MEDICAL IMAGE ANALYSIS

FOR ILLNESS DIAGNOSTICS AND MONITORING

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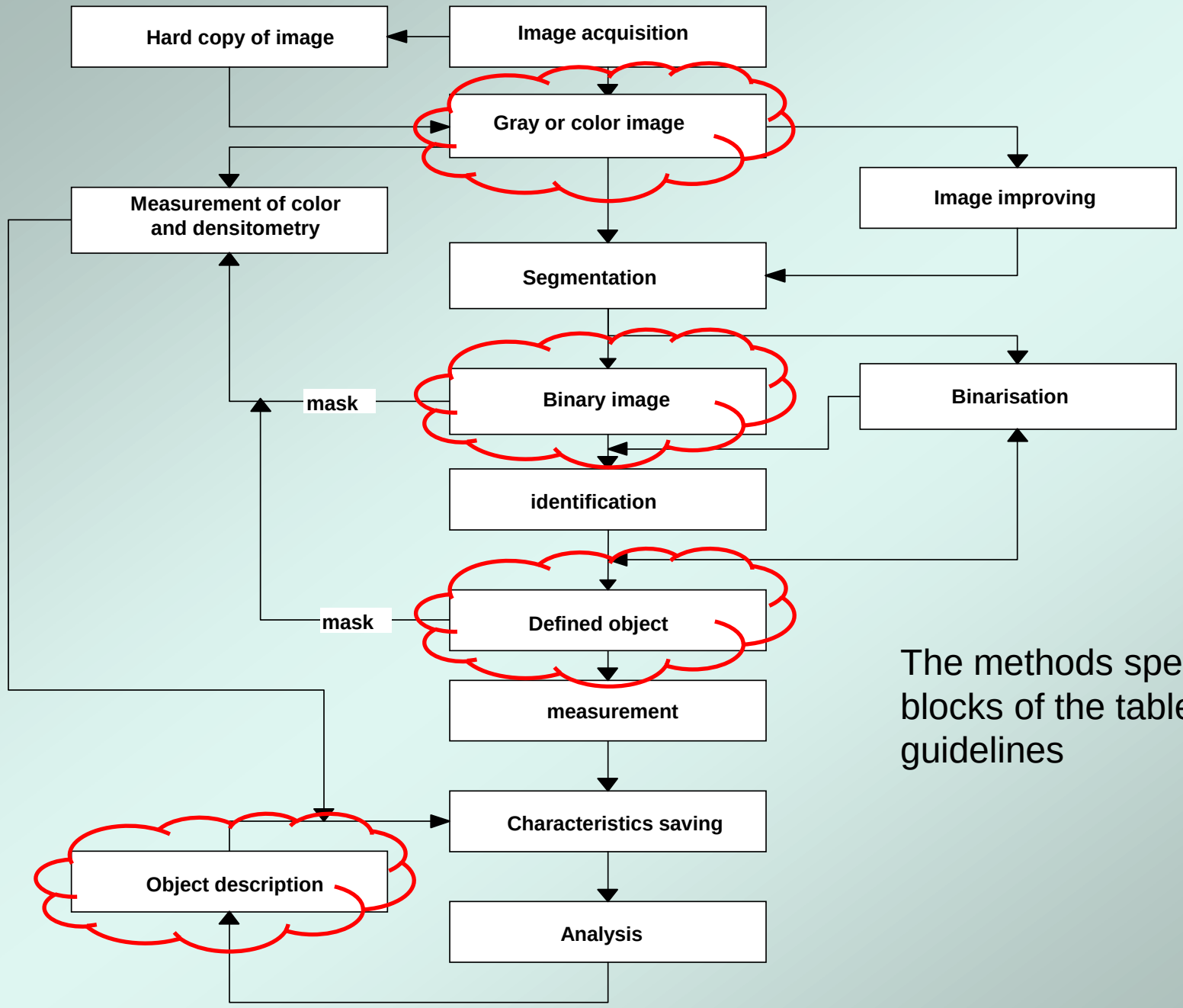
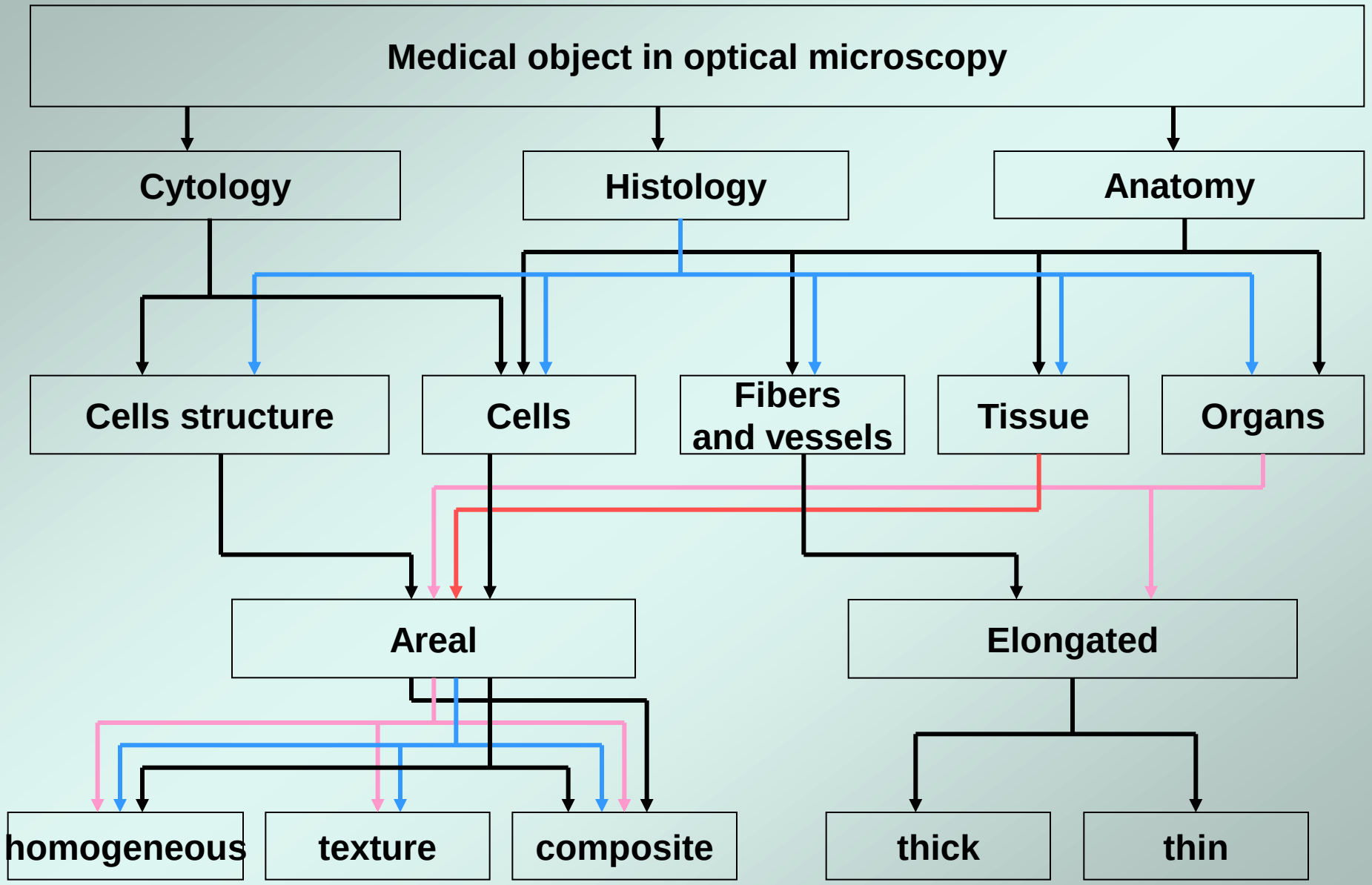
Common description of image analysis

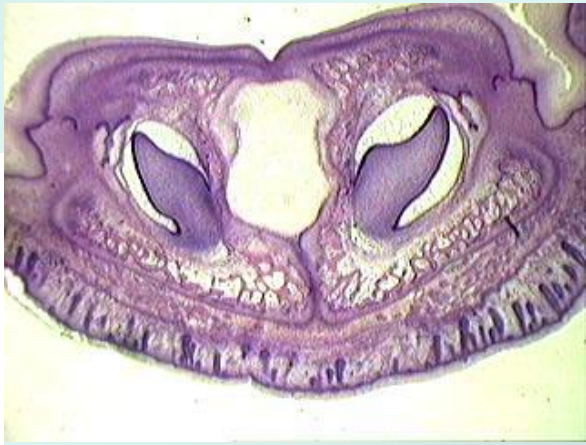


The methods specified in the blocks of the tables and guidelines

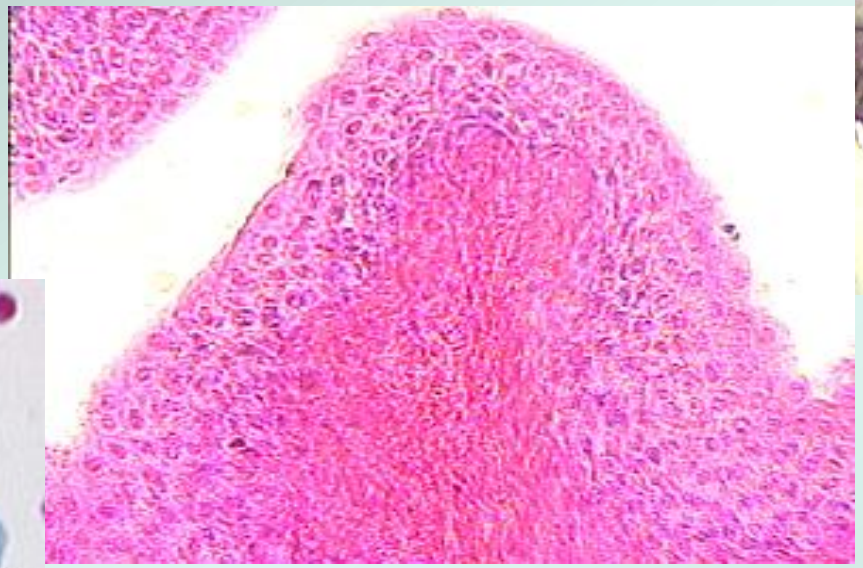
Biomedical images classification



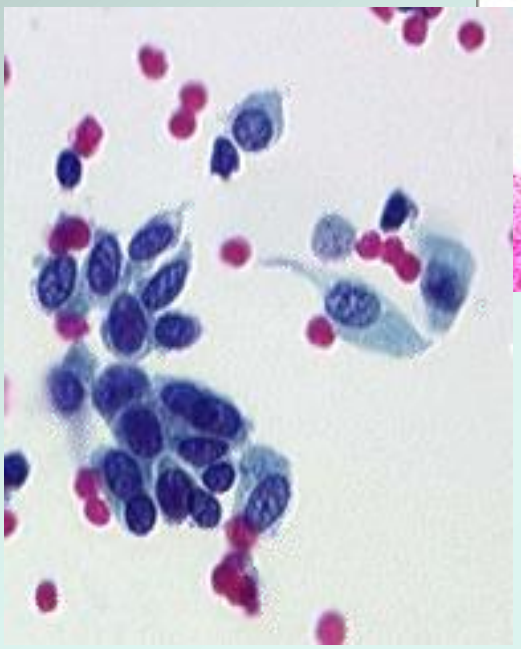
Medical microscopic images



Anatomic image



Histological image



Cytological image

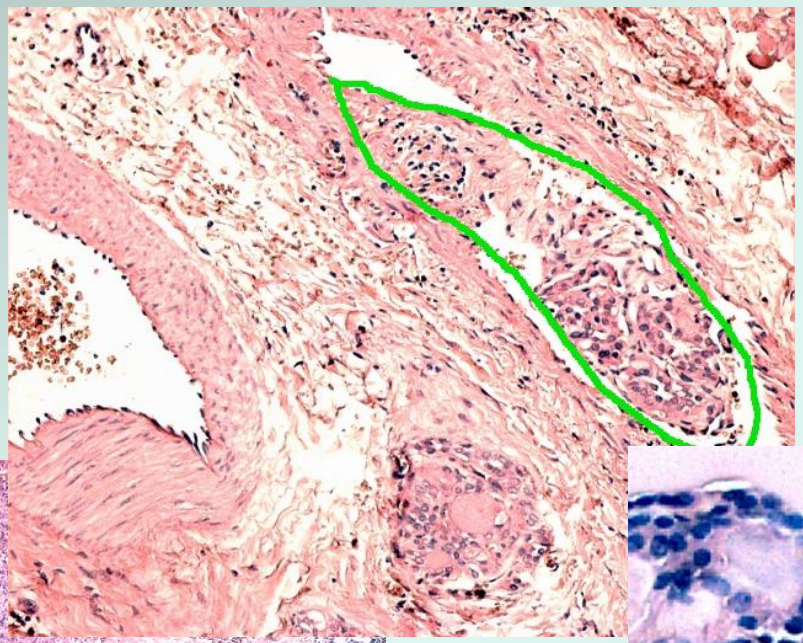
Histological-cytological attributes of oncological diseases

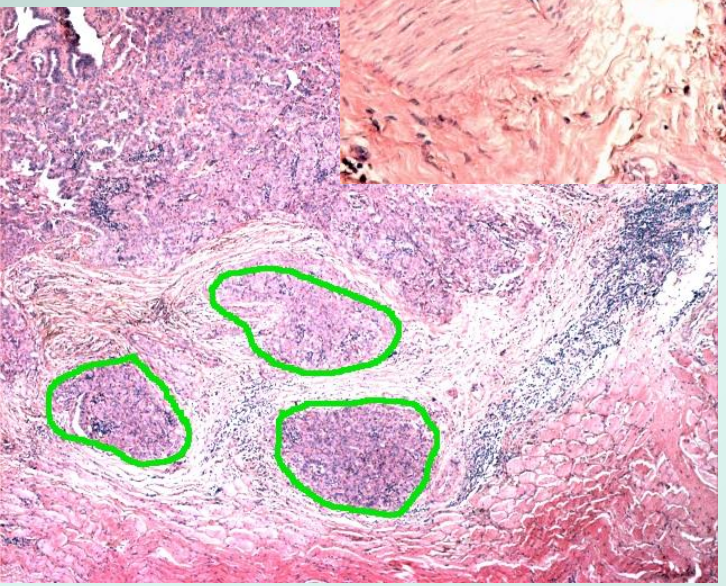
- Each kind of the morphological attributes of a histologic fragment of body, tissue, etc. is separated from all other kinds. Usually there is not transition of characteristic attributes to anther kinds of characteristic attributes of another.
- Analyze of all morphological forms of similarity and relationship allow to allocate most close and similar kinds of cells and tissues. The further expansion to bodies and their fragments uses wider generalizing attributes.
- The basic method of research of any group is the rather-morphological. At the same time in the group of morphological attributes considerably extends. Improvement of computer facilities and modern microscopes open new opportunities of studying of cellular structures.
- Morphological research of histologic preparations is usually carried out at two essentially different levels corresponding to different optical resolution.

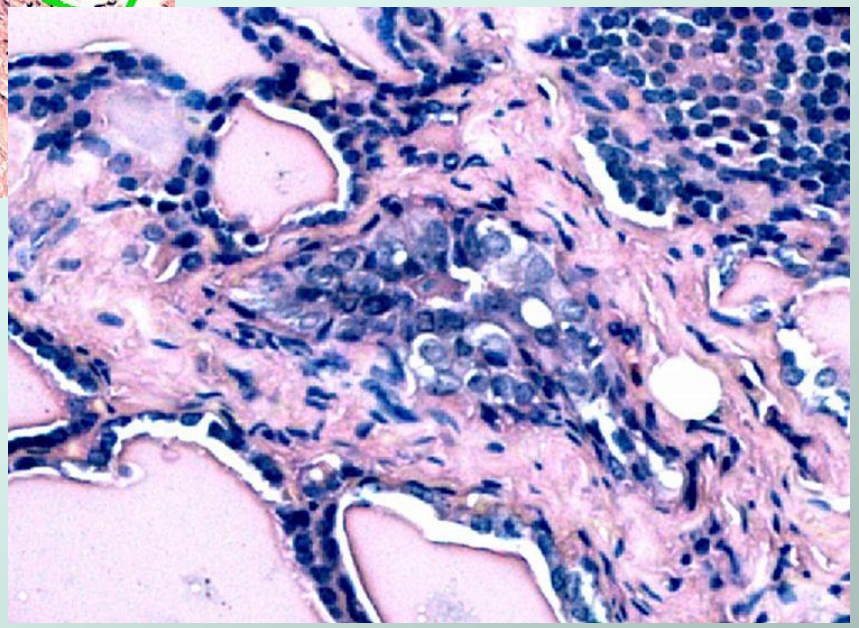
Histological attributes of oncological diseases

