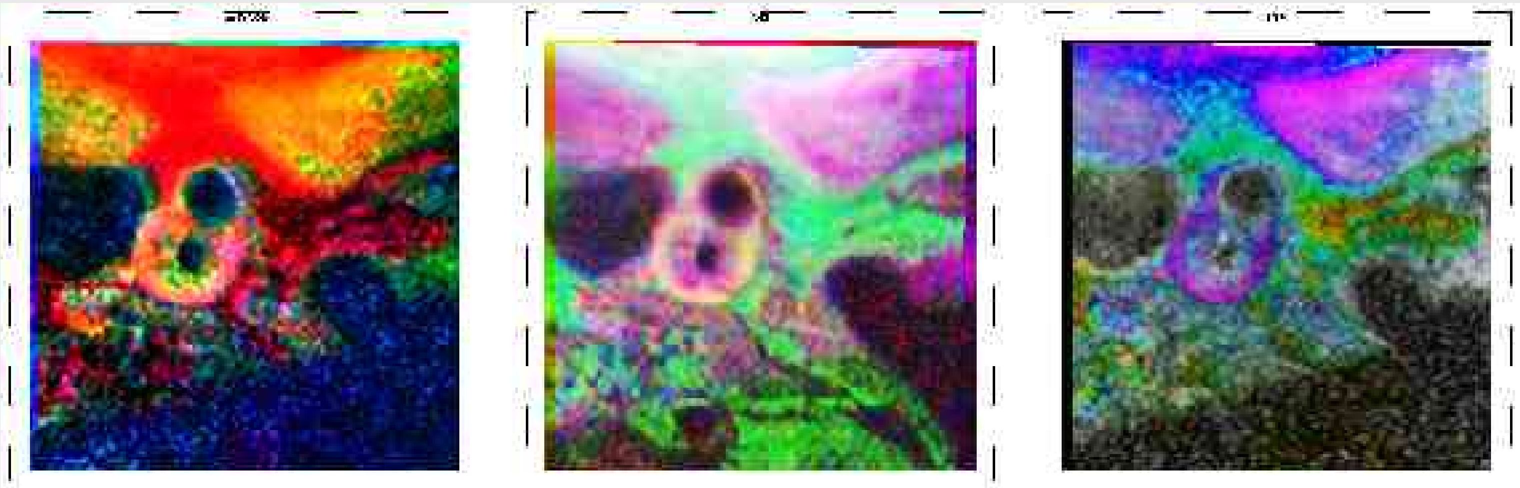






Thank you for your attention

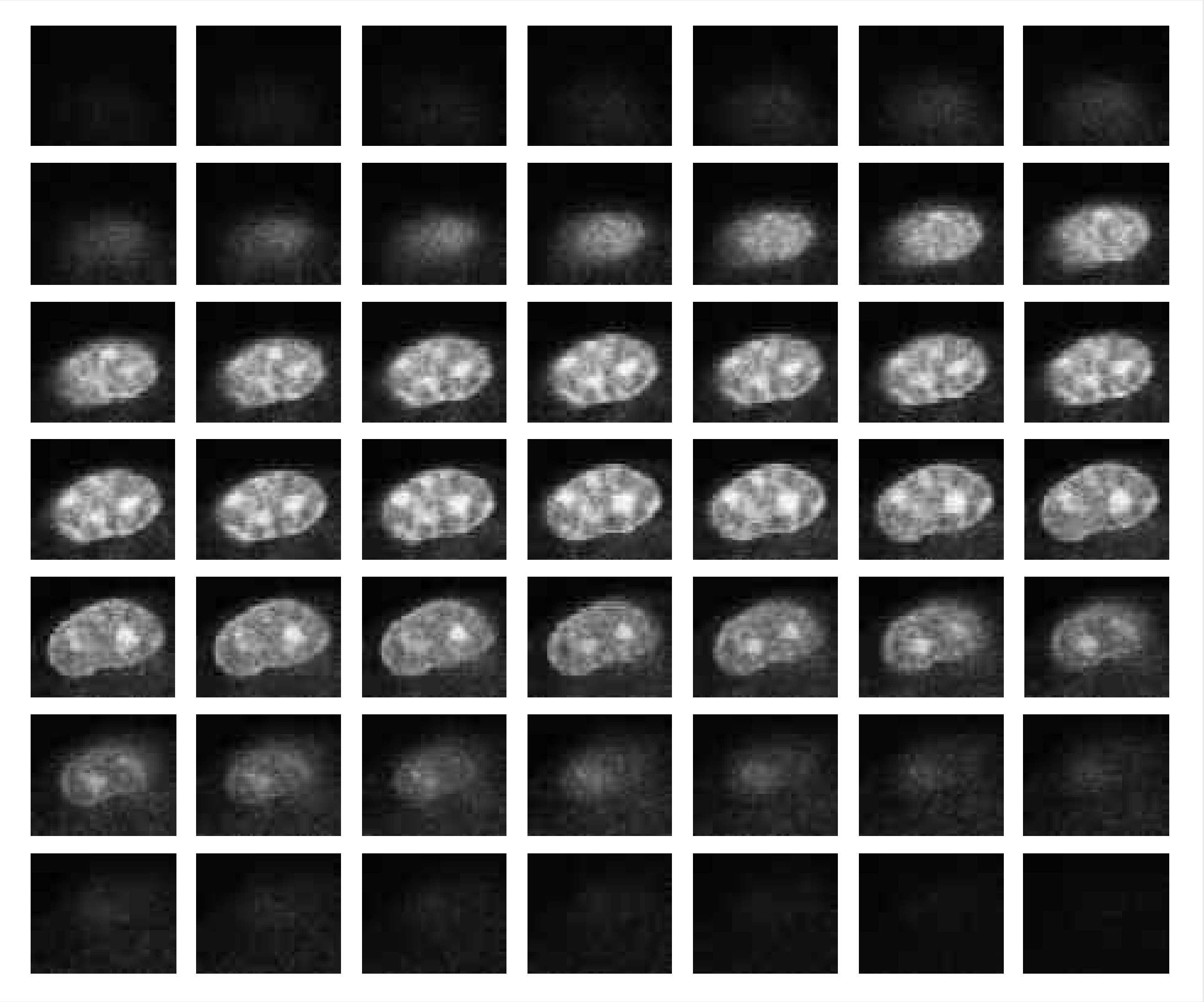
Exploiting our retinal RGB multi-spectral analyzer:



