

Cytomine for collaborative and semantic analysis of multi-gigapixel images

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cytomine



@cytomine



github.com/cytomine



www.cytomine.be



info@cytomine.be



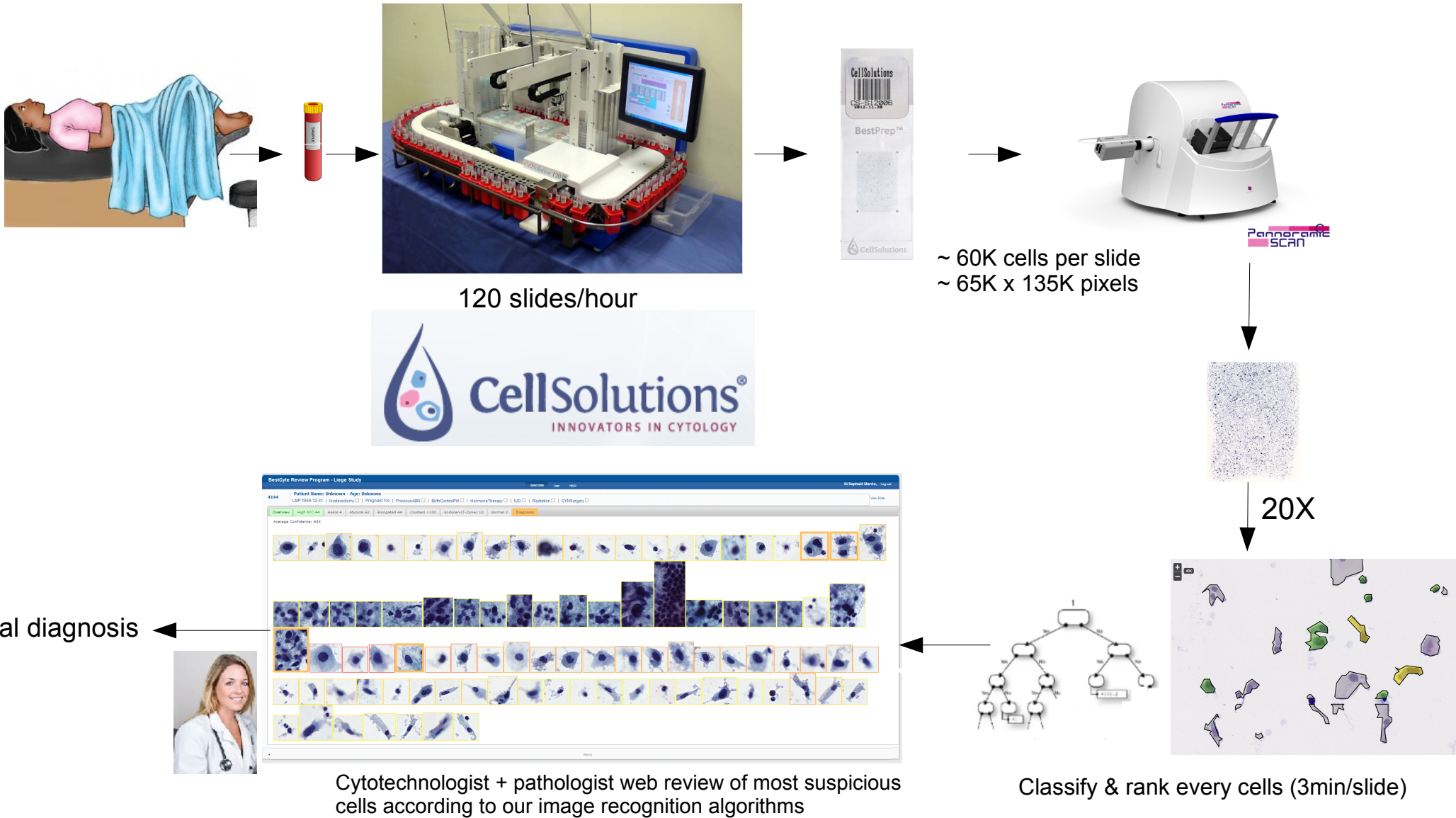
+32 4 366 26 44

June 9th, 2016. ISP Group @ UCL



Previous work : cervical cancer screening

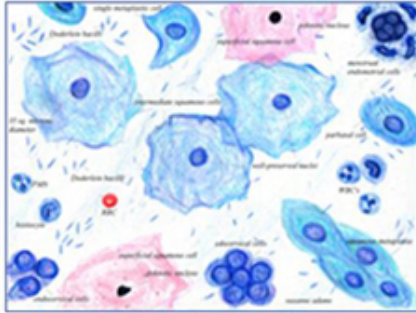
(specific, proprietary classifier developed with CellSolutions : 2008-2014)



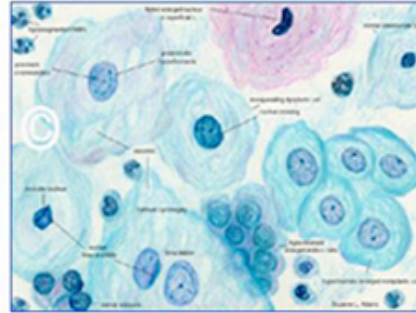
Evaluation of CellSolutions BestPrep Automated Thin-Layer Liquid-Based Cytology Papanicolaou Slide Preparation and BestCyte Cell Sorter Imaging System, A. Delga, F. Goffin, F. Kridelka, R. Marée, C. Lambert, P. Delvenne, Acta Cytologica, 2014;58(5):469-77

The world of cytology

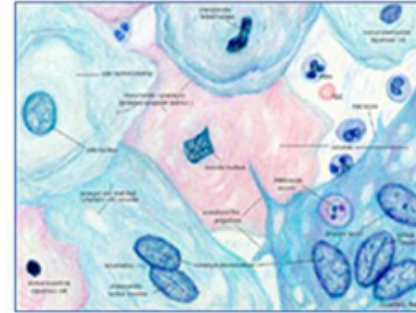
Many sample types,
preparation protocols, cell
types, ...



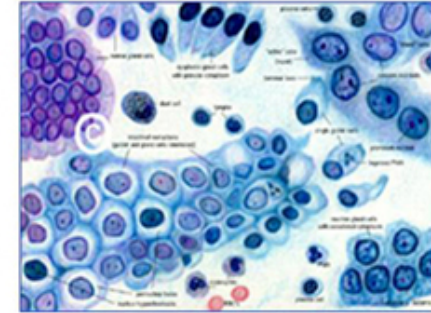
Normal Cervical Cells



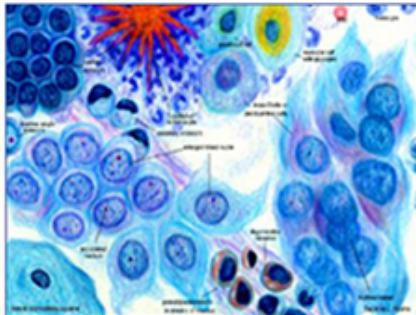
Folic Acid/B12 Deficiency



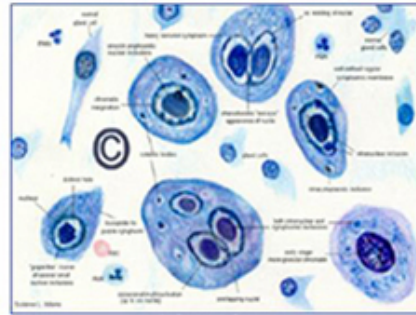
Radiation/Chemo Effect



Atrophic Gastritis/Intestinal Metaplasia



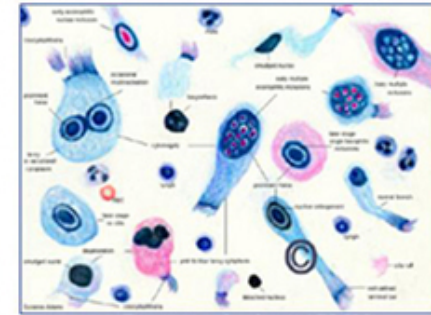
Hormone Effect (Cervical Cells)



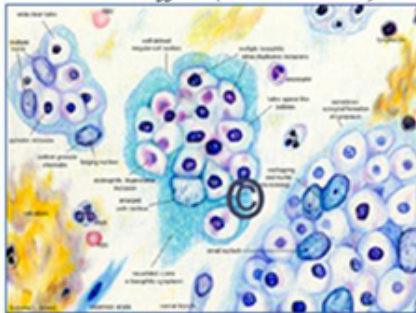
Adenovirus



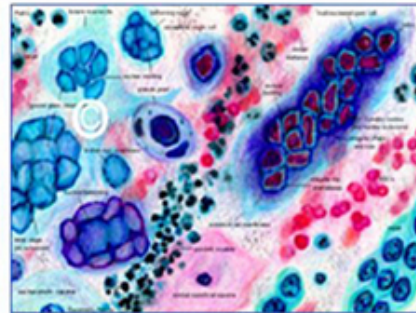
Human Papilloma Virus (HPV)



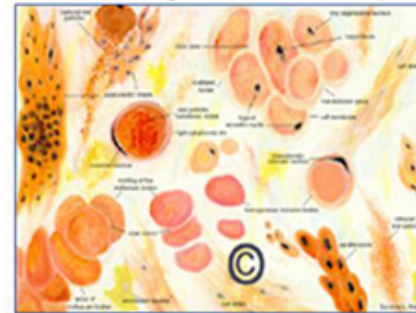
Cytomegalovirus (CMV)



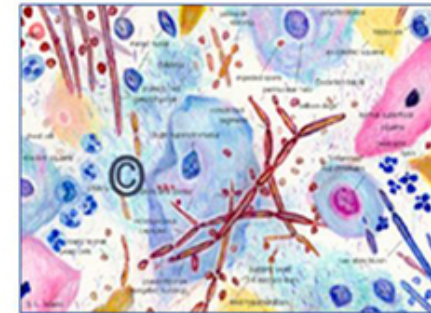
Respiratory Syncytial Virus (RSV)



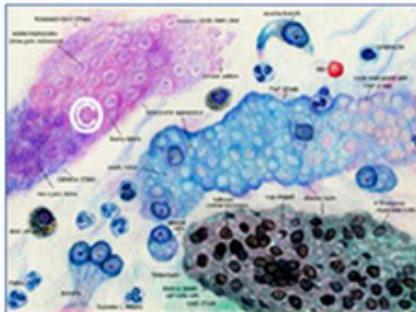
Herpes Simplex Virus (HSV)



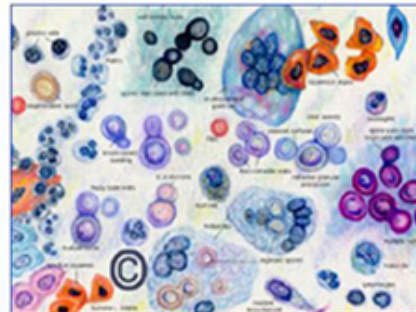
Molluscum Contagiosum



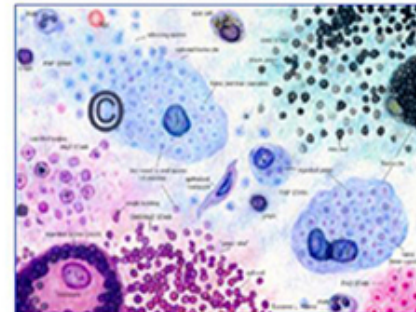
Candida Albicans



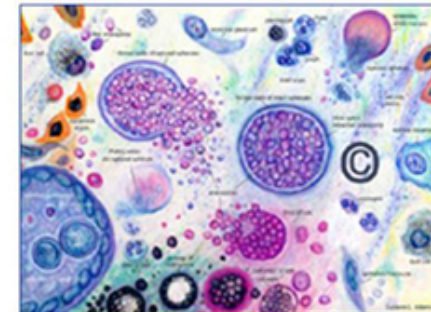
Pneumocystis carinni



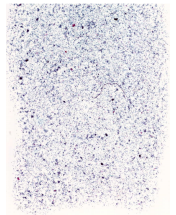
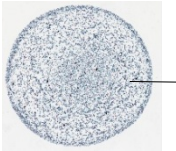
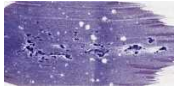
Blastomyces dermatitidis



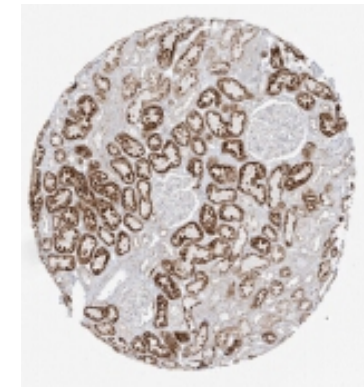
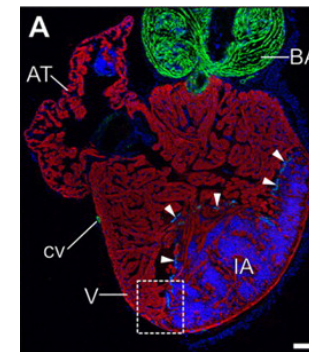
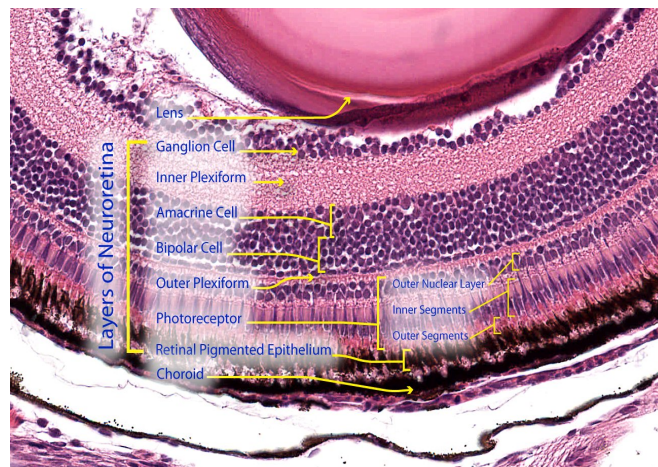
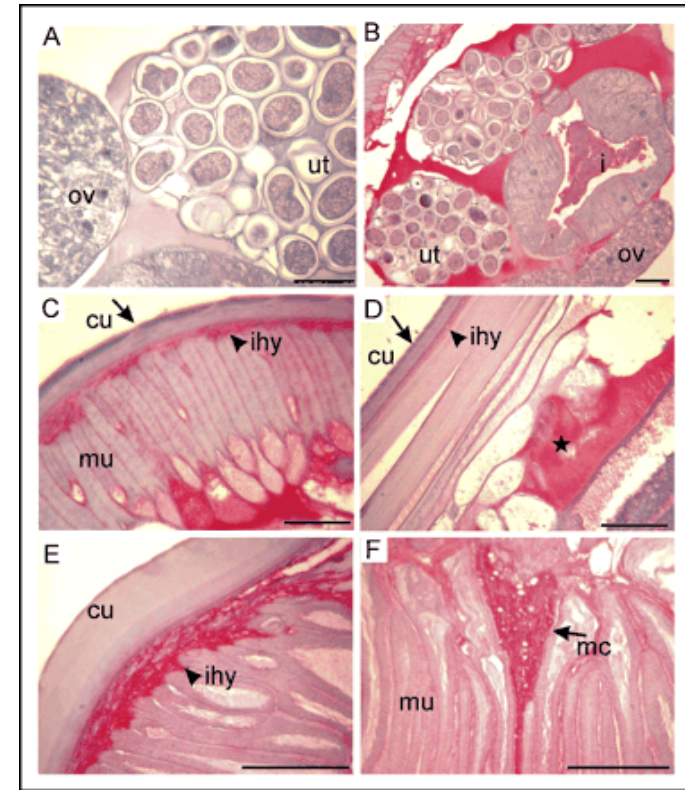
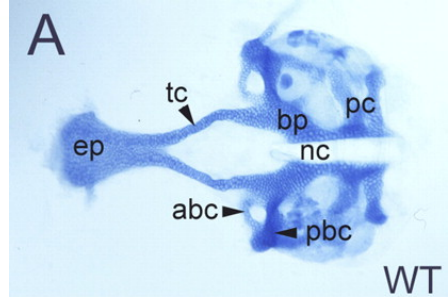
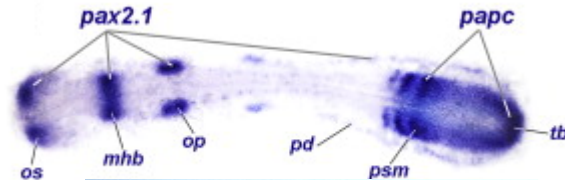
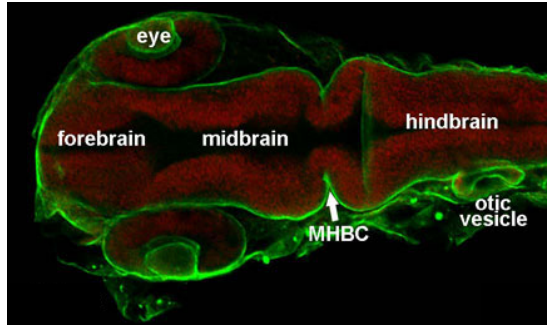
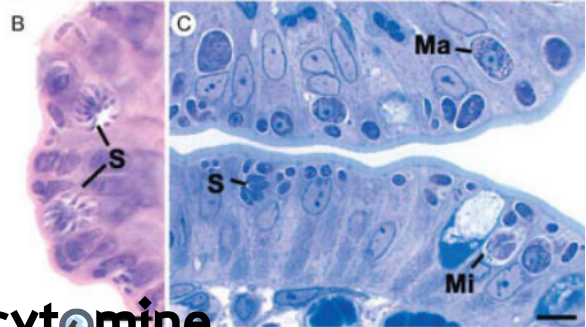
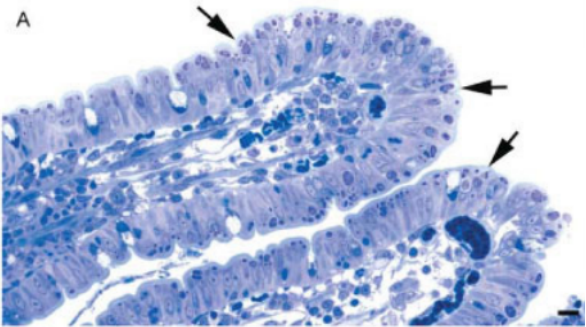
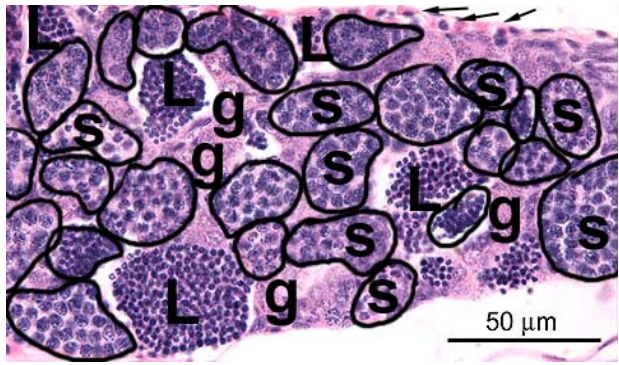
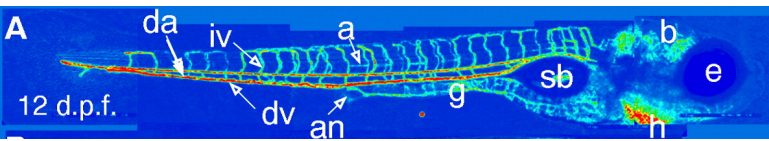
Histoplasma capsulatum



Coccidioides immitis

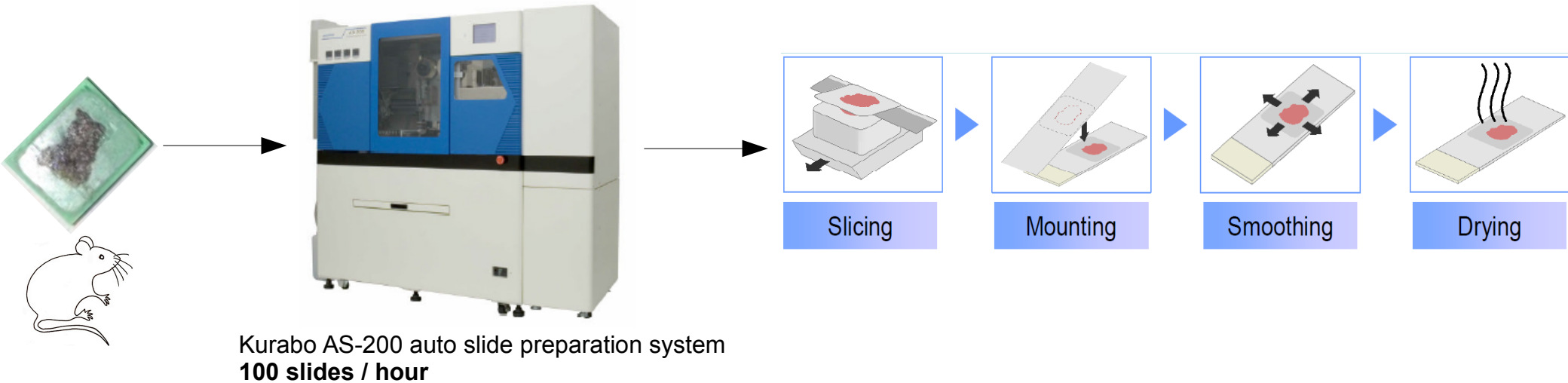


Biological/biomedical research heavily rely on semantic annotation & quantification of images