ATTRIBUTES

- invasion of tumoral complexes in a vessel or a capsule,



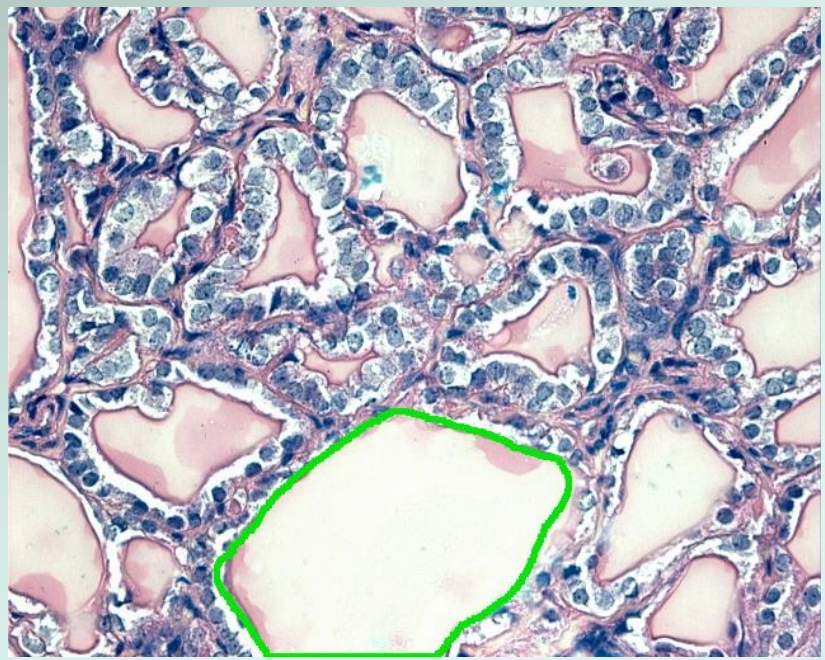


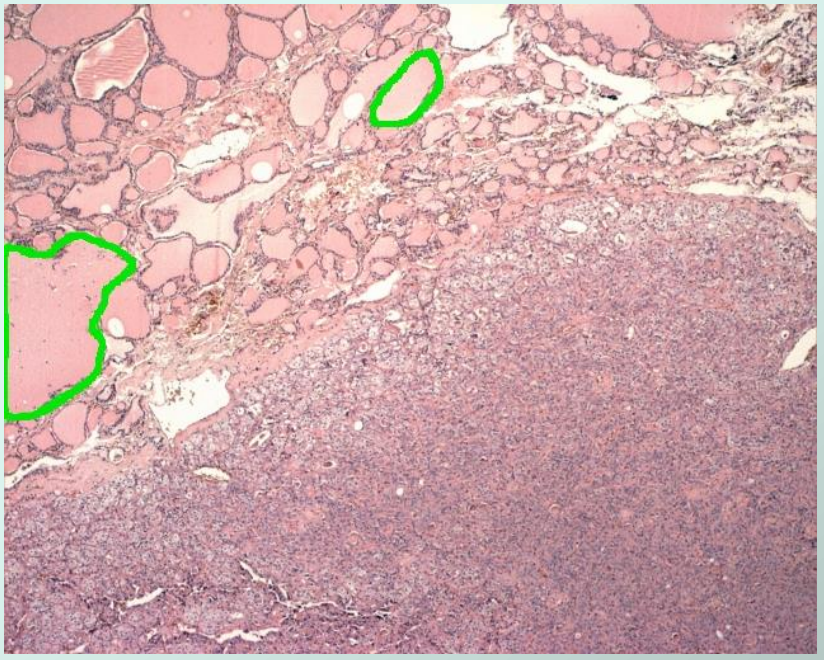


Histological attributes of oncological diseases

ATTRIBUTES

- The different color of follicles in the tumor and in the normal tissue,

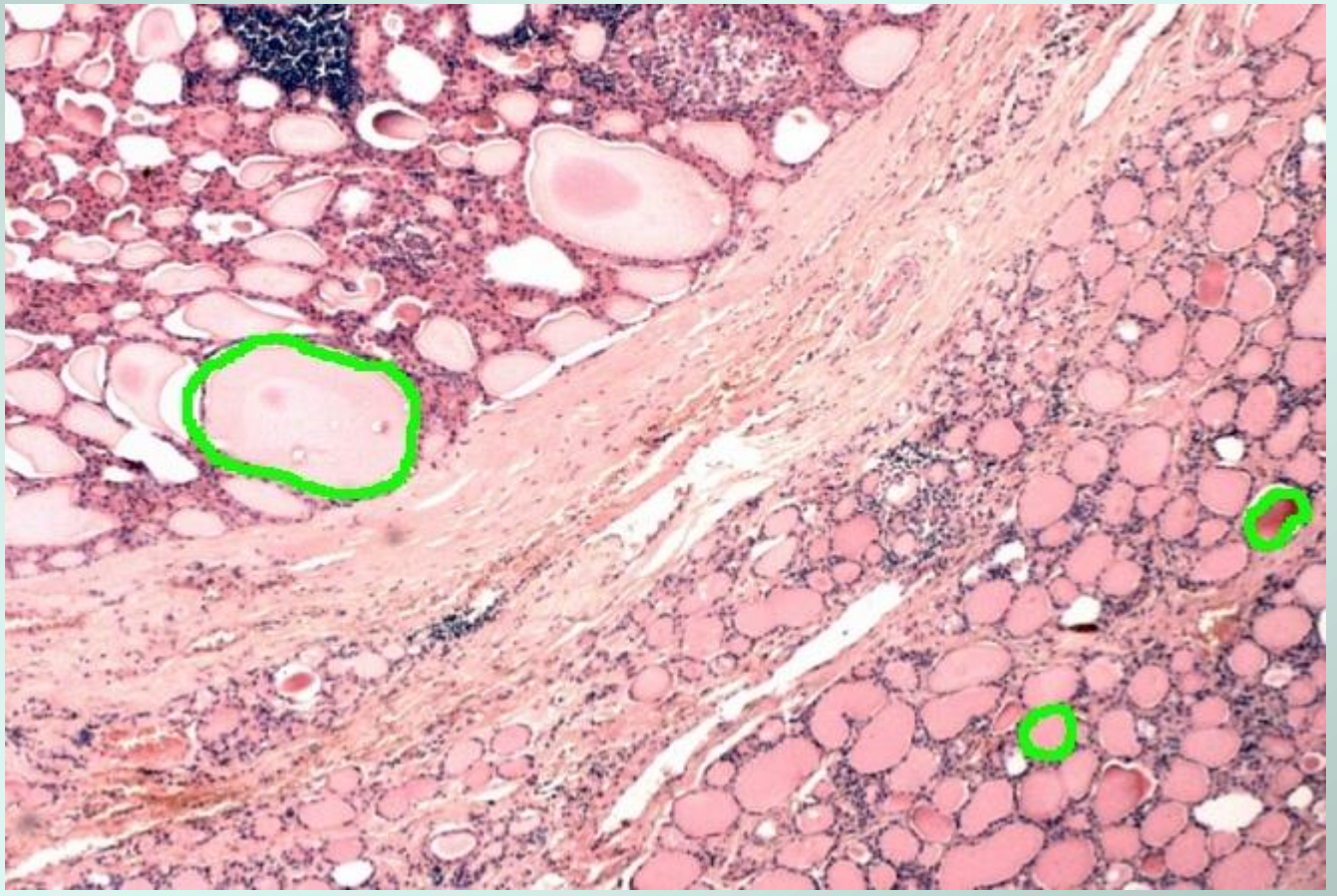




Histological attributes of oncological diseases

ATTRIBUTES

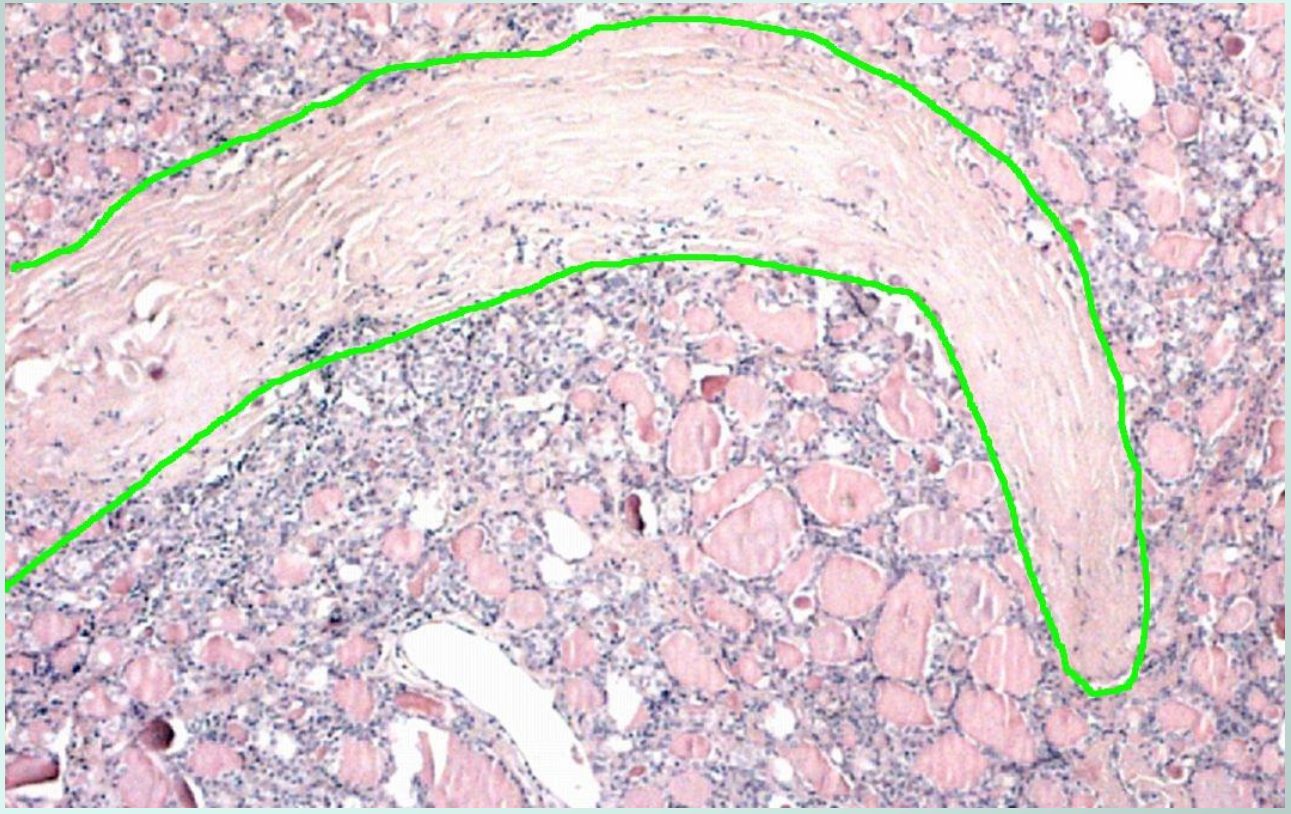
- The different sizes of follicles,



Histological attributes of oncological diseases

ATTRIBUTES

- Presence of fibrosis (a uniform sclerotic tissue surrounding cells),,

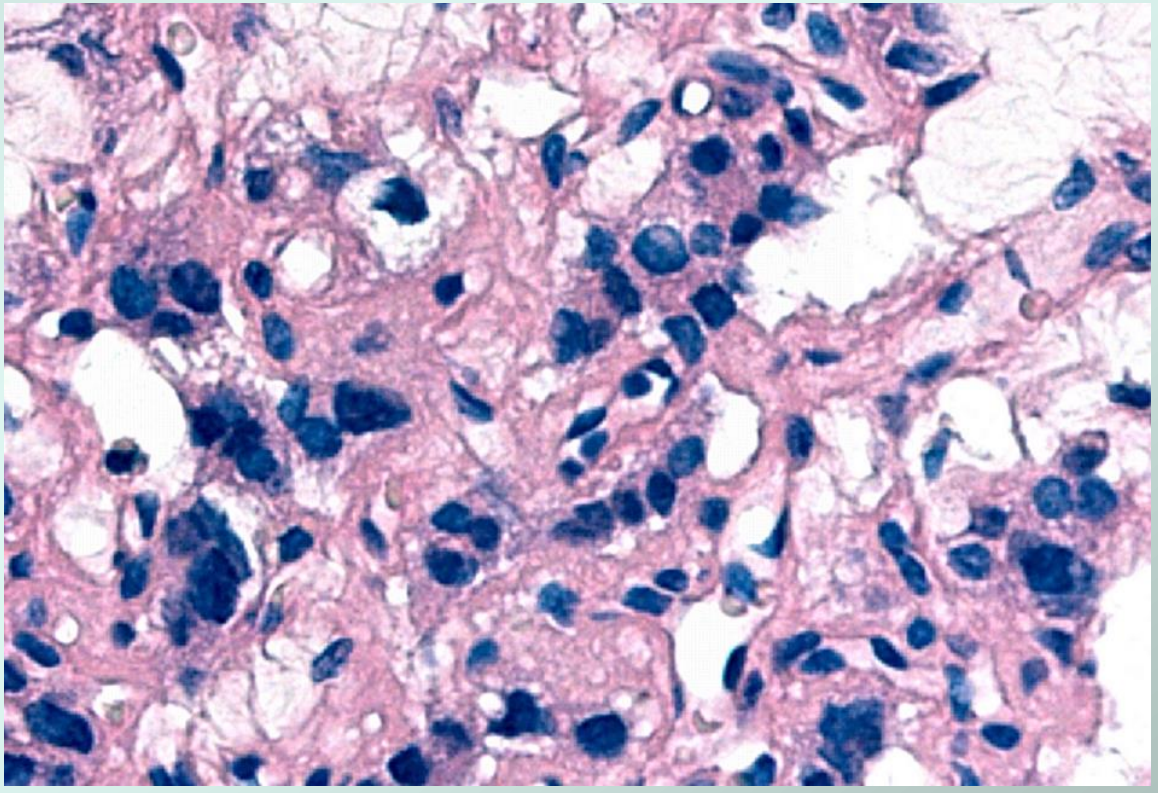


Histological attributes of oncological diseases

ATTRIBUTES OF CELLS

- Common cells attributes

Properties:
•Polymorphism - the different sizes and shape of cells;
•Polychromasia - different painting (color);
•Anaplasia - strong differences of a cell;

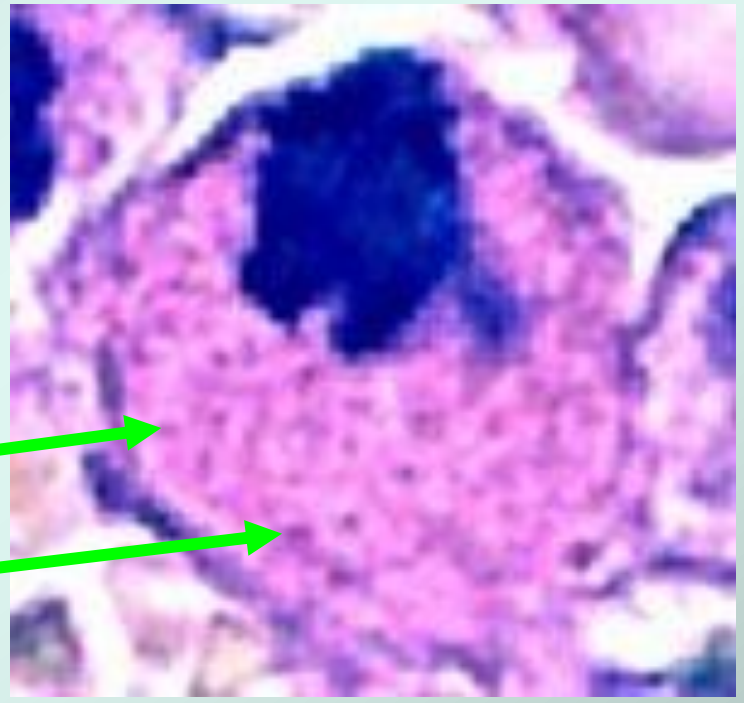


Histological attributes of oncological diseases

ATTRIBUTES OF CELLS

- oxyphillic cells

Properties:
- Colored cytoplasm;
- Giant mitochondria in cytoplasm;
- Polygonal shape of nuclear
- Size;

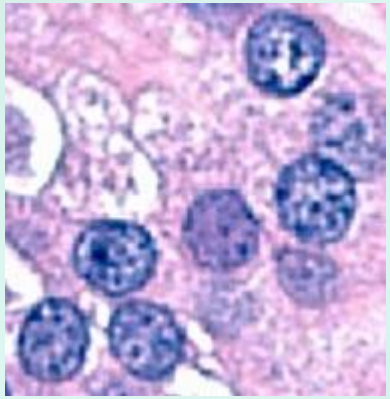


Giant mitochondria

Histological attributes of oncological diseases

ATTRIBUTES OF NUCLEUS

- Nucleus



adenoma

Shape and orientation of nucleus places important role in cancer diagnostic.
Elongated (ovoid) shape of nucleus is a one of the signs of papillary carcinoma.
Oval shape of nucleus is a one of the signs of goiter or adenoma

Papillary thyroid carcinoma

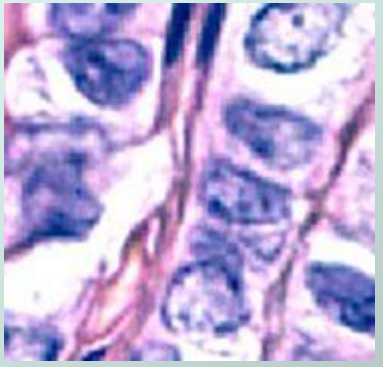
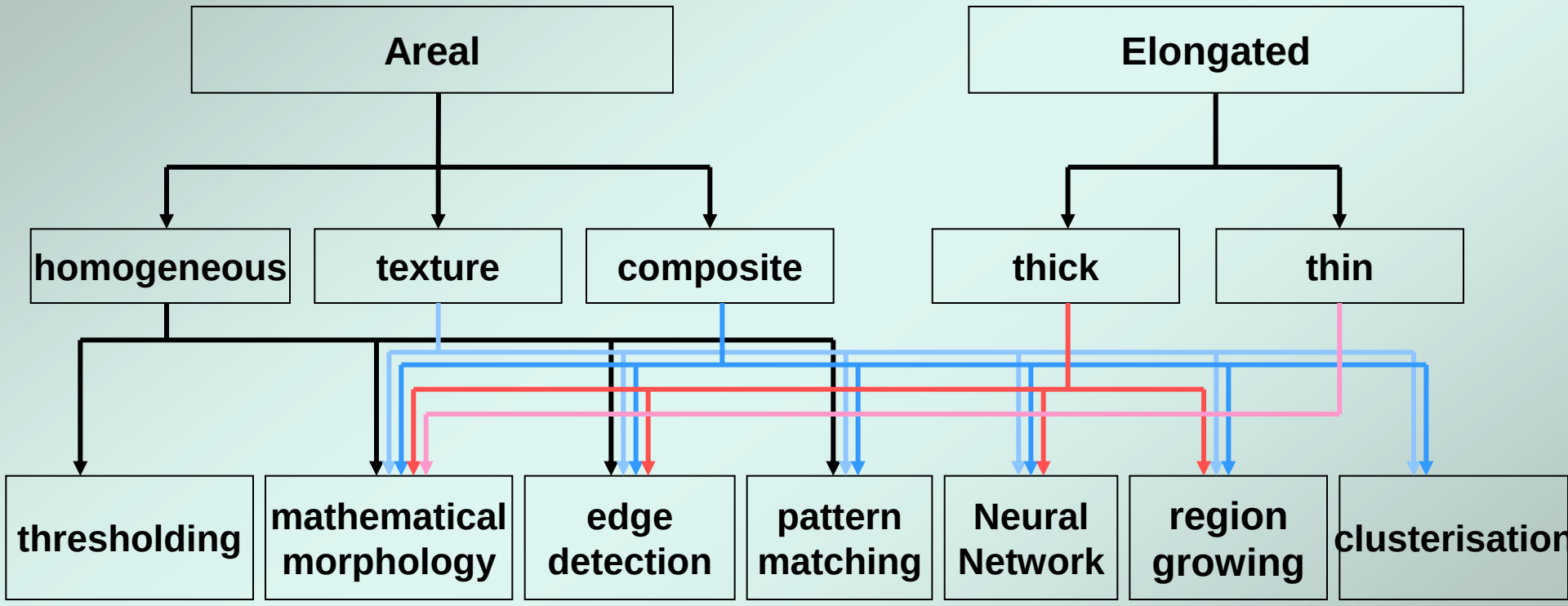


Image Processing Algorithms Classification

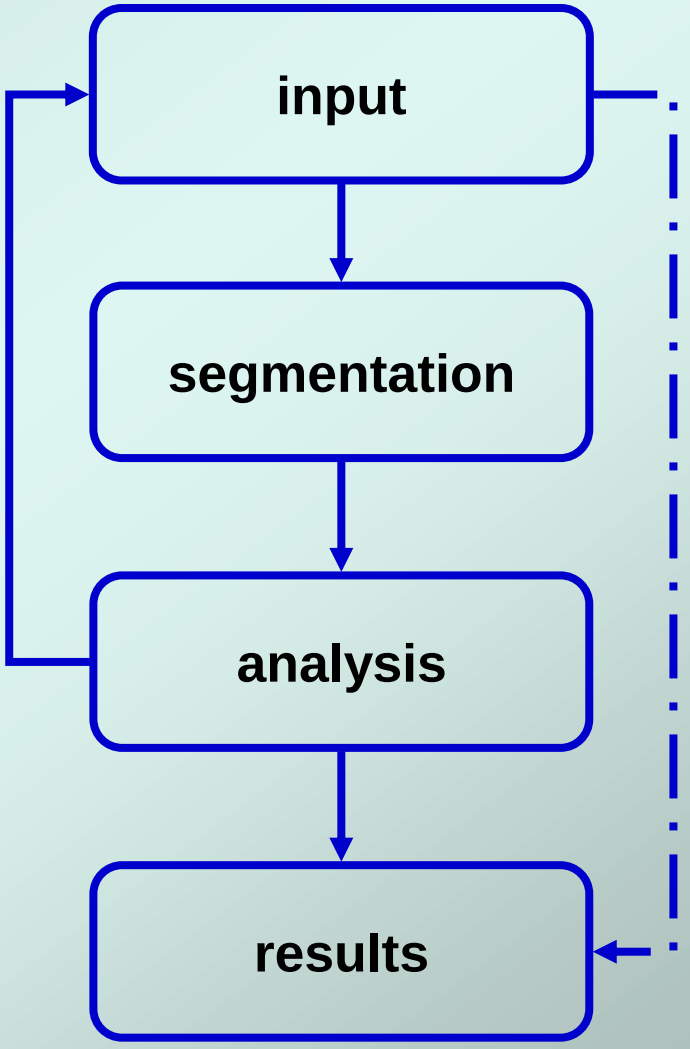


Comparison of Techniques

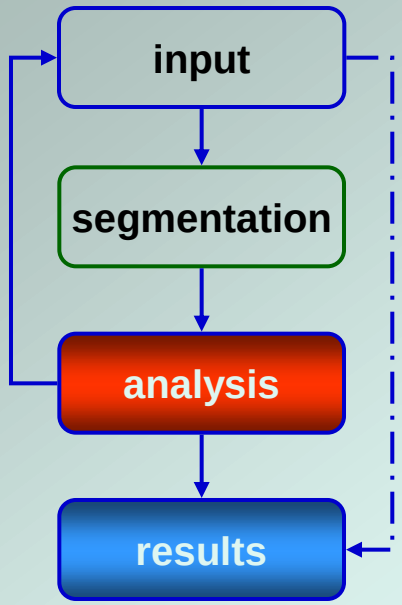
Mathematical morphology	Cells, nucleus, vessels and fibers in longitudinal and cross section	fast, easy impl.	absence of exact forms of morph. objects
Edge detection	Cells, vessels and fibers in cross section	simple and easy	simple objects detection
Neural Networks	Cells, nucleus, vessels and fibers in longitudinal and cross section (specific objects only)	Classification time	Training data and time
Region growing	Cells, vessels, fibers	Image sequences extraction	Long time
Clasterisation	Cells, nucleus, nucleolus vessels and fibers, tissue organs	unsupervised, flexible	iterative
Pattern matching	Cells, tissue organs	Precise cells extraction	Complex and slow

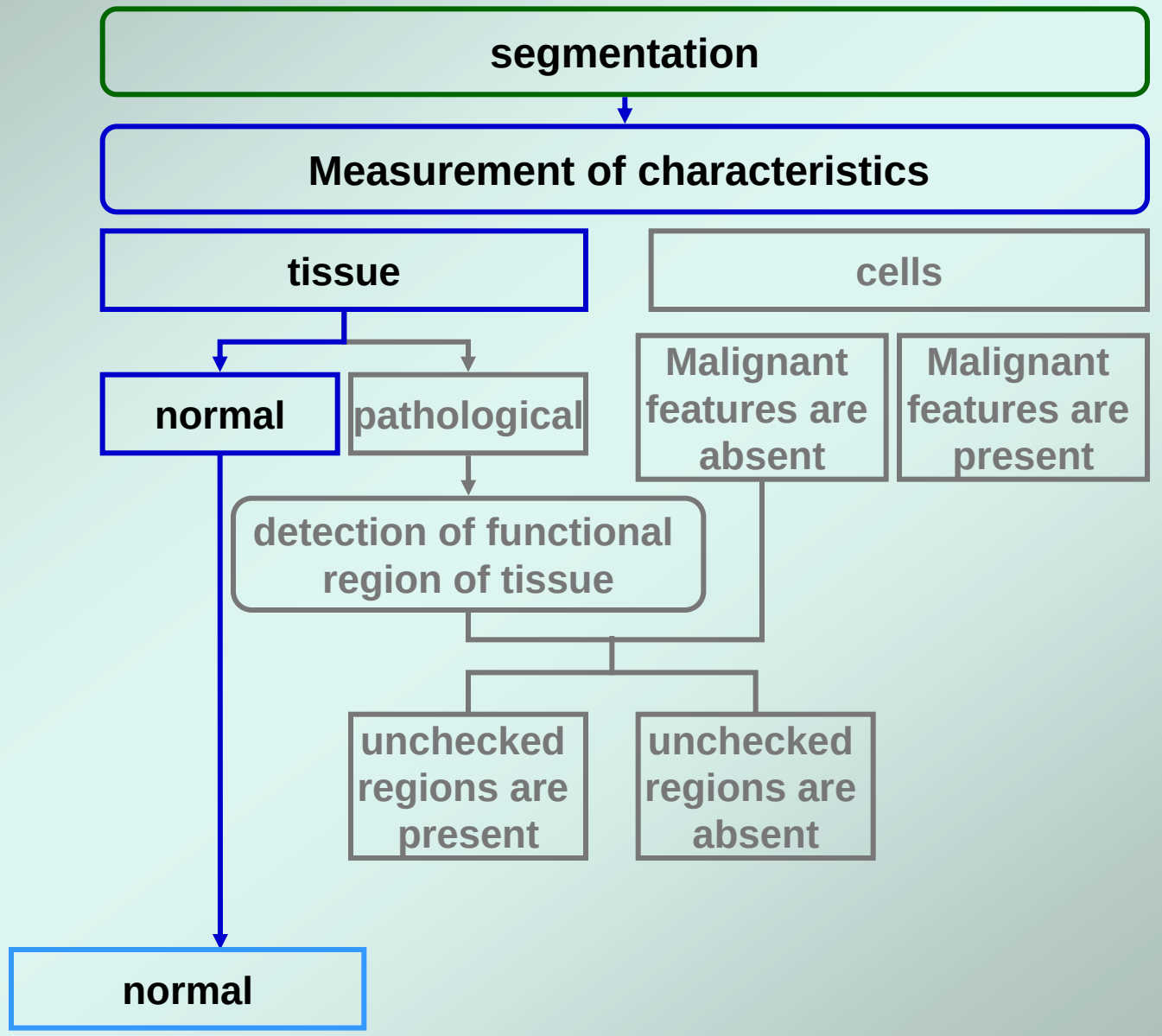
The principal scheme

An idea of stepwise processing of several images of one preparation under different magnification is described here