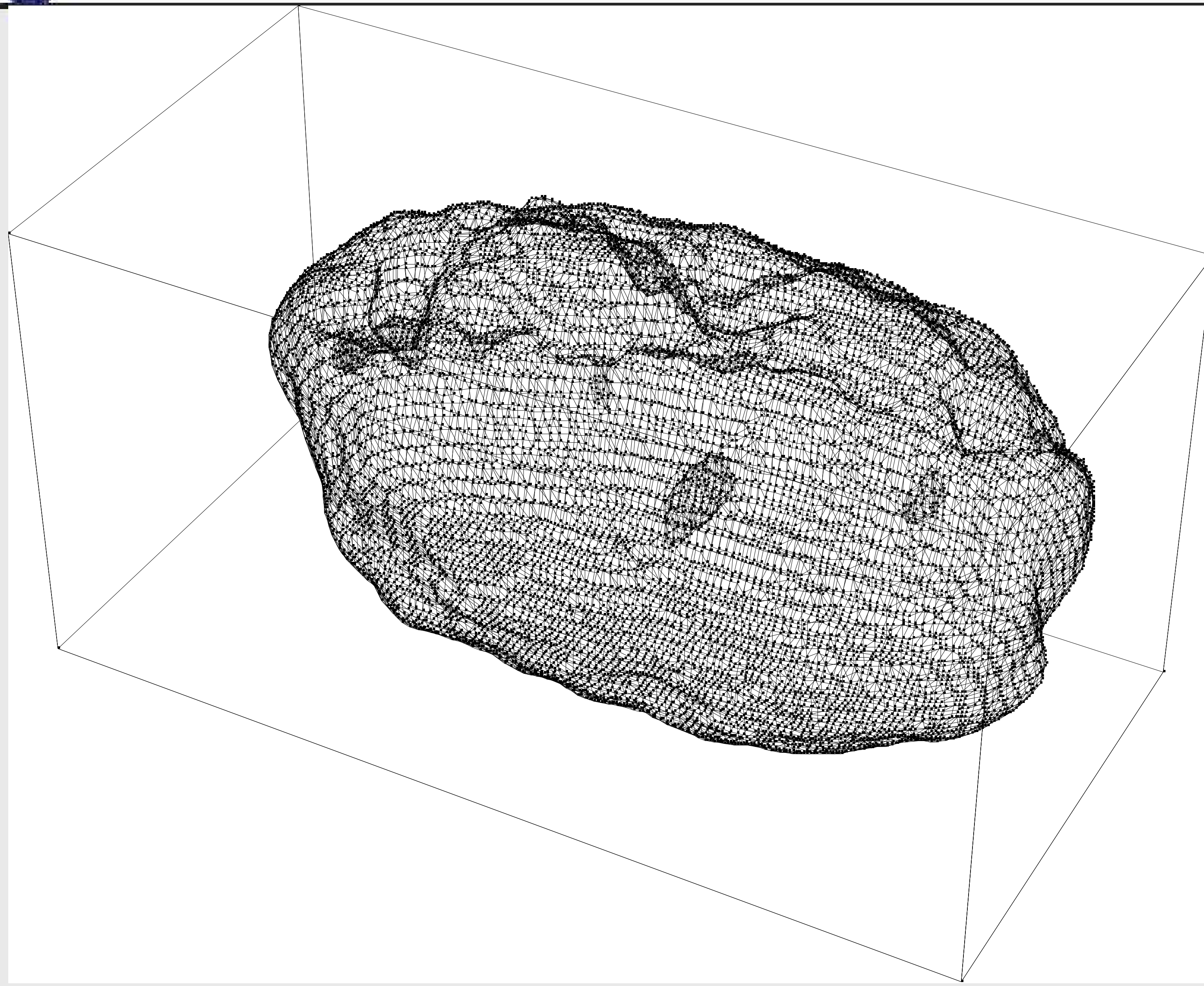
Thijs van Driel
TU/e - BME

What is best color space? Which 3 of 5? Validation of results.

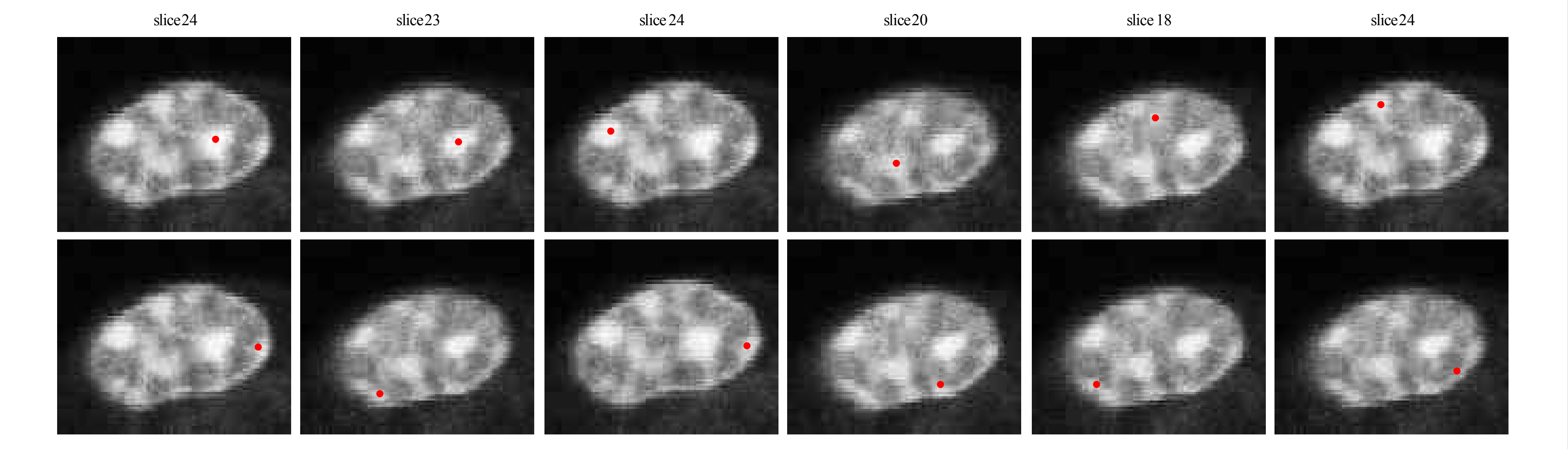
Task: Lysosome detection in a macrophage