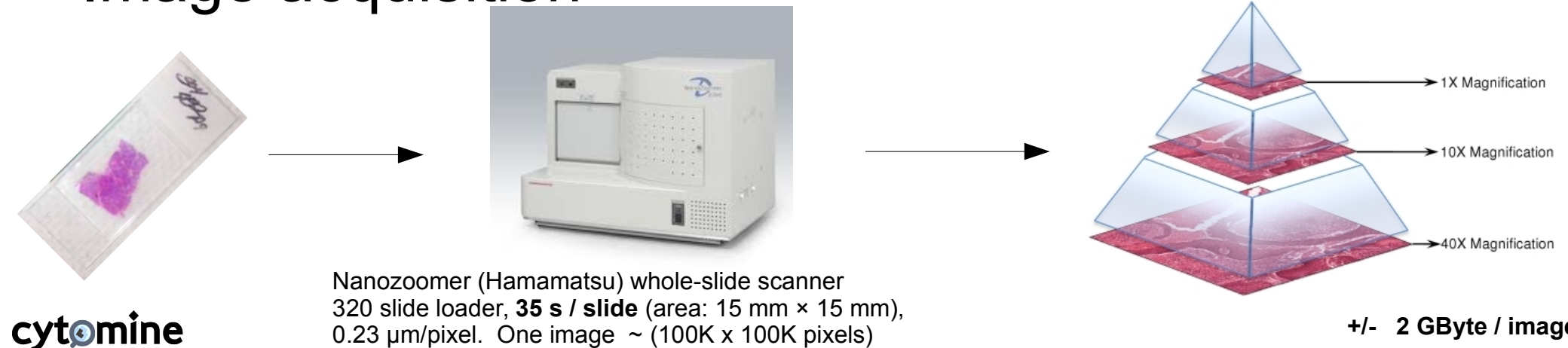
Automated tissue bioimaging

Sample preparation



200 GByte/hour → 5TByte/day

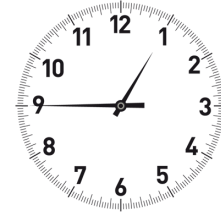
Image acquisition



Scientists and pathologist's daily work

Slide annotations/quantifications are still often :

- performed manually (through a microscope)



- performed within tissue subregions in small sample groups
(might not be statistically significant or one might miss specific patterns)

- created by isolated experts and stored locally
(sometimes lost)



- not saved, or in proprietary format so hardly reusable
(e.g. Photoshop draws for paper figures)

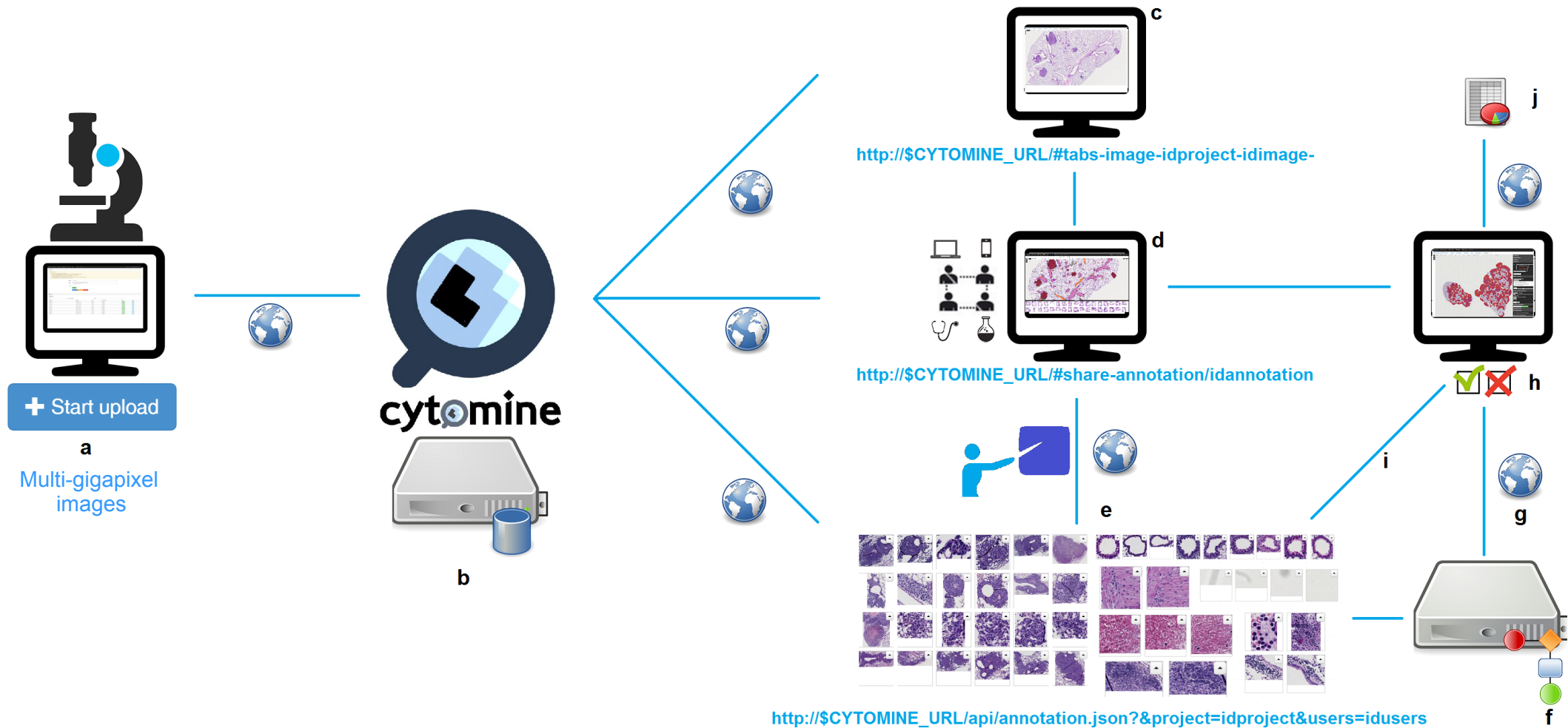
cyt^omine

Objective : *to make life easier for both life scientists, pathologists, and computer scientists*

- Continuous development since 2010
- Academic project but **industrial-grade software**
(modern & proven software libraries, user-driven, code quality control,...)
- **General-purpose**
- A rich internet application (**web-based**)
 - Google Maps-like visualization of digital slides
 - **Collaborative, semantic**, annotation of regions of interest
 - **Semi-automated analysis**
 - Generic machine learning algorithms
 - Proofreading
- User-authentication for **secure sharing** of images, annotations, results
- Documented, **Free and Open-source** (www.cytomine.be)
*A computer software with its **source code made available** with a license in which the copyright holder provides the **rights to study, change, and distribute the software to anyone and for any purpose.***



cyt@mine



cyt_omine



Html 5



Javascript



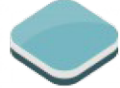
Jquery



Backbone.js



AngularJS



Openlayers

Cytomine-WebUI



Scikit-learn



OpenCV



Redis



Java



Python

Content-based Image retrieval
Cell Classifier
Landmark Detection
Tissue Segment
Annotation Stats
...

Cytomine-DataMining



Python



Java

Cytomine-clients

REST API HTTP

NGINX



Message broker

REST API HTTP

NGINX



Grails



Groovy



Java



Spring



Postgis



Tomcat



PostgreSQL

Cytomine-Core



MongoDB



Grails



MEMCACHED



Java



IIP + OpenSlide

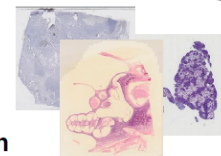


Cytomine-IMS



GlusterFS

File system



Docker

Cytomine Install/Deploy



Node.js



MongoDB

Cytomine Monitoring



cyt_omine

Collaborative analysis
of gigapixel images

www.cytomine.be

cyt@mine features : Organize and centralize on the web

Create and manage multiple **projects** :

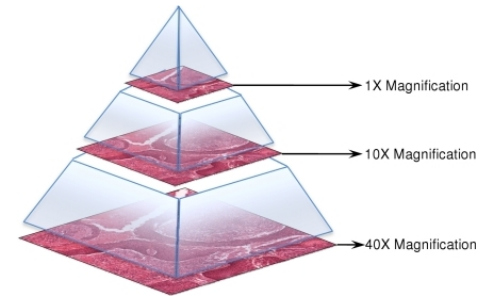
- **Upload** images to centralized server or keep data local (distributed image tile servers)
- Support for **various formats** (TIFF, JP2000, Aperio SVS, Hamamatsu NDPI/VMS, 3DHistech MRXS, Leica SCN, Roche TIF...)
- Users with **authentication** (e.g. LDAP), **access rights**, and **roles**
- **Specific ontologies** with user-defined, vocabulary terms

The screenshot displays the cyt@mine web interface, which is a dashboard for managing biological projects. On the left, there is a 'New project' button. The main area is a grid of project cards, each representing a different project. Each card contains the following information:

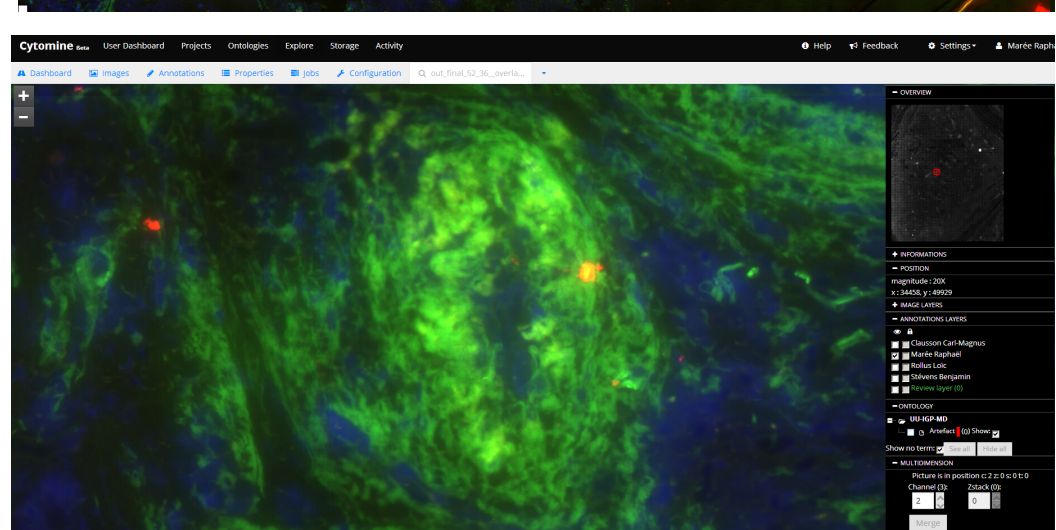
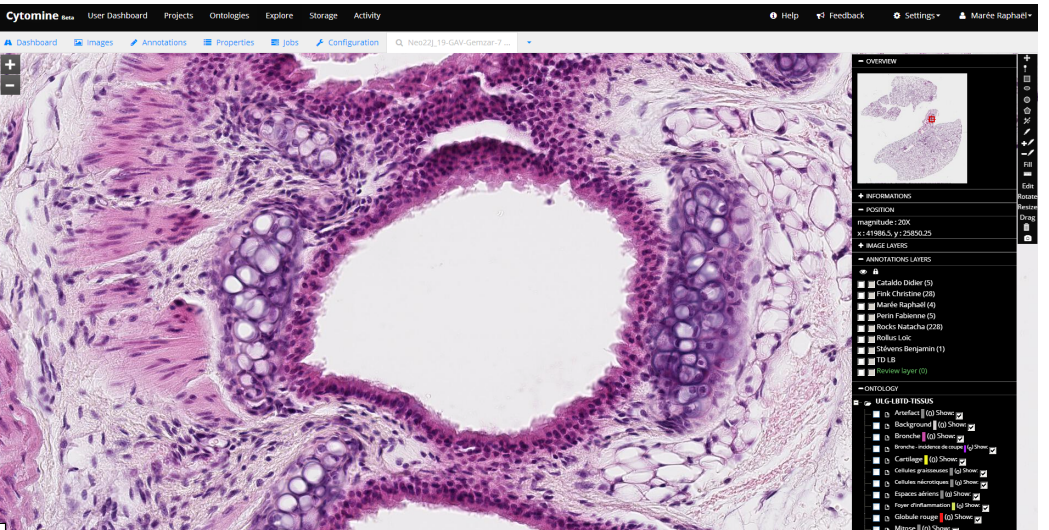
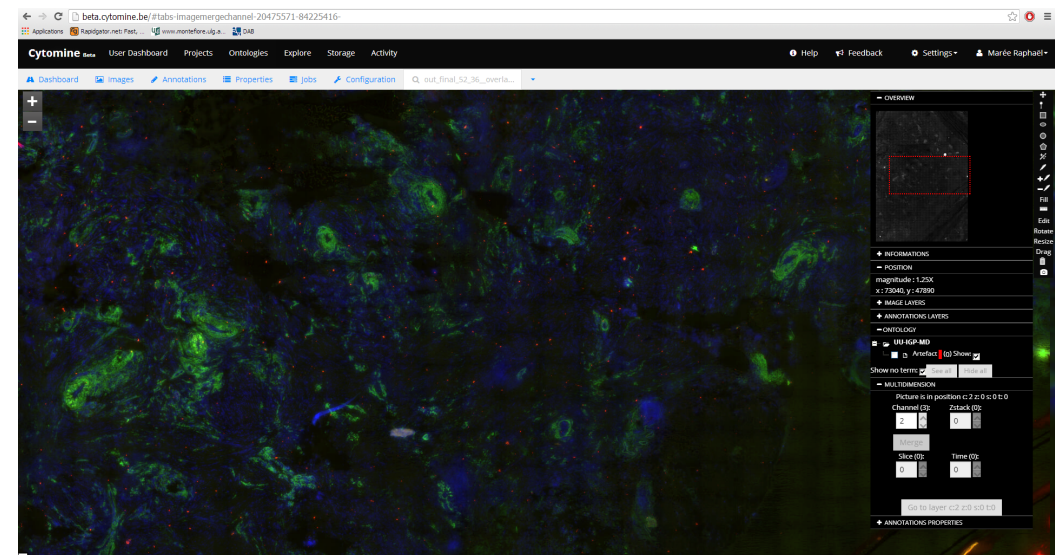
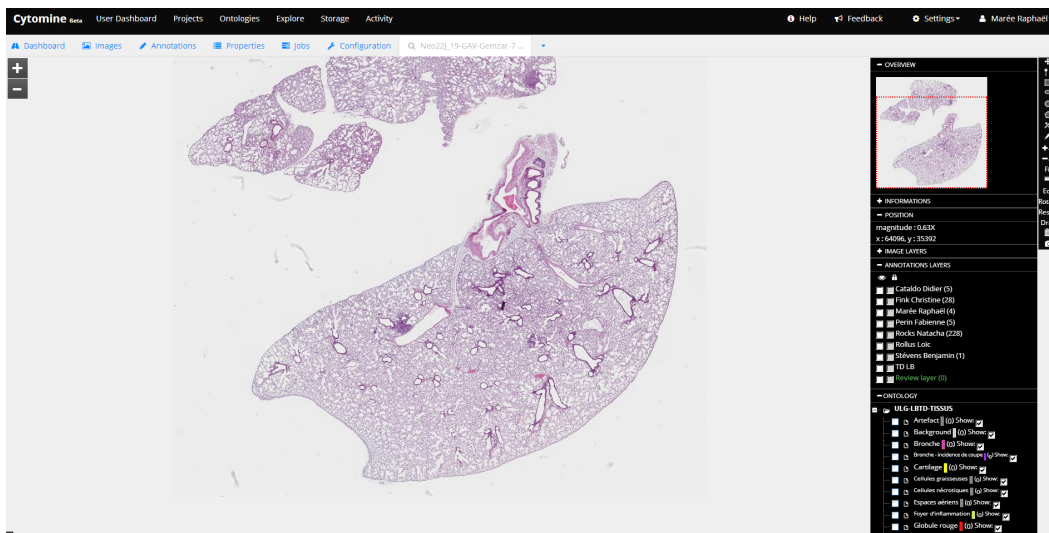
- Name:** Project name (e.g., ULG-LBTD-E2B-NOV2013)
- Discipline:** HISTOLOGY
- Ontology:** ULG-LBTD-TISSUS
- Number of images:** 29
- Number of user annotations:** 133
- Number of job annotations:** 4594
- Number of validated annotations:** 692

At the bottom of each card are buttons for 'Info', 'Edit', 'Delete', and 'Open'. To the right of the grid, there is a sequence of histology images, with an arrow pointing from the top-right card to the first image. Below the grid, there is another row of project cards, and an arrow points from the bottom-right card to a sequence of histology images.

cyt^omine features : Visualize



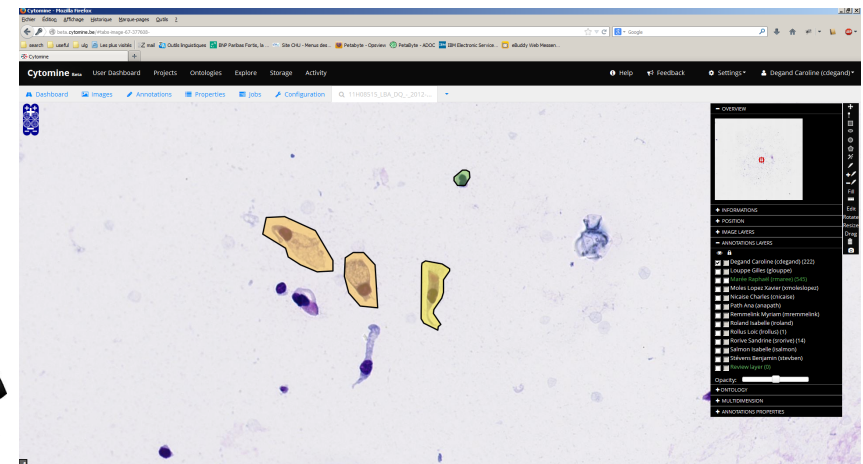
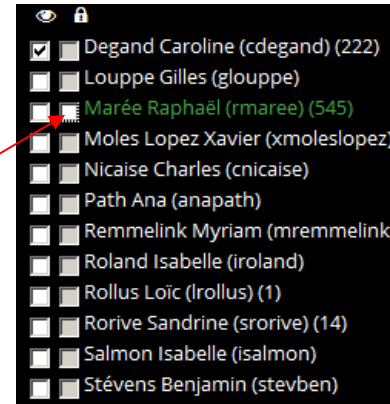
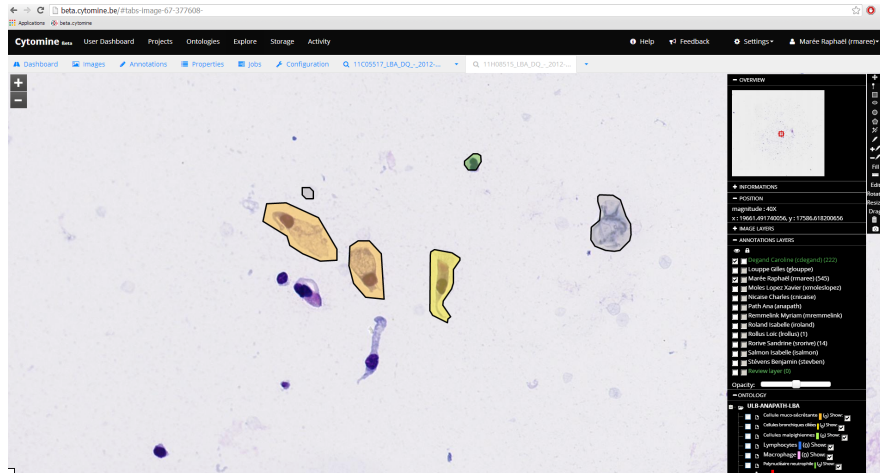
- Explore **large** (>gigabyte) images at multiple resolutions, **remotely**
- GoogleMaps/OpenStreetmap browsing style (zoom in/out, pyramid tile-based)



1 tissue slice = 35000 x 30000 pixels (0.23 μ m/pixel)

4 fluo channels 83000 x 100 000 pixels = 4 x 16GB image
(image from O.Söderberg group, Uppsala)

cyt^omine features : Live broadcast



Start following Marée Raphaël (rmaree)

cyt@mine features : Annotate

- **Annotate** images using various **drawing tools**, with **user-specific layers**
- Describe ROIs with **ontology terms**
- Describe images and ROIs with any **key-value properties** or **text description**