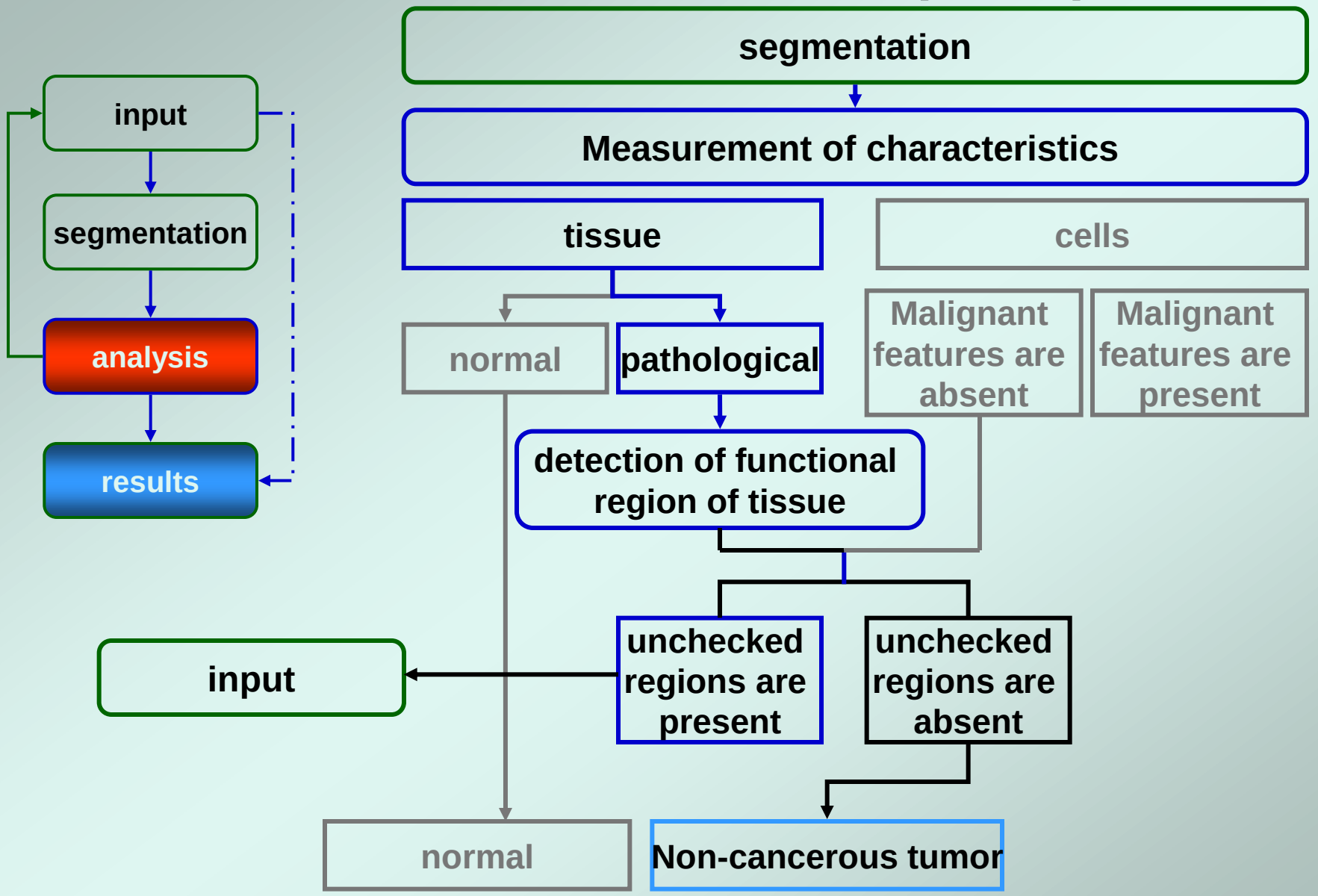


The principal scheme

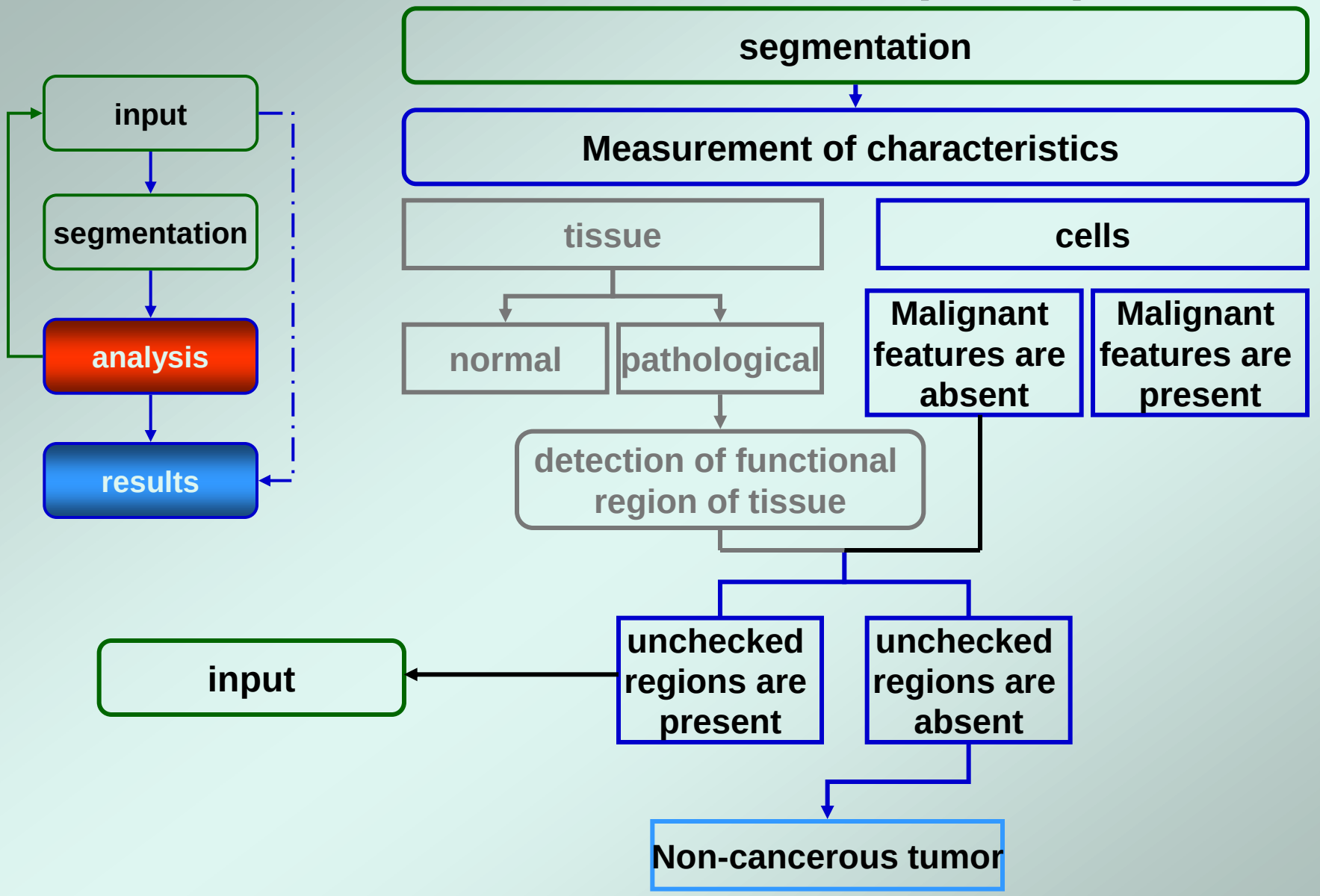




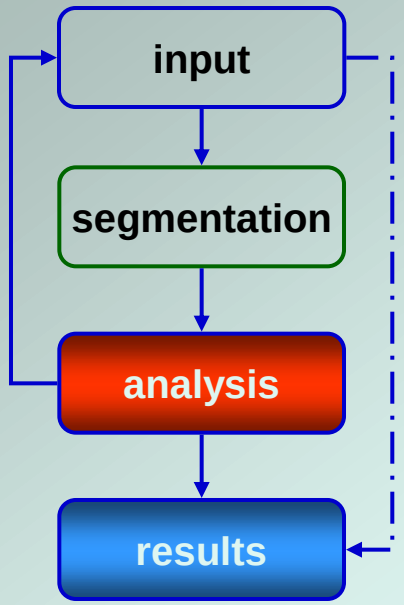
The principal scheme

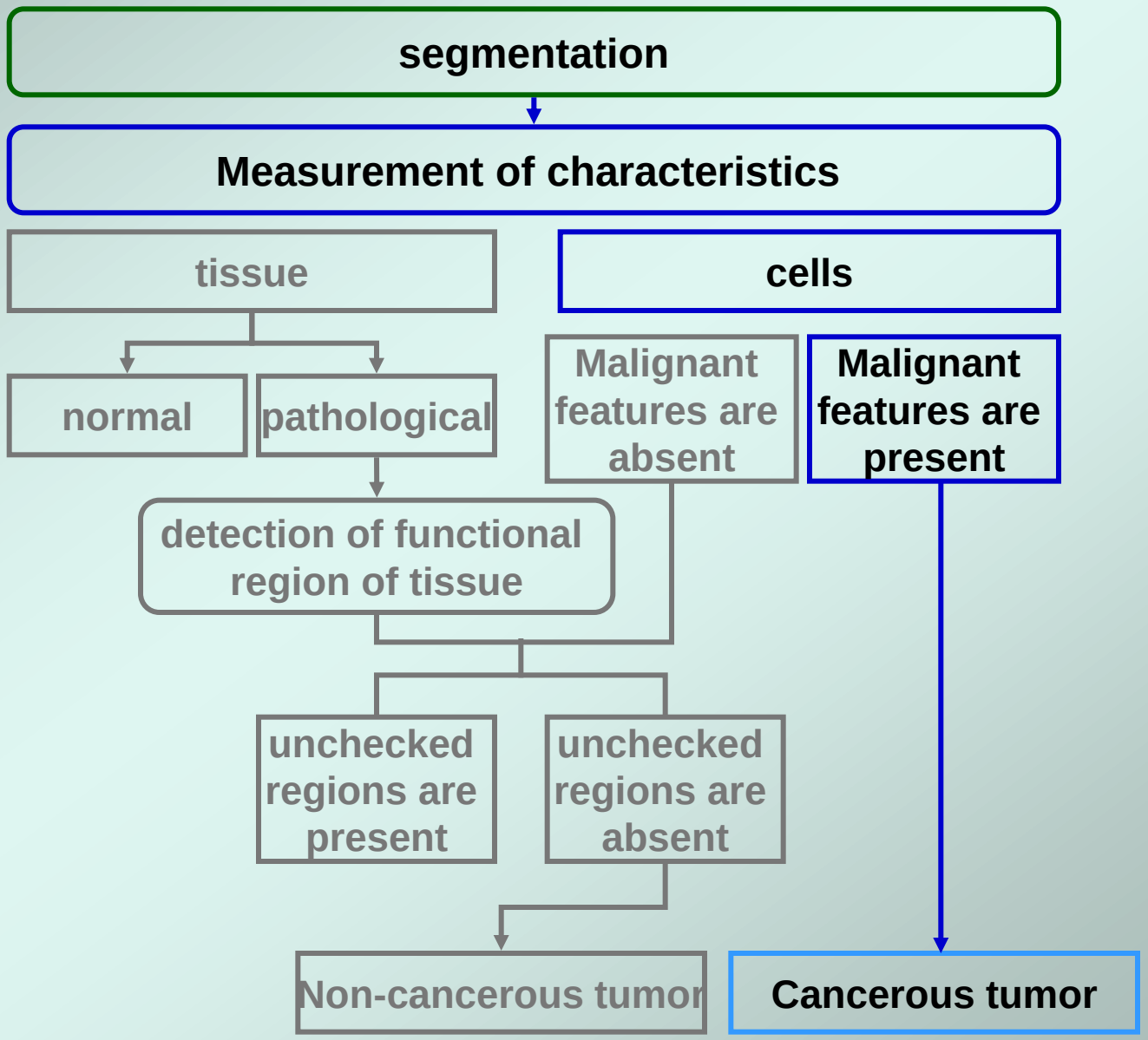


The principal scheme



The principal scheme





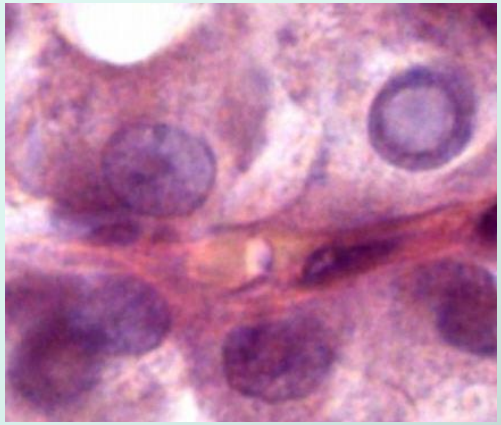
Segmentation of color image

To obtain binary image of a nucleus, the threshold segmentation is used in color system coordinates LCH. Threshold segmentation for lightness L is performed automatically. Threshold of chromatic components is determined on the CH coordinates circle of color space. threshold is exposed by a component of chromaticity H and functionally dependency from saturation C. Difference in color tone is less than π/4.

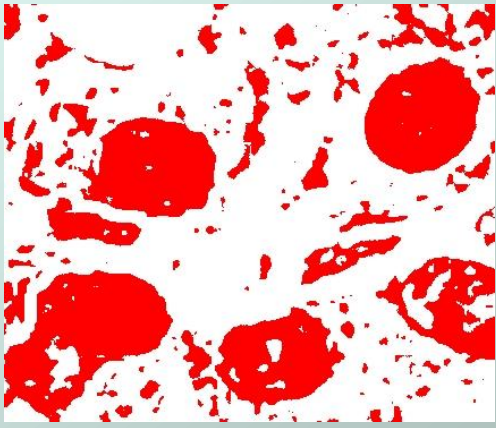
The corner of close color perception grows with reduction of color saturation :

$$H=H_{old}\ C_{max}/C,$$

where H - color pseudo-angle, H_{old} - real hue, C_{max} - the maximal change of a chromaticity, C - chromaticity.

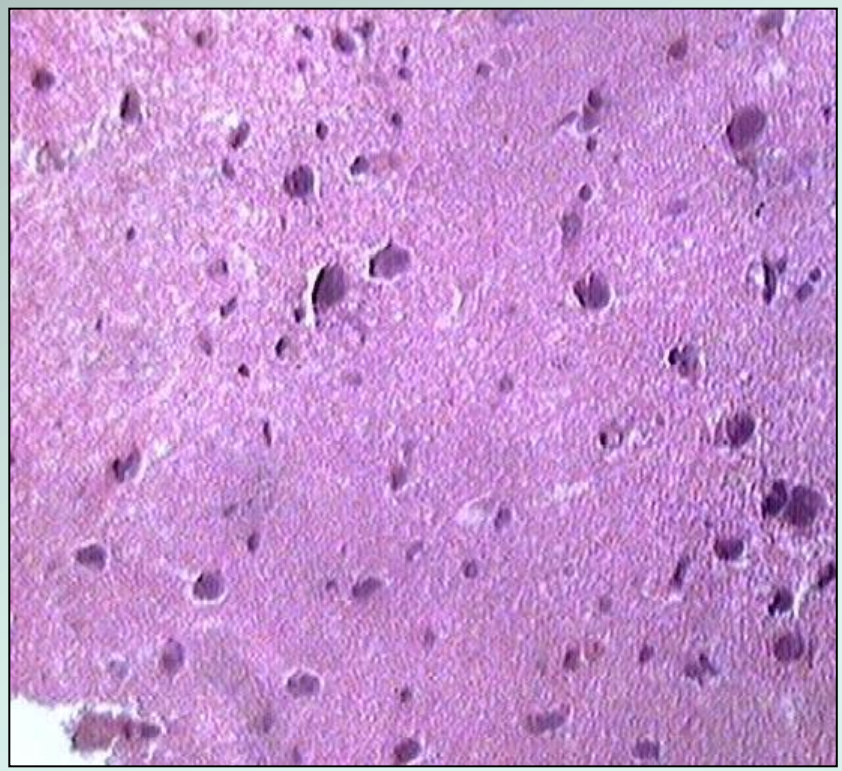


Fragment
of histology image

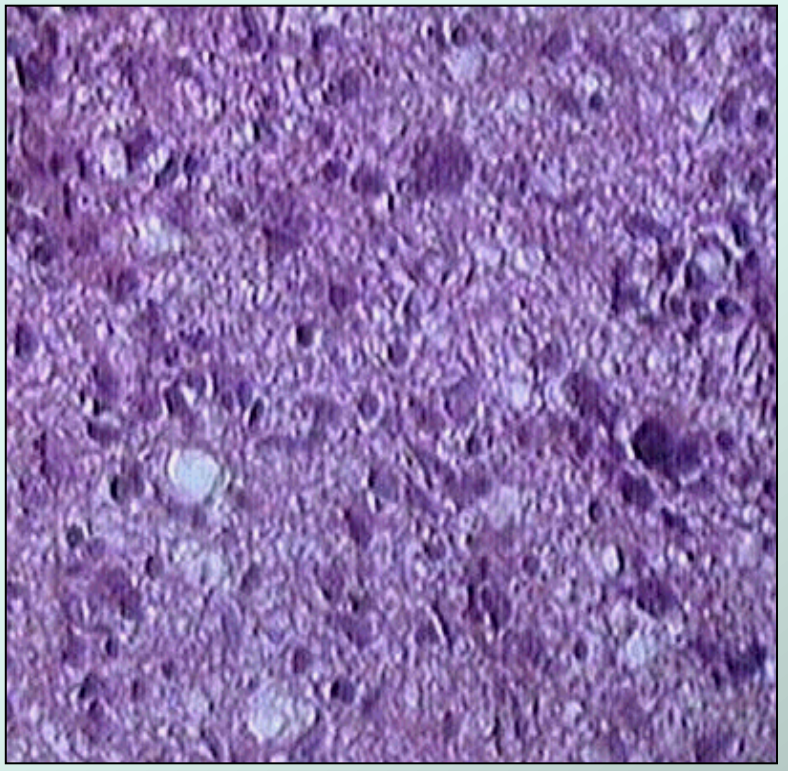


result of binarization

Images of histological samples

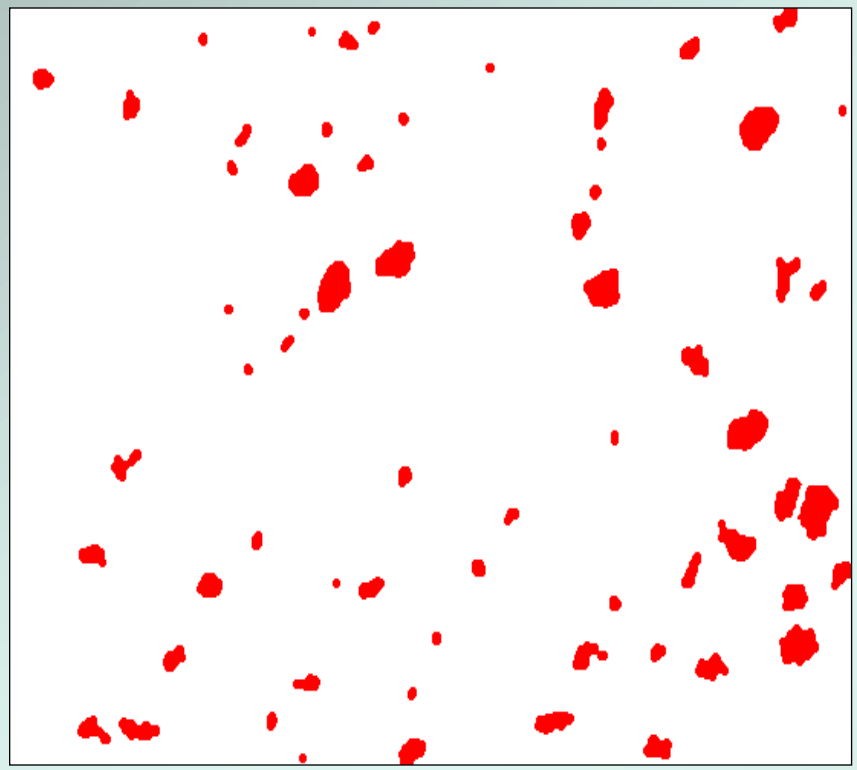


normal tissue

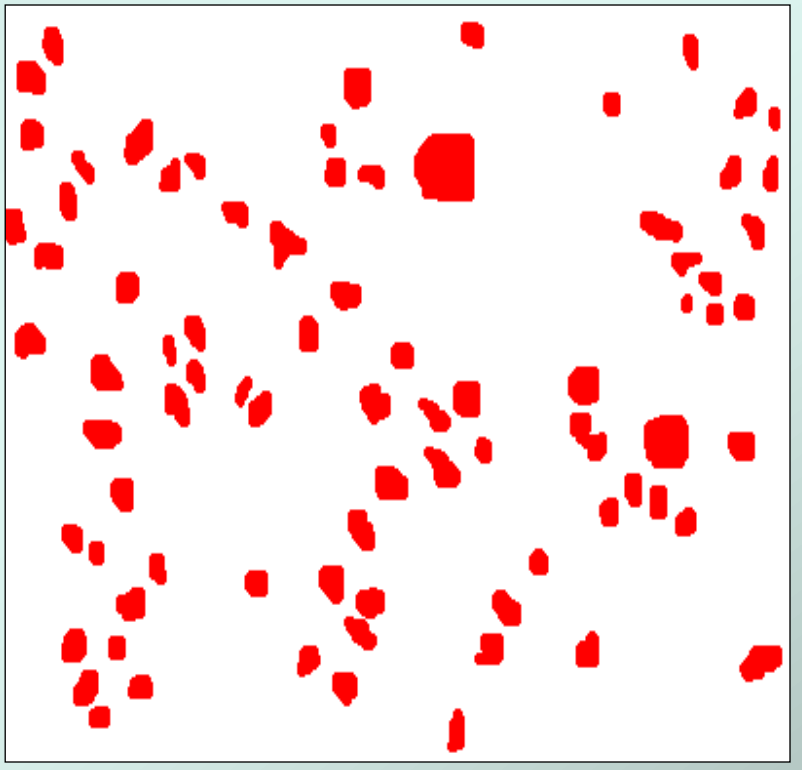


gliablastoma with cells polymorphism.

Binary images of histological samples after segmentation

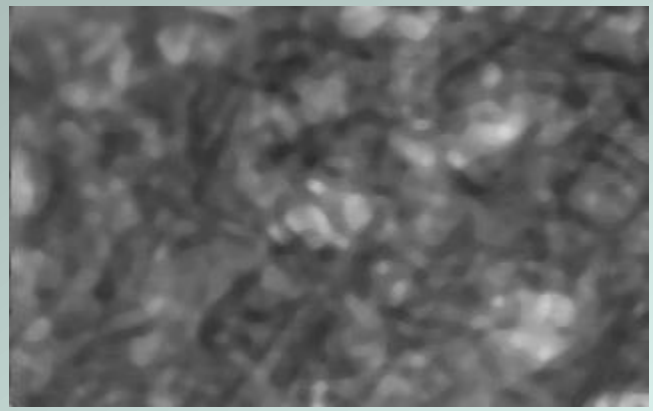


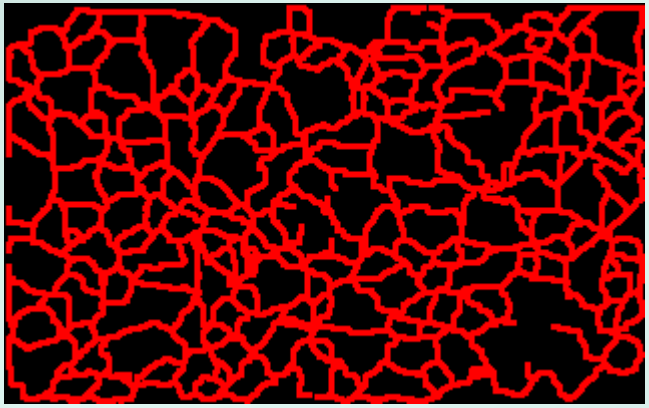
normal tissue

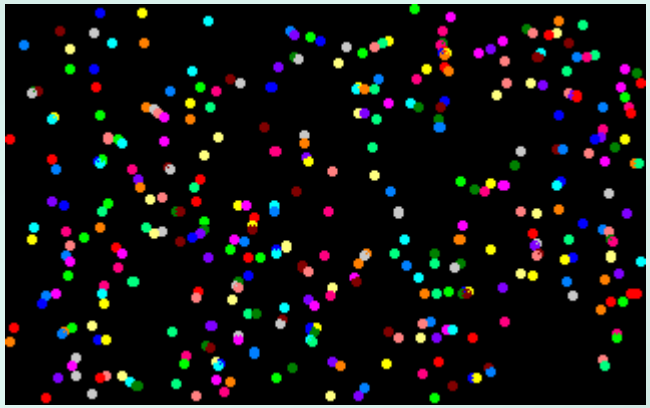


gliablastoma with cells polymorphism.

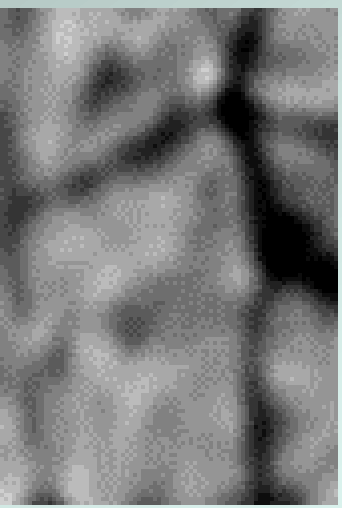
Segmentation of elongated objects

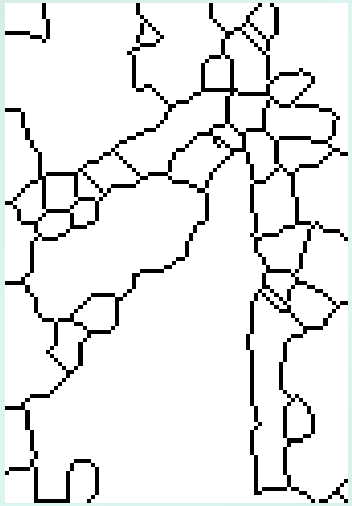
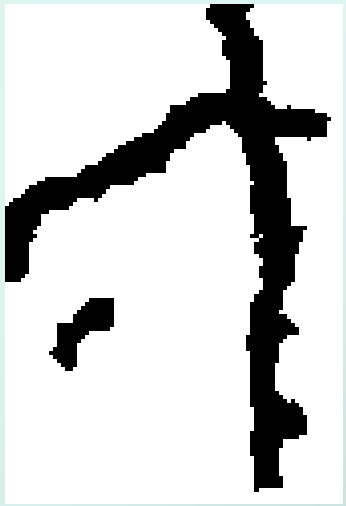
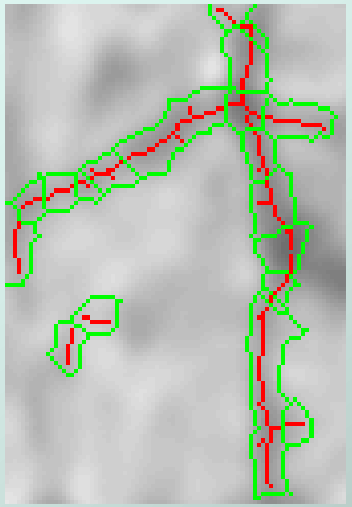




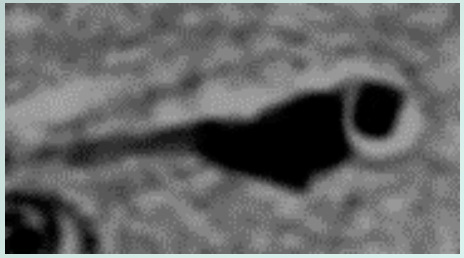


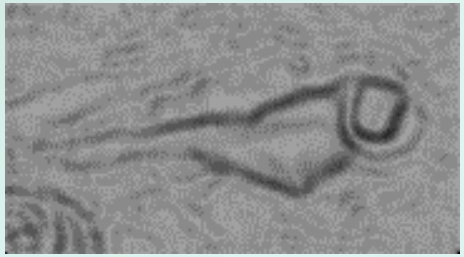
Morphological segmentation of image fibers under large resolution