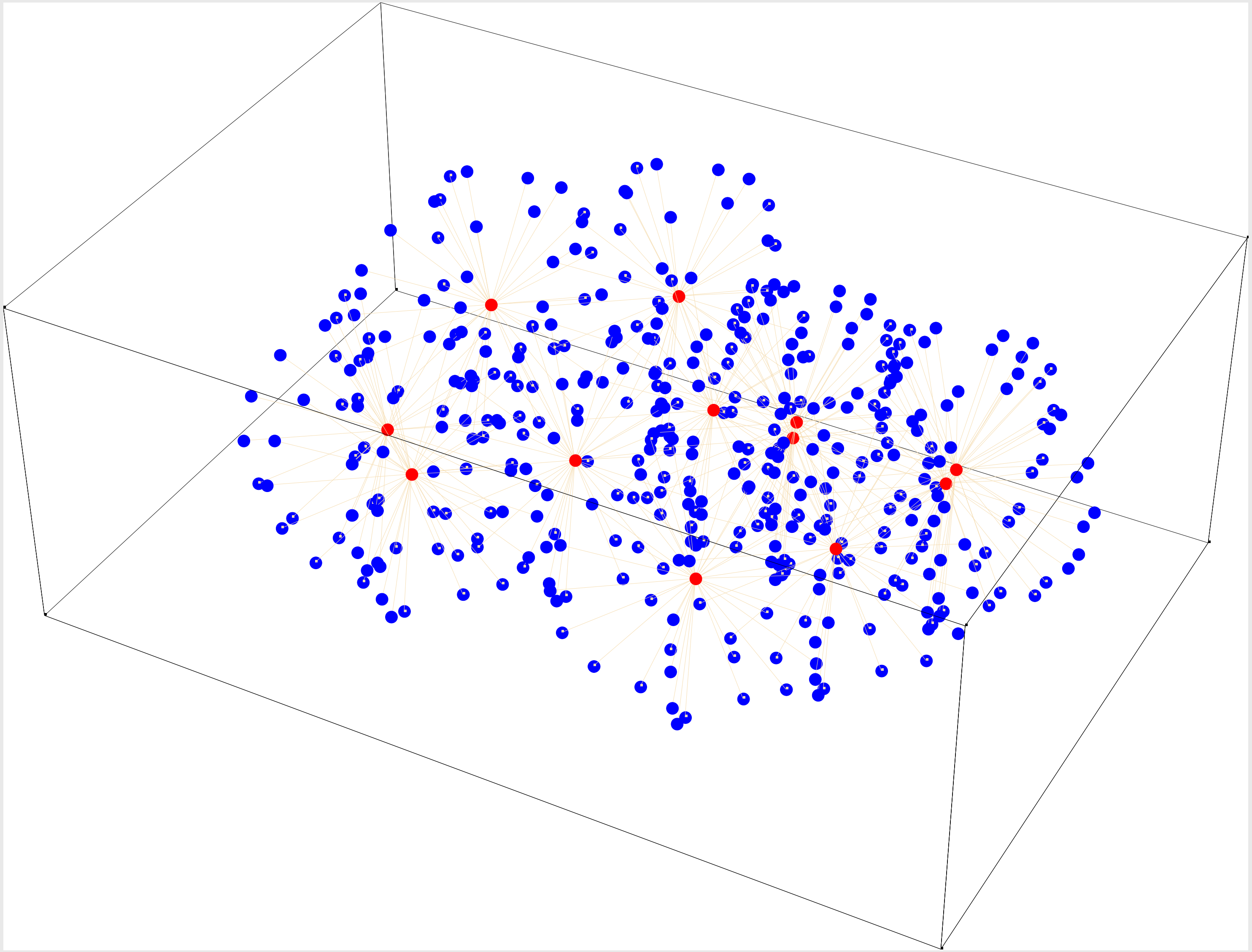
Wim Engels, UM



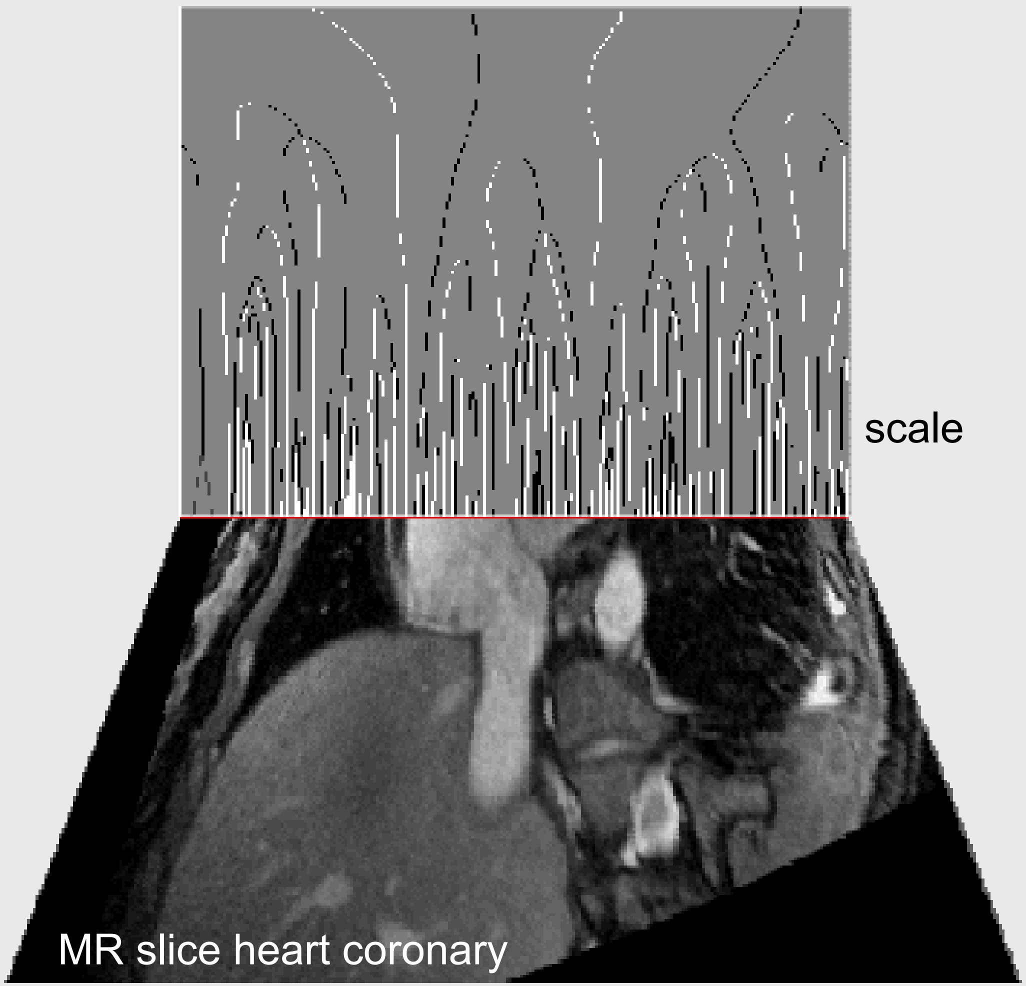
N-Maxima detection:

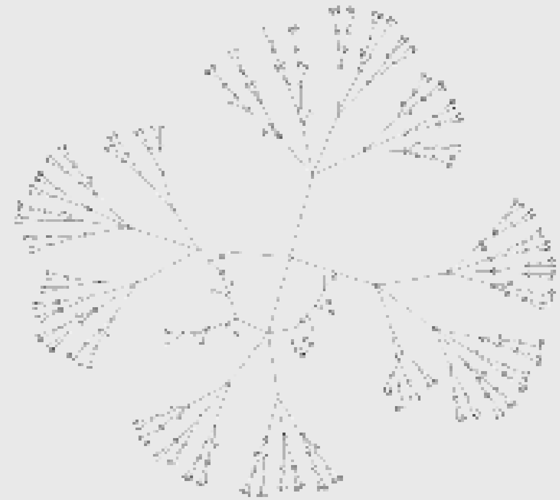


35 profiles in a star of directions are sampled for each maximum



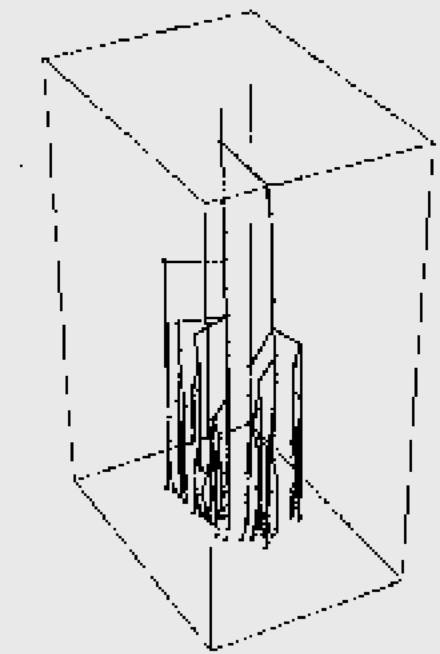
- toppoints



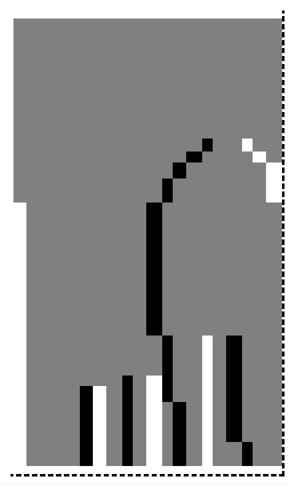


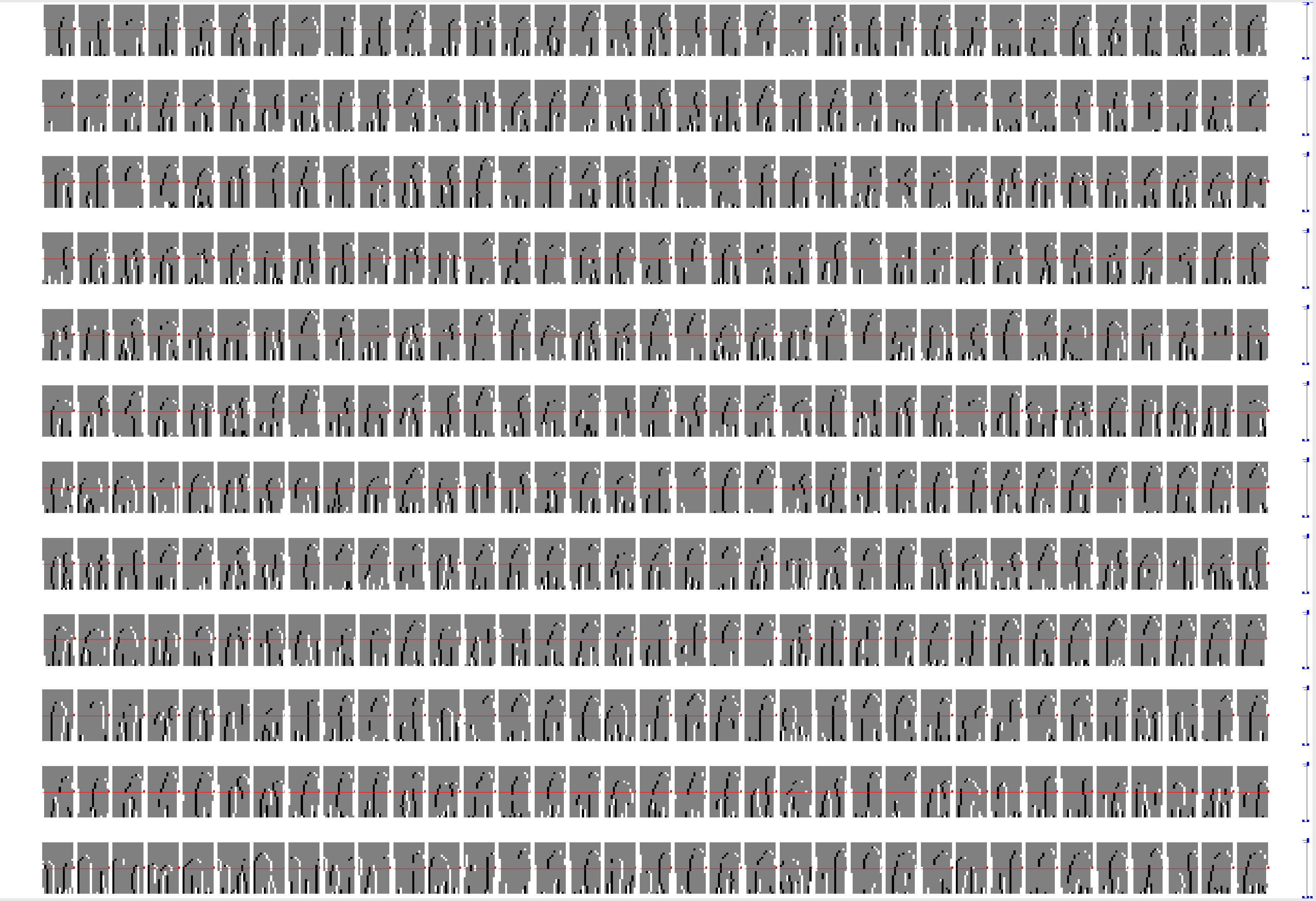
- graph theory

- EC project

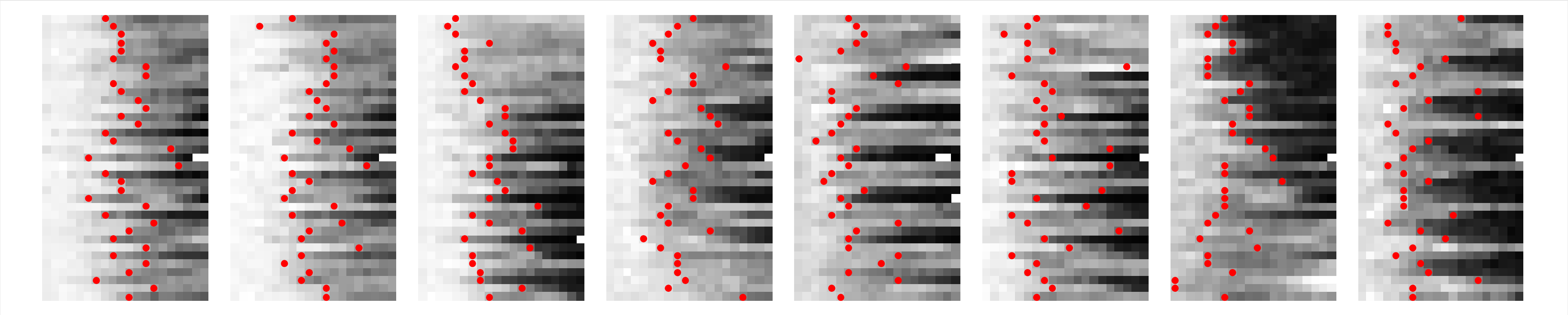


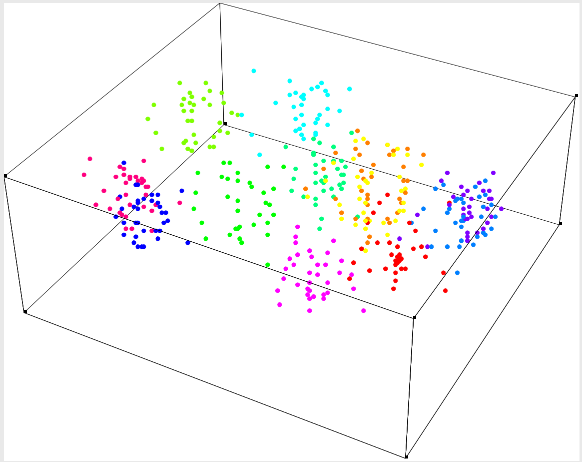
Edge focusing





Noisy edge detection: results





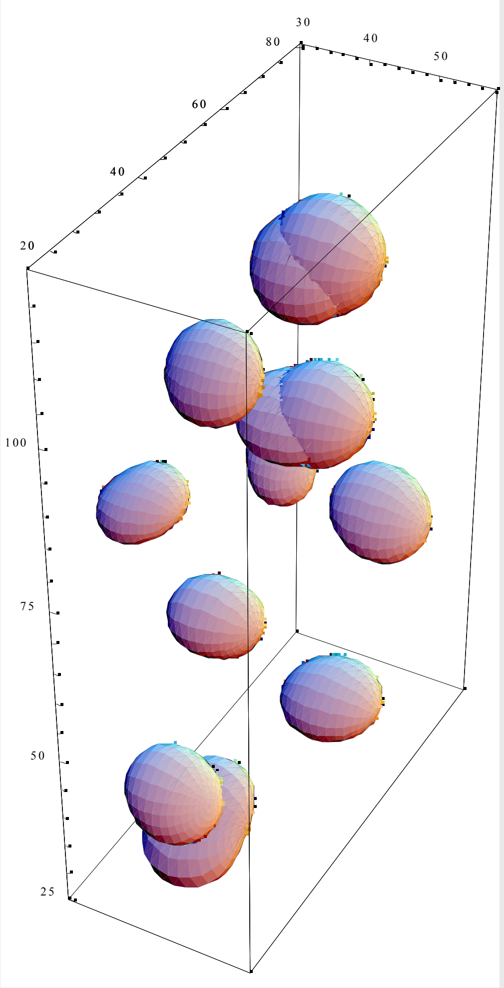
Fitting 3D Spherical Harmonics functions

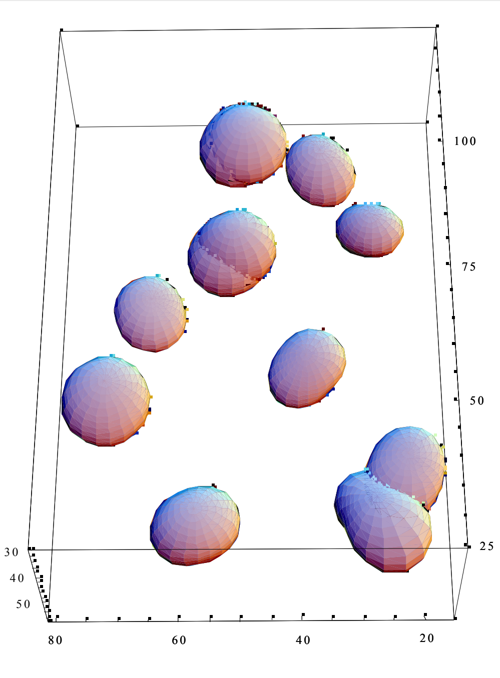
```
order = 2;
fitfunctions = Flatten[Table[SphericalHarmonicY[l, m, θ, ϕ], {l, 0, order}, {m, -l, l, 1}]]
```

$$\left\{\frac{1}{2\sqrt{\pi}},\ \frac{1}{2}e^{-i\phi}\sqrt{\frac{3}{2\pi}}\,\mathrm{Sin}[\theta],\ \frac{1}{2}\sqrt{\frac{3}{\pi}}\,\mathrm{Cos}[\theta],\ -\frac{1}{2}e^{i\phi}\sqrt{\frac{3}{2\pi}}\,\mathrm{Sin}[\theta],\ \frac{1}{4}e^{-2i\phi}\sqrt{\frac{15}{2\pi}}\,\mathrm{Sin}[\theta]^2,\ \frac{1}{2}e^{-i\phi}\sqrt{\frac{15}{2\pi}}\,\mathrm{Cos}[\theta]\,\mathrm{Sin}[\theta],\ \frac{1}{4}\sqrt{\frac{5}{\pi}}\,(-1+3\,\mathrm{Cos}[\theta]^2),\ -\frac{1}{2}e^{i\phi}\sqrt{\frac{15}{2\pi}}\,\mathrm{Cos}[\theta]\,\mathrm{Sin}[\theta],\ \frac{1}{4}e^{2i\phi}\sqrt{\frac{15}{2\pi}}\,\mathrm{Sin}[\theta]^2\right\}$$