The screenshot displays the cyt@mine software interface. On the left, a sidebar titled 'ONTOLOGY' lists various biological terms under categories like 'ULG-LBTD-TISSUS', 'Tumeurs', and 'Vaisseaux'. The main area shows a histology image with several regions highlighted in different colors (red, orange, purple, green). The interface includes a top navigation bar with options like 'Dashboard', 'Projects', 'Ontologies', 'Explore', 'Storage', 'Activity', and 'Search'. A toolbar at the top of the image area provides drawing tools such as 'Select', 'Point', 'Arrow', 'Rectangle', 'Ellipse', 'Circle', 'Polygon', 'MagicWand', 'Fill', 'Ruler', 'Edit', 'Rotate', 'Resize', and 'Drag'. A 'SHOW TOOLS' button is visible in the top right corner of the image area. At the bottom, a grid of small thumbnail images shows different views or zoom levels of the annotated regions. The user's name 'Marée Raphaël (mareae)' is visible in the top right corner.

cyt@mine features : Ontology editor

Ontologies + Add Refresh

- ALCIAN BLUE
- ALIZARIN RED
- ATEST
- AUSTRALIAN-MUSEUM-INSECT-SOUP
- BLABLA
- BM-01
- BUDÉSONIDE 1 BALF
- BUDÉSONIDE 1 SCORE INFLAMMATOIRE
- CELLSOLUTIONS-PROSTATE
- CMU-BE-DEMO
- CVM
- CellSolutions-PAP
- DEFAUTSSHEARIOGRAPHIE
- DEMO
- DEMO-OXFORD-ZEGAMI
- DEMO-UMINN-TPENGO
- DEMO-VARIOUS
- DEMO_2014
- EDEMA
- FRAUNHOFER-IIS-DEMO
- GHDC-PLANCANCER
- HISTOLOGIE DIVERS
- HUBBLE
- IPASTEUR-DEMO
- LABSETDEMO
- LS4-NEWANNOTATIONS
- MEDEX-CHEST-CCD
- MEDUNIGRAZ-BONE-MARROW
- MUMC-CARIM-PATHOLOGY
- NANJING-DEMO
- OPENCONNECTOME-KASTHURI11
- PHYSIO 1 BALF
- PROJET_DEMO
- RHTEST
- ROSTOCK-HJTHIESEN-KIDNEY-TMA
- RWTH-METROPOL-CRYSTAL
- SEGMENT_FISH
- TB
- TEST-CZI
- TEST-MERGE
- TEST-MERGE-TIFF

ULG-LBTD-TISSUS

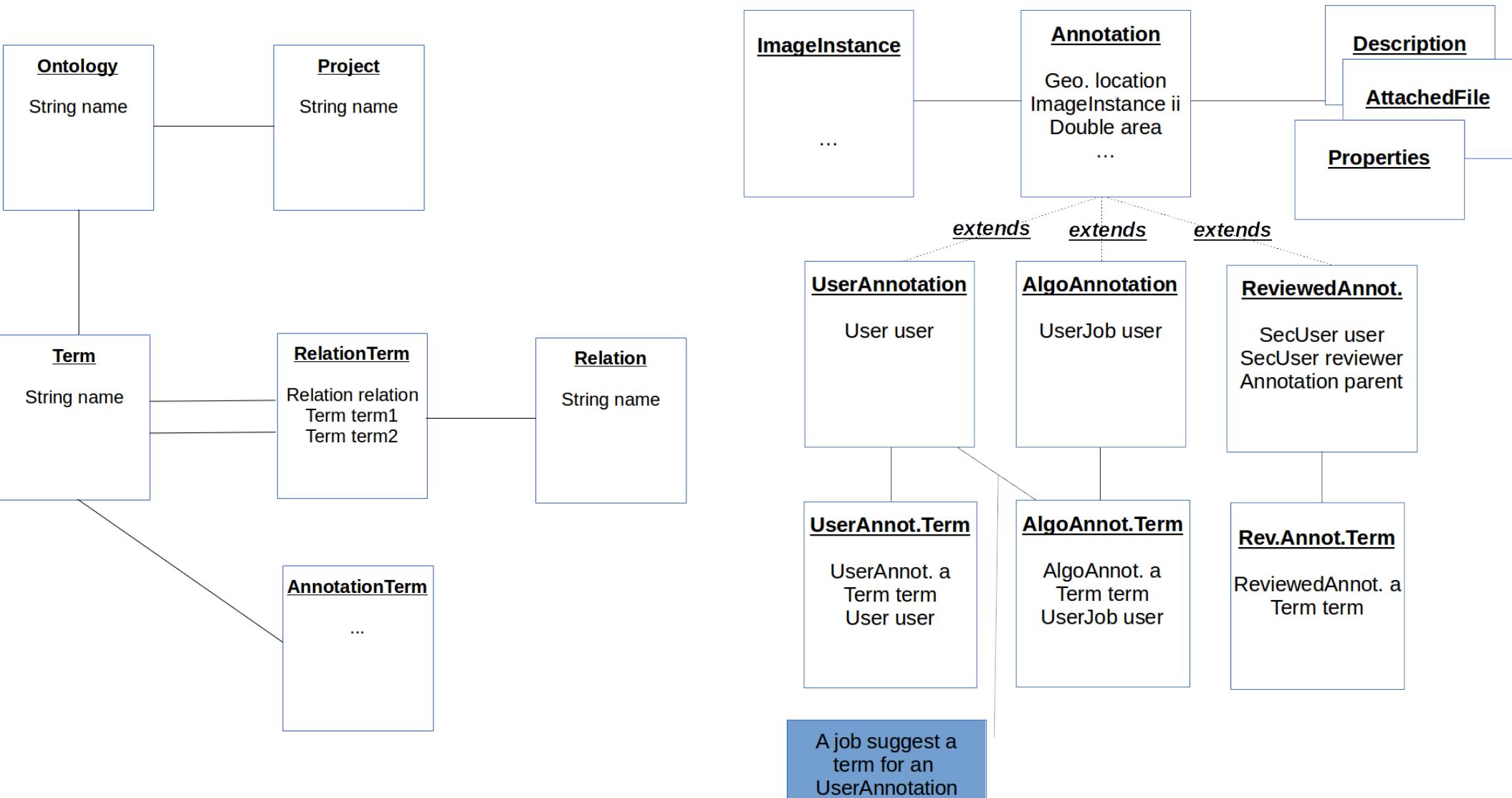
Ontology ▼ Term ▼

Ontology : ULG-LBTD-TISSUS
Creator : Stéve
Shared with :
Projects : ULG-LBTD-NEO13, ULG-TEST-PHL, ULG-LBTD-NEO22, ULG-LBTD-HDM1-HE, ULG-LBTD-CS7, BORDET, ULG-LBTD-AGAR15-POUMON, ULG-LBTD-W18-HE, ULG-LBTD-W18-CR, ULG-LBTD-CR1-HISTO, ULG-LBTD-O3, ULG-LBTD-PGP, ULG-LBTD-G1-HE POU, PGPTTEST, ULG-LBTD2-BALBC-4T1, ULG-LBTD-LIDOCAINE, ULG-LBTD-AS6, ULG-LBTD-AGAR23, ULG-LBTD-AGAR25, TESTAGA, ULG-LBTD-AGAR28, ULG-LBTD-SH1-IV-POUMON, ULG-LBTD-SH1-SC-POUMON-TUMEUR, ULG-LBTD-E2A-FEB2013, ULG-LBTD-TRANSFERT-ADOPTIF, ULG-DEMO-HE-LUNG, TESTSTATS, ULG-LBTD-E2B-NOV2013, ULG-LBTD-E2C-FEB2014, ULG-LBTD-AGAR29, ULG-LBTD-AD28_2, ULG-LBTD-E2E-JUN2014, ULG-LBTD-ADAM 28 4, ULG-LBTD-E2F-AOUT 2014, ULG-LBTD-AD28_8, ULG-LBTD-AGIC3, ULG-LBTD-AGIC1, ULG-LBTD-AGIC2, ULG-LBTD-AGIC6, ULG-LBTD-IT MC IV 4T1 G1, ULG-LBTD-AGIC5, ULG-LBTD-AGIC7, ULG-LBTD-AGIC8, ULG-LBTD-AGCT1, ULG-TEST-RABBIT-SEGMENT, ULG-LBTD-AGDC1bis, ULG-LBTD-AGDC2, ULG-LBTD-AGDC5, ULG-LBTD-AGDC6, ULG-LBTD-MT1, ULG-LBTD-MT3, ULG-LBTD-MT2, ULG-LBTD-AGIC9, ULG-LBTD-AGDC10, ULG-LBTD-MT5, ULG-LBTD-MT5', ULG-LBTD-AGDC9, ULG-LBTD-MT4, ULG-LBTD-IT IL16 10NG GR3

ULG-LBTD-TISSUS

- Artefact
- Background
- Bronche
- Bronche - incidence de coupe
- Cartilage
- Cellules graisseuses
- Cellules nécrotiques
- Coupe
- Espaces aériens
- Foyer d'inflammation
- Globule rouge
- Mitose
- Muscle
- NotAdeno
- Poumon
- Poumon non insufflé
- Unknown
- Zone floue
- Marquage**
 - Alpha-smooth muscle actin
 - Collagen
- Tumeurs**

cyt@mine



cyt@mine features : Share

- **Share images** through simple URLs

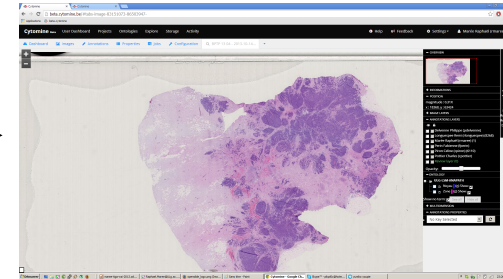
<http://beta.cytomine.be/#tabs-image-83151073-86503947-> →

Sign in to Cytomine

Username

Password

Remember me



- **Share and comment annotations** through simple URLs & e-mail mechanisms

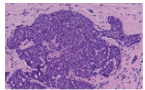
<http://beta.cytomine.be/#share-annotation/77044>

Comment/Share an annotation

- Delvenne Philippe (pdelvenne)
- Longuespee Remi (rlonguespee)
- Marée Raphaël (rmaree)
- Perin Fabienne (fperin)
- Piron Celine (cpiron)
- Pottier Charles (cpottier)

What do you think it is?

Comments



Cancel Share



From: cytomine.ulg@gmail.com To: raphael.maree@ulg.ac.be
Subject: Cytomine : Marée Raphaël (rmaree) shared an annotation with you Date: Fri, 29 Nov 2013 23:12:05 +0100 (CET)

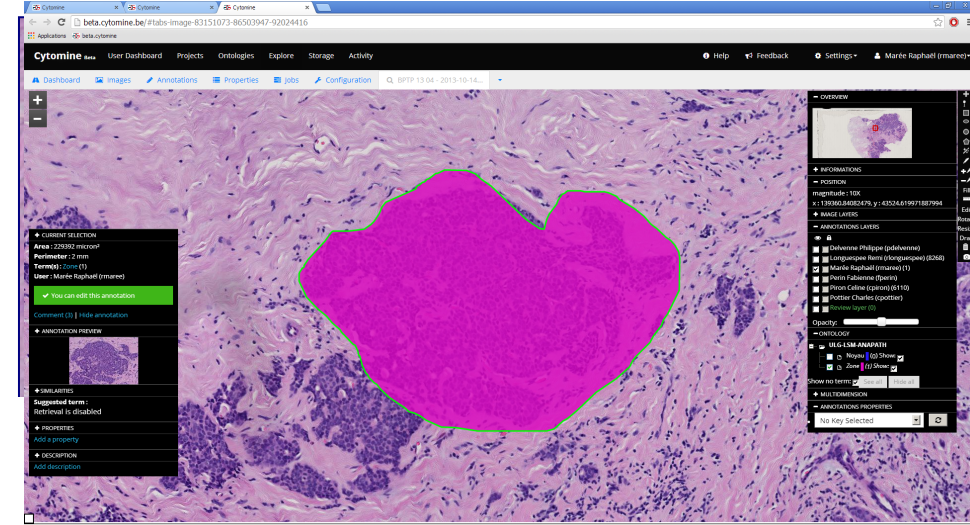
Dear Marée Raphaël (rmaree),

Marée Raphaël (rmaree) shared an annotation with you and said :

Dear colleague, Do you think it is grade C ?

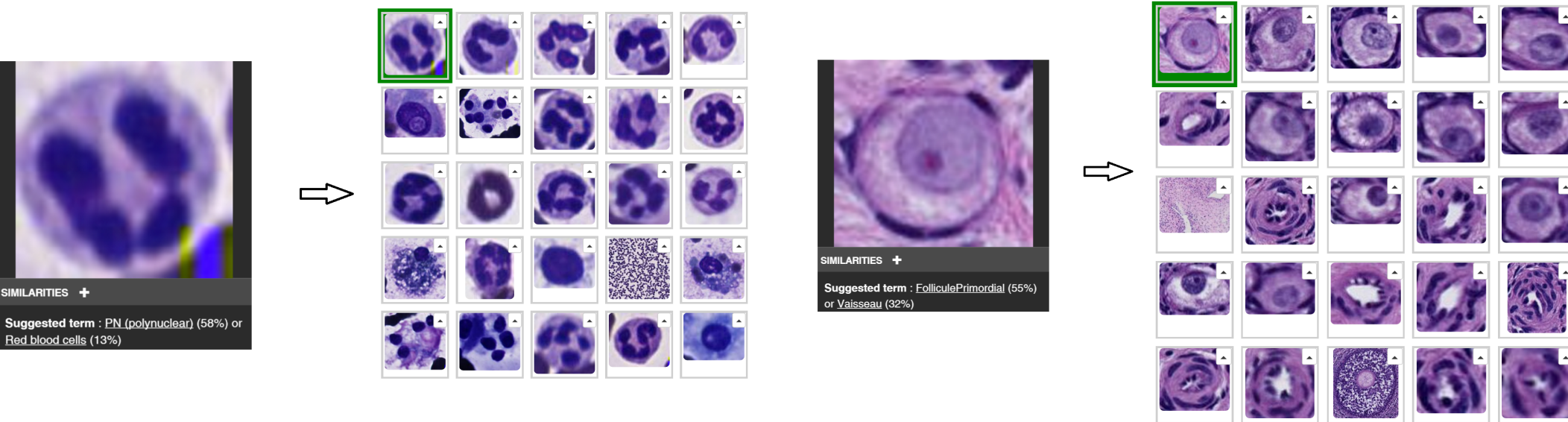
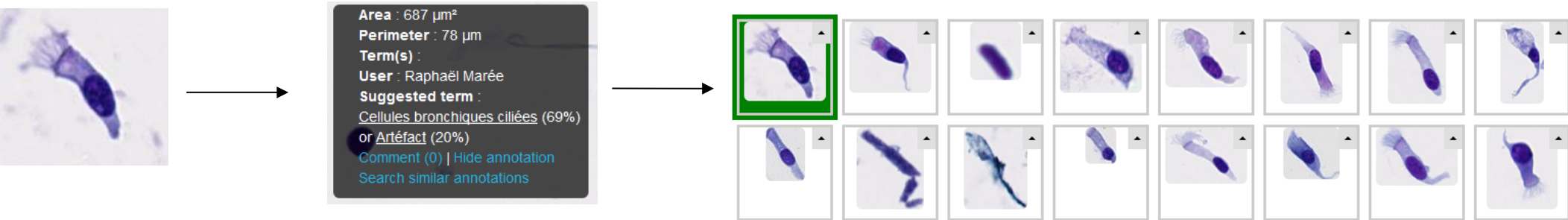
Navigate to <http://beta.cytomine.be/#share-annotation/92024416> in order to reply.

Navigate to <http://beta.cytomine.be/#tabs-image-83151073-86503947-92024416> in order to view the annotation within its context, or click on the thumbnail.



cyt@mine features : Search

- **Text search** (projects, images, annotations)
- **Visual search** (CBIR) of regions of interest and **ontology term suggestion**



cytomine : Fully open

JSONDoc <http://current.cytomine.be/jsondoc/apiproduct#> | [Get documentation](#)

API INFO
Base path: <http://localhost:8080/api>
Version: 1.0

APIs

- [abstract image services](#)
- [algo annotation services](#)
- [annotation filter services](#)
- [annotation index service](#)
- [annotation term service](#)
- [discipline services](#)
- [generic annotation services](#)
- [image group services](#)
- [image instance services](#)
- [image sequence services](#)
- [nested image services](#)
- [ontology services](#)
- [project services](#)
- [property services](#)
- [relation services](#)
- [relation term services](#)
- [reviewed annotation services](#)
- [sample services](#)
- [storage abstract image services](#)
- [term services](#)
- [uploaded file services](#)
- [user annotation services](#)

OBJECTS

- [\[annotation_listing\]](#)
- [\[project_sharing_same_image\]](#)
- [\[sequence_possibilities\]](#)
- [abstract image](#)
- [algo annotation](#)
- [anno_annotation term](#)

GENERIC ANNOTATION SERVICES
Methods for managing an annotation created by a software

[/annotation.json](#) POST

[/annotation/{id}.json](#) PUT

[/imageinstance/{idImage}/annotation/included.json](#) GET

Path `/imageinstance/{idImage}/annotation/included.json`

Description Get all annotation that intersect a geometry or another annotation. See [/annotation/search](#) for extra parameter (show/hide).

Method GET

Produces application/json

Query parameters

- idImage** Required: true
Type: long
Description: The image id
- geometry** Required: true
Type: string
Description: (Optional) WKT form of the geometry (if not set, set annotation param)
- annotation** Required: true
Type: long
Description: (Optional) The annotation id for the geometry (if not set, set geometry param)
- user** Required: true
Type: long
Description: The annotation user id (may be an algo)
- terms** Required: true
Type: list
Description: The annotation terms id
- max** Required: false
Type: int
Description: Pagination: Number of record per page (default 0 = no pagination)

PLAYGROUND
[/imageinstance/{idImage}/annotation/included.json](#)

Accept
application/json

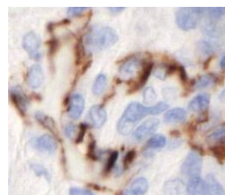
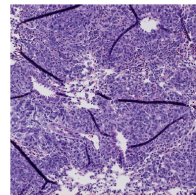
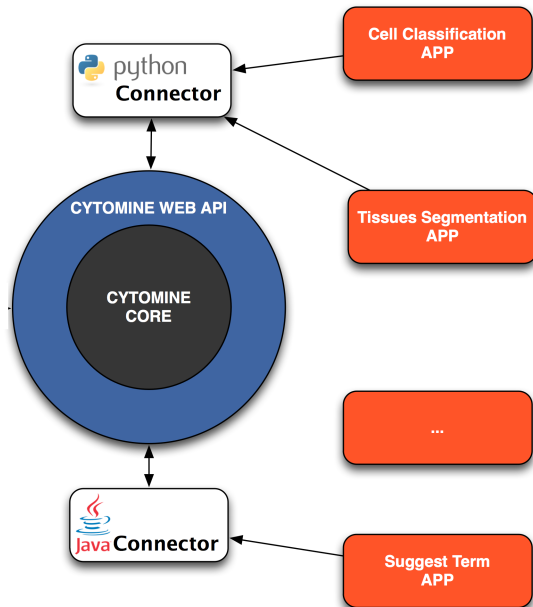
Query parameters

idImage	idImage
geometry	geometry
annotation	annotation
user	user
terms	terms
max	max
offset	offset

[Submit](#)

- Documentation wiki (doc.cytomine.be)
- User guide
- Open REST API
- Open source code