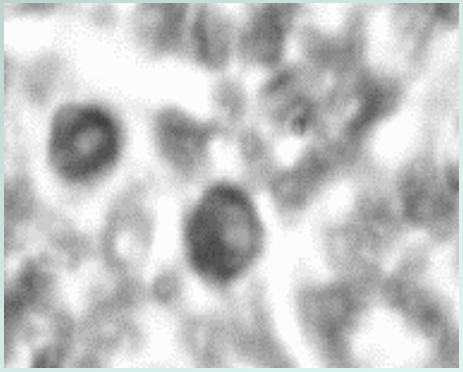




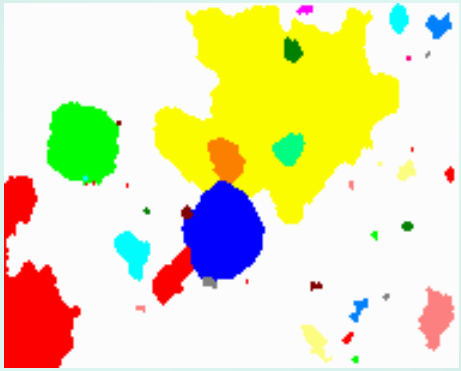
Morphological segmentation of area objects

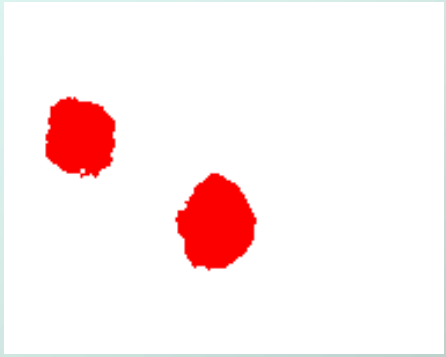




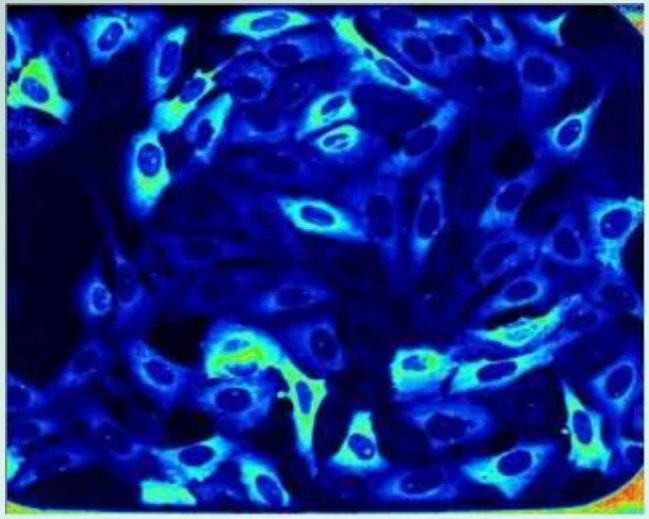
Segmentation of low-contrast images by region growing method

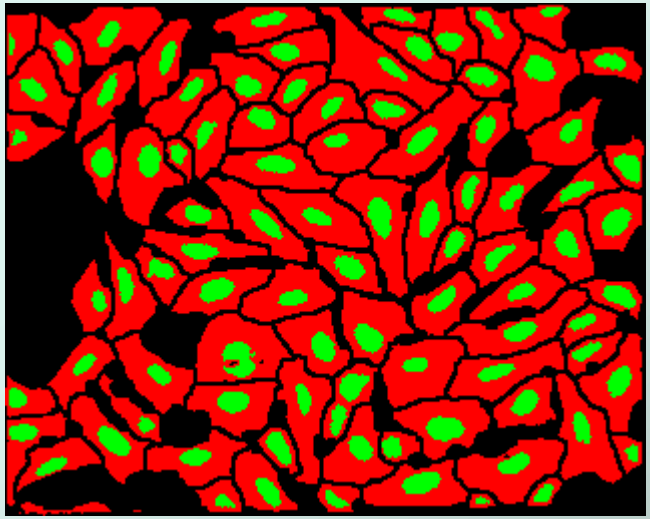






Morphological segmentation of cell images





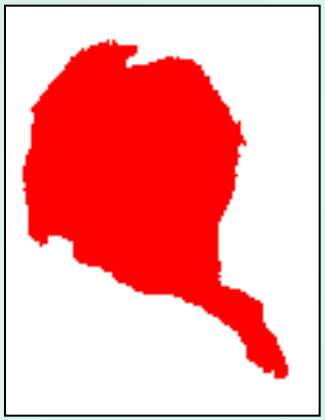
Feature extraction

The following types of features can be extracted:

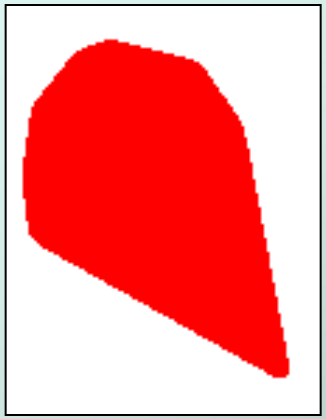
- Geometrical
- Topology
- Texture
- Densitometry

Feature extraction

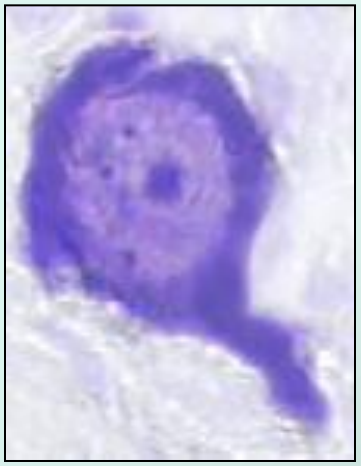
simple or net area



fill area

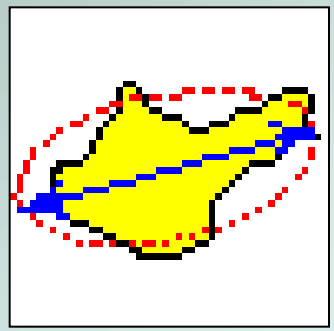


convex area



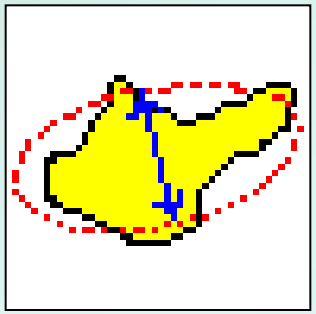
Feature extraction

Major Axis



- **Major Axis Length** (object length)
- **Major Axis Angle**

Minor Axis

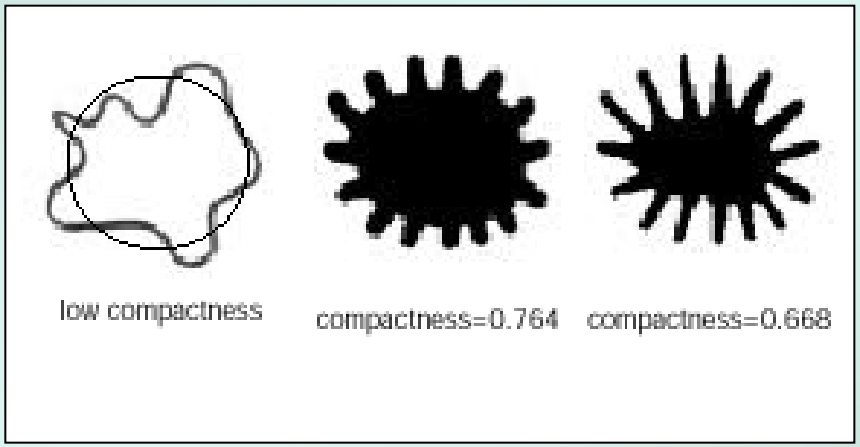


- **Minor Axis Length** (object width)
- **Minor Axis Angle**

Feature extraction

Compactness

defined as the ratio of the area of an object to the area of a circle with the same perimeter



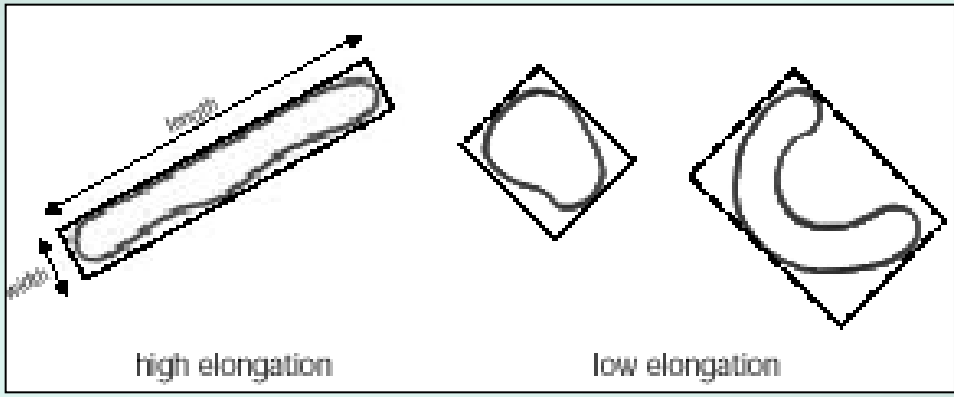
• A circle is used as it is the object with the most compact shape.
• The measure takes a maximum value of 1 for a circle
• Objects which have an elliptical shape, or a boundary that is irregular rather than smooth, will decrease the measure.

An alternate formulation:
• The measure takes a minimum value of 1 for a circle
• Objects that have complicated, irregular boundaries have larger compactness

Feature extraction

Elongation

is the ratio between the length and width of the object bounding box



– The result is a measure of object elongation, given as a value between 0 and 1.

– If the ratio is equal to 1, the object is roughly square or circularly shaped. As the ratio decreases from 1, the object becomes more elongated

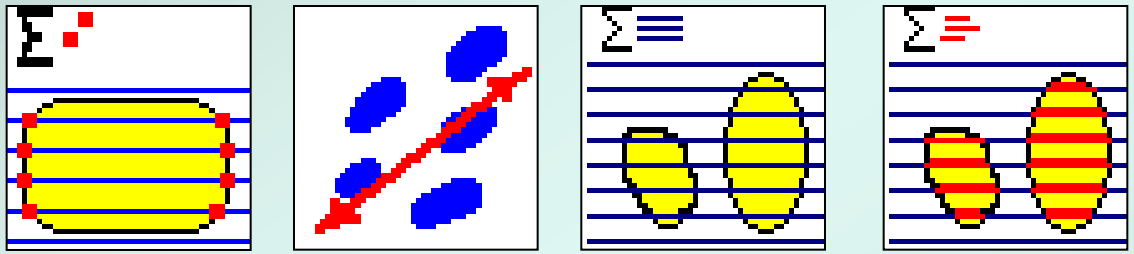
This criterion cannot succeed in curved regions, for which the evaluation of elongatedness must be based on maximum region thickness.

– Elongatedness can be evaluated as a ratio of the region area and the square of its thickness.

– The maximum region thickness (holes must be filled if present) can be determined as the number **d** of erosion steps that may be applied before the region totally disappears.

Feature extraction

Texture description



Intercept ***Anisotropy*** ***ChordSum*** ***ChordRef***

Intercept is a stereological parameter which is defined as the number of times the horizontal or vertical grid crosses the phase boundary. The spacing of the grid is defined by the global variable *GridSpace* which has a default value of 1.

Anisotropy is derived from the intercept and defines the general anisotropy of the phase relative to the coordinate axes.

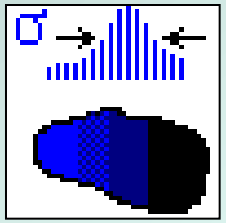
The sum of chords is a stereological parameter defined as the total length of horizontal grid lines falling inside the objects belonging the phase The spacing of the grid is defined by the global variable *GridSpace* which has a default value of 1

ChordSum returns the length of grid lines crossing the phase, in calibrated units:

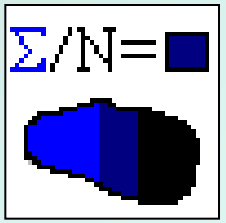
ChordRef returns the total length of grid lines in the image or selection, in calibrated units

Feature extraction

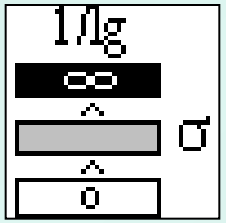
Densitometry description



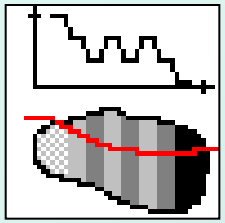
Histograme of intensity



Average intensity



Optical dencity



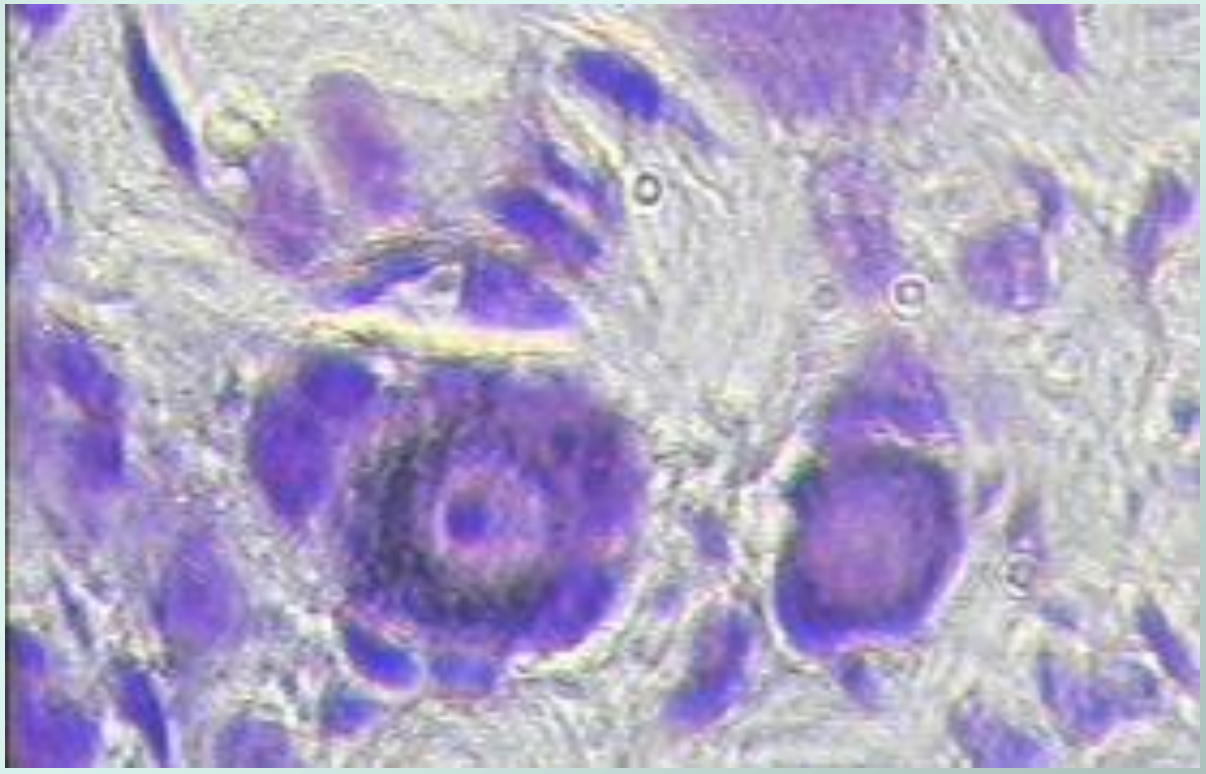
Profile

- the average scaled intensity of an object or phase
- the integral scaled intensity of an object or phase
- the maximum scaled intensity within an object or phase
- the minimum scaled intensity within an object or phase
- the standard deviation of scaled intensity within an object or phase
- the average value of the scaled green component of an object or phase
- the standard deviation of the green component within an object or phase
- histogram - the vector of pixel intensity distribution within an object
- Profile - the vector of intensities along the object's contour

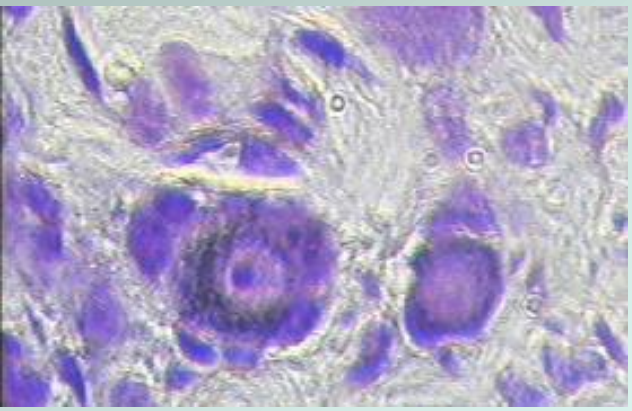
EXTRACTION OF CELL AND NUCLEAR STRUCTURE IN COLOR HISTOLOGICAL IMAGES

Color image of nervous cells a spinal cord

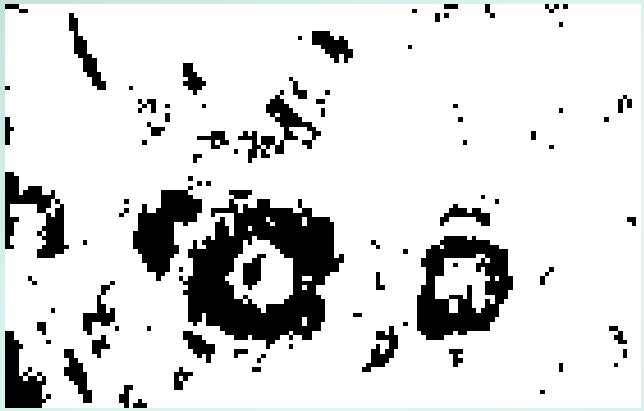
The nucleus is usually located in center of cells. The gray characteristics of nucleus differ from cell characteristics. In a nucleus, there exist one or some rounded dark particles, that is named nucleolus.



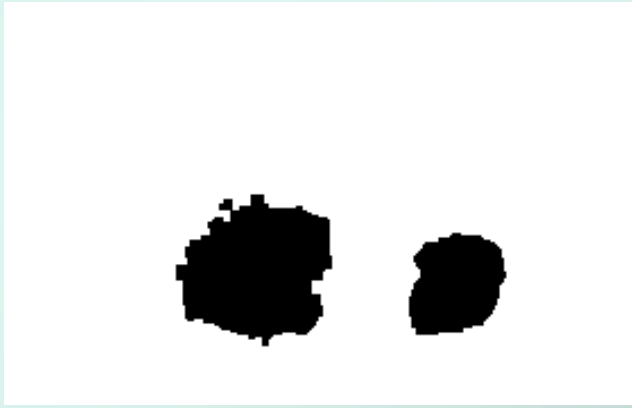
Extraction of cell structure



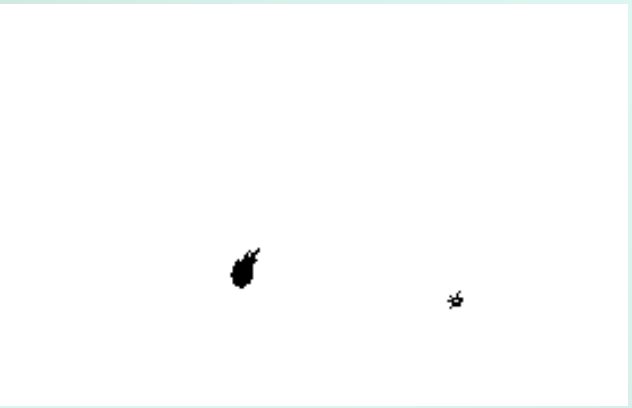
Color image of nervous cells a spinal cord



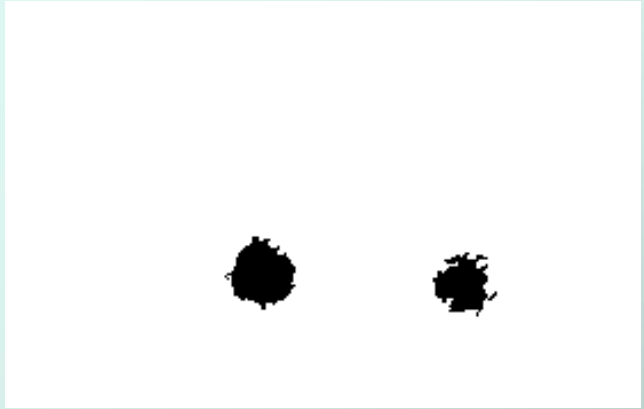
Binary image – result of segmentation.



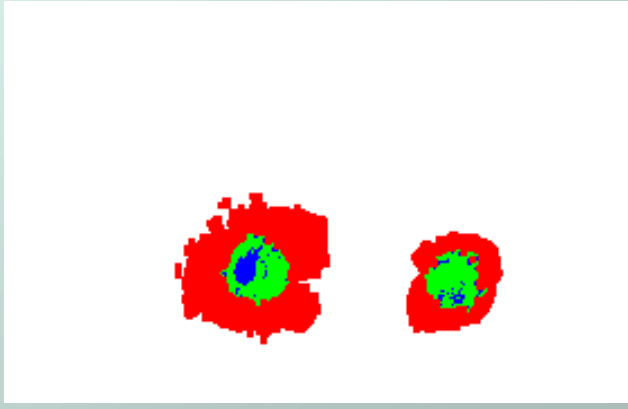
Binary image of nervous cells



Binary image of nucleolus



Binary image of nucleus of cells.



Hierarchical image of nervous cells in spinal cord.

Extraction of cell structure

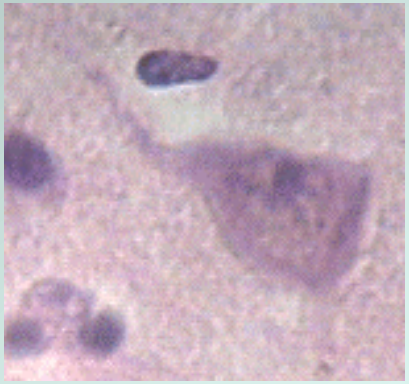
For obtain to binary nucleolus images it is necessary to execute logic "**AND"** operation between the initial binary image and the binary image of a nucleus, having removed dot noise.
The idea of hierarchy of areas is easily realized in computer facilities using bits.

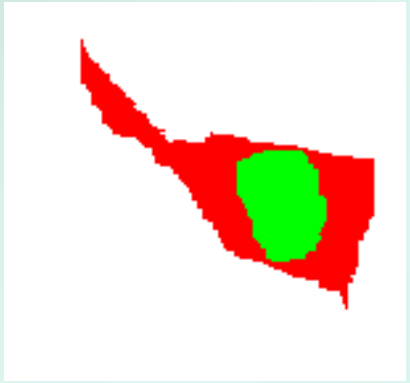
Object	*Operation*	*Separate value*	*Result of association*
Cell	1 < < 0	1	1
Nucleus	1 < < 1	2	3
Nucleolus and inclusions	1 < < 2	4	7

Hierarchical image of nervous cells in spinal cord.