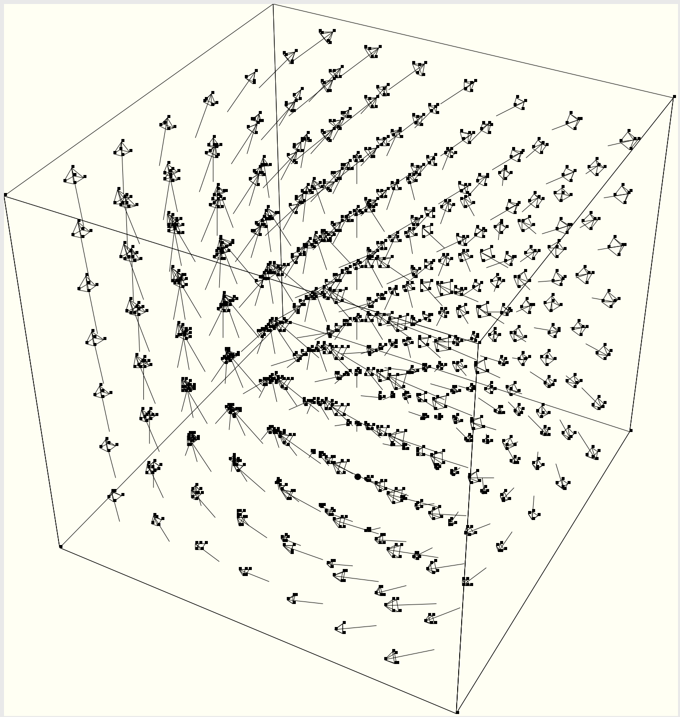
$$48.5375 + 1.36246\,\mathrm{Cos}[\theta] - 0.346201\,\mathrm{Cos}[\theta]^2 + 0.371463\,\mathrm{Cos}[\phi]\,\mathrm{Sin}[\theta] - 1.34494\,\mathrm{Cos}[\theta]\,\mathrm{Cos}[\phi]\,\mathrm{Sin}[\theta] - 0.998947\,\mathrm{Cos}[2\phi]\,\mathrm{Sin}[\theta]^2 + 0.162299\,\mathrm{Sin}[\theta]\,\mathrm{Sin}[\phi] + 4.52912\,\mathrm{Cos}[\theta]\,\mathrm{Sin}[\theta]\,\mathrm{Sin}[\phi] - 1.16299\,\mathrm{Sin}[\theta]^2\,\mathrm{Sin}[2\phi]$$

Lysosomes detected





A. Multi-scale optic flow



How can we find a dense optic flow field from a motion sequence in 2D and 3D?

Many approaches are taken:

- gradient based (or differential);
- phase-based (or frequency domain);
- correlation-based (or area);
- feature-point (or sparse data) tracking.

The Lie derivative (denoted with the symbol $\mathcal{L}_{\vec{v}}$) of a function $F(g)$ with respect to a vectorfield $\vec{v}$ is defined as $\mathcal{L}_{\vec{v}} F(g)$. The optic flow constraint equation (OFCE) states that the luminance does not change when we take the derivative along the vectorfield of the motion:

$$\mathcal{L}_{\vec{v}} F(g) \equiv 0$$

Multi-scale optic flow constraint equation:

For scalar images:

$$\mathcal{L}_{\vec{v}}\, F(g) = \vec{\nabla} F.\vec{v}$$

For density images:

$$\mathcal{L}_{\vec{v}}\, \rho = \rho\, \mathrm{Div}\, \vec{v} + \vec{v}.\vec{\nabla}\rho = 0$$

The velocity field is unknown, and this is what we want to recover from the data. We like to retrieve the velocity and its derivatives with respect to x, y, z and t.

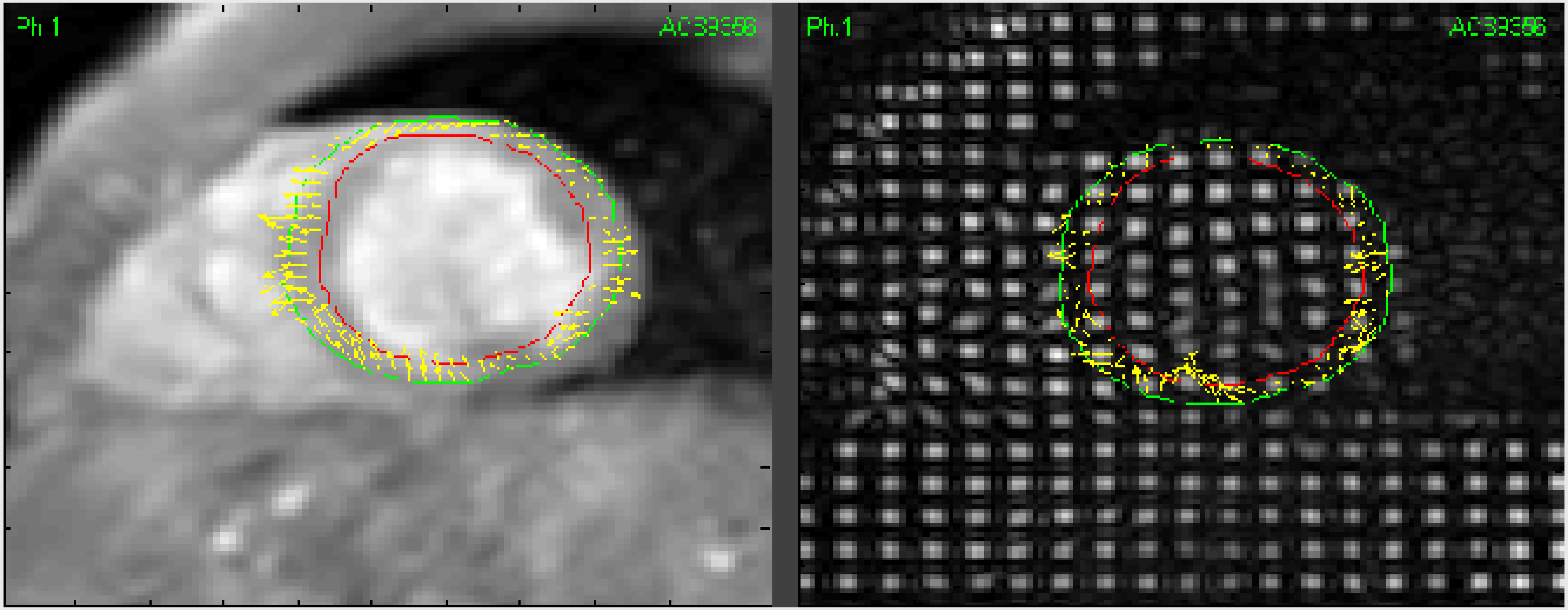
We insert this unknown velocity field as a truncated Taylor series, truncated at first order.