- Extensible
- Interoperable



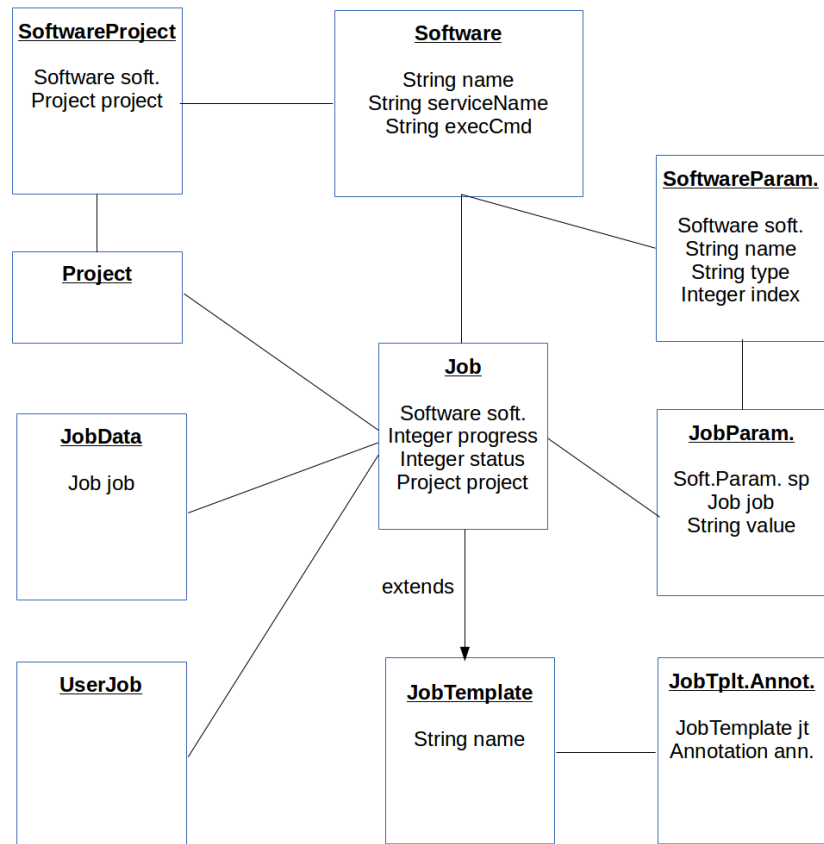
```

{"class": "be.cytomine.ontology.UserAnnotation", "id": "95189319", "created": "1390233213025", "location": "POLYGON ((83409.75 96490.375, 83412.75 96492.375, 83412.75 96481.375, 83411.75 96476.375, 83408.75 96473.375 ... 96489.375, 83409.75 96490.375))", "image": "95062074", "project": "94152784", "container": "94152784", "user": "94115159", "area": "8953.0", "perimeterUnit": "mm", "areaUnit": "micron", "perimeter": "1.0", "centroid": {"x": "83426.59663300458", "y": "96382.22057123308"}, "term": "[95062790]", "cropURL": "http://beta.cytomine.be/api/userannotation/95189319/crop.jpg", "reviewed": "true"}
  
```

- [http://\\$HOST/api/imageinstance/7889452/window-10000-10000-1500-1500.jpg](http://$HOST/api/imageinstance/7889452/window-10000-10000-1500-1500.jpg)
- [http://\\$HOST/api/userannotation/95189319/crop.png?zoom=0](http://$HOST/api/userannotation/95189319/crop.png?zoom=0)
- [http://\\$HOST/api/userannotation/95189319/crop.png?mask=true](http://$HOST/api/userannotation/95189319/crop.png?mask=true)
- [http://\\$HOST/api/userannotation/95189319.json](http://$HOST/api/userannotation/95189319.json)

Write and plug your own algorithms (Java/Python/...) or design your own user interfaces

cytominer features : Third-party software integration



The screenshot shows the Cytomine web interface. The top navigation bar includes 'Cytomine', 'Dashboard', 'Projects', 'Explore', 'Storage', and 'Activity'. The main content area is titled '_DEMO-SEGMENTATION-TISSUE' and contains a list of software jobs under the 'Jobs' tab. The list includes '0Segmentation_Model_Builder', '2Segmentation_Model_Builder', '5Segmentation_Model_Predict', 'AutoLung2', 'TissueDetect', 'TissueSegment_Model_Builder', and 'TissueSegment_Model_Predict'. The 'TissueSegment_Model_Builder' job is highlighted with a left-pointing arrow. Below the list is an 'Actions' section with a 'Run job' button, also highlighted with a left-pointing arrow. To the right of the job list is a 'Launch new job' section with a right-pointing arrow. Below this is a configuration form for 'Run TissueSegment_Model_Builder on project _DEMO-SEGMENTATION-TISSUE'. The form has a table with columns 'Name', 'Value', and 'Required'. The table contains the following rows:

Name	Value	Required
cytomine_annotation_projects	278366	
cytomine_zoom_level	2	
cytomine_predict_terms	Tumor	
cytomine_excluded_terms	Section	
pyxit_target_width	16	
pyxit_target_height	16	
pyxit_colorspace	2	
pyxit_n_jobs	10	
pyxit_transpose	<input type="checkbox"/>	
pyxit_fixed_size	<input checked="" type="checkbox"/>	
pyxit_interpolation	1	
forest_n_estimators	10	
forest_max_features	28	
forest_min_samples_split	1	
pyxit_n_subwindows	100	
cytomine_reviewed	<input type="checkbox"/>	

cyt@mine features : Algorithm evaluation (e.g. class conf matrix)

• Average (per class) : 76.80

View confusion matrix

View predicted galleries

X	Amas.	Amas. non-.	Amas. susp.	Arté.	Autr.	Bact.	Cell. muco.	Cell. bron. cili.	Cell. malp.	Cell. tumo.	Cham.	Lymp.	Macr.	Mucu.	Non. smal. cell. carc.	Poly. neut.	Smal. cell. carc.	total
Amas.	0																	
Amas. non-.		44						2	7						5	5		70%
Amas. susp.			5												10	3		19%
Arté.		2	1	597		1	5	21				3	12		5	7		91%
Autr.					0													
Bact.		2		7		20	4	3										64%
Cell. muco.		1		9		1	126	27	9				2		1			72%
Cell. bron. cili.		1		6			6	265	1				3		9	7		89%
Cell. malp.		2		5			6	1	320				2		3			94%
Cell. tumo.										0								
Cham.											0							
Lymp.								2				06	3		5	20		71%
Macr.		1		4			2	2	7			1	385		4	7		93%
Mucu.														0				
Non. smal. cell. carc.			1	3				5	5			1	5		270	13		89%
Poly. neut.		1		2				3	2			12	4		10	413		92%
Smal. cell. carc.																	0	



- 98% : Annotation 2182594 is predicted Cellules malpighiennes instead of Amas non-suspects
- 97% : Annotation 2511070 is predicted Cellules malpighiennes instead of Amas non-suspects
- 96% : Annotation 1814853 is predicted Non small cell carcinoma instead of Artéfact
- 96% : Annotation 1815026 is predicted Non small cell carcinoma instead of Amas suspects
- 96% : Annotation 59515 is predicted Macrophage instead of Artéfact
- 96% : Annotation 673307 is predicted Non small cell carcinoma instead of Polynucléaire neutrophile
- 96% : Annotation 2017832 is predicted Non small cell carcinoma instead of Amas non-suspects
- 96% : Annotation 2177840 is predicted Cellules malpighiennes instead of Amas non-suspects
- 96% : Annotation 796313 is predicted Macrophage instead of Artéfact
- 95% : [Annotation 682189](#) is predicted Cellules bronchiques ciliées instead of Cellule muco-sécrétante

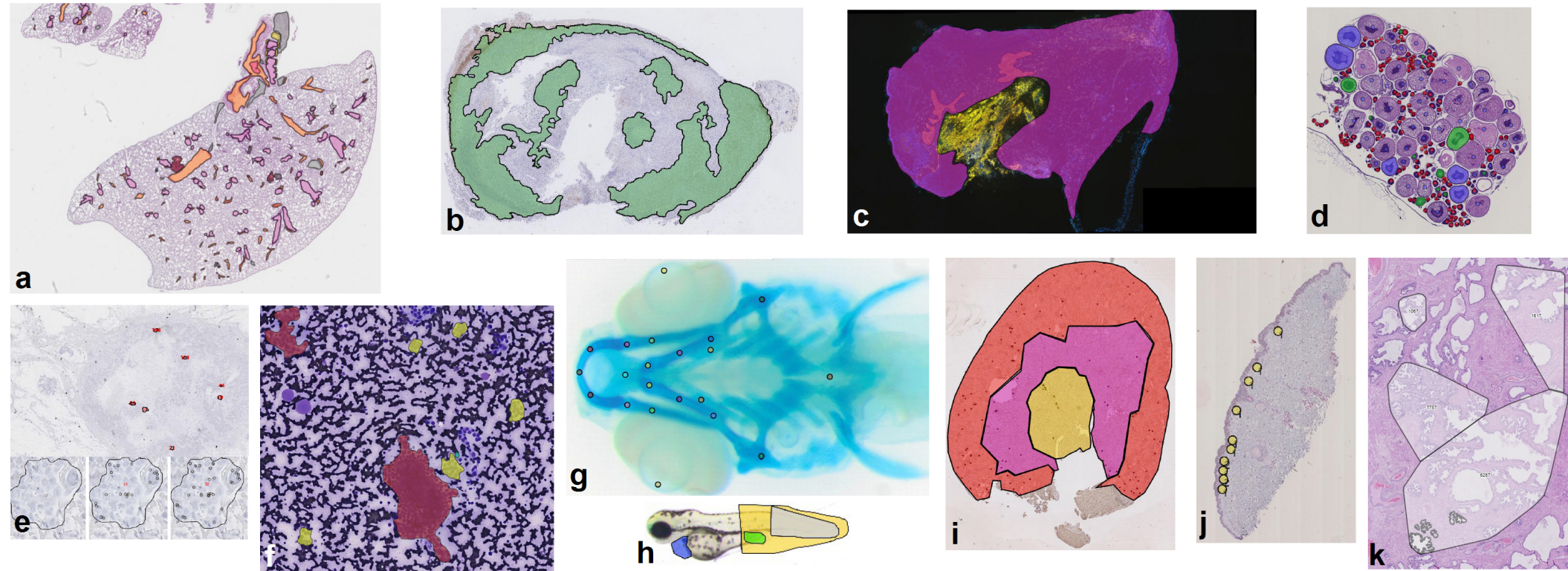


s predicted Non small cell carcinoma instead of Amas suspects
s predicted Polynucléaire neutrophile instead of Non small cell carcinoma
predicted Artéfact instead of Bactérie
predicted Cellules bronchiques ciliées instead of Artéfact
predicted Cellules bronchiques ciliées instead of Cellule muco-sécrétante
predicted Non small cell carcinoma instead of Lymphocytes

+ proofreading
(see applications)

cyt^omine research applications :

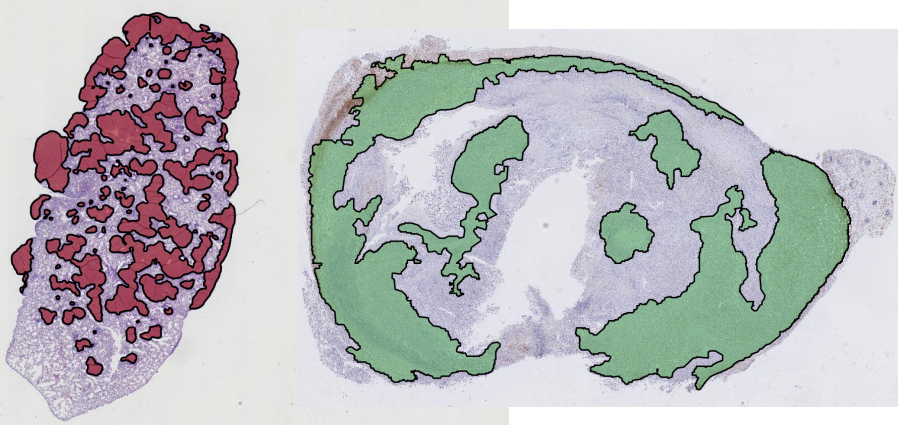
As of March 2016 :
> 200 registered users, > 300 projects,
> 21 000 images, > 700 000 manual annotations
> 6 000 000 algorithm annotations



- a:** H&E mice lung cancer research (D.Cataldo's lab, GIGA-Research) @ ISBI 2014.
- b:** IHC mice lung cancer research (P. Martinive's lab, GIGA-Research) @ OncoTarget 2015.
- c:** Immunofluorescent mouse ear sponge assays in tumor angiogenesis. @ Journal of Pathology 2015.
- d:** H&E Chondrostoma nasus sexual maturation research (Gennotte's lab, CEFRA).
- e:** in situ hybridization assays in human breast cancer research (C.Josse's lab, GIGA-Research) @ BMC Cancer 2015
- f:** Human thyroid cytology (I.Salmon's lab, ULB Anatomical Pathology Department) @ ECDP 2016.
- g:** Danio rerio embryo development (M. Muller's lab, GIGA-Research) @ PLoS ONE 2015.
- h:** Danio rerio toxicology research (M.Muller's lab, GIGA-Research) @ PLoS ONE 2015.
- i:** IHC renal ischemia/reperfusion research (F.Jouret's lab, GIGA-Research) @ Am J Transl Res. 2015.
- j:** IHC in melanoma microenvironment research (P.Quatresooz's lab, GIGA-Research).
- k:** H&E in human breast cancer research (R. Longuespée, GIGA-Research) @ Methods. 2016

cyt_omine features :

Semi-automated analysis using machine learning and proofreading



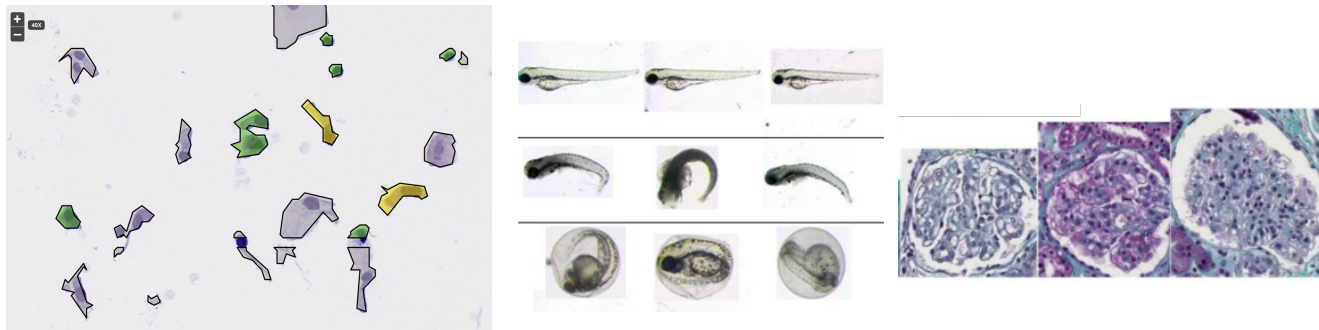
Tissue segmentation

Dumont et al., VISAPP 2009
Marée et al., ISBI 2014
Leroi et al., Oncotarget 2015



Landmark detection

Vandaele et al., Submitted
Huang et al., IEEE TMI 2015

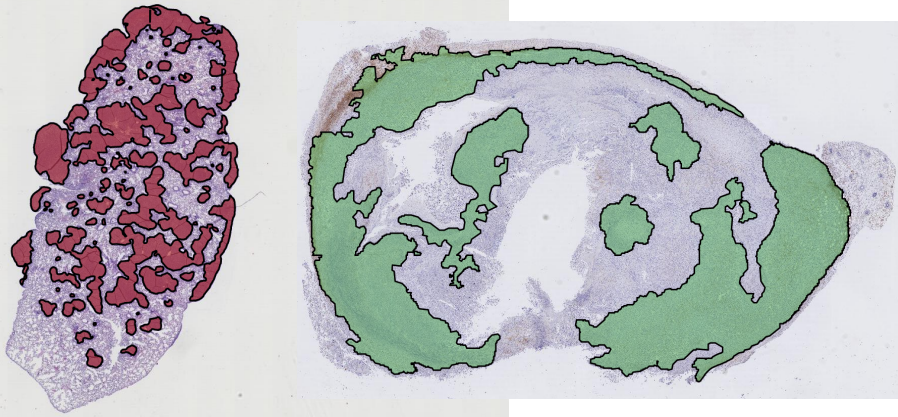


Object classification

Marée et al. Pattern Recognition Letters 2016 ; ISBI 2016
Delga et al., 2014 ; Jeanray et al., PLoS ONE 2015 ;

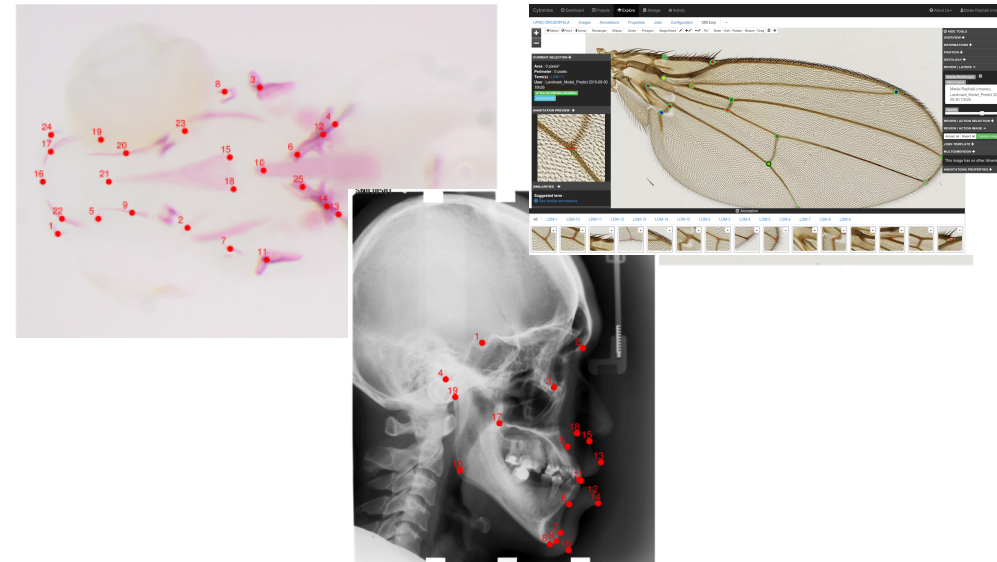
cyt_omine features :

Semi-automated analysis using machine learning and proofreading



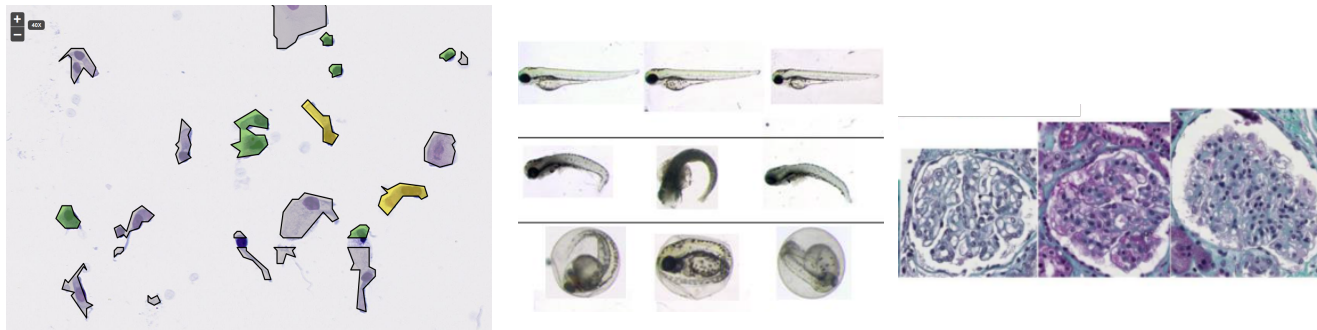
Tissue segmentation

Dumont et al., VISAPP 2009
Marée et al., ISBI 2014
Leroi et al., Oncotarget 2015



Landmark detection

Vandaele et al., Submitted
Huang et al., IEEE TMI 2015

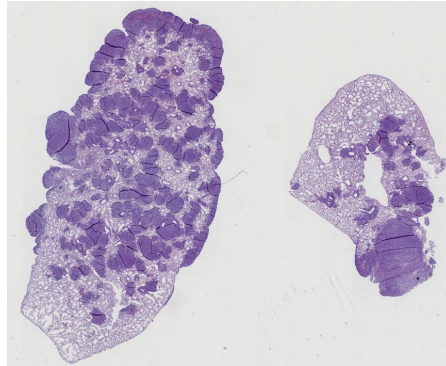
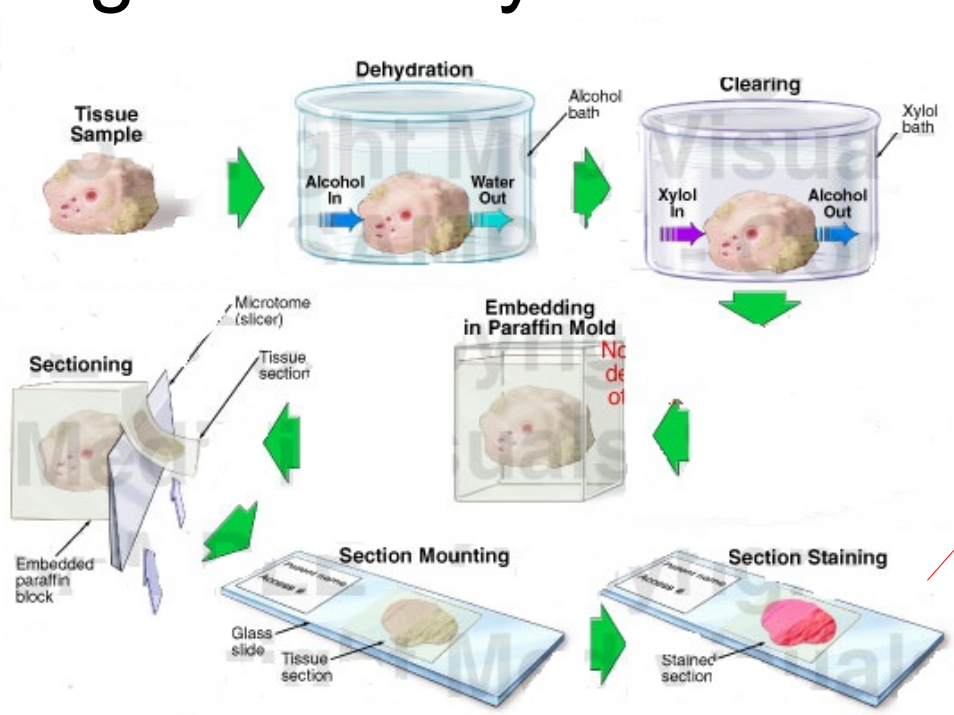