Optimum condition for pixel P an ideal cell is:
(P **AND** 1) **OR** (P **AND** 3) **OR** (P **AND** 7),

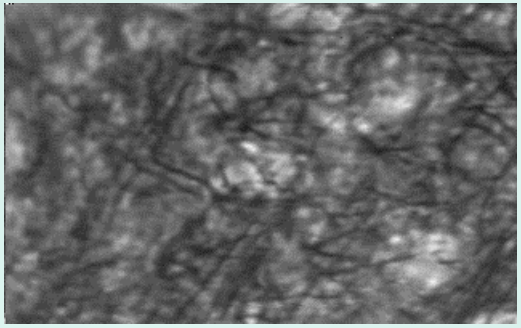
Extraction of pyramidal neurons of a head brain



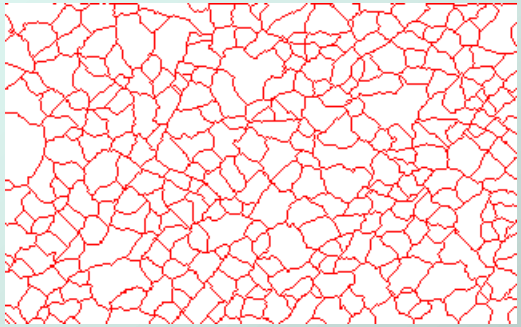


Neural cells with extracted neurons,

Determination of density of radial and tangential fibers of a brain tissue

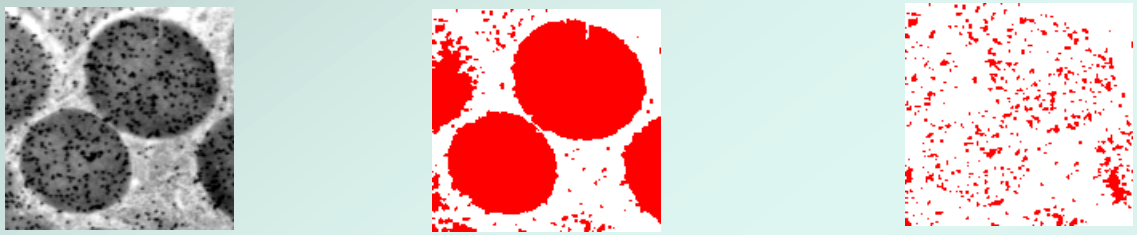


Radial and tangential fibers of a brain fabric



Result of gray-scale thinning of an image of fibers with

Observation of exchange of substances in a cell with help of radioavtography



a) b) c)

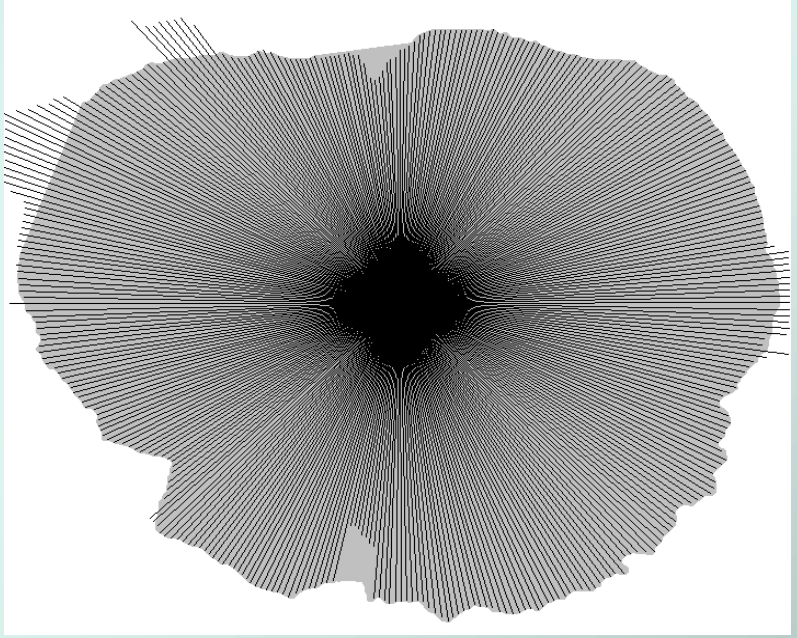
Cell of blood with radioisotope labels: a) a gray scale image b) result of threshold segmentation c) a binary image of radioisotope labels obtained by threshold segmentation

a) b)

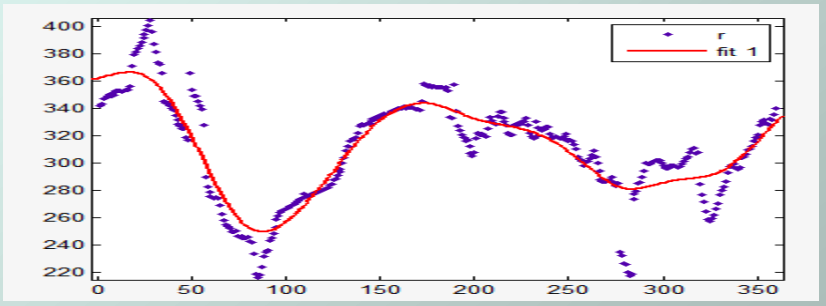
a) Image of blood cells b) image of radio-isotope labels in cells

The set of segmentation algorithms for objects with a fuzzy borders on a microscopic image.

This is based on the methods of definition of borders and their subsequent contour correction.



Using the contour scanning giving a more accurate shape of microscopic objects for such complex objects with broken boundaries as sections of organs, cells and nuclei in histological sample images.

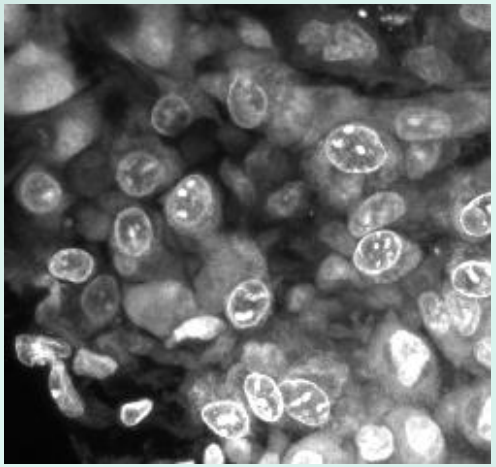


The algorithm constructs a smooth border facility

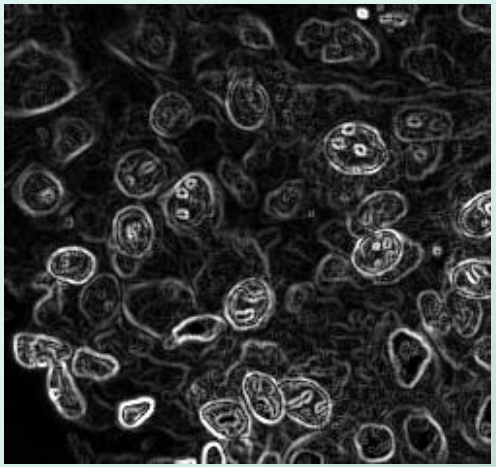
The set of algorithms of segmentation of textured objects

The algorithm is based on methods of regions growing and regions association. Its uniqueness consist of synthesis of an artificial image, which characteristics that are shown simultaneously boundaries and texture on the image. For every pixel first and second derivatives are define properties of neighborhood.

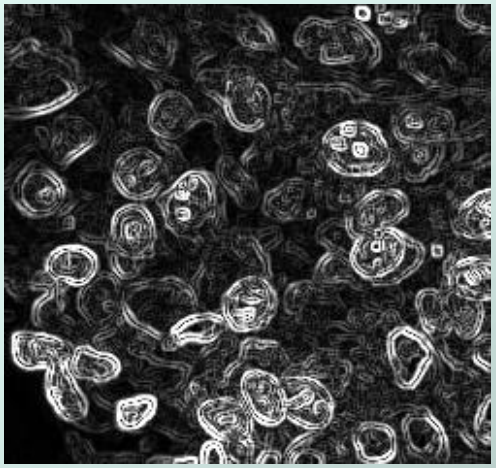
As a result of this modification the algorithm identifies objects with very small details on a new qualitative level.



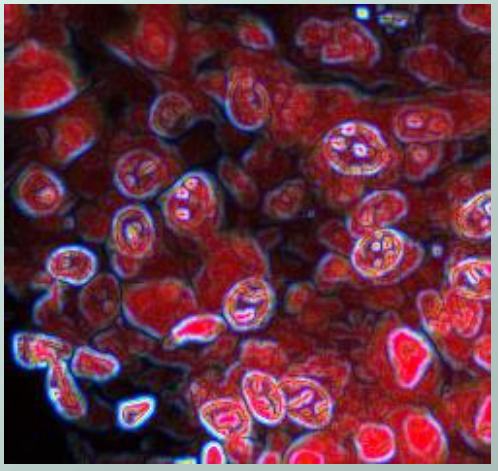
source



First derivative

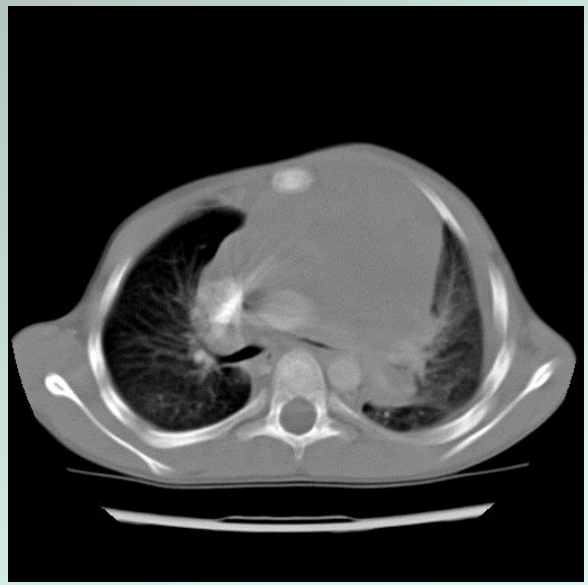


Second derivative

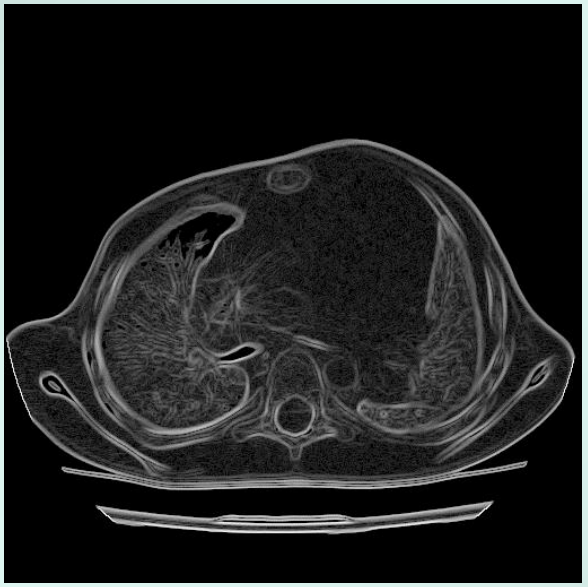


synthesized

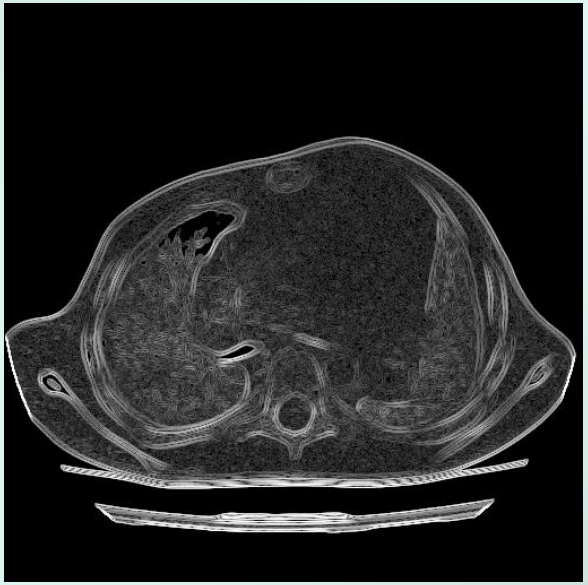
Stages of image processing



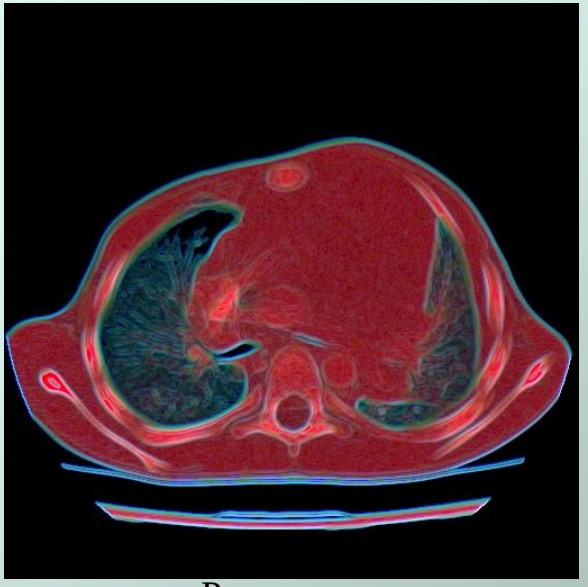
R



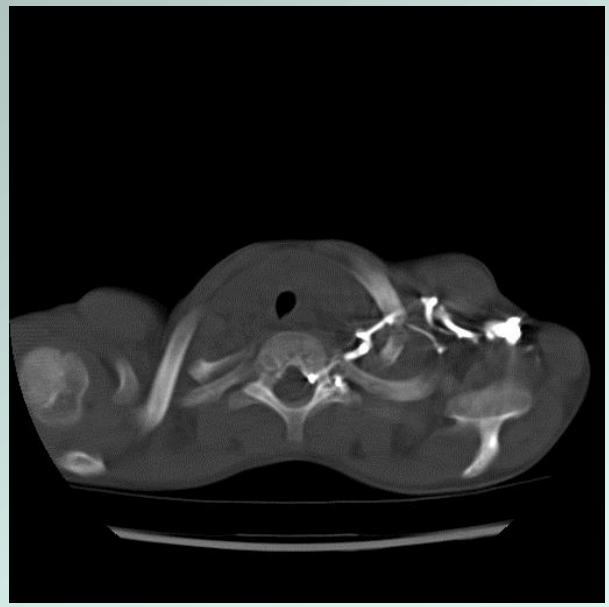
G



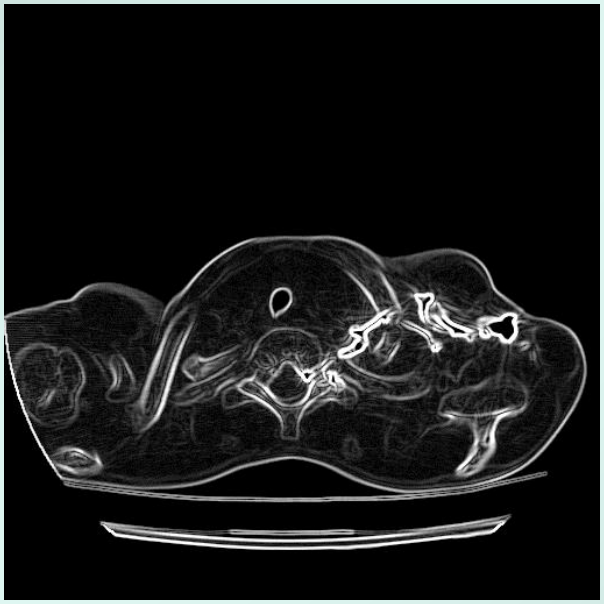
B



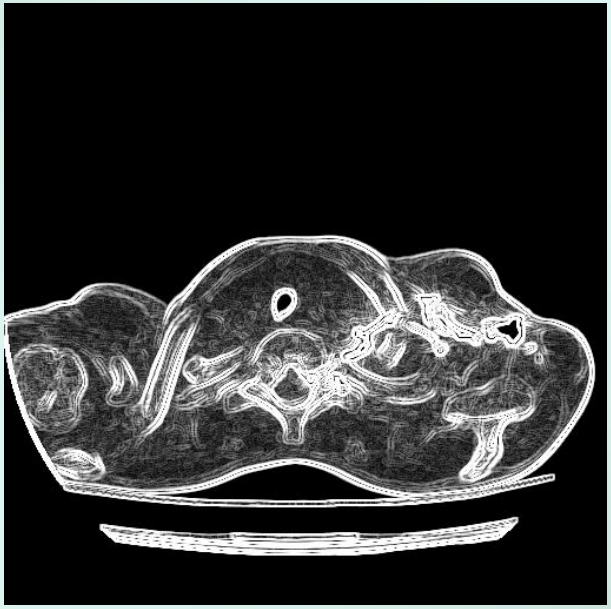
P



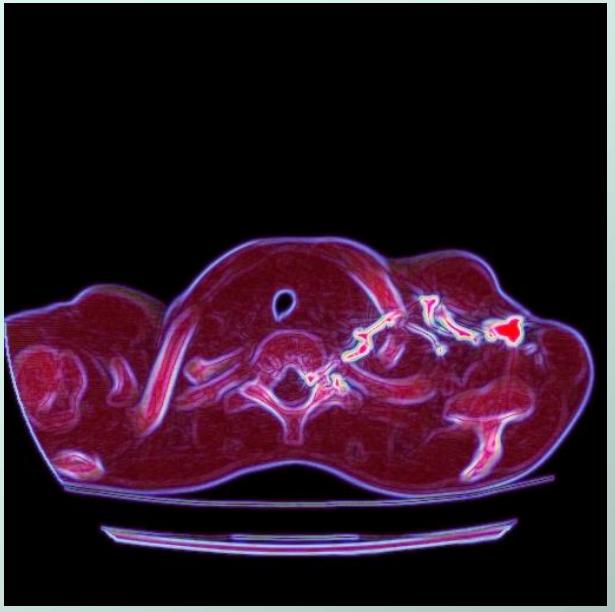
R



G

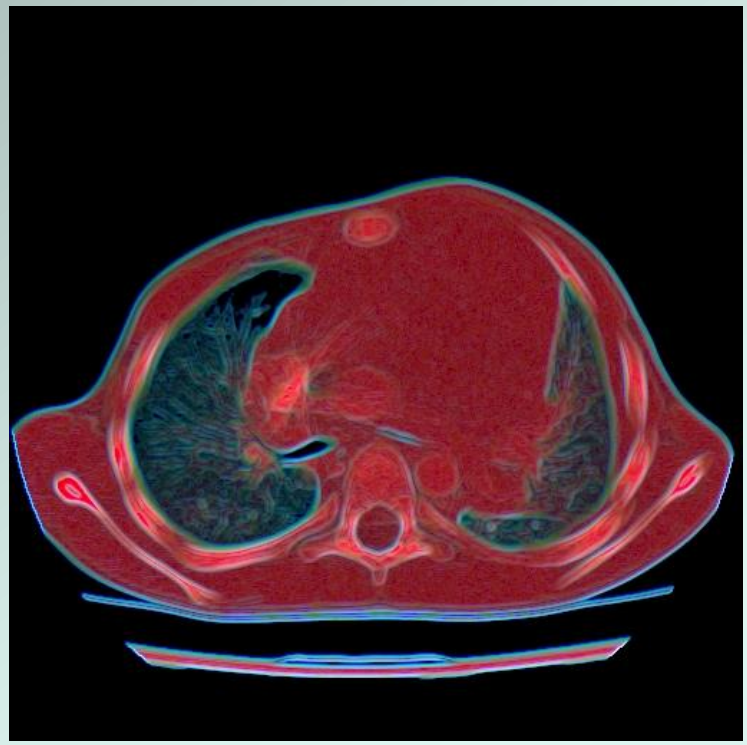


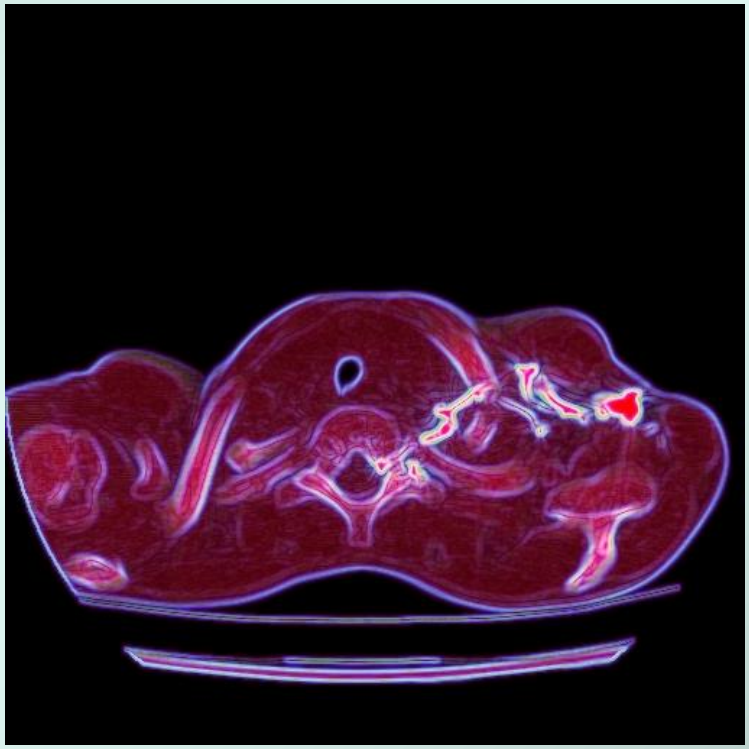
B

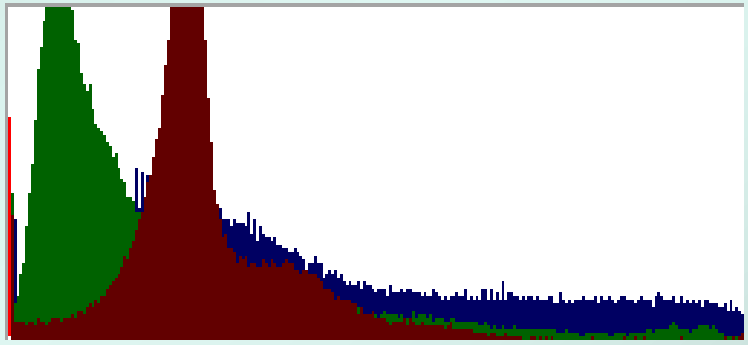


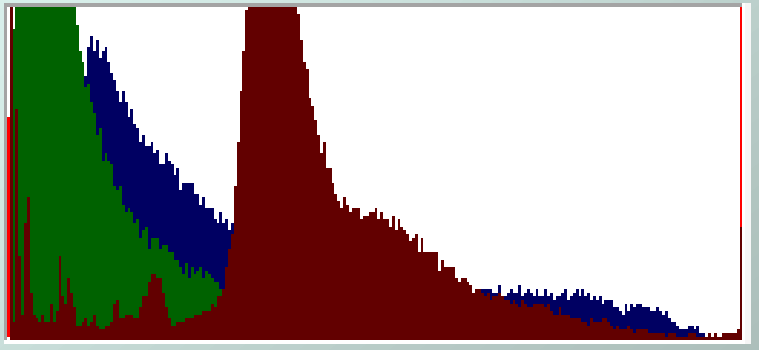
P

Analysis of results





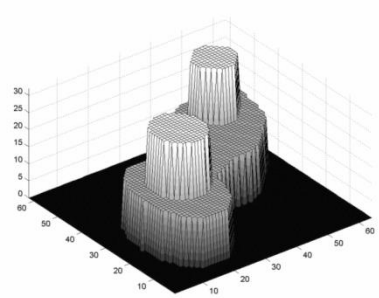




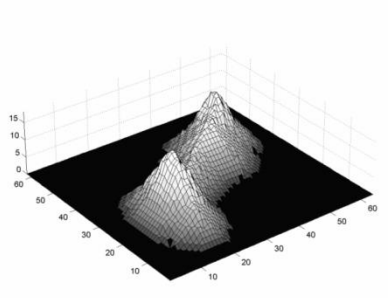
The set of algorithms of algorithm on base gray and color thinning

The result of thinning operation is a skeleton. For gray thinning algorithm, it is necessary to build special distance map, which includes all necessary properties of a skeleton. Skeleton reflects the following topological properties of an object.

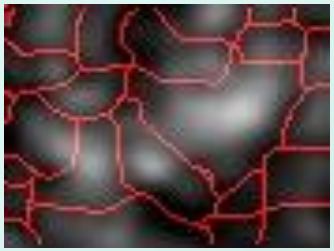
We propose to use pseudodistance map (PDM) instead of distance map.
PDM should preserves all these properties and can be built in a more effective and easier way



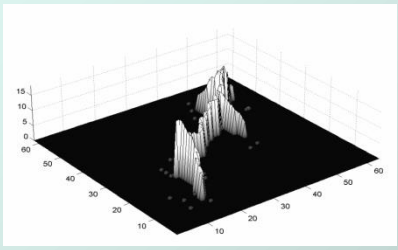
Тестовый объект



PDM



Скелет на изображении



Скелет объекта

algorithms:	Working time (ms)	Relation time coefficient
PDM	51	0.08
Zhang-Suen	480	0.76
4 scanning method	630	1

Building a pseudo-distance map

0	0	0	0	0	0	0	0
0	255	255	255	255	255	255	0
0	255	255	255	511	511	255	0
0	255	255	255	511	511	255	0
0	255	255	255	511	511	255	0
0	255	255	255	511	511	255	0
0	255	255	255	255	255	255	0
0	0	0	0	0	0	0	0

a)

0	0	0	0	0	0	0	0
0	1	1	1	1	1	1	0
0	1	2	2	256	256	1	0
0	1	2	3	256	256	1	0
0	1	2	3	256	256	1	0
0	1	2	2	256	256	1	0
0	1	1	1	1	1	1	0
0	0	0	0	0	0	0	0

b)

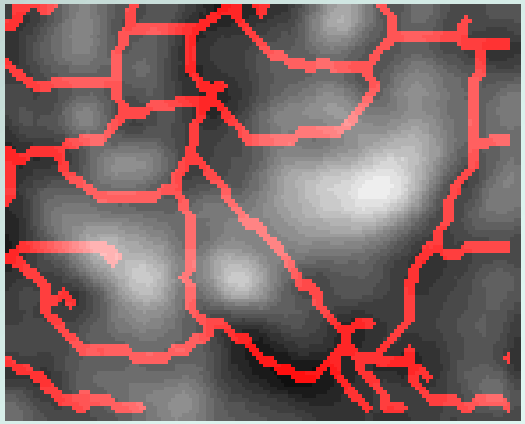
Stages of pseudo-distance map construction:

a) A gray-scale image multiplied by 256

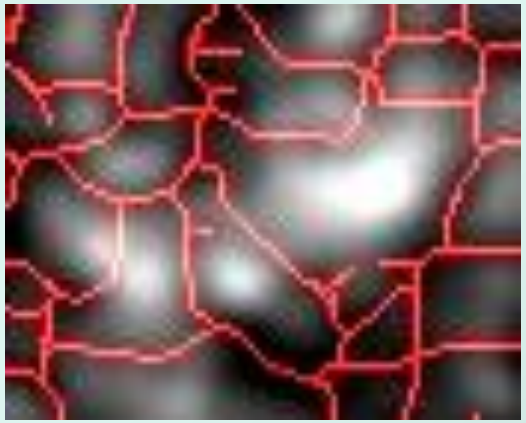
b) pseudo-distance map.