Multi-scale density flow: in each pixel 8 equations of third order and 8 unknowns:

$$
\begin{pmatrix}
L_x & \sigma_x^2 L_{xx} & \sigma_y^2 L_{xy} & \tau^2 L_{xt} & L_y & \sigma_x^2 L_{xy} & \sigma_y^2 L_{yy} & \tau^2 L_{yt} \\
-L_{xx} & -L_x-\sigma_x^2 L_{xxx} & -\sigma_y^2 L_{xxy} & -\tau^2 L_{xxt} & -L_{xy} & -\sigma_x^2 L_{xxy}-L_y & -\sigma_y^2 L_{xyy} & -\tau^2 L_{xyt} \\
-L_{xy} & -\sigma_x^2 L_{xxy} & -L_x-\sigma_y^2 L_{xyy} & -\tau^2 L_{xyt} & -L_{yy} & -\sigma_x^2 L_{xyy} & -L_y-\sigma_y^2 L_{yyy} & -\tau^2 L_{yyt} \\
-L_{xt} & -\sigma_x^2 L_{xxt} & -\sigma_y^2 L_{xyt} & -L_x-\tau^2 L_{xtt} & -L_{yt} & -\sigma_x^2 L_{xyt} & -\sigma_y^2 L_{yyt} & -L_y-\tau^2 L_{ytt} \\
L_y & \sigma_x^2 L_{xy} & \sigma_y^2 L_{yy} & \tau^2 L_{yt} & -L_x & -\sigma_x^2 L_{xx} & -\sigma_y^2 L_{xy} & -\tau^2 L_{xt} \\
-L_{xy} & -\sigma_x^2 L_{xxy}-L_y & -\sigma_y^2 L_{xyy} & -\tau^2 L_{xyt} & L_{xx} & L_x+\sigma_x^2 L_{xxx} & \sigma_y^2 L_{xxy} & \tau^2 L_{xxt} \\
-L_{yy} & -\sigma_x^2 L_{xyy} & -L_y-\sigma_y^2 L_{yyy} & -\tau^2 L_{yyt} & L_{xy} & \sigma_x^2 L_{xxy} & L_x+\sigma_y^2 L_{xyy} & \tau^2 L_{xyt} \\
-L_{yt} & -\sigma_x^2 L_{xyt} & -\sigma_y^2 L_{yyt} & -L_y-\tau^2 L_{ytt} & L_{xt} & \sigma_x^2 L_{xxt} & \sigma_y^2 L_{xyt} & L_x+\tau^2 L_{xtt}
\end{pmatrix}
\begin{pmatrix} u \\ u_x \\ u_y \\ u_t \\ v \\ v_x \\ v_y \\ v_t \end{pmatrix}
=
\begin{pmatrix} -L_t \\ L_{xt} \\ L_{yt} \\ L_{tt} \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}
$$

Motion analysis:

Extraction of dense optic flow field, multi-scale technique



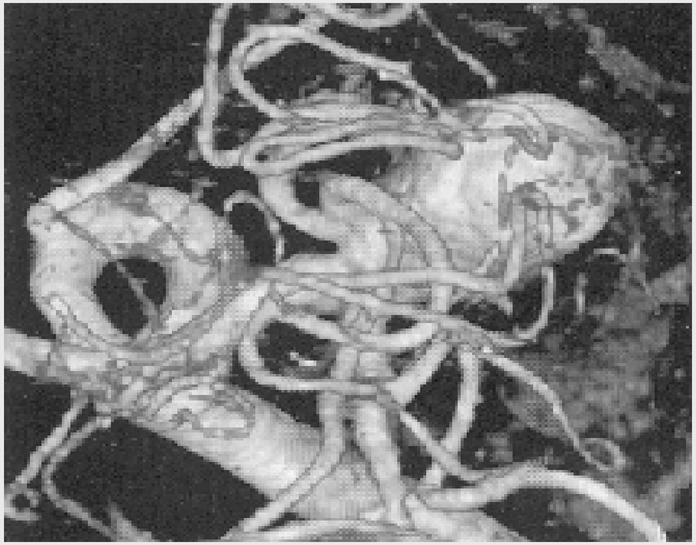
MRI left ventricular wall motion, phase velocity

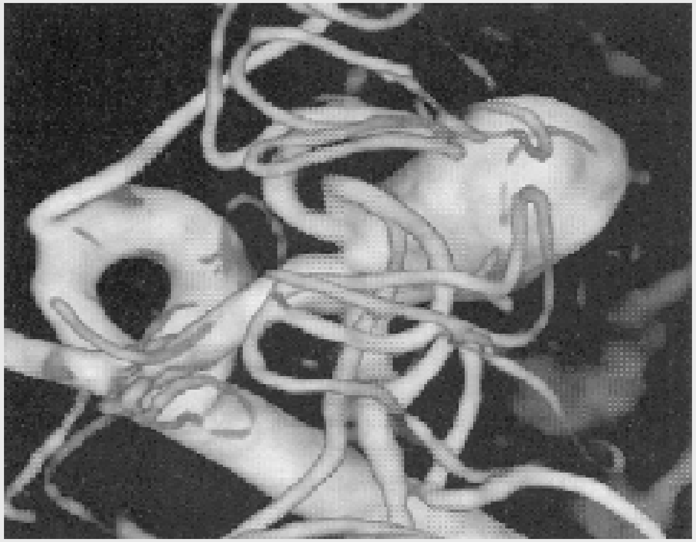
MRI tagging

A. Suinesiaputra, ter Haar Romeny, MICCAI 200

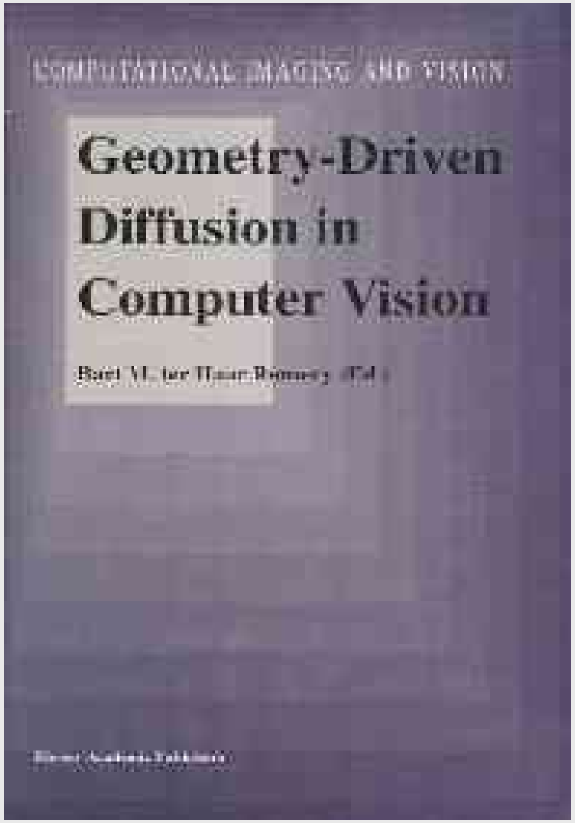
Edge preserving smoothing:

cerebral
aneurysm
clean-up
for coiling

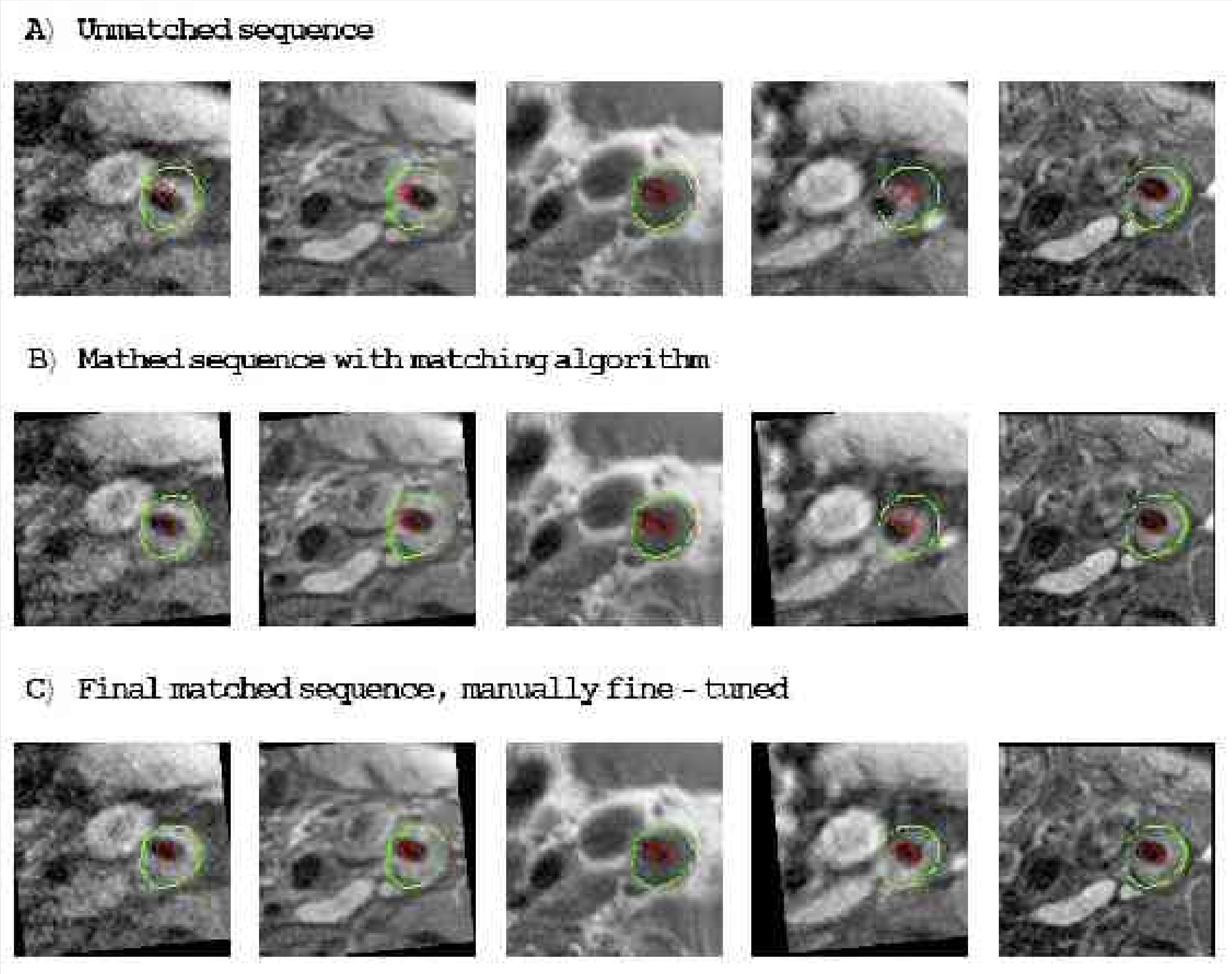




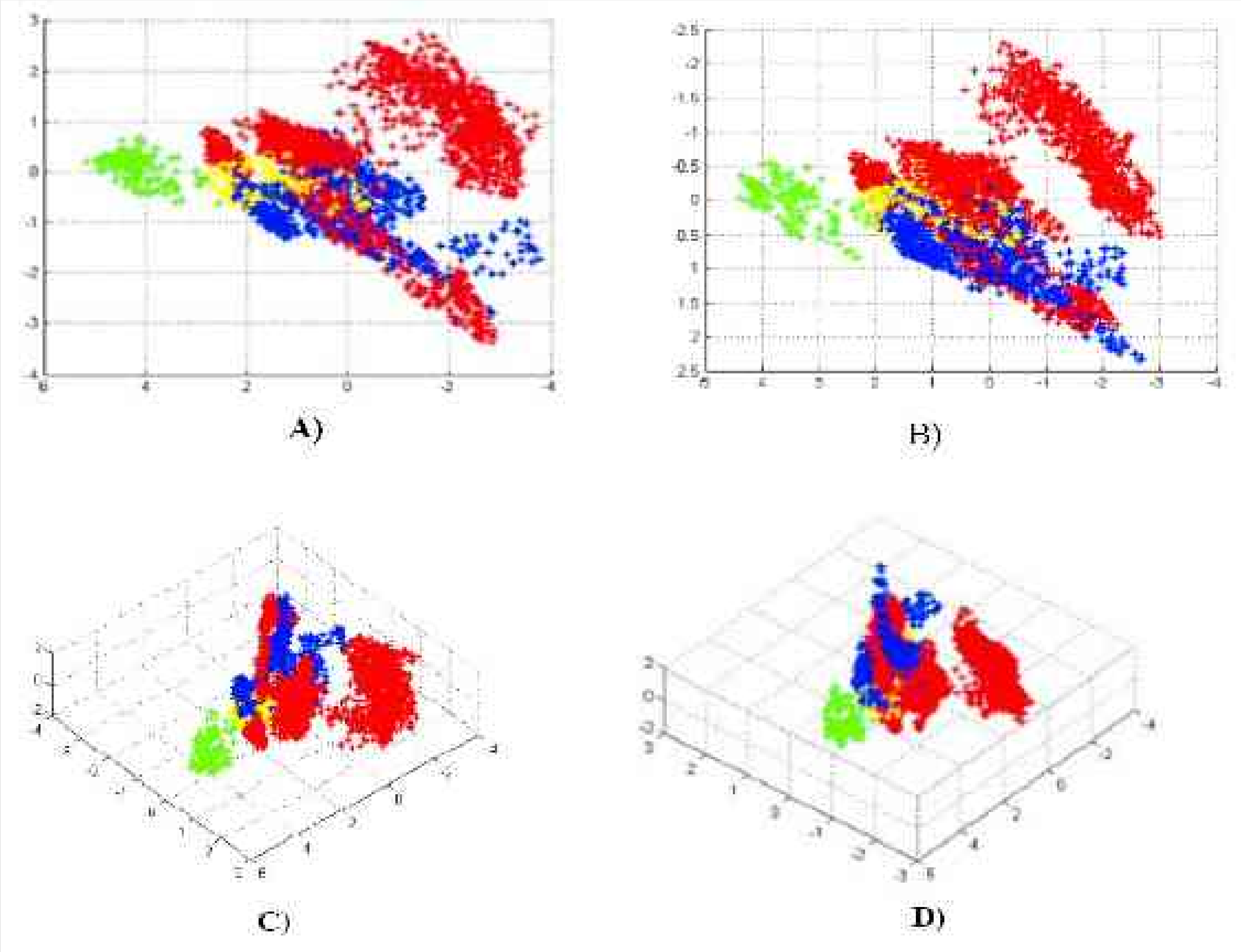
E. Meijering, ISI

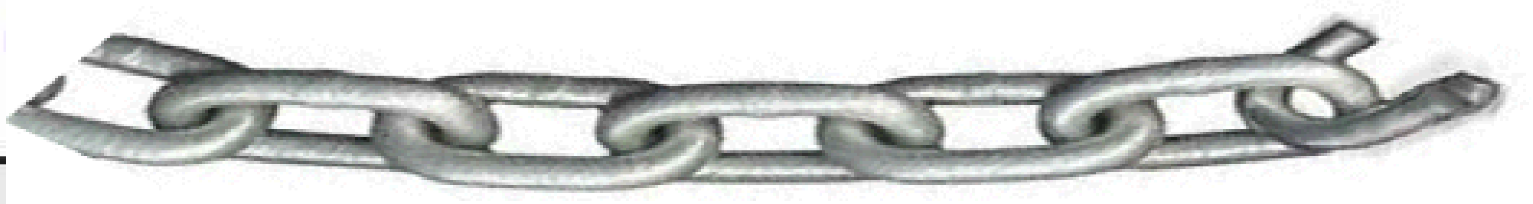


Matching with normalized mutual information maximization



Principal Component Analysis





Look

image acquisition
& storage

See

image analysis
computer vision

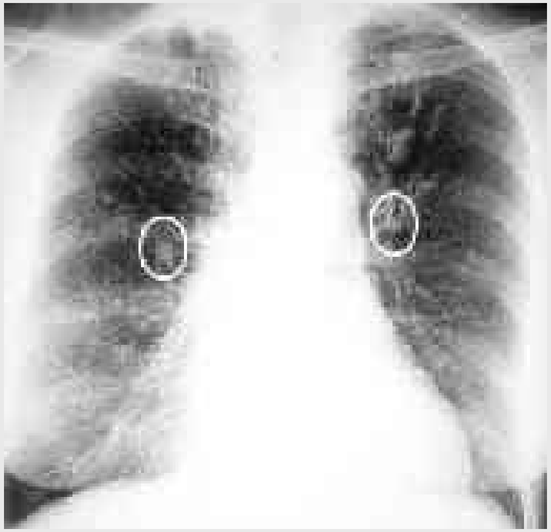
Decide

visualization
diagnosis

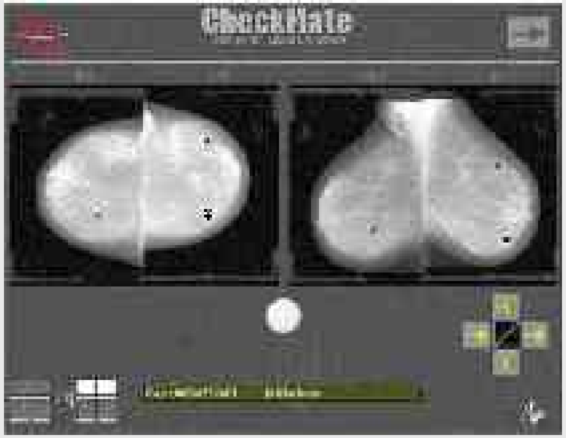
Computer aided diagnosis


Deus Technologies


R2 Technologies



Nodules
Sarcoidosis
Embolisms
…



Microcalcifications
Stellate tumors
Masses
…

Examples

- **Text is mixed with code and graphics.**

In[1]:= 234^{123}

Out[1]= 25914955143308114635177098802178395597060844178058237280525326180\
9028715616176137986680793513381639184099672798955490919248903334\
4614984624210141436210516217232746250724250378953402460057610397\
1859512134938220645562373823638281210359896611908026405889059881\
4138101408543005638210417517291104