Object classification

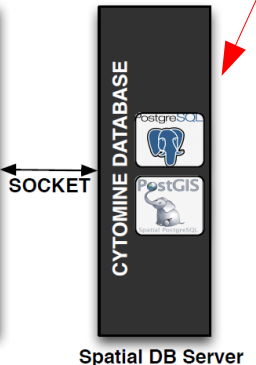
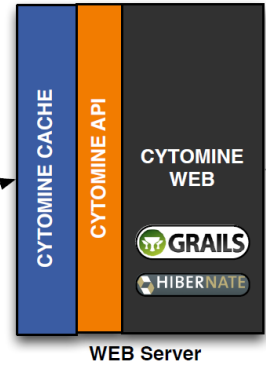
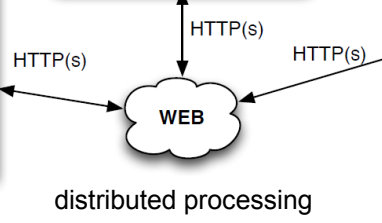
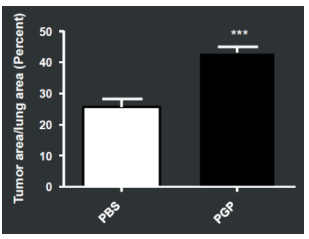
Marée et al. Pattern Recognition Letters 2016 ; ISBI 2016
Delga et al., 2014 ; Jeanray et al., PLoS ONE 2015 ;

Tissue recognition : Hybrid human-computer workflow

Treated with X



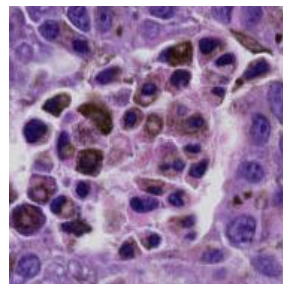
40K x 30K pixels



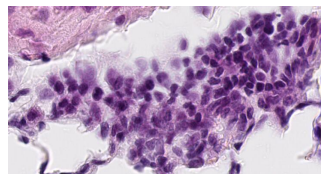
A hybrid human-computer approach for large-scale image-based measurements using web services and machine learning, Marée et al. Proc. IEEE International Symposium on Biomedical Imaging, 2014

Hybrid human-computer workflow

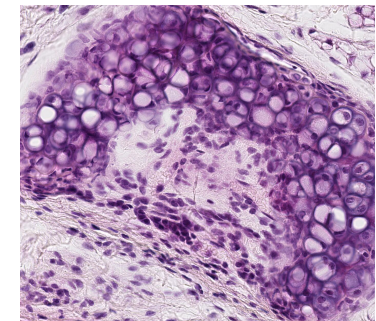
Manual region contouring and labelling to provide training examples



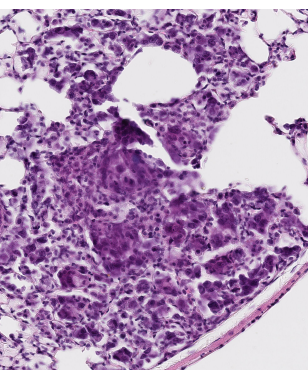
necrosis



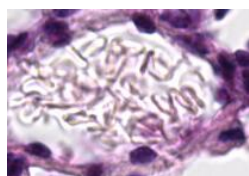
inflammatory cells



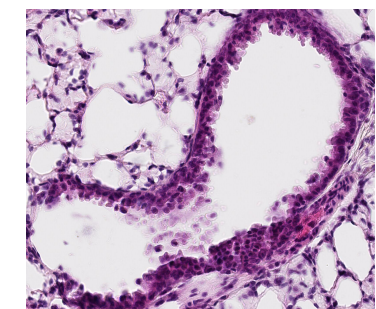
cartilage



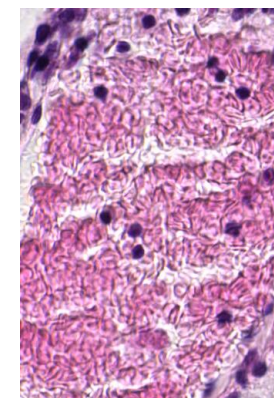
adenocarcinoma



blood vessel



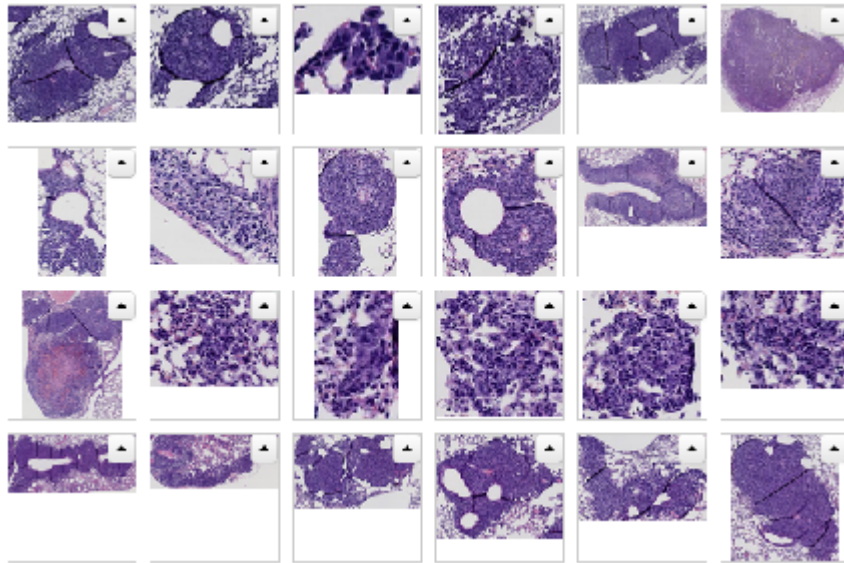
bronchus



red-blood

Hybrid human-computer workflow

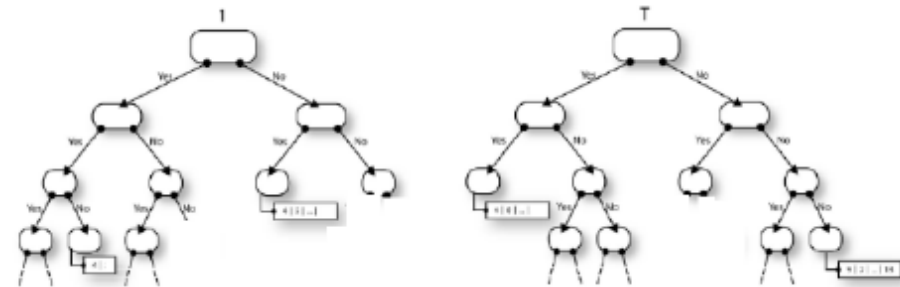
Automatic training of image recognition model based on training examples



VS



A machine-learned classifier that recognizes tumor/nontumor pixels using local patches



Key ingredients :

Standardized preparation/acquisition protocols

Random Subwindows & Extremely randomized trees with multiple outputs (Dumont et al., 2009)

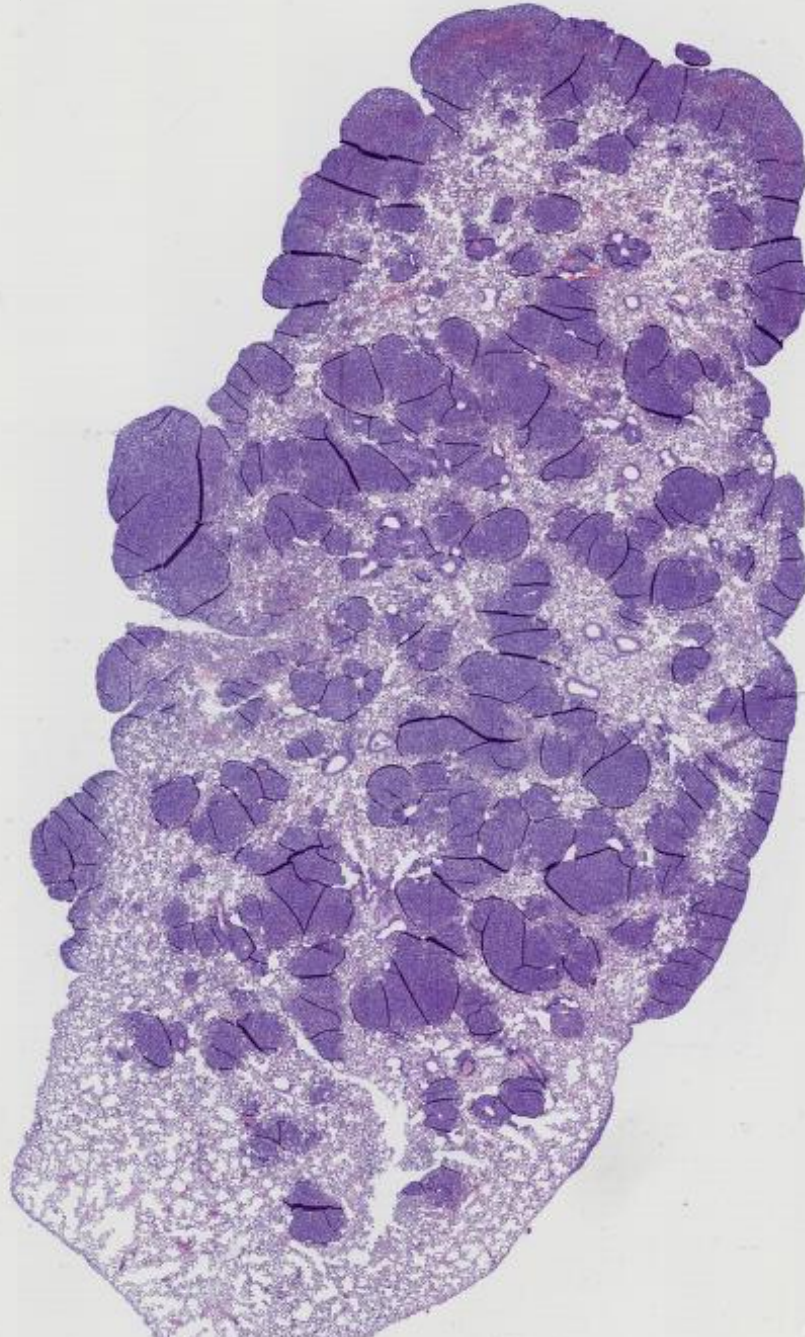
Rapid tuning of parameters :
number/size of subwindows, color space, number of trees, ...

Multi-threaded implementation



Hybrid human-computer workflow

3. Automatic segmentation (pixel classification) of tumors in new images



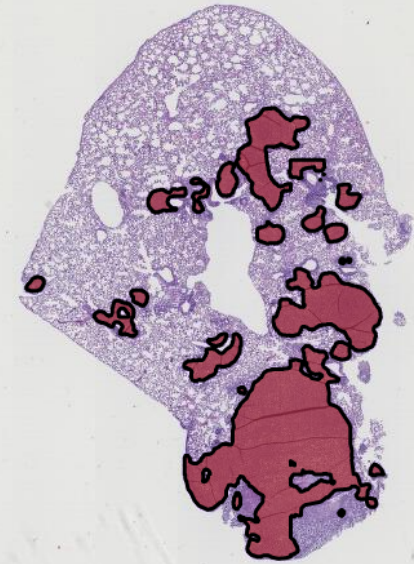
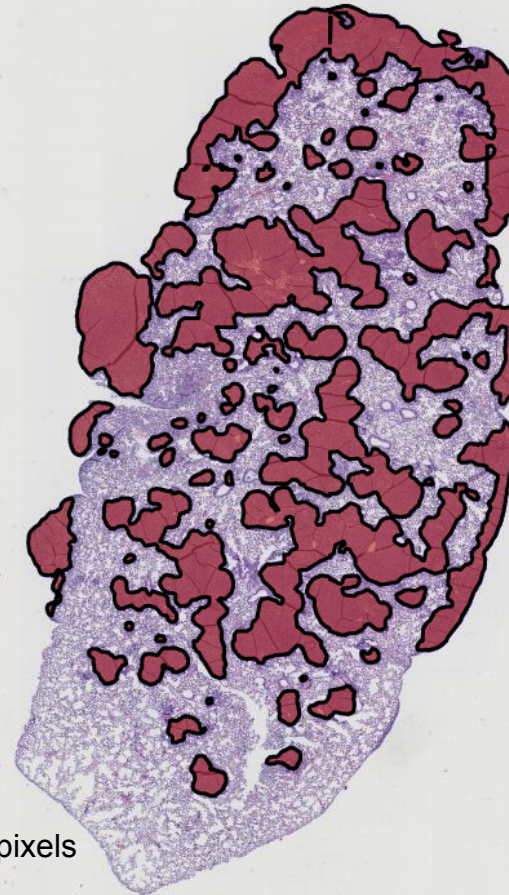
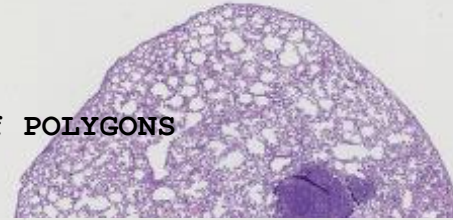
```
Fetch http://is.cytomine.be/.../TileGroup97/2-1-7.jpg
```

```
...{processing : Random Subwindows and Extra-Trees}...
```

```
POST http://beta.cytomine.be/api/annotation.json  
DATA image: 7889452 location: "POLYGON((29672 26176,  
34980 24902,29580 ...))"
```

```
...
```

```
Union of POLYGONS
```

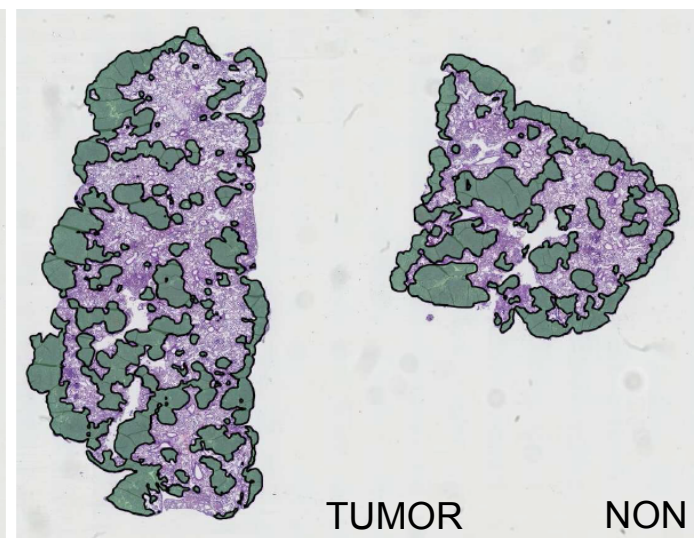
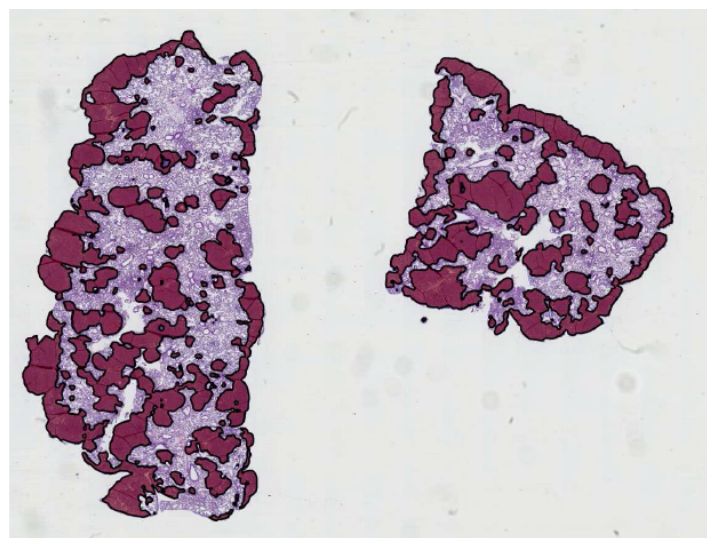
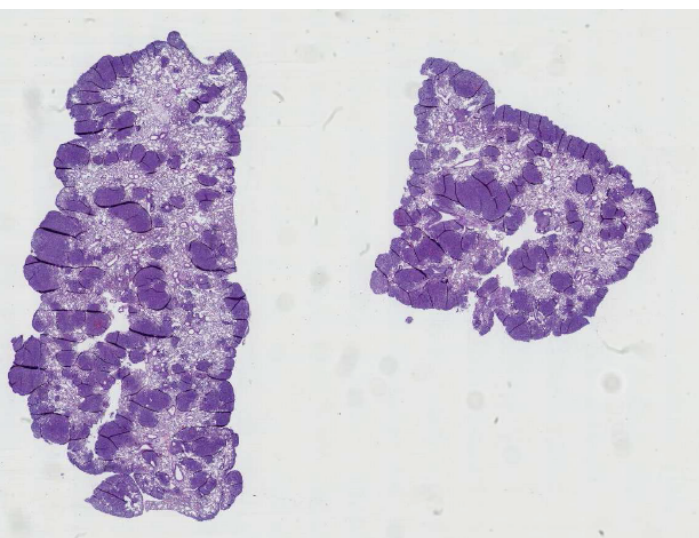


One image ~ 40 K x 30 K pixels

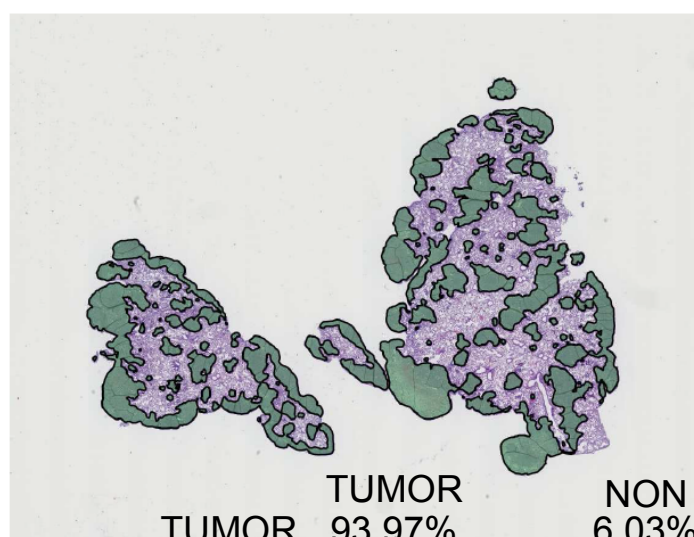
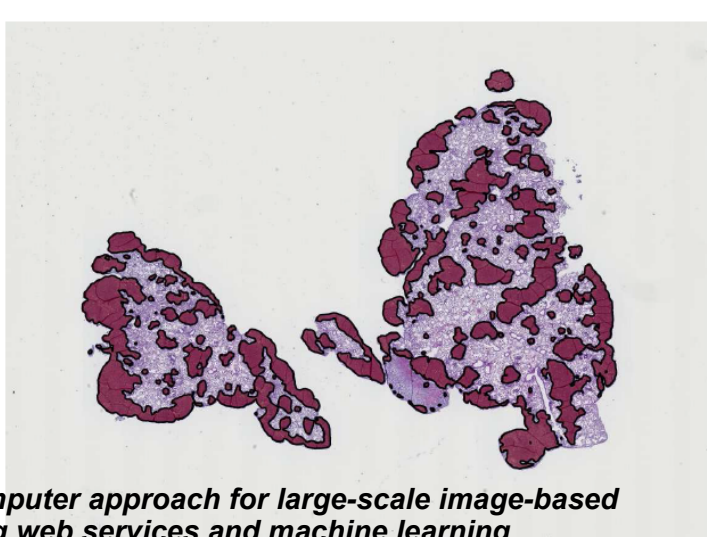
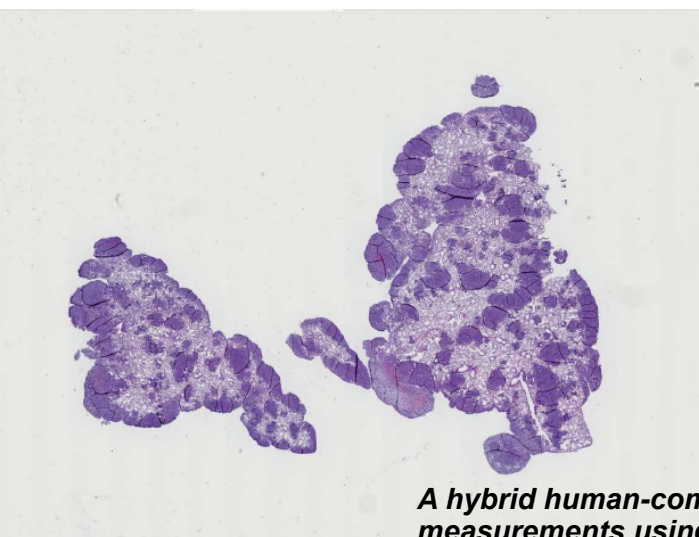


Hybrid human-computer workflow

Recognition performances



	TUMOR	NON
TUMOR	98.51%	1.49%
NON	2.78%	97.22%



	TUMOR	NON
TUMOR	93.97%	6.03%
NON	0.01%	99.99%

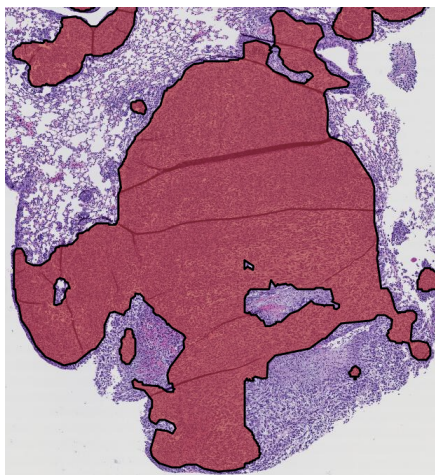
A hybrid human-computer approach for large-scale image-based measurements using web services and machine learning,

Marée et al.