Conclusion and discussion

a)

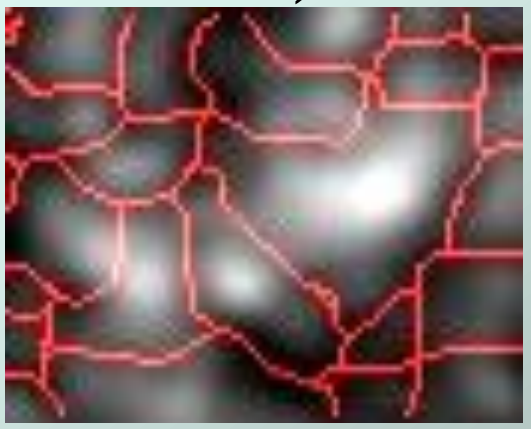


b)



c)

Result of thinning: a) source image, b) Zhang-Suen method, c) algorithm by pseudodistance map, d) algorithm by pseudodistance map with prunning

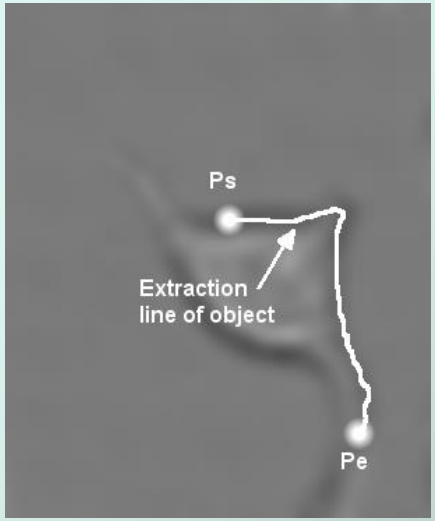


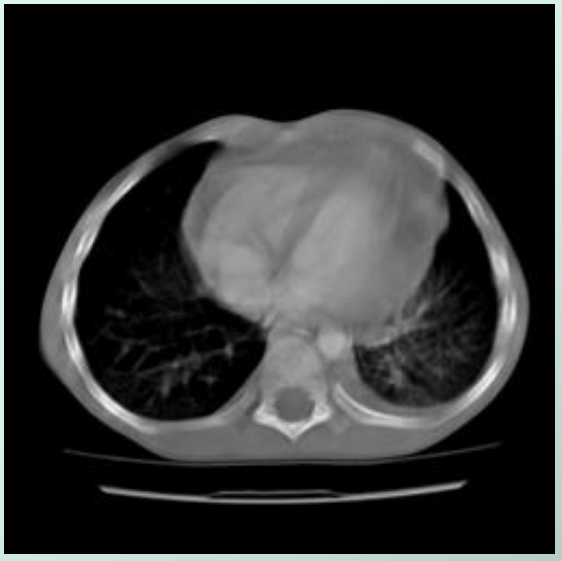
d)

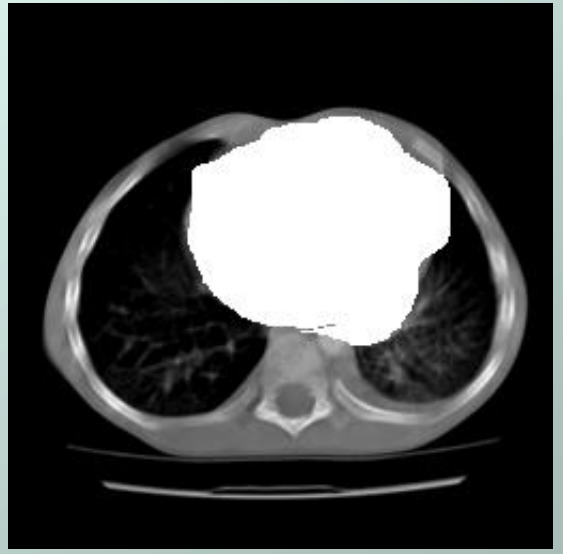
The algorithm has been widely tested to thin biomedical vascular images. The pictures shows result of thinning of biomedical image by our algorithm. As one can see, the algorithm correctly extracted all ridge pixels. There exist several open branches bounded by end and node pixels. However, they can be easily removed by pruning procedure.

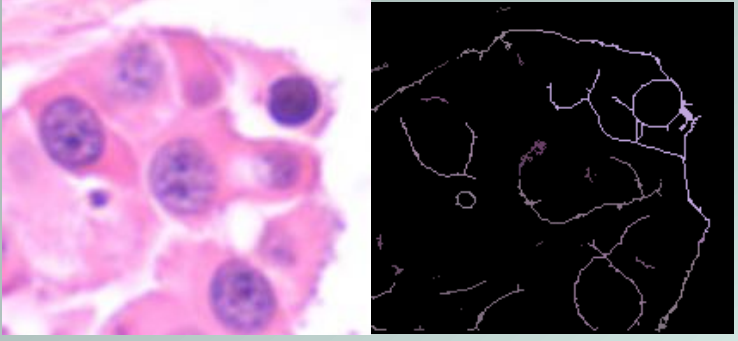
Pseudo-distance map transformation for interactive object tracing

In the proposed method, a user firstly specifies a start point and an end point of the target road on a bitmap image. This is the only step manually performed by the user. The remaining steps will be done by automatically. Then a regular-mesh graph is prepared on a bitmap image by treating every pixel as a node and putting an edge between every pair of adjacent nodes wpipj
The weight is assigned with the proposed pixel value on pseudo-distance map.



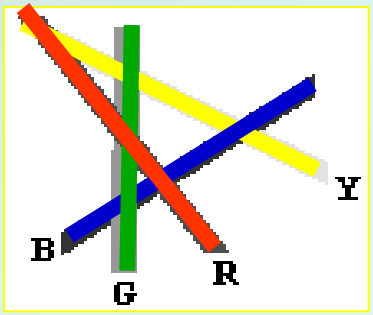




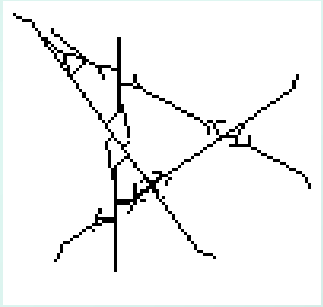


Thinning of color medical images

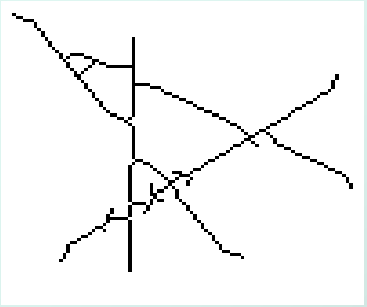
The thinning algorithm for color image is unique, because it defines the connection to such a complex characteristics as color. The result of thinning correspond to the correct skeleton of the object that based on the color characteristics and served its topological evaluation.



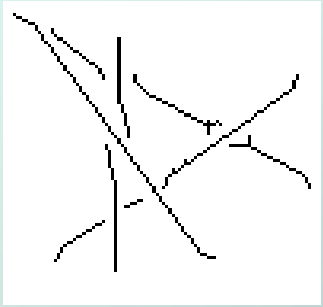
source



Thinning in RGB



Thinning by BITMIX method



Result of proposed algorithm

It uses a specific angular value of color :

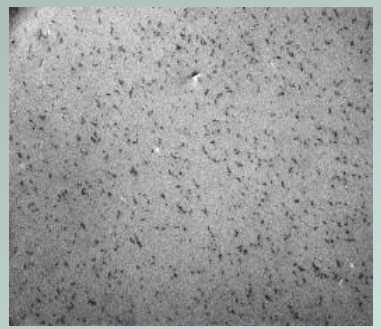
$$A=H\ C_{max}/C,$$

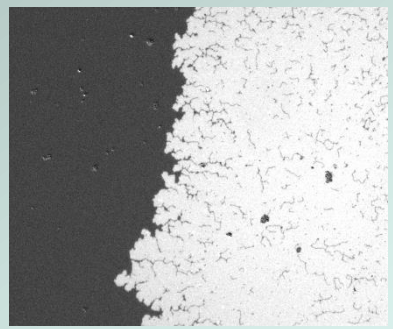
where A– specific angular value, H – hue, C_{max} – maximum of saturation, C – saturation in pixel.
As a result, the condition of pixel connectedness is determined as follows :

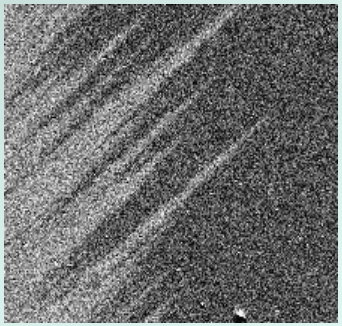
$$(L_j>=L_x \text{ AND } |A_j-A_x| < \pi/4)$$

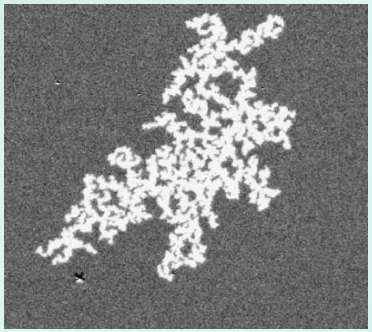
where L_j – the brightness of neighboring pixels, Lx – the brightness of source pixels .

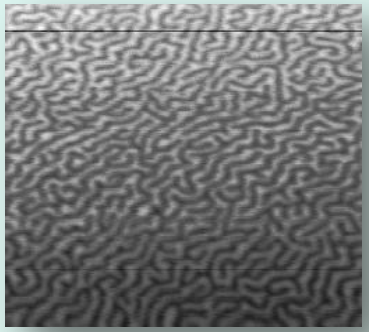
Structure Shape Description Approach for Magnification Images


Blobs

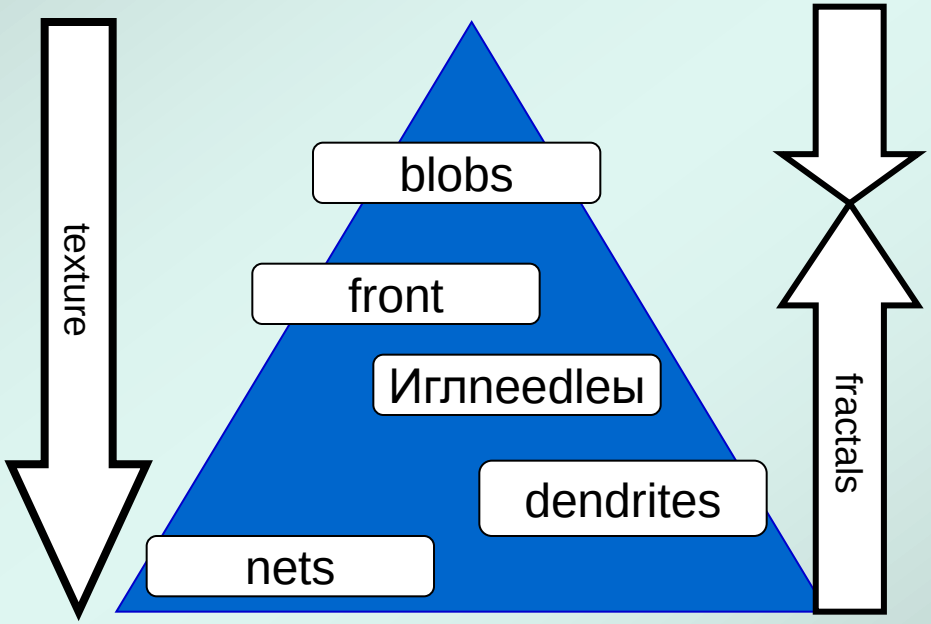

front


needle


dendrites


nets

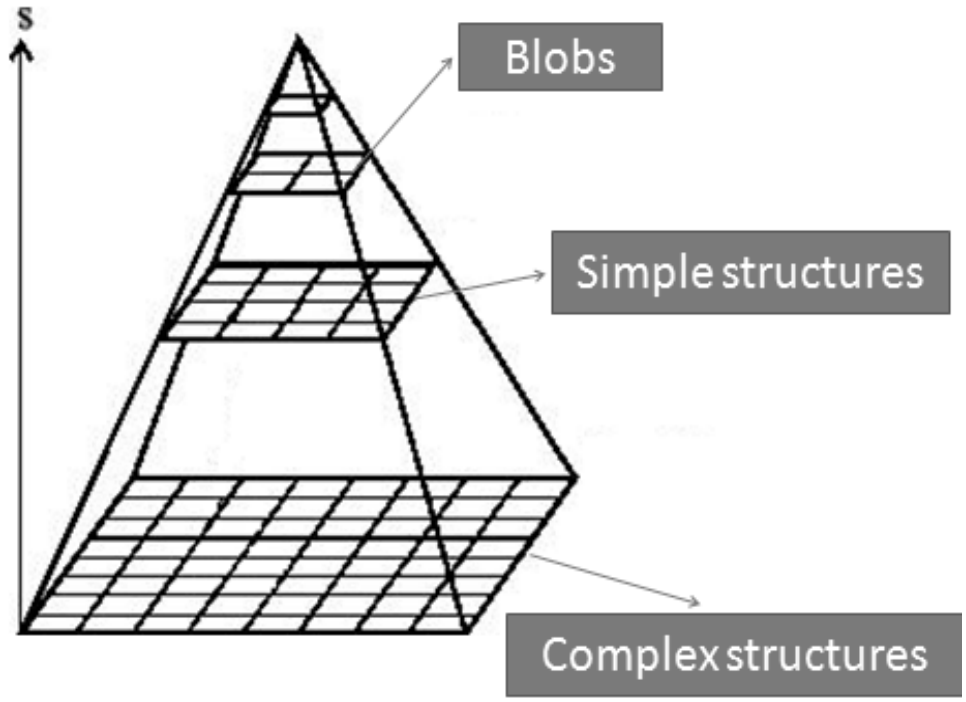
The structures are divided into five major classes. Each class has its individual set of characteristics to describe them, are defined in the work.

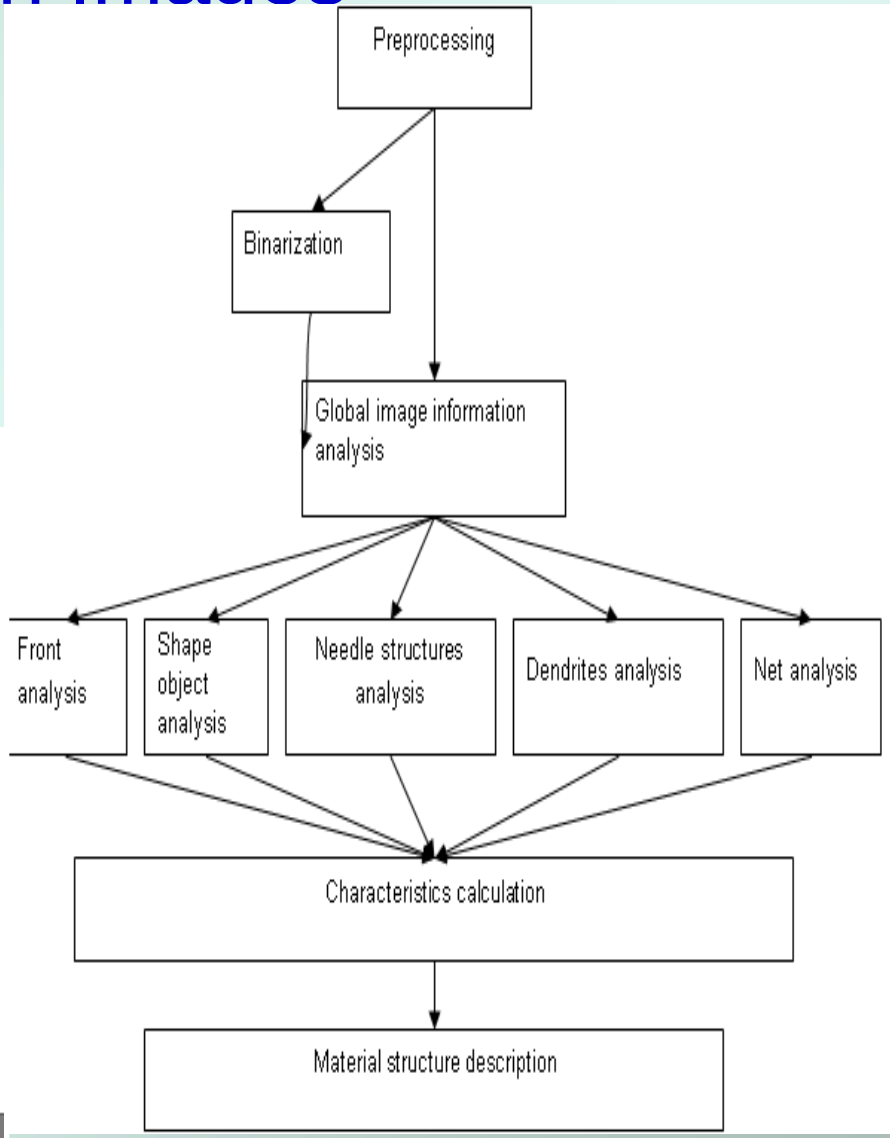


Defects are evaluated:
- geometric displacement;
- offset brightness;
- residual noise;
- uneven brightness;
- limited region of interest.

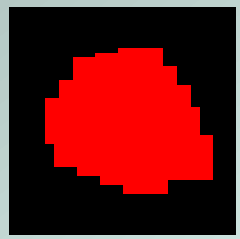
Structure Shape Description Approach for Magnification Images

Determination of the presence of these structures gives an indication of the local organization of the nature of fabric or material.

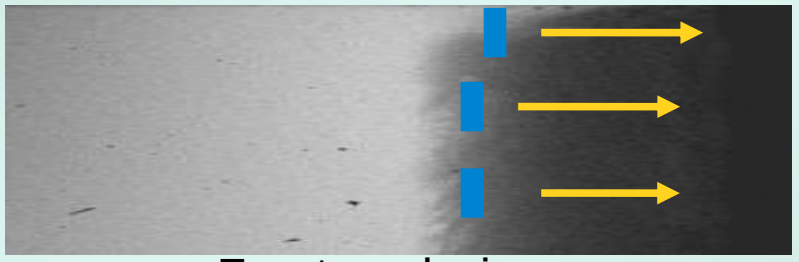




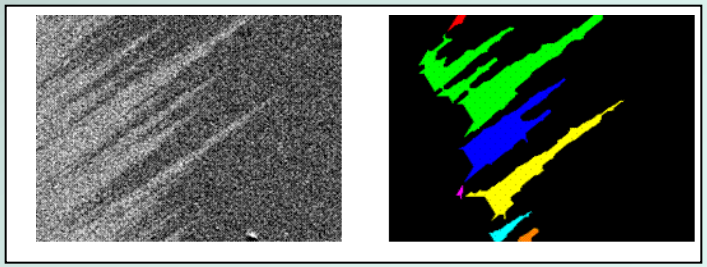
Sets of structure analysis algorithms.

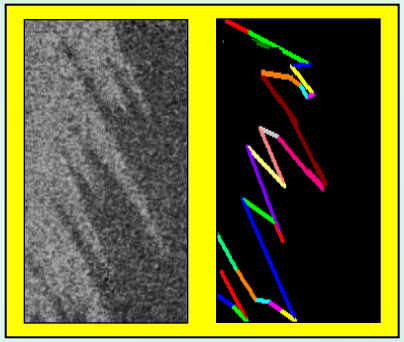


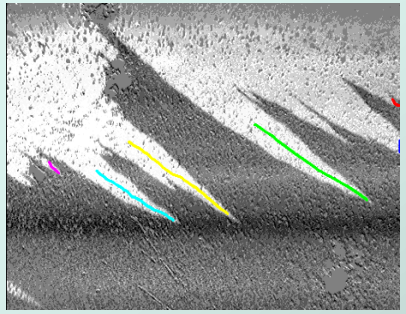
Blobs analysis



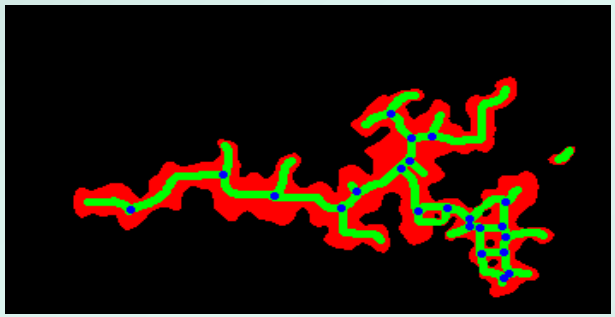
Front analysis



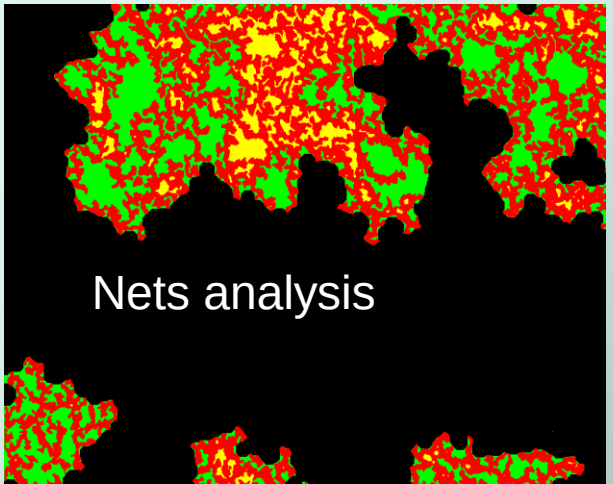


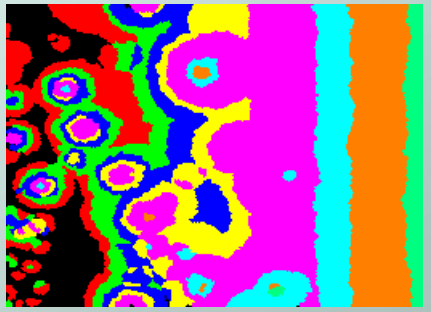


Needle analysis



Dendrites analysis

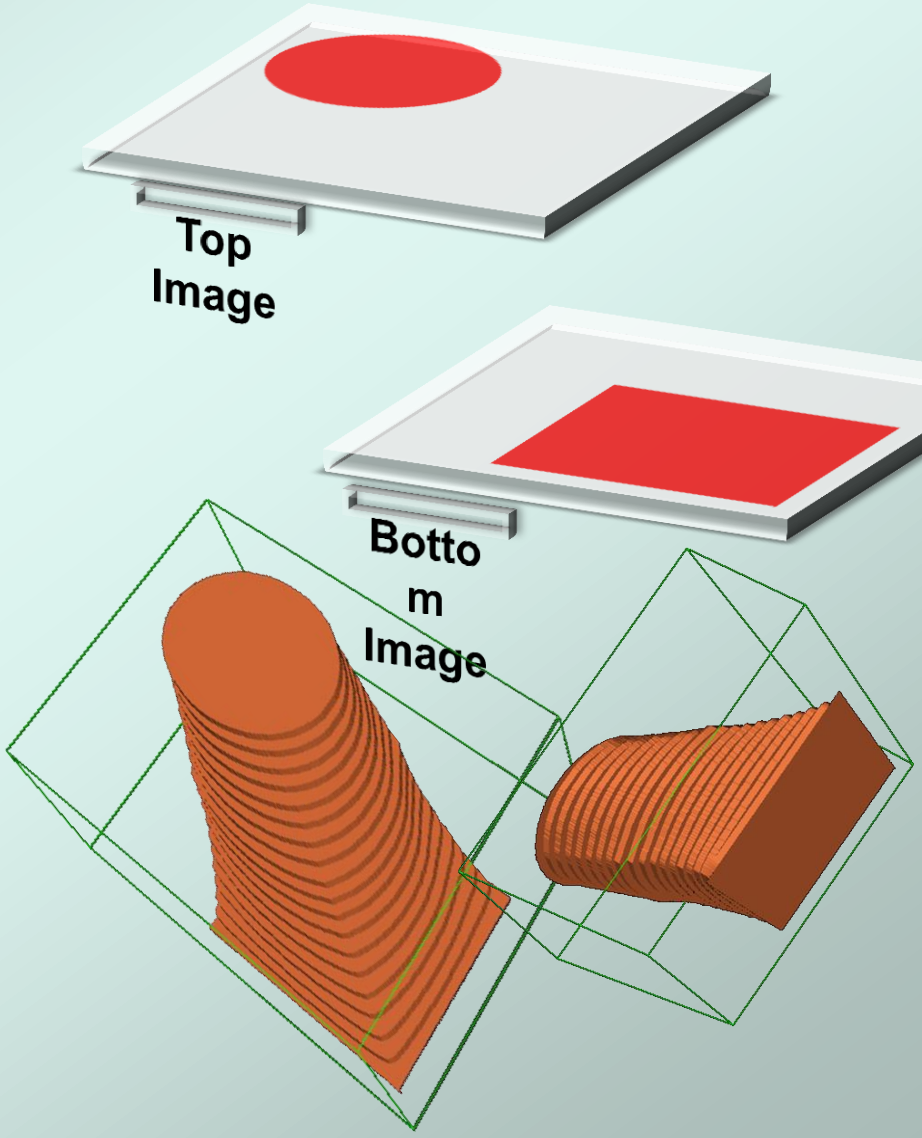




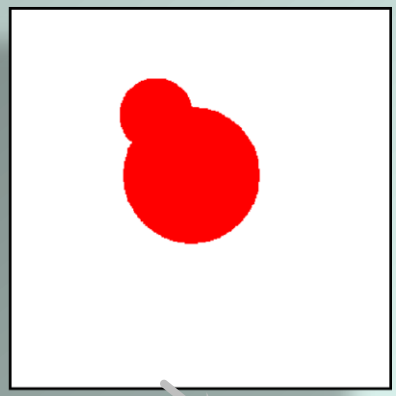
Analysis of nuclear grow

Reconstruction of 3D Medical Object Shapes from 2D Cross-Sections

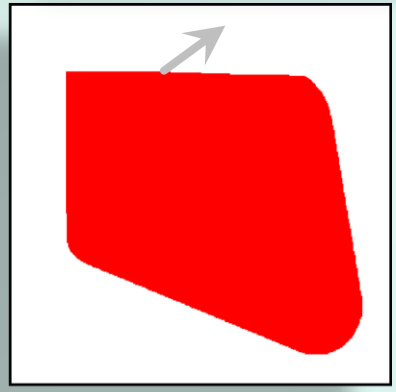
- The task of three-dimensional object surface reconstruction is well known in different applications, especially in medicine
- It is used in MRI, CT, 3D USI, etc.
- Usually segmented object of interest is represented by 2D cross-sections on medical image slices
- Achievement of these cross-sections can be the challenging problem, and can be performed either manually or automatically