In[2]:= `N[π, 100]`

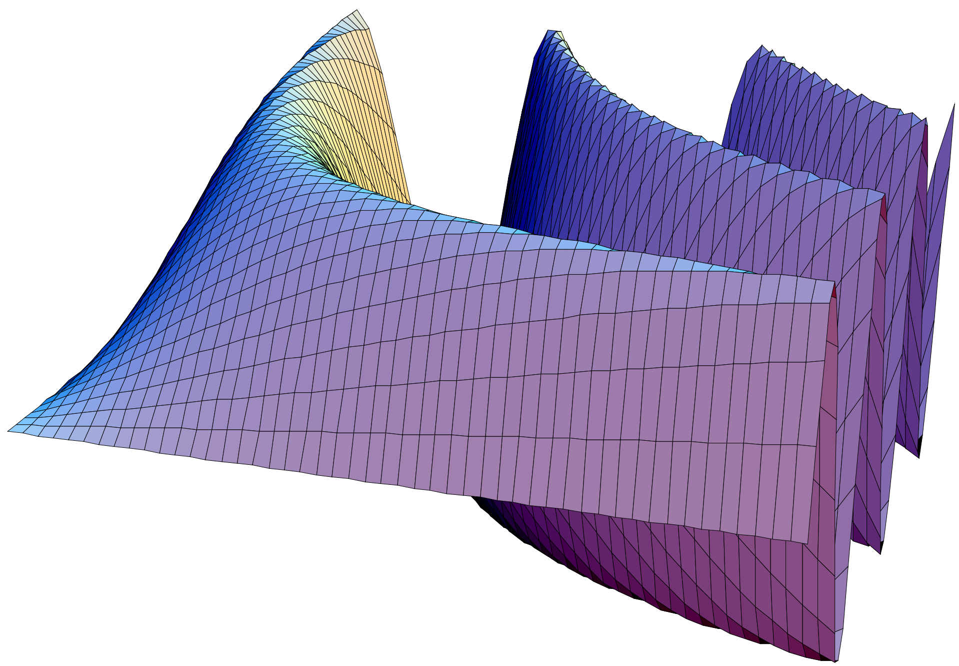
Out[2]= 3.141592653589793238462643383279502884197169399375105820974944592\
3078164062862089986280348253421170 68

- **Full symbolic and graphics/animations capabilities:**

In[3]:= $\int_a^b \mathbf{Sin[x]\ Exp[-3\,x]}\ dx$

Out[3]= $\frac{1}{10}\left(e^{-3\,a}\,(\mathrm{Cos}[a] + 3\,\mathrm{Sin}[a]) - e^{-3\,b}\,(\mathrm{Cos}[b] + 3\,\mathrm{Sin}[b])\right)$

In[4]:= **Plot3D[Sin[x y], {x, 0, π}, {y, 0, 2 π}, PlotPoints → 50];**

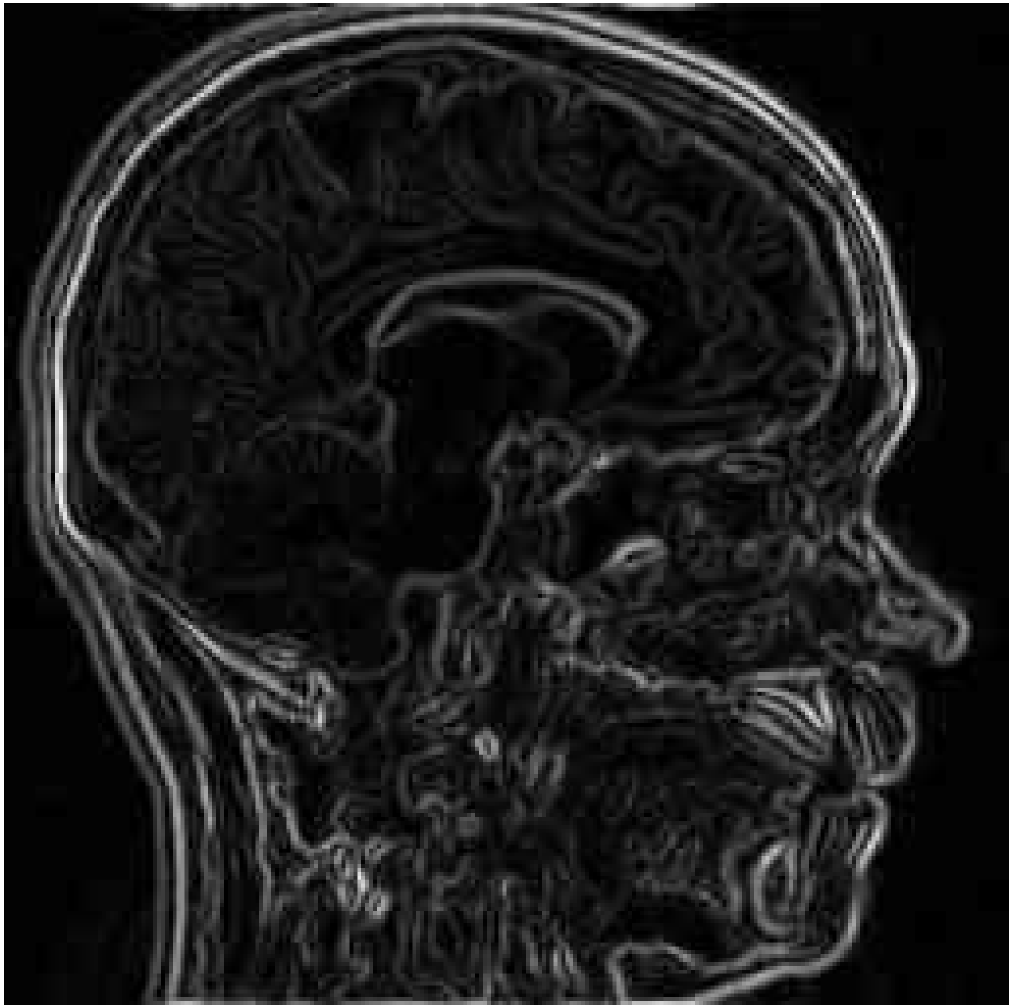


$$\int \sqrt{x}\ \mathrm{ArcTan}[x]\, dx$$

$$\frac{1}{6}\Big(-8\sqrt{x} - 2\sqrt{2}\,\mathrm{ArcTan}\big[1-\sqrt{2}\sqrt{x}\big] + 2\sqrt{2}\,\mathrm{ArcTan}\big[1+\sqrt{2}\sqrt{x}\big] + 4x^{3/2}\,\mathrm{ArcTan}[x] - \sqrt{2}\,\mathrm{Log}\big[-1+\sqrt{2}\sqrt{x}-x\big] + \sqrt{2}\,\mathrm{Log}\big[1+\sqrt{2}\sqrt{x}+x\big]\Big)$$

In[8]:= σ = 1;

$$\text{ListDensityPlot}\left[\sqrt{\text{gD}[\text{im}, 1, 0, \sigma]^2 + \text{gD}[\text{im}, 0, 1, \sigma]^2}\right];$$



```
Show[{ListDensitgyPlot[im],
   ListContourPlot[gD[im, 2, 0, σ] + gD[im, 0, 2, σ], Contours → {0},
    ContourStyle -> Red]}];
```