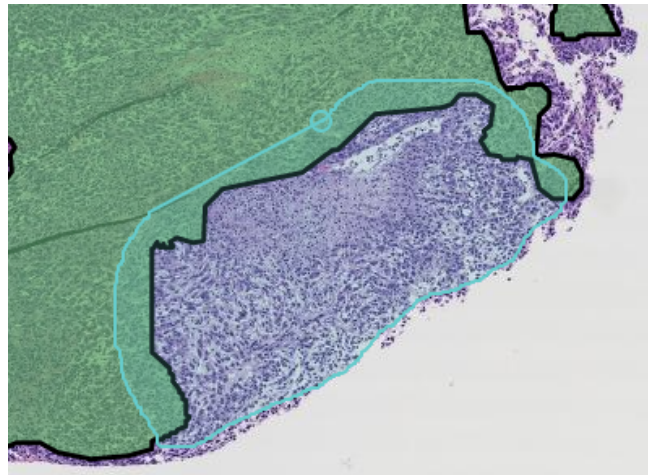
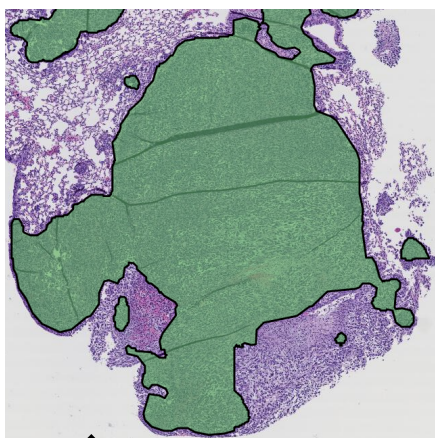
Proc. IEEE International Symposium on Biomedical Imaging, 2014

cyt@mine features : Algorithm proofreading

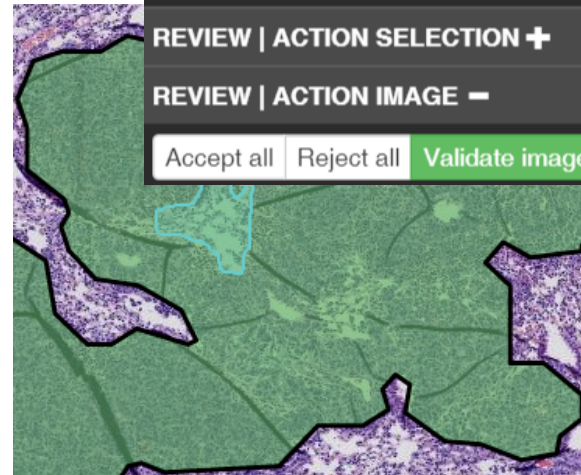
Edit Rotate Resize Drag Fill + Extend - Subtract Delete



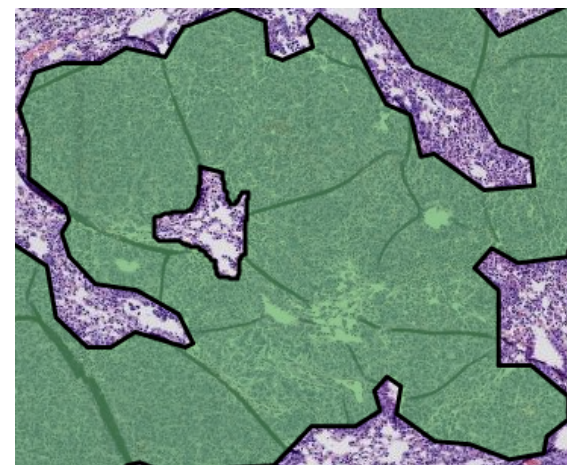
Fill



+ Extend



- Subtract



REVIEW | LAYERS +

Display Review layer :

Others layers :

Snow Jon (jsnow),
TissueSegment_Model_Predict
2015-06-12 11h16

Opacity

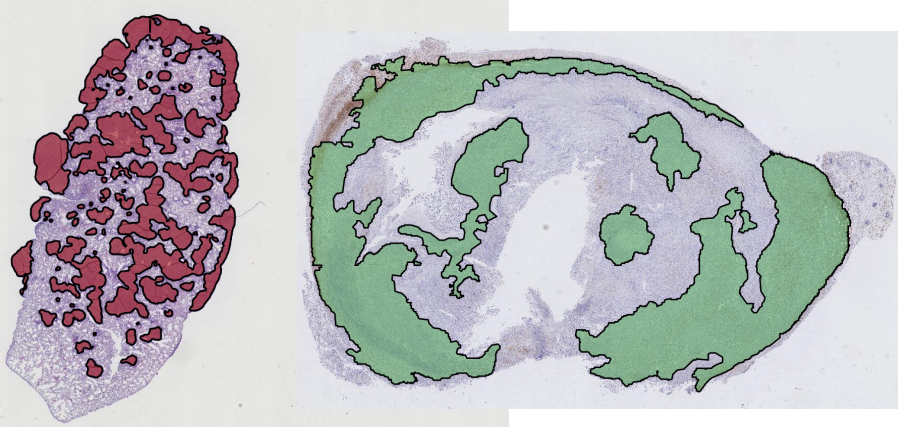
REVIEW | ACTION SELECTION +

REVIEW | ACTION IMAGE -

Accept all Reject all **Validate image**

cyt_omine features :

Semi-automated analysis using machine learning and proofreading



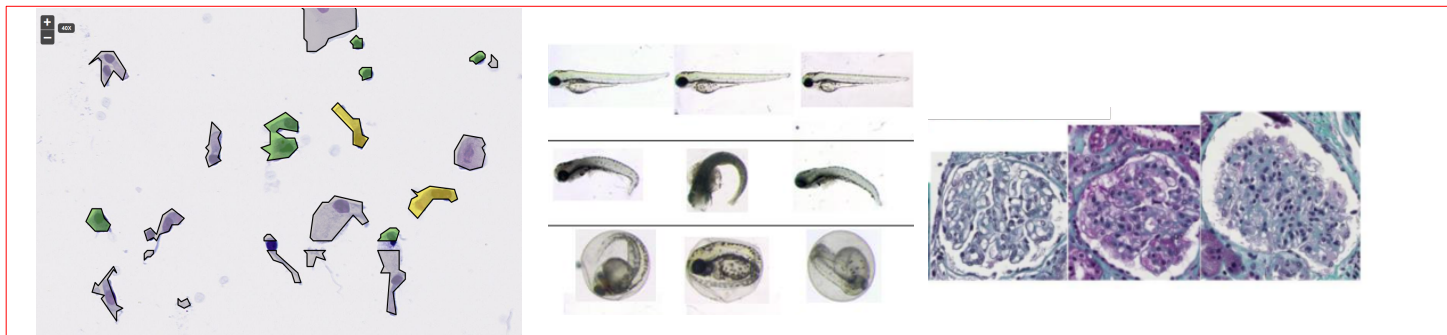
Tissue segmentation

Dumont et al., VISAPP 2009
Marée et al., ISBI 2014
Leroi et al., Oncotarget 2015



Landmark detection

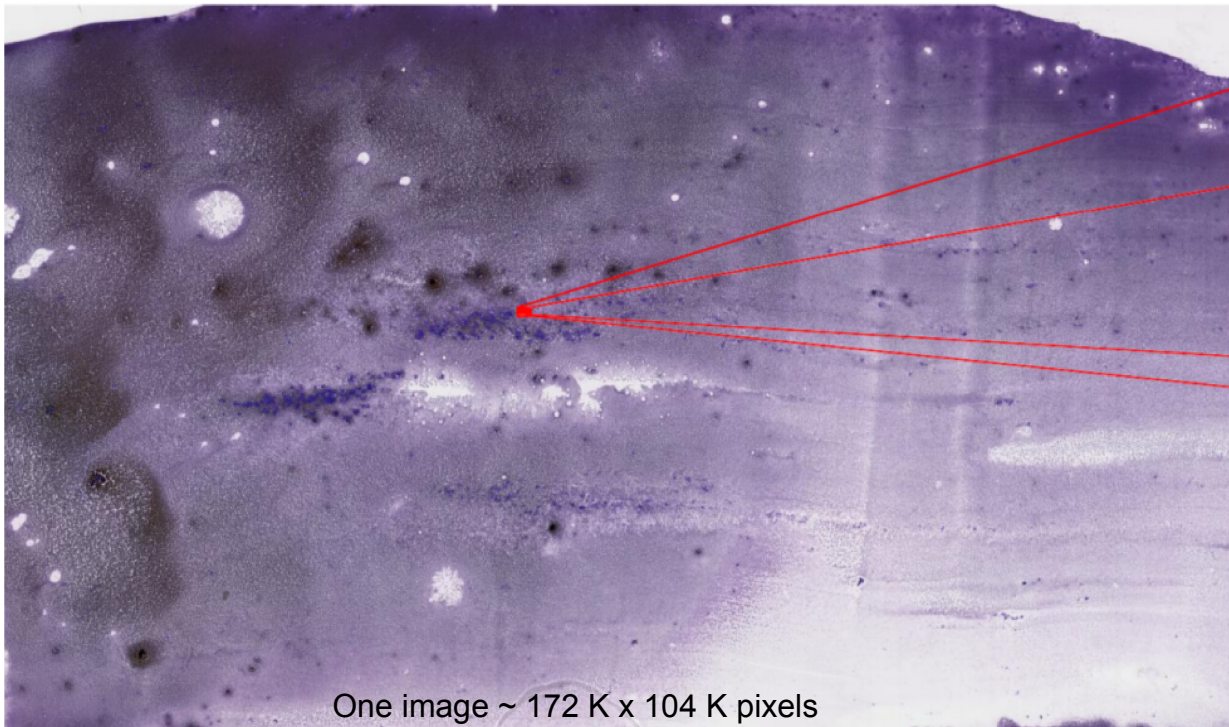
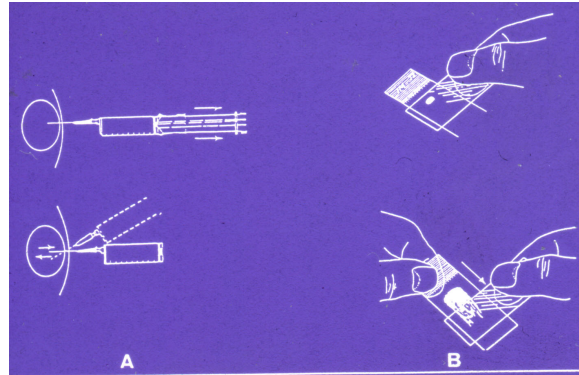
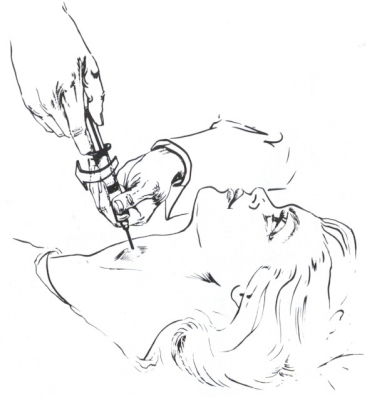
Vandaele et al., Submitted
Huang et al., IEEE TMI 2015



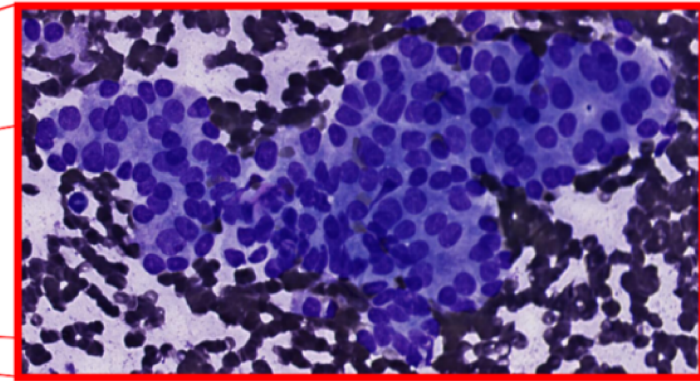
Object classification

Marée et al. Pattern Recognition Letters 2016 ; ISBI 2016
Delga et al., 2014 ; Jeanray et al., PLoS ONE 2015 ;

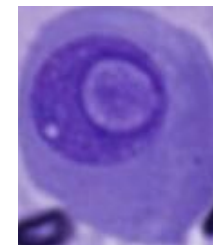
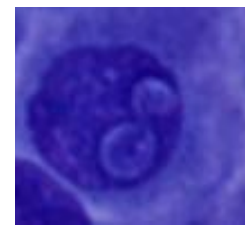
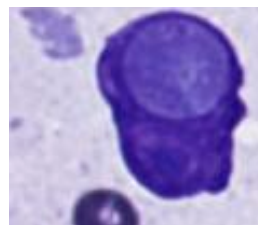
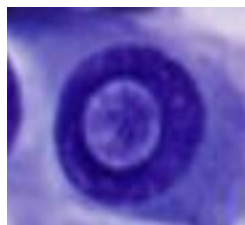
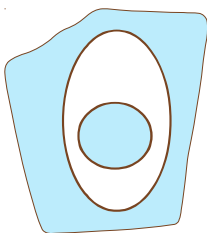
Object classification in multi-gigapixel images



One image ~ 172 K x 104 K pixels

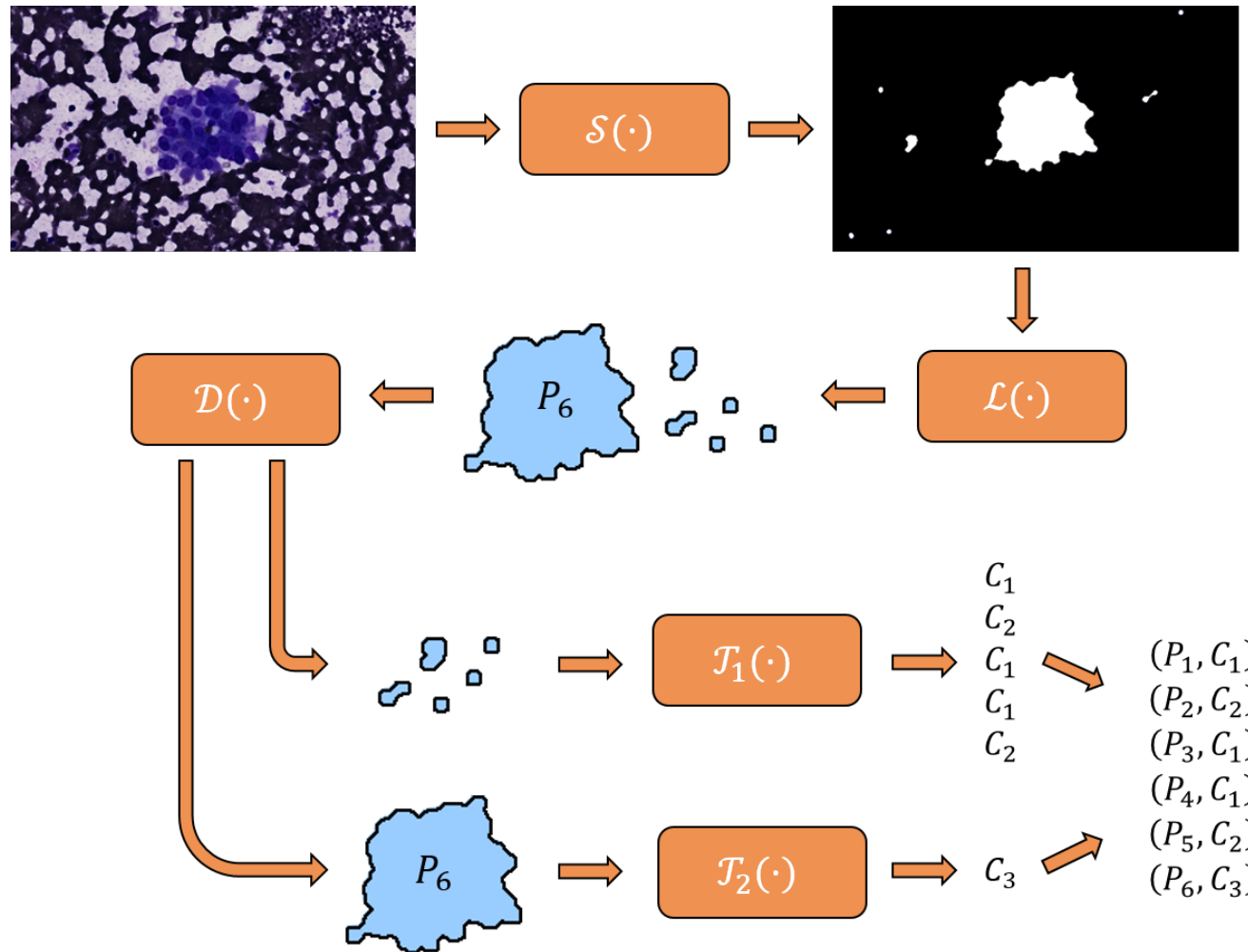


x130



Thyroid FNAB project with ULB Erasme (Prof. I. Salmon)

SLDC : a workflow for object detection & classification in multi-gigapixel images



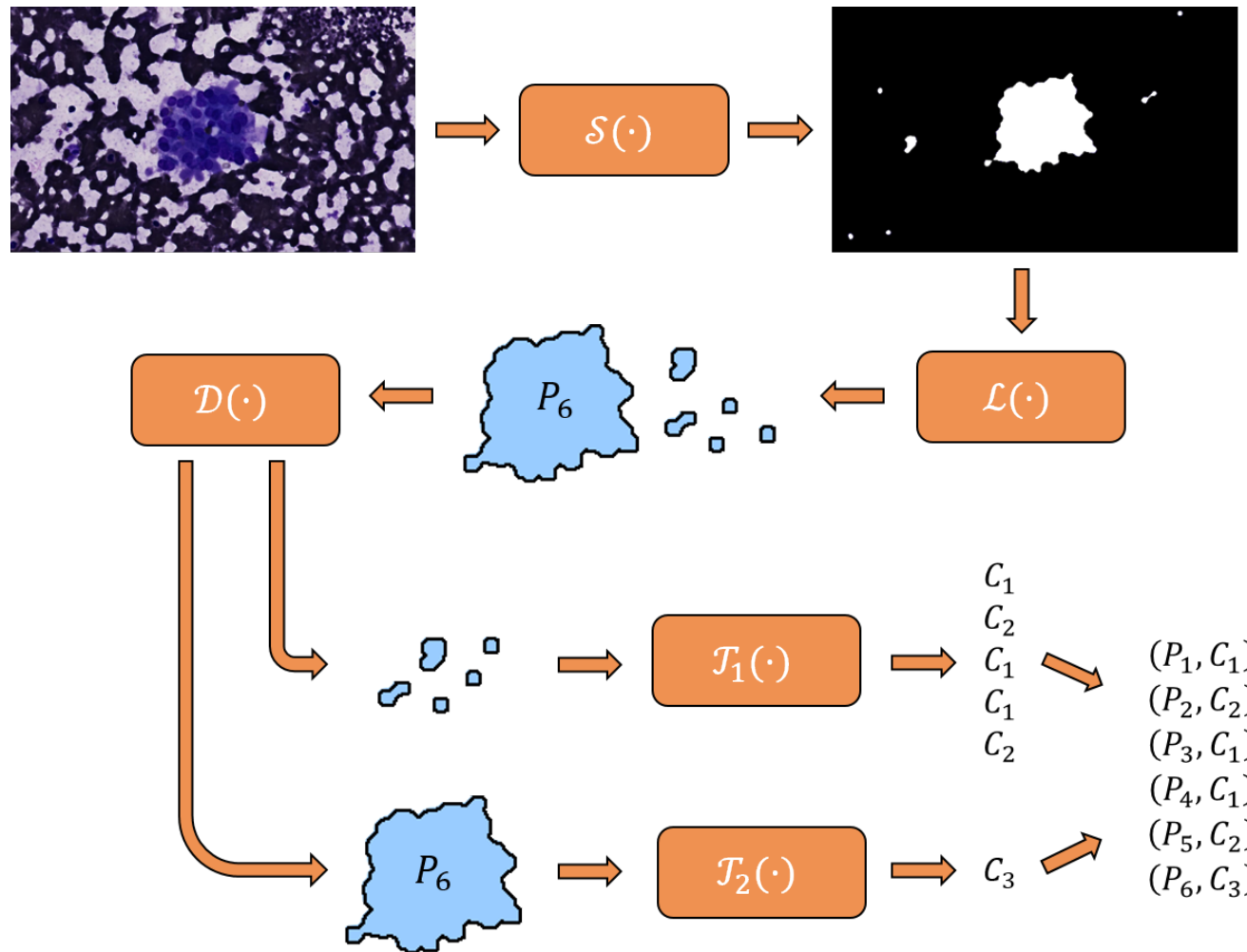
Segment : Produces binary masks

Locate : Extracts polygons representing the objects of interest from binary masks