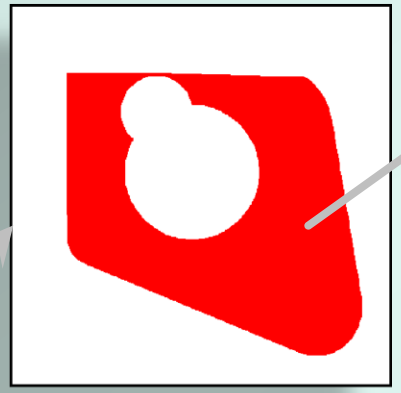


MAIN IDEA

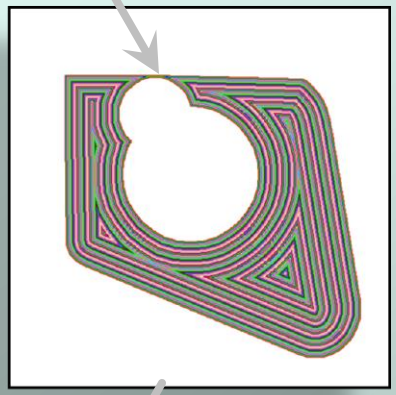


XOR

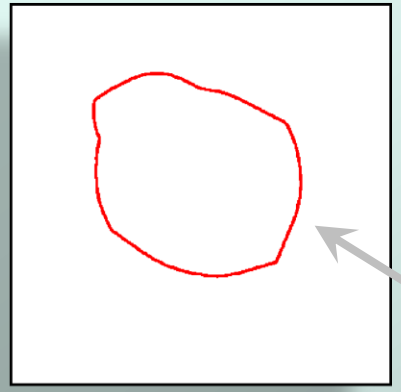




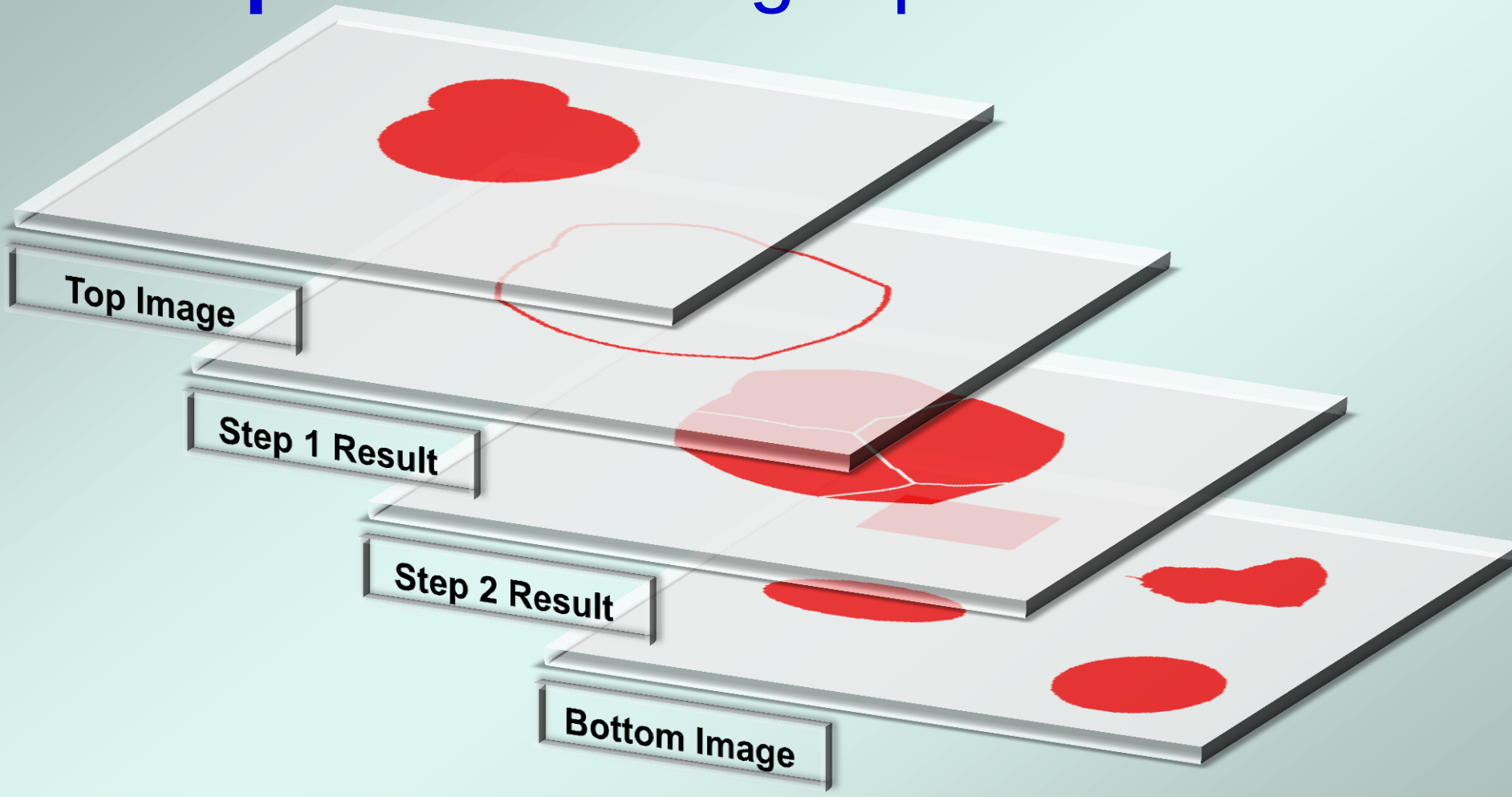
DISTANCE MAP



WATERSHED



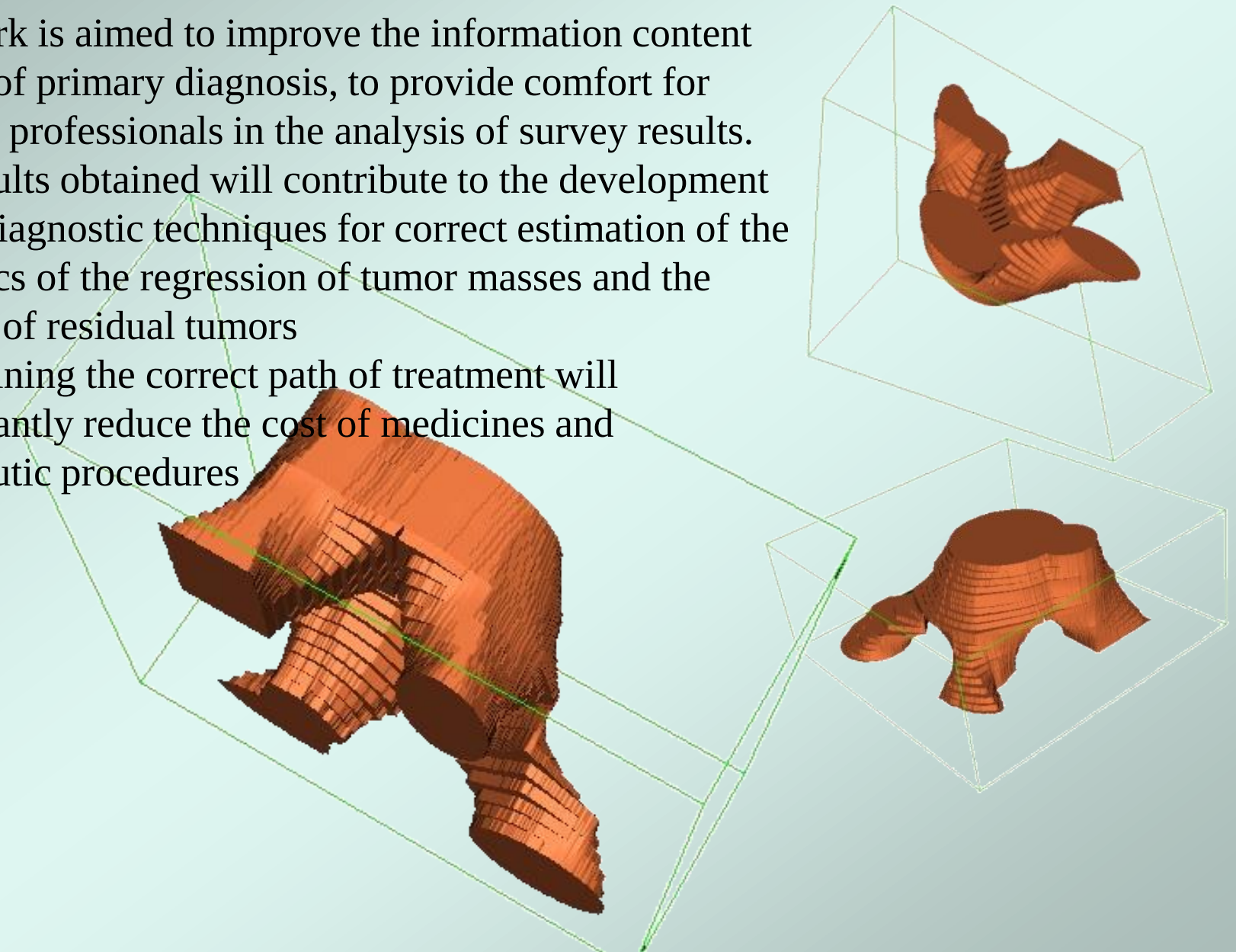
Sample: branching Input Data



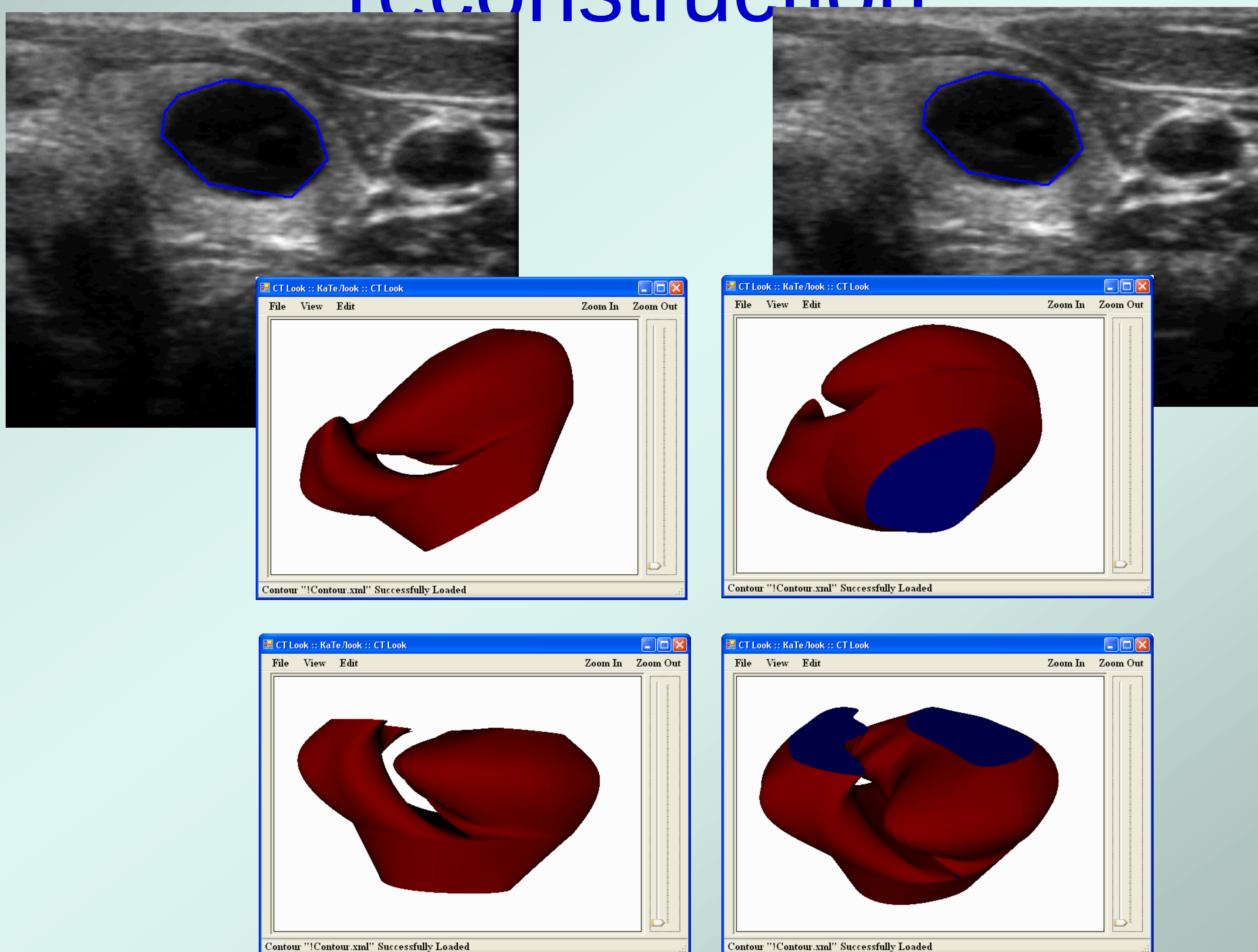
3D reconstruction

The work is aimed to improve the information content of data of primary diagnosis, to provide comfort for medical professionals in the analysis of survey results. The results obtained will contribute to the development of ray diagnostic techniques for correct estimation of the dynamics of the regression of tumor masses and the amount of residual tumors

Determining the correct path of treatment will significantly reduce the cost of medicines and therapeutic procedures

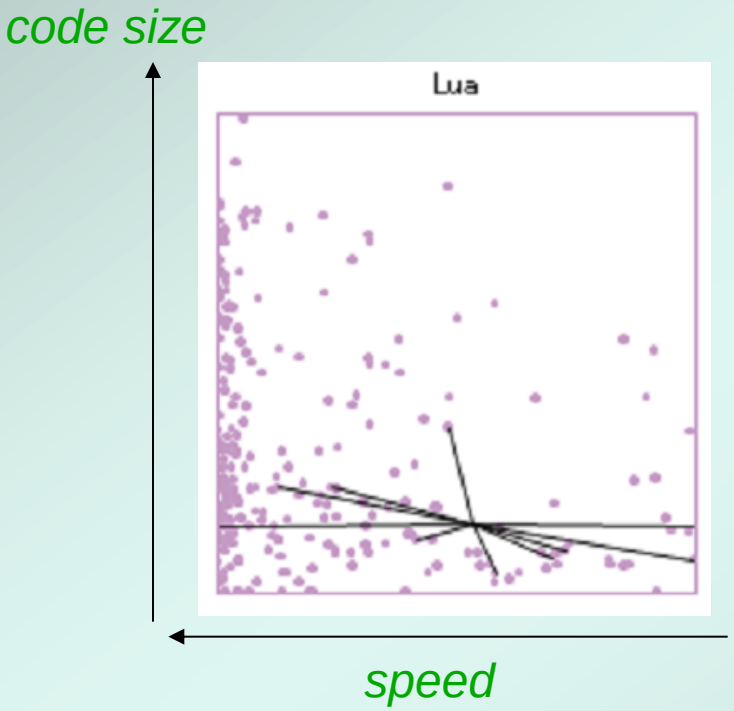


Real sample of branching 3D reconstruction



Realization

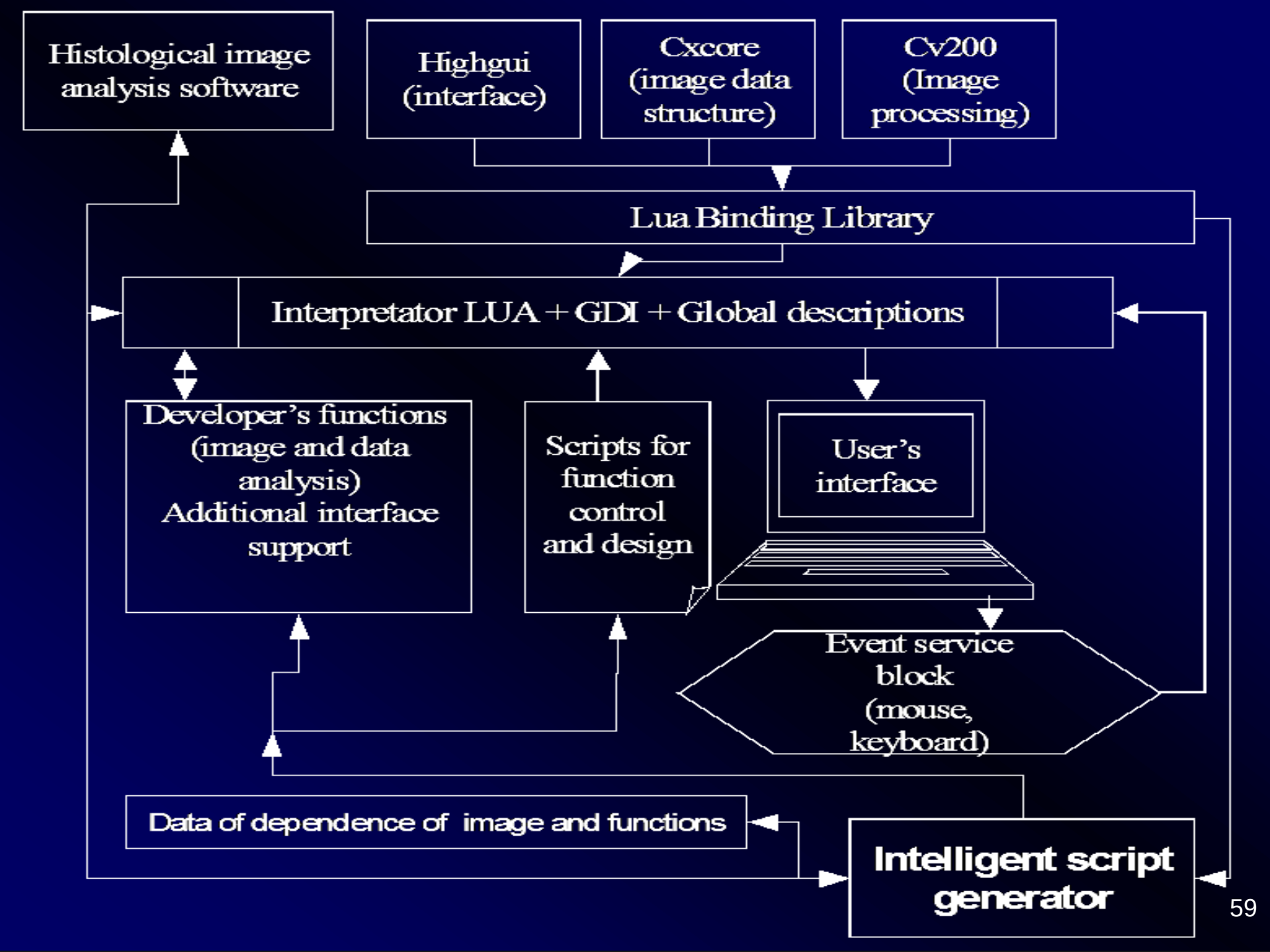
For elaboration of a structural scheme of a software basic interface an estimation of functionality and compatibility of existed software development tools were done. Lua is a good choice for core. Tasks which may be solved with the software to be developed, initial data, diagnostic features and characteristics have been observed.