Dispatch : Identifies the most appropriate classifier for processing each polygon

Classify : Produces a classification label (and probability estimates) for each polygon

SLDC : a workflow for object detection & classification in multi-gigapixel images



Segment : Color deconvolution (Ruifrok & Johnston, Anal Quant Cytol Histol., 2001)

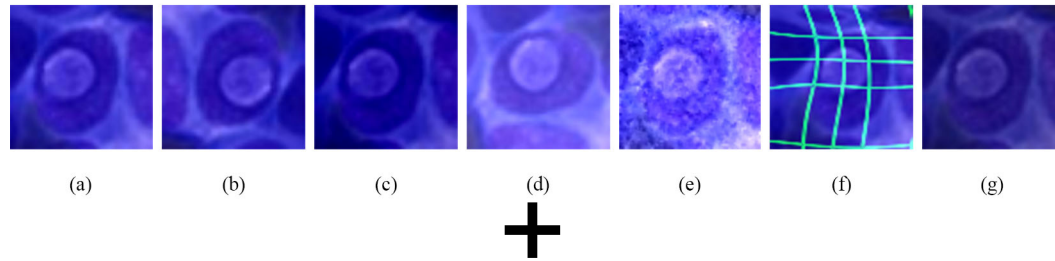
Locate : Connected components + polygon merging (tiles)

Dispatch : Classifier* to sort Cells / Patterns / Artefacts

Classify : Classifier* Inclusion vs Normal ; Classifier Proliferative pattern vs Normal pattern

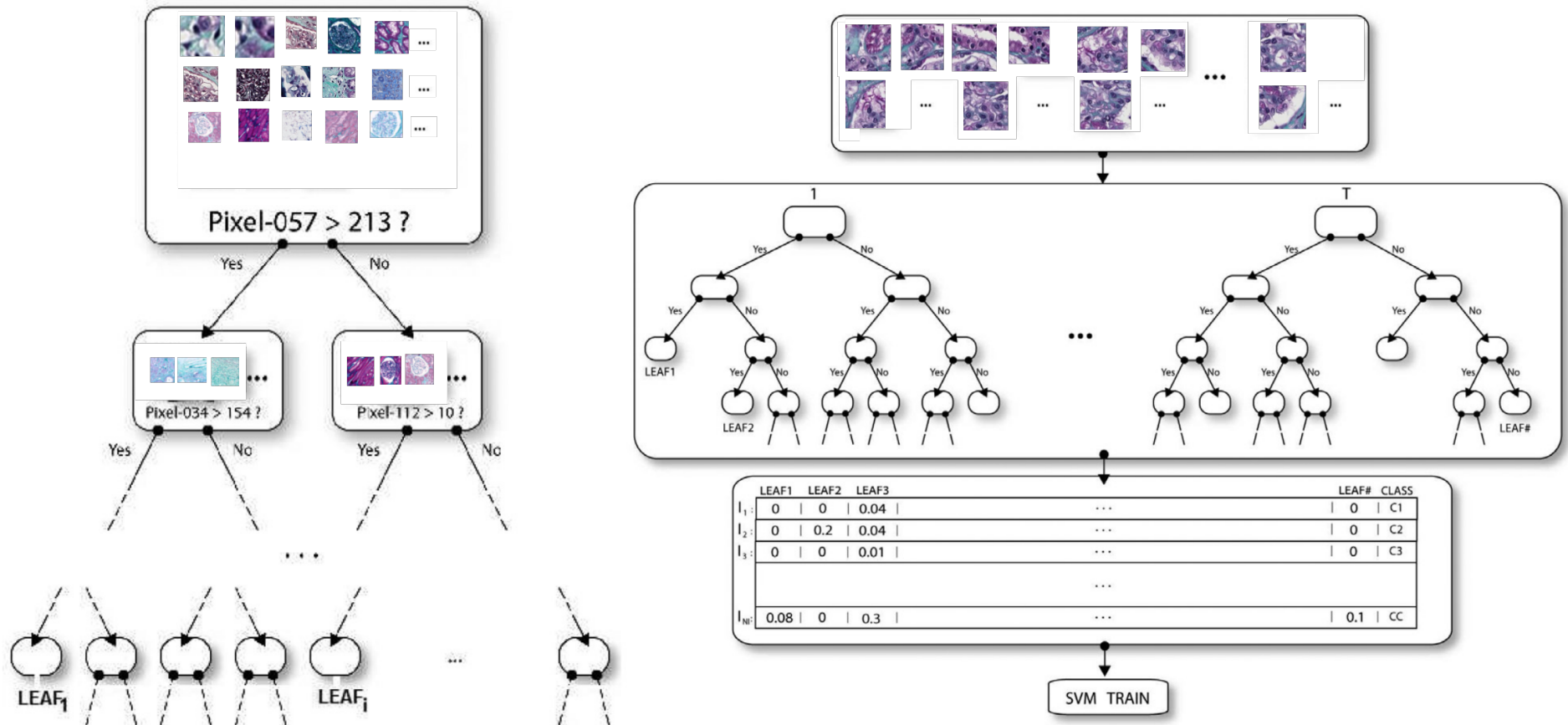
*Based on Random subwindows and Extra-Trees (Marée et al., Pattern Recognition Letters ; 2016)

Generic classifier



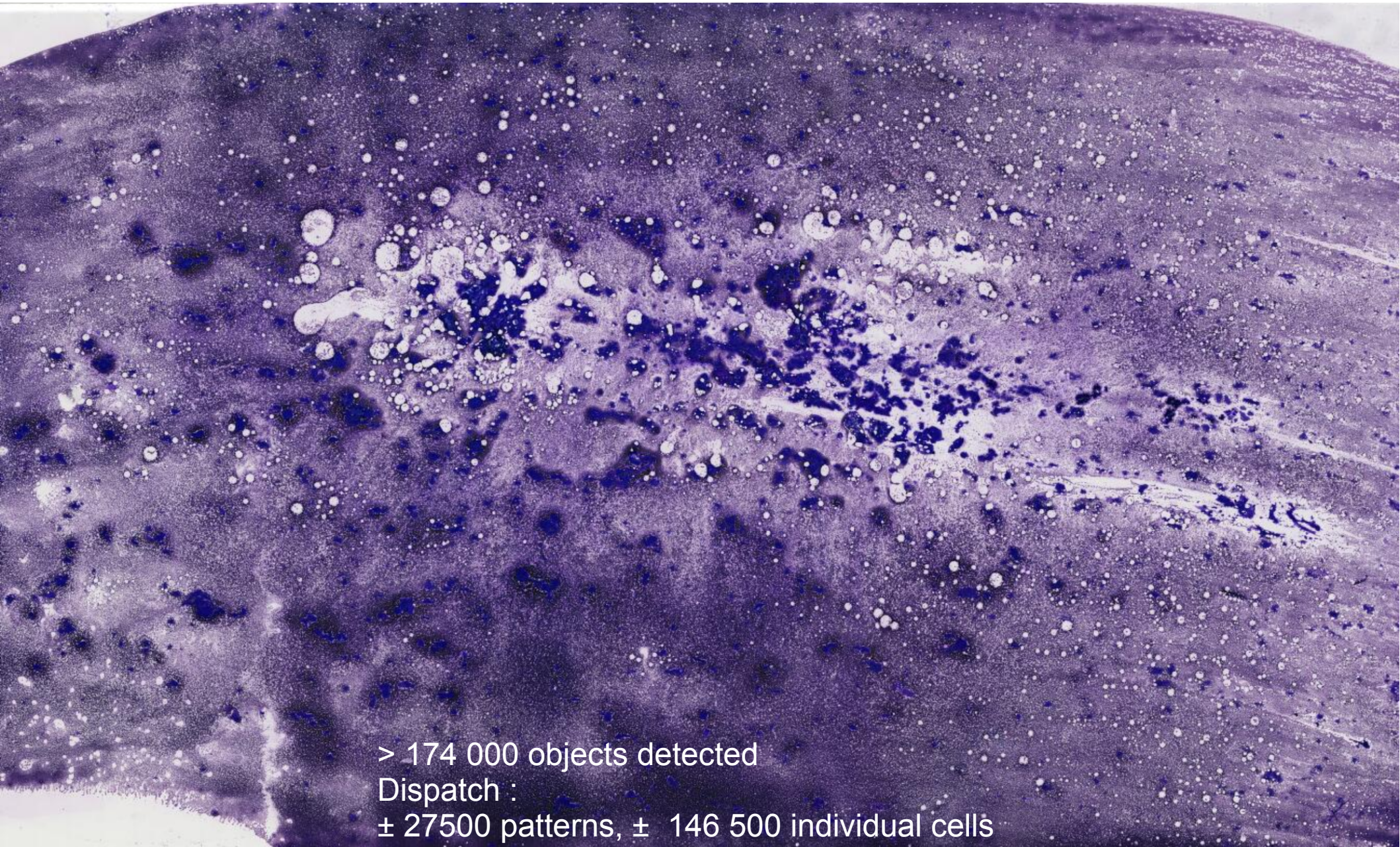
Random subwindows (patches) extracted in images
 Described by raw pixel values

Extremely Randomized Trees for feature learning + Final linear SVM classifier

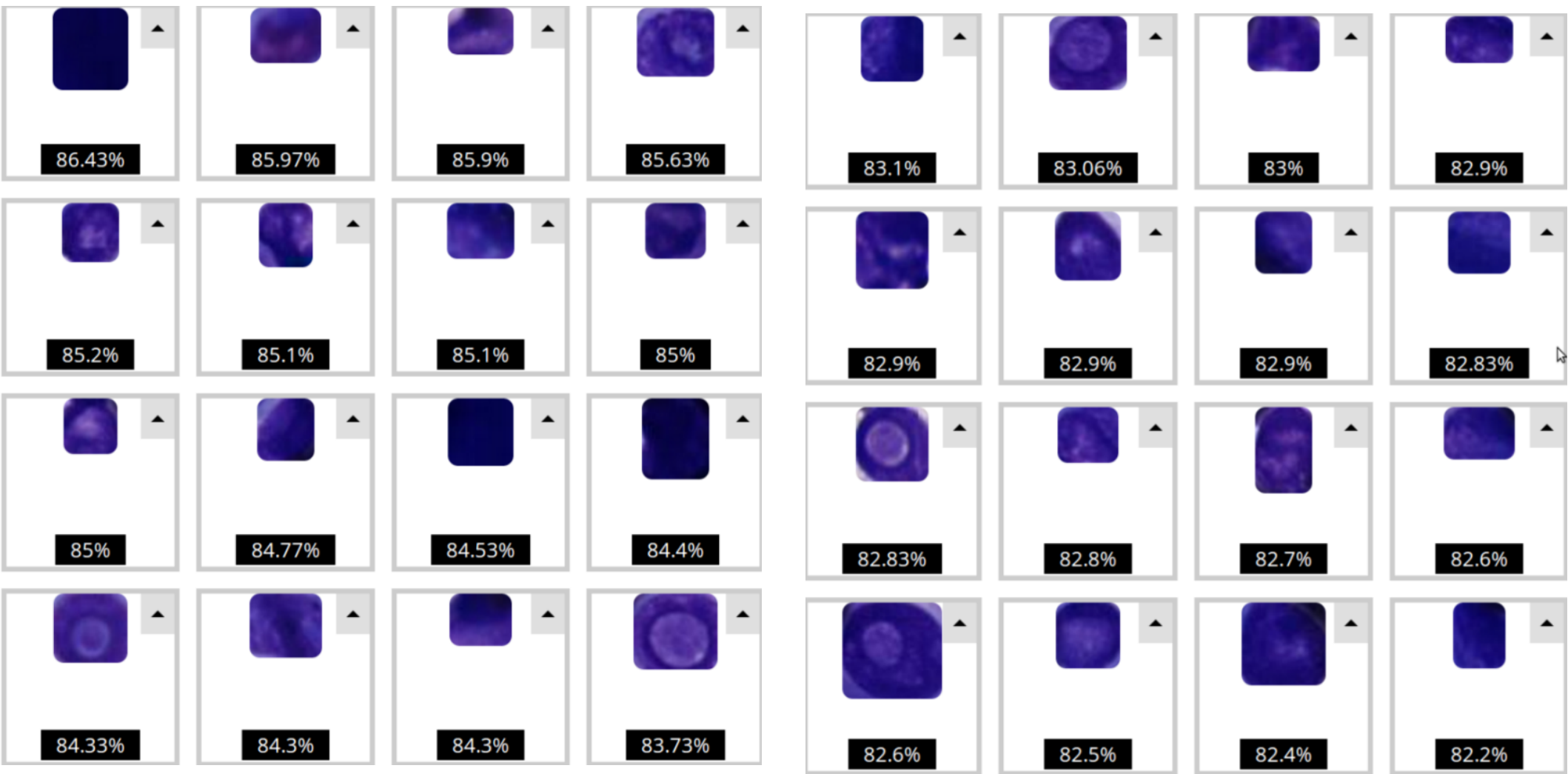


(Marée et al., Pattern Recognition Letters 2016)

Application on a whole-slide image



Application on a whole-slide image : Detected intranuclear inclusions



cyt@mine features : Algorithm proofreading : classification

Cytomine Dashboard Projects Ontologies Explore Storage Activity Search About Us Marée Raphaël (rmaree)

ULB-ANAPATH-THYROID-FNAB Images Annotations Properties Jobs Configuration Review 016-CP_11C09223_1B-2012...

Review for project ULB-ANAPATH-THYROID-FNAB

You are reviewing image 016-CP_11C09223_1B-2012-08-16-23.53.39.jp2.

User: Test 2016-05-25 16h56 Term: Proliferative follicular architectural pattern

Test 2016-05-23 12h39: 1671 / 183782 reviewed
Test 2016-05-25 16h56: 8 / 76212 reviewed
Deblire Antoine (adeblire): 1 / 21 reviewed
Degand Caroline (cdegand): 0 / 264 reviewed

Annotation details:
Created by: Test
Date: 2016-05-25 21h28
Term associated: Test has associated Proliferative follicular architectural pattern

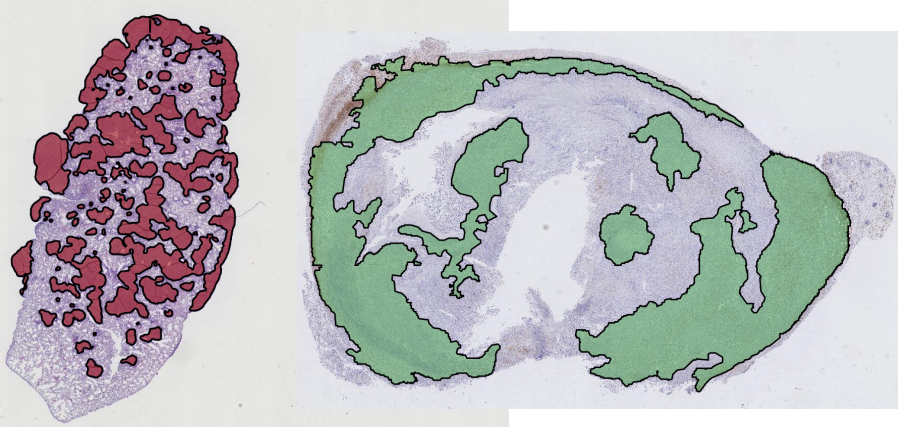
NonInclusion	Papillary cell with inclusion	Proliferative follicular architectural pattern (minor sign)	Normal follicular architectural pattern
Architectural pattern to classify	Cell to classify	Aggregate	Background
		Colloid	Macrophages

Your last review for this project:

- Reviewed Artefacts 2016-05-25 22h19
- Reviewed Artefacts 2016-05-25 22h19
- Reviewed Artefacts 2016-05-25 22h19

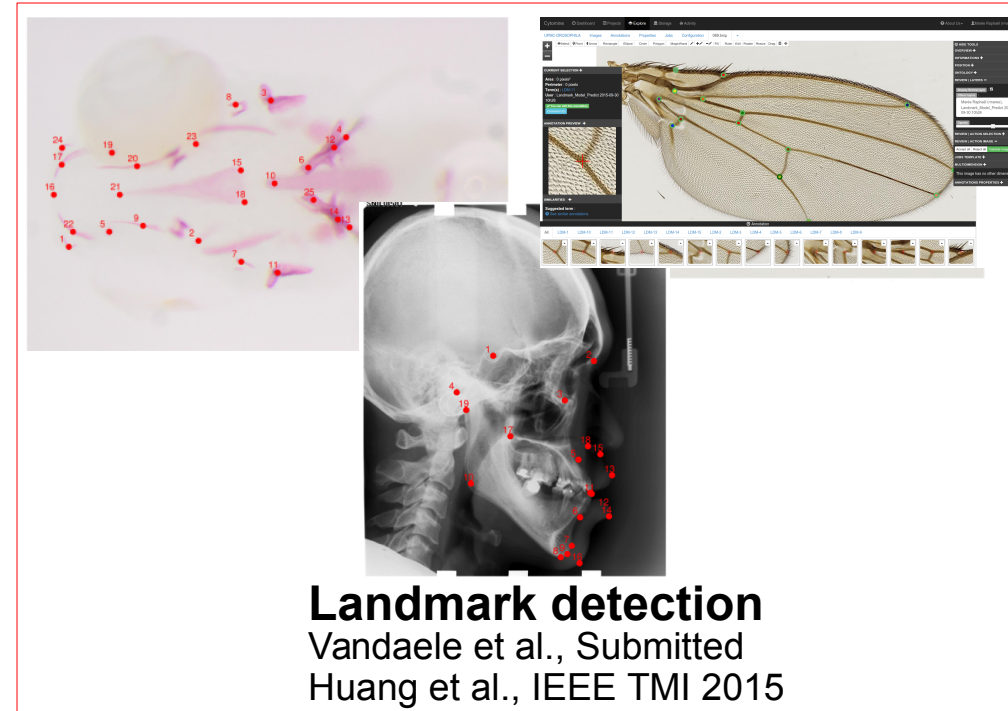
cyt_omine features :