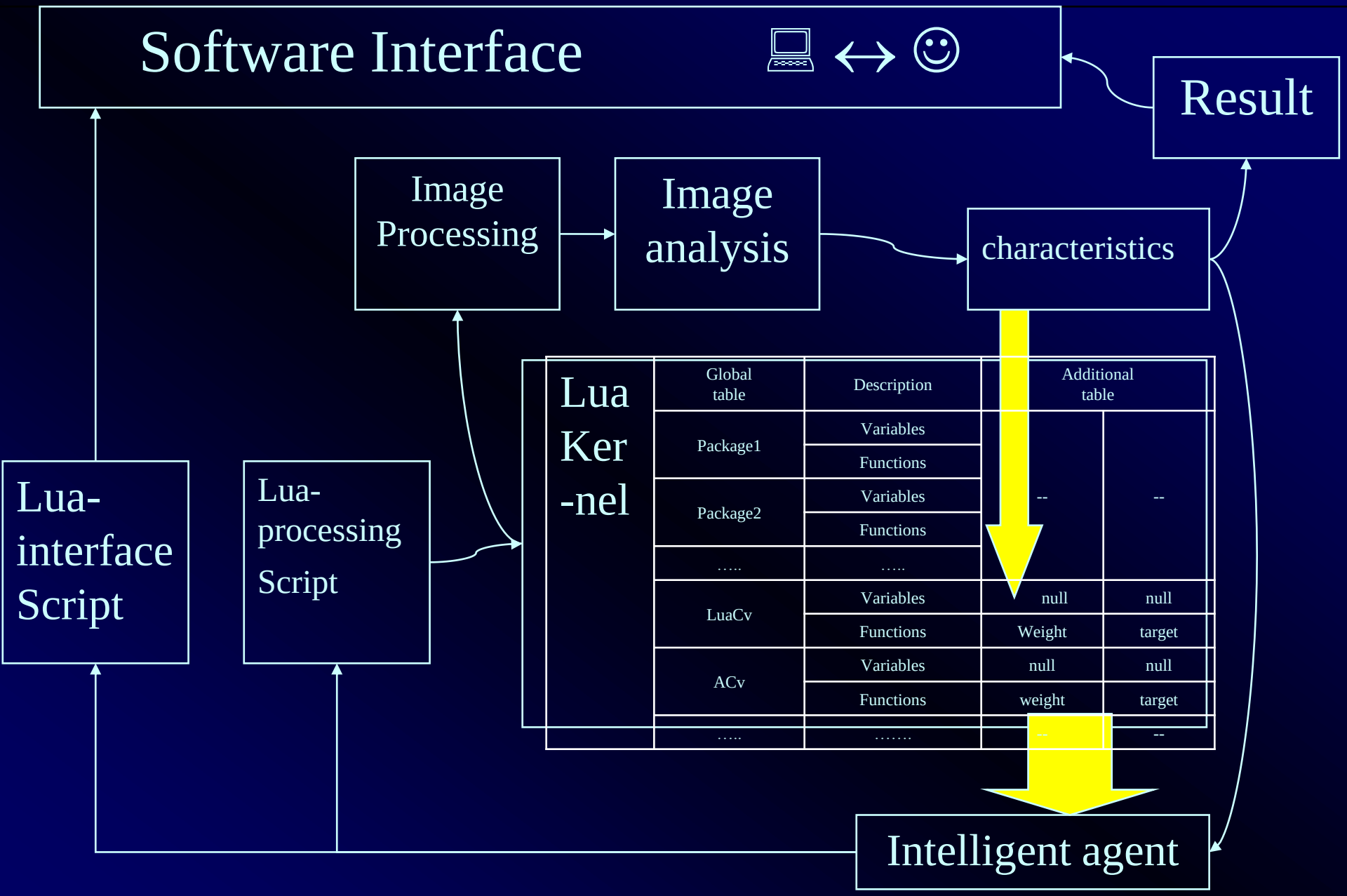


G. Marceau, The speed, size and dependability of programming languages
(33 programming languages were compared)

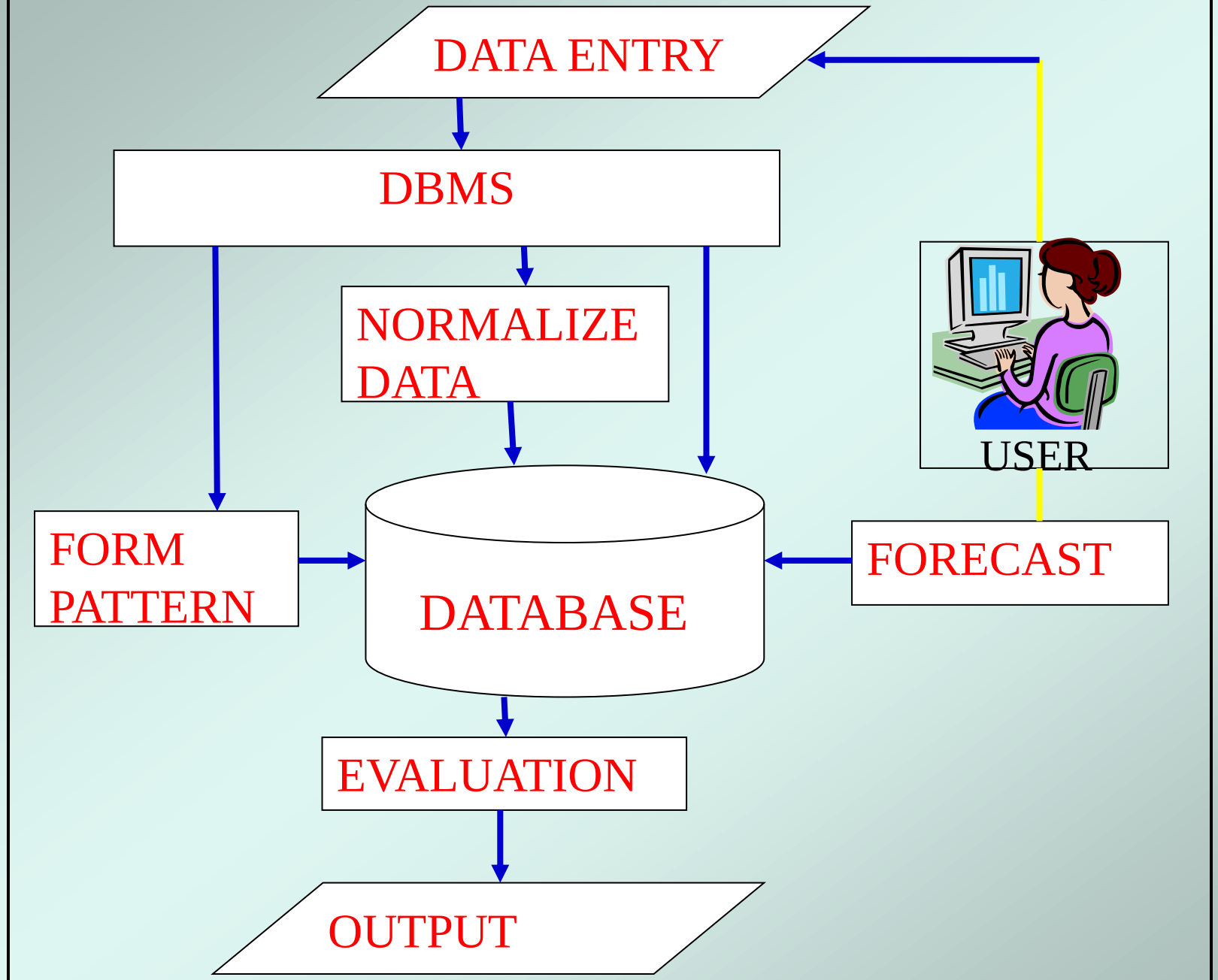
We used in our soft :

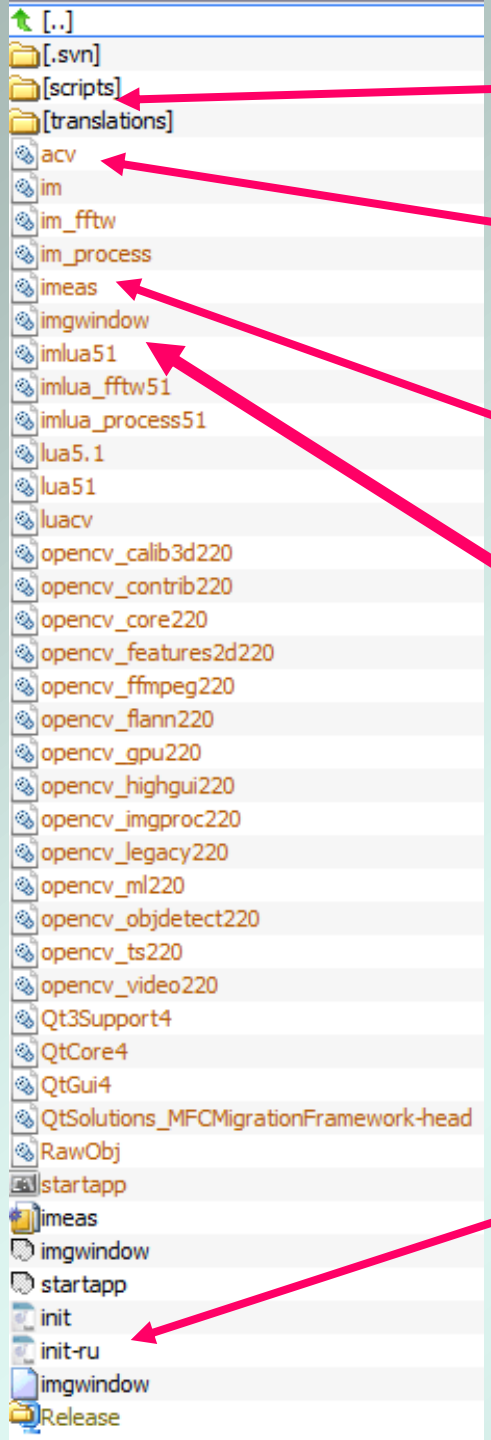
- Lua – kernel interpreter
- OpenCV – image processing and intellectual network library
- Imeasure – a measurement library
- Qt - GUI


Histological image analysis software
Highgui (interface)
Cxcore (image data structure)
Cv200 (Image processing)
Lua Binding Library
Interpretator LUA + GDI + Global descriptions
Developer's functions (image and data analysis) Additional interface support
Scripts for function control and design
User's interface
Event service block (mouse, keyboard)
Data of dependence of image and functions
Intelligent script generator


Software Interface
Result
Image Processing
Image analysis
characteristics
Lua-interface Script
Lua-processing Script
Lua Ker -nel
Global table
Description
Additional table
Package1
Variables
Functions
Package2
Variables
Functions
…..
…..
LuaCv
Variables
Functions
ACv
Variables
Functions
…..
…….
--
--
null
null
Weight
target
null
null
weight
target
--
--
Intelligent agent

A Block Diagram of the intellectual agent





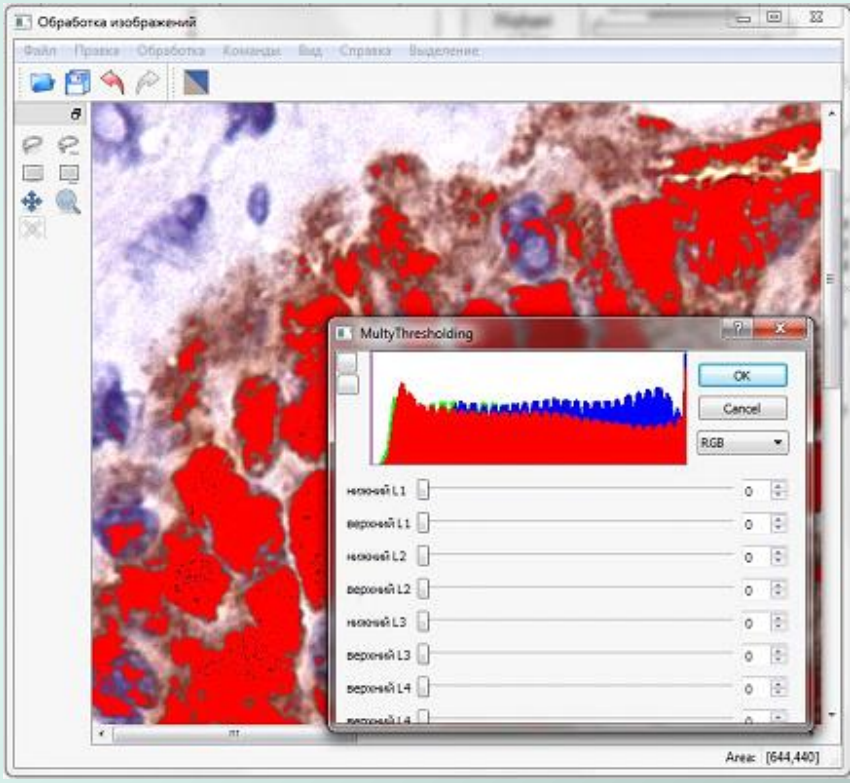
Scripts

User lua-extention

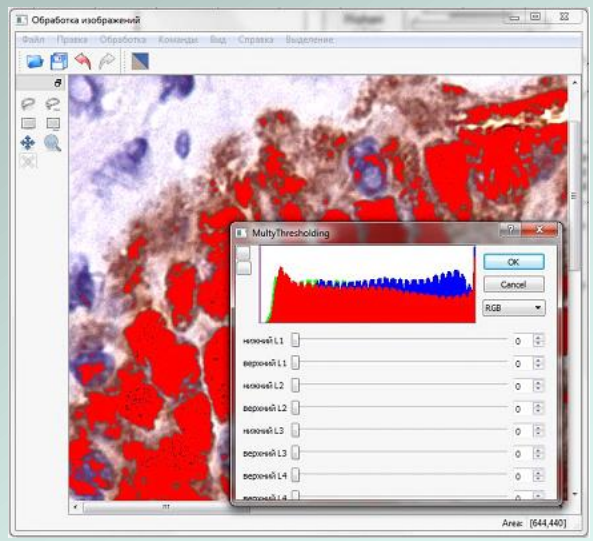
Measurement of Objects characteristics

GUI

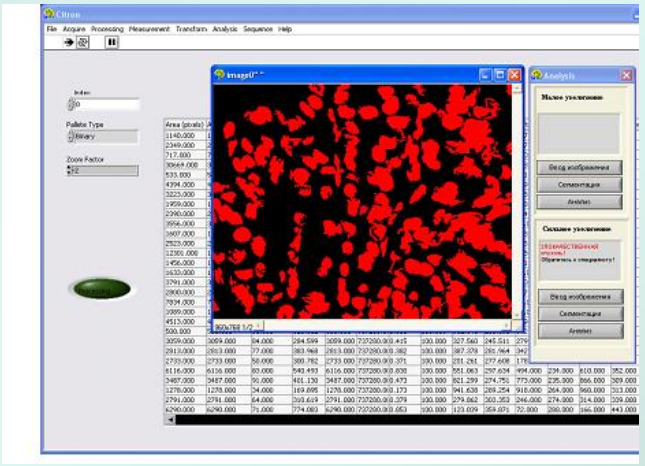
INIT-RU.LUA



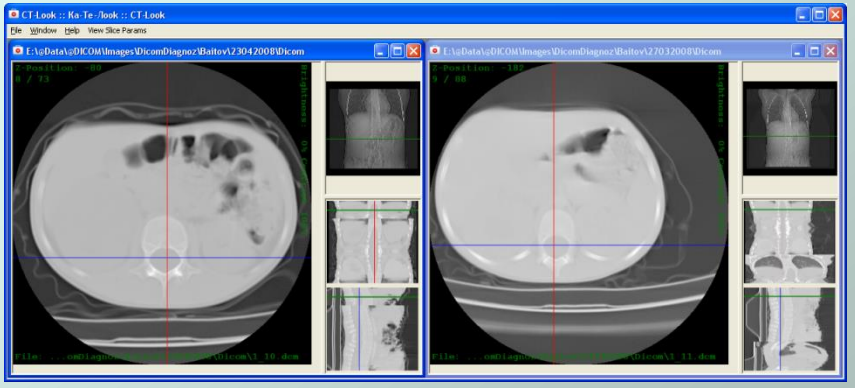
Different interfaces produced by our intellectual script generator



Interface for histological measurement

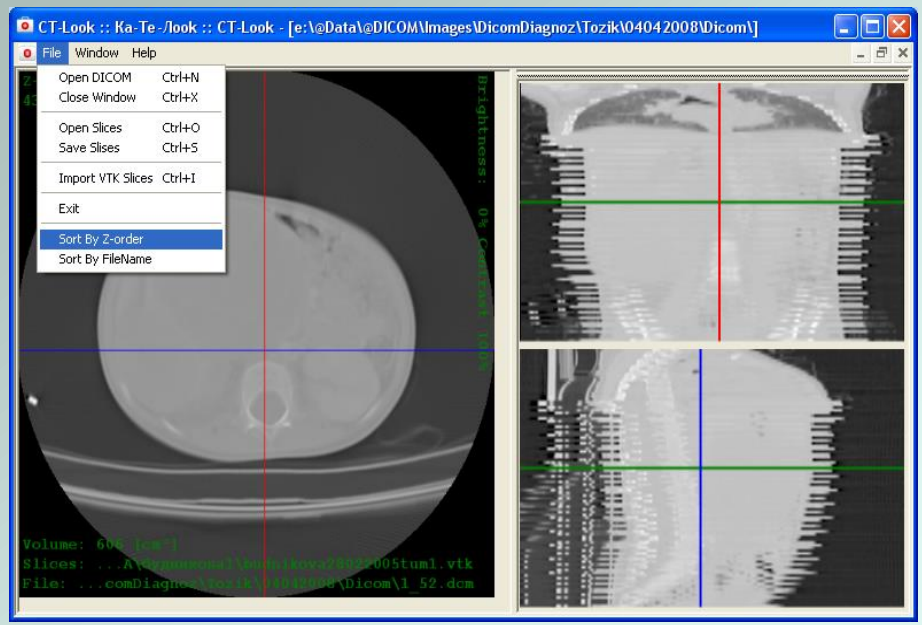


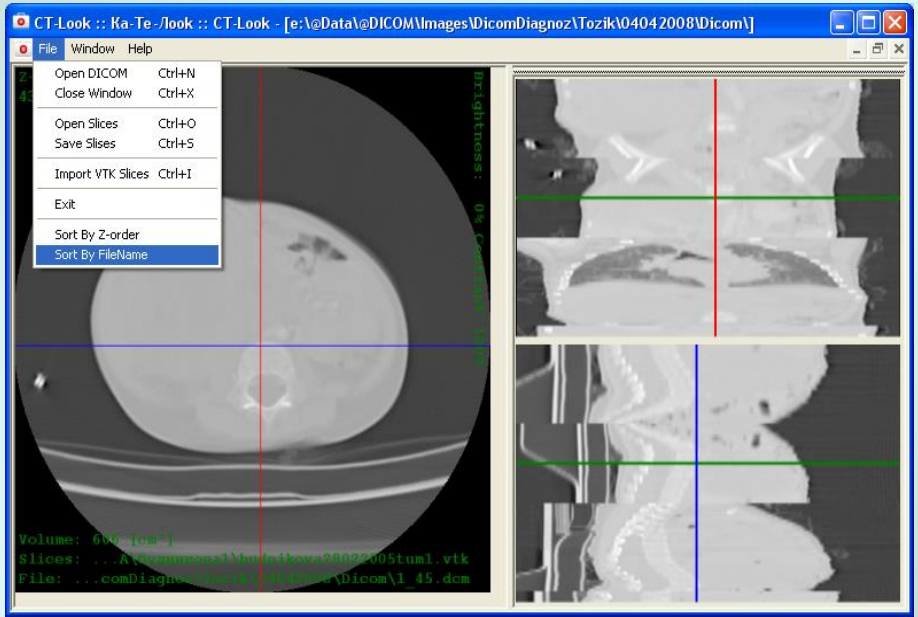
Similar to a LabVIEW interface



Interface for multi-patient viewing

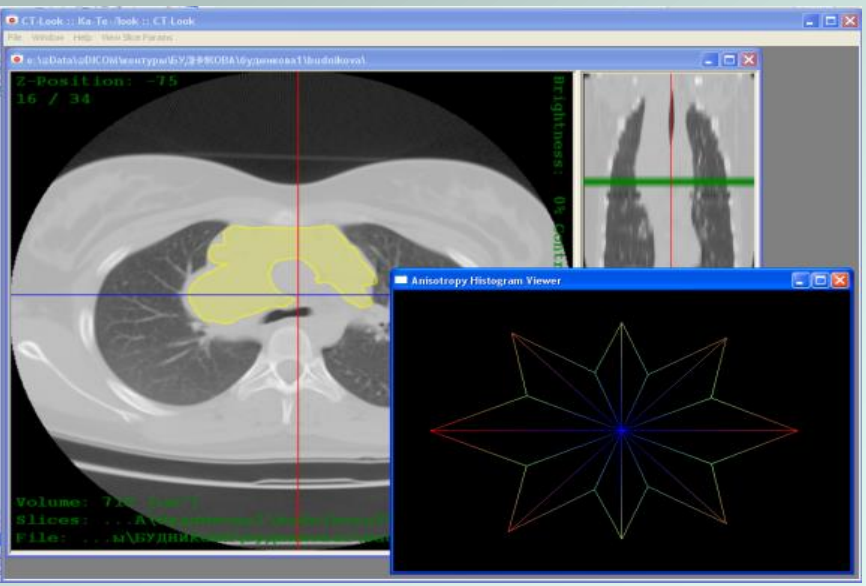
Changing interface by Lua script

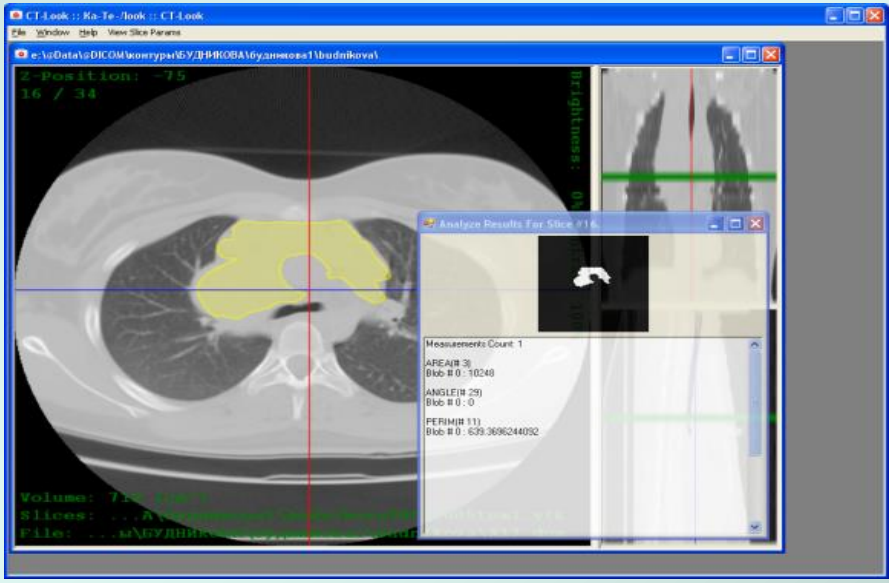


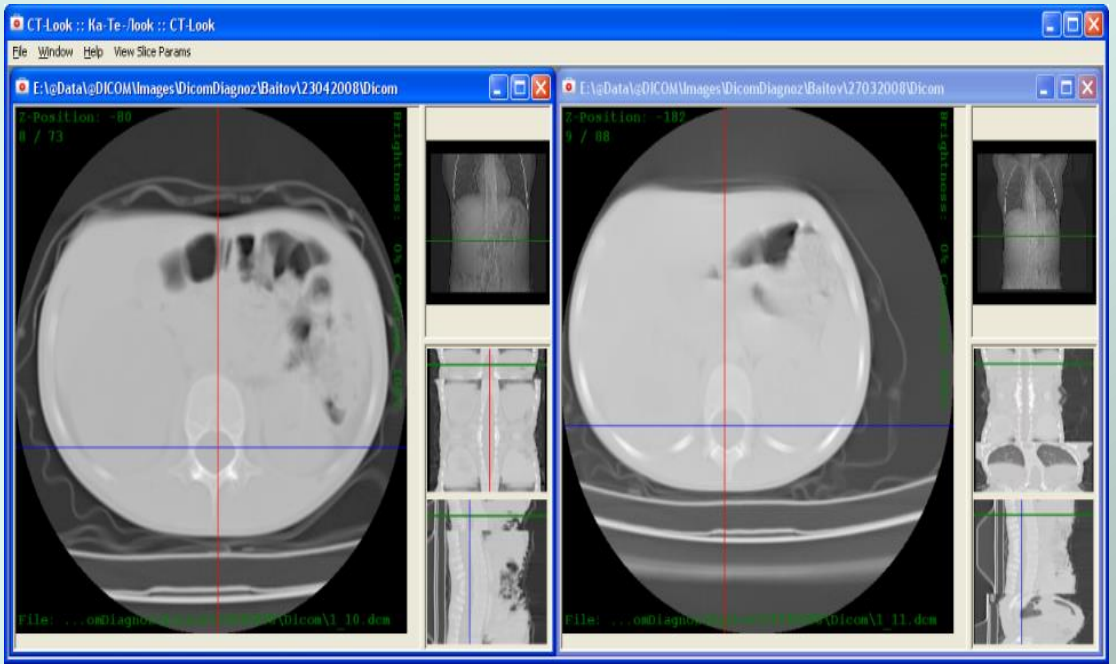



```
function SortByZorderEvent(sender,data)

MainWindow.MdiChildren[0].dicomList:Sort(Dico
mFileSorting.SortByZedOrder());

MainWindow.MdiChildren[0]:UpdateOrthoPlanesC
ut();
end
function SortByFileNameEvent(sender,data)

MainWindow.MdiChildren[0].dicomList:Sort(Dico
mFileSorting.SortByFileNumber());

MainWindow.MdiChildren[0]:UpdateOrthoPlanesC
ut();
end
MainWindow.menuFile.MenuItems:Add('-');
MainWindow.menuFile.MenuItems:Add('ϕSort By
Z-order', SortByZorderEvent);
MainWindow.menuFile.MenuItems:Add('Sort By
FileName', SortByFileNameEvent);
```

Changing interface by Lua script







Testing

Now an experimental software based on these ideas is developing. We are studying different capabilities of the software.

We tested our software on three types of histological images (see Table). Histological images are divided into the types by cell density: high density - more than 70% of the image area is occupied by cells, medium density - between 40% and 70% image area for cells, low density - less than 40%.

After testing values of successive image processing by the generated scripts were tabulated. Rate of correct analysis was evaluated by an empiricall way.

The software was testes on 248 color medical images.

Image type	Correct image type definition	Correct image analysis
Histological images with high density of cells	98%	83%
Histological images with middle density of cells	99%	90%
Histological images with low density of cells	87%	90%

Summary

We have proposed a scheme of automatic generation of image processing function sets for analysis of images and design an experimental software for this.

The software is based on principles of open architecture and allows to change design and its possibilities in real time on physician work place without a compilation stage.

On the other hand the runtime of our soft is similar to compiled versions solving the same tasks.

The suggested software architecture is flexible and simplifies development of modular programs for image analysis of histological images.