Semi-automated analysis using machine learning and proofreading



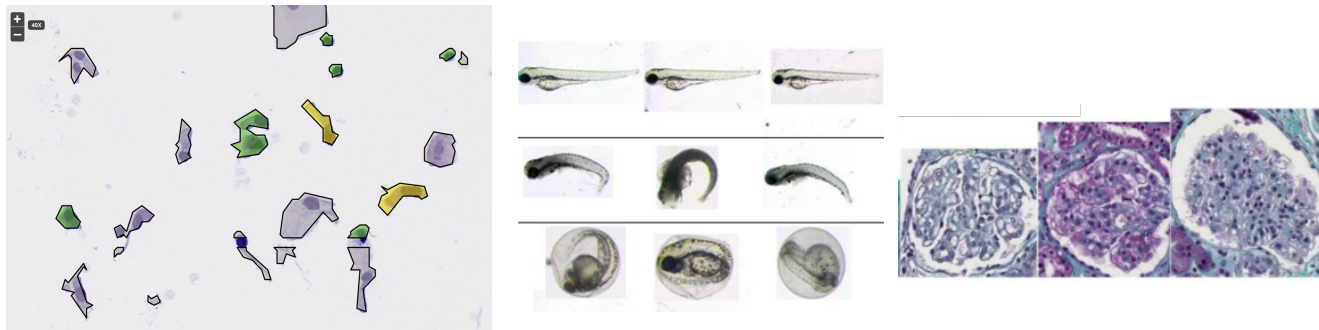
Tissue segmentation

Dumont et al., VISAPP 2009
Marée et al., ISBI 2014
Leroi et al., Oncotarget 2015



Landmark detection

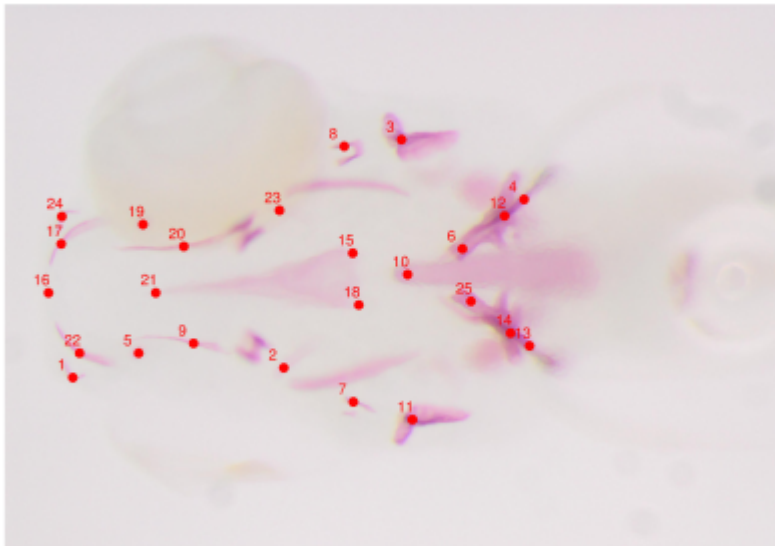
Vandaele et al., Submitted
Huang et al., IEEE TMI 2015



Object classification

Marée et al. Pattern Recognition Letters 2016 ; ISBI 2016
Delga et al., 2014 ; Jeanray et al., PLoS ONE 2015 ;

Supervised landmark detection



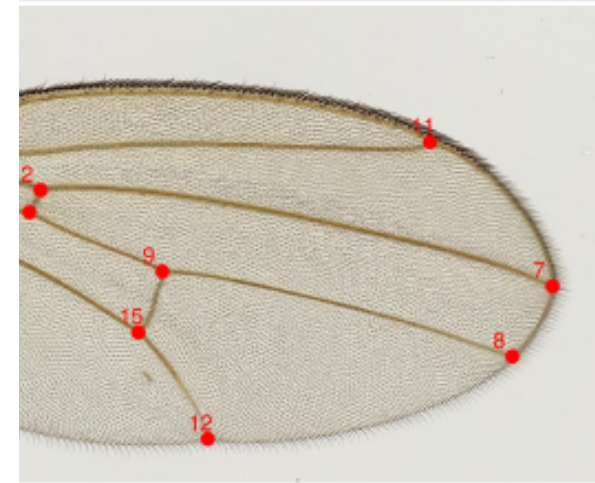
ZEBRA
(M.Muller's lab, GIGA)



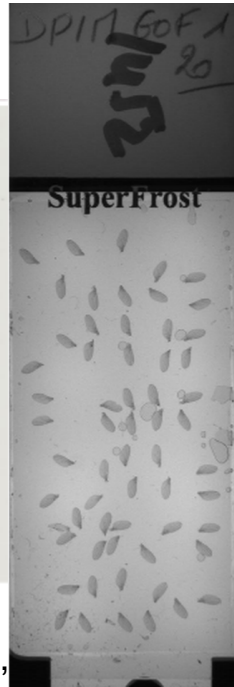
ALIZARIN RED

- Anguloarticular down ■
- Anguloarticular up ■
- Anterior ■
- Background ■
- Branchiostegal ray 1 down ■
- Branchiostegal ray 1 up ■
- Branchiostegal ray 2 down ■
- Branchiostegal ray 2 up ■
- Ceratobranchial down ■
- Ceratobranchial up ■
- Ceratohyal down ■
- Ceratohyal up ■
- Cleithrum down ■
- Cleithrum up ■
- Dentary down ■
- Dentary up ■
- Entopterygoid down ■
- Entopterygoid up ■
- Eye down ■
- Eye up ■
- Hyomandibular down ■
- Hyomandibular up ■
- Maxilla down ■
- Maxilla up ■
- Notochord ■
- Opercul down ■
- Opercul up ■
- Parasphenoid a ■
- Parasphenoid b ■
- Parasphenoid c ■
- Superposition down ■
- Superposition up ■

(C-T Huang's lab, NTUST)



DROSO
(F.Peronnet's lab, UPMC)



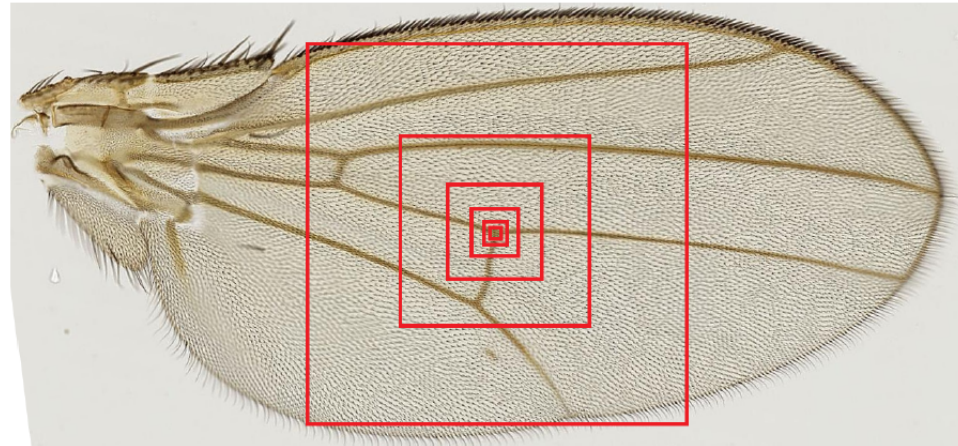
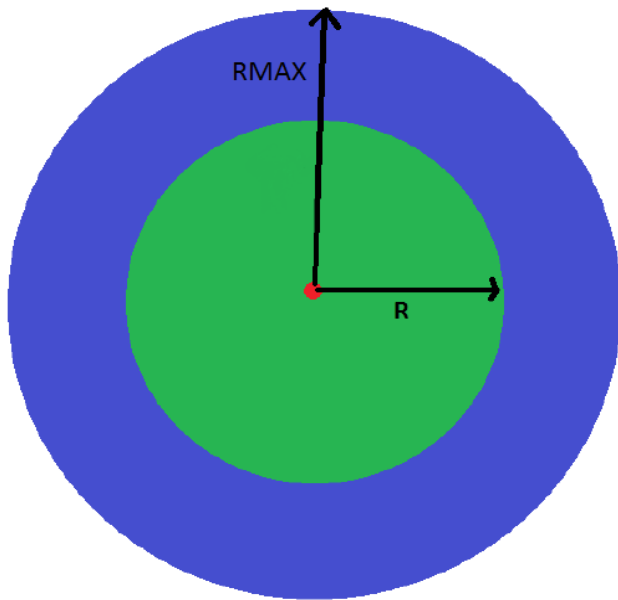
Vandaele et al., Landmark detection in 2D images : a tree-based approach. To be submitted

Training

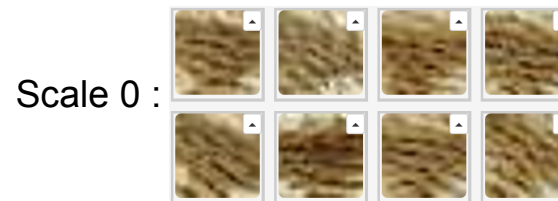
Binary classification problems using Extremely Randomized Trees classifier

Training dataset for each landmark:

Positive examples : n pixels in the neighborhood $((x,y) < R)$ of the landmark from each training images.



Each pixel is described by
6 multiresolution subwindows (16x16)



Negative examples : $p \cdot n$ pixels beyond the neighborhood but within a certain distance to balance the training set ($R < (x,y) < R_{MAX}$)

Prediction

For each landmark :

Subsample NP candidate pixels (multivariate normal distribution, centered on observed mean position in the training set), described by multiresolution features.

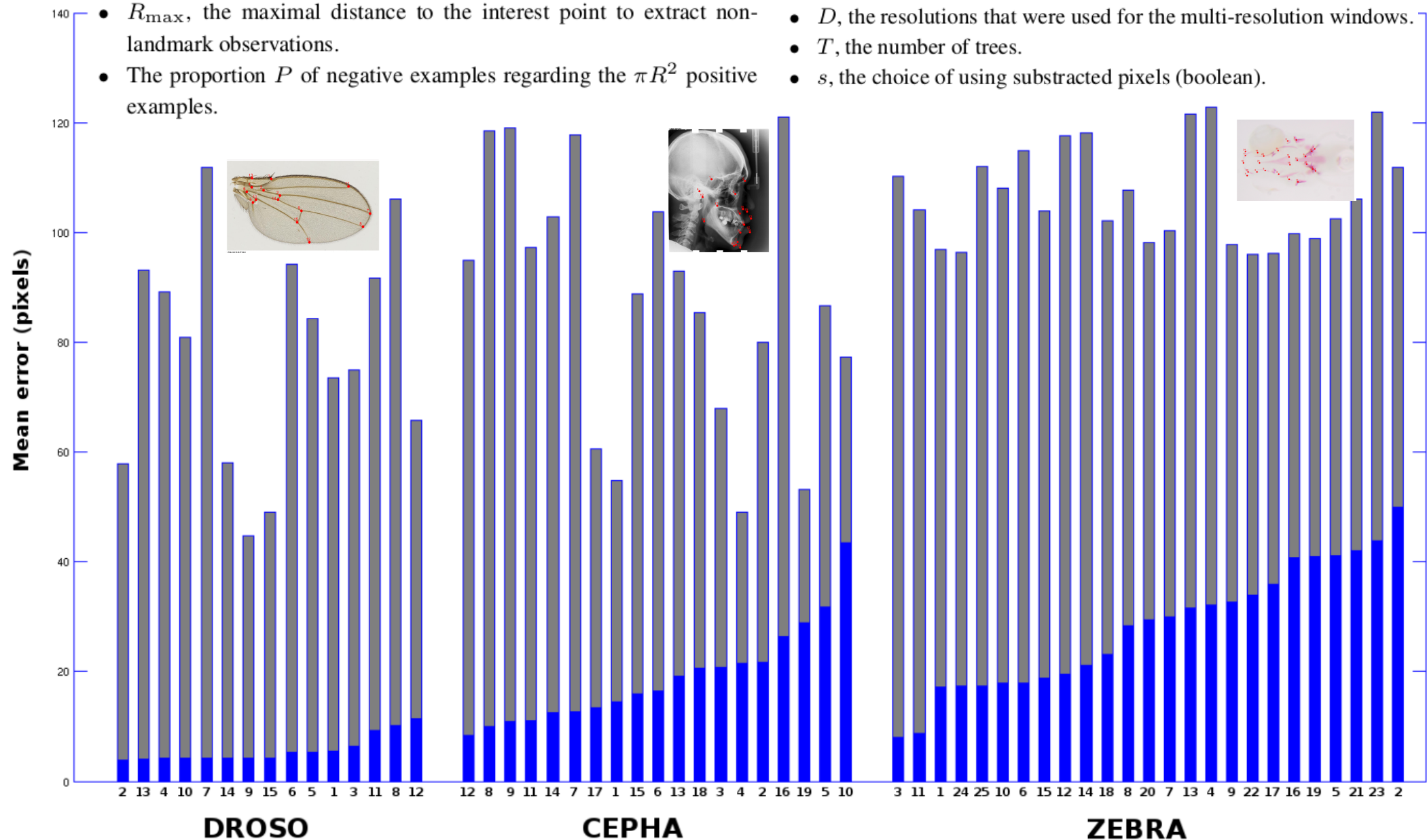


Classify each candidate pixel into positive/negative using the Extra-Trees classifier

Predicted landmark position is the median position of the pixels predicted as positive with the highest probability

Empirical evaluation

- W , the size of the multi-resolution windows.
- R , the distance to the landmark position determining the training pixel output class.
- R_{\max} , the maximal distance to the interest point to extract non-landmark observations.
- The proportion P of negative examples regarding the πR^2 positive examples.
- N_p , the number of pixels randomly extracted during prediction.
- N_r , the number of repetitions with rotation to add to the dataset.
- α the maximal angle of the rotations (in degree).
- D , the resolutions that were used for the multi-resolution windows.
- T , the number of trees.
- s , the choice of using subtracted pixels (boolean).

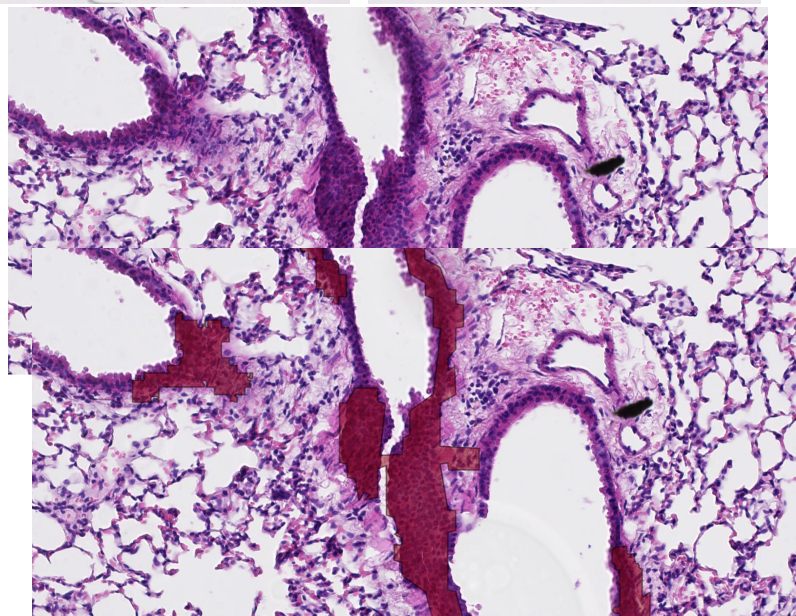
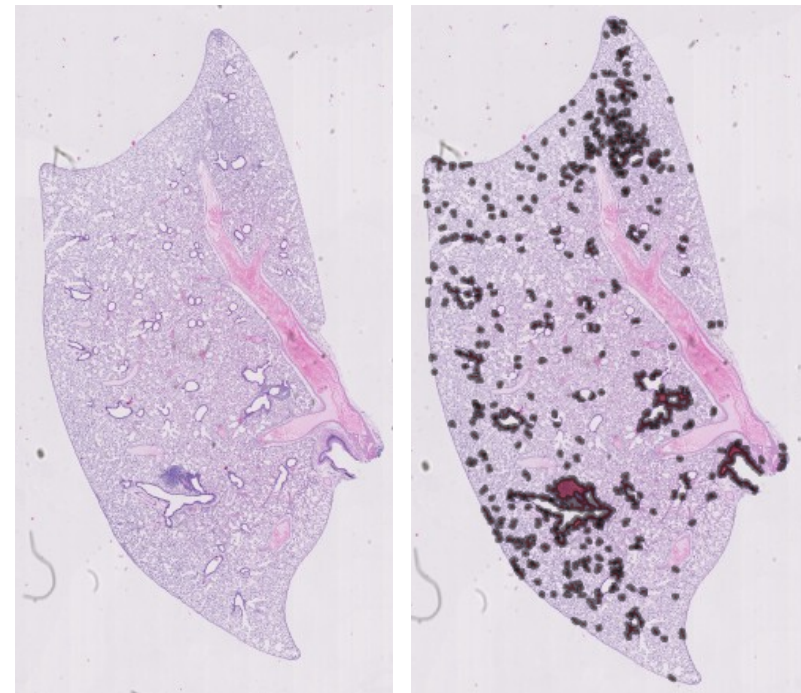


cyt^omine features :

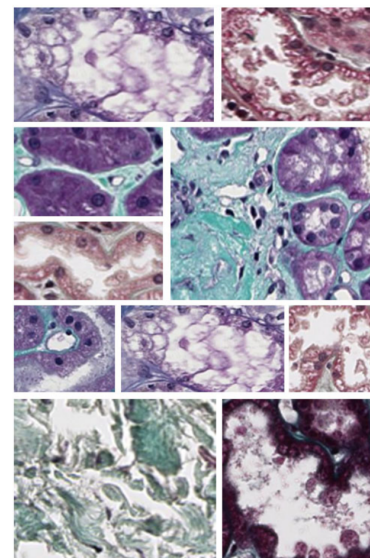
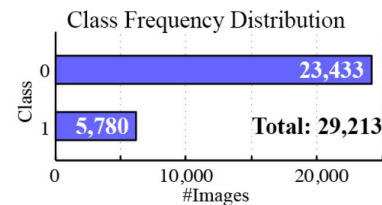
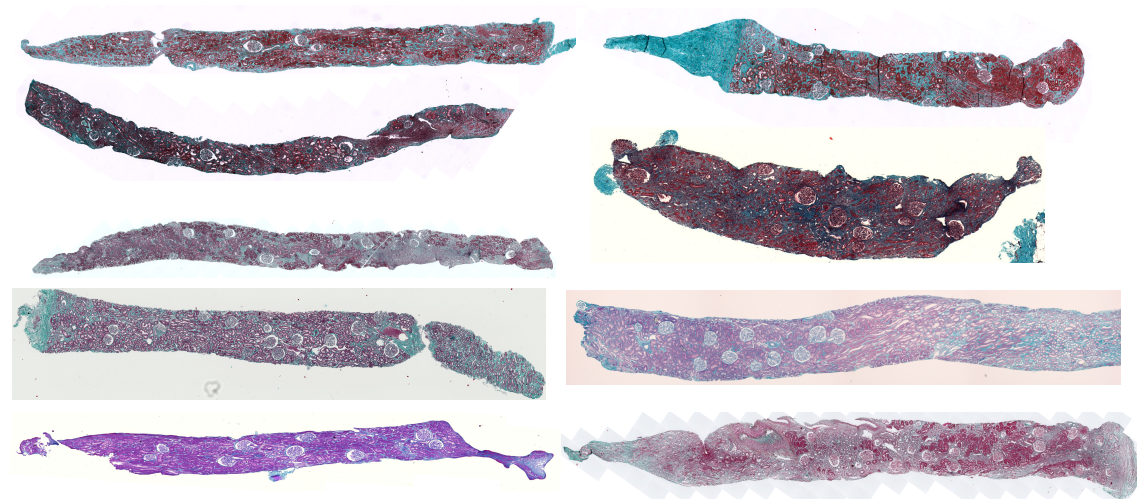
Algorithm proofreading : interest point detection

The screenshot displays the cyt^omine web application interface. At the top, the navigation bar includes 'Cytomine', 'Dashboard', 'Projects', 'Explore', 'Storage', and 'Activity'. The main header shows the current project 'UPMC-DROSOPHILA' and the image '089.bmp'. A toolbar with various tools like Select, Point, Arrow, Rectangle, Ellipse, Circle, Polygon, MagicWand, Fill, Ruler, Edit, Rotate, Resize, and Drag is visible. The central image is a detailed view of a fly wing with several colored dots (green, red, blue, yellow) marking specific points of interest. On the left, a 'CURRENT SELECTION +' panel shows metadata for the selected point: Area: 0 pixels², Perimeter: 0 pixels, Term(s): LDM-11, User: Landmark_Model_Predict 2015-09-30 10h26, and a 'You can edit this annotation' message. Below it is an 'ANNOTATION PREVIEW +' showing a zoomed-in view of the selected point with a red crosshair. At the bottom left, a 'SIMILARITIES +' panel shows a 'Suggested term : LDM-1' and a link to 'See similar annotations'. On the right, a sidebar contains a 'HIDE TOOLS' button and several expandable sections: 'OVERVIEW +', 'INFORMATIONS +', 'POSITION +', 'ONTOLOGY +', 'REVIEW | LAYERS -' (with a 'Display Review layer' checkbox checked and a dropdown menu showing the user 'Marée Raphaël (rmarée)' and the timestamp '2015-09-30 10h26'), 'REVIEW | ACTION SELECTION +', 'REVIEW | ACTION IMAGE -' (with 'Accept all', 'Reject all', and 'Validate image' buttons), 'JOBS TEMPLATE +', 'MULTIDIMENSION +' (with the text 'This image has no other dimension.'), and 'ANNOTATIONS PROPERTIES +'. At the bottom, a row of thumbnails labeled 'All', 'LDM-1', 'LDM-10', 'LDM-11', 'LDM-12', 'LDM-13', 'LDM-14', 'LDM-15', 'LDM-2', 'LDM-3', 'LDM-4', 'LDM-5', 'LDM-6', 'LDM-7', 'LDM-8', and 'LDM-9' shows different views of the annotated wing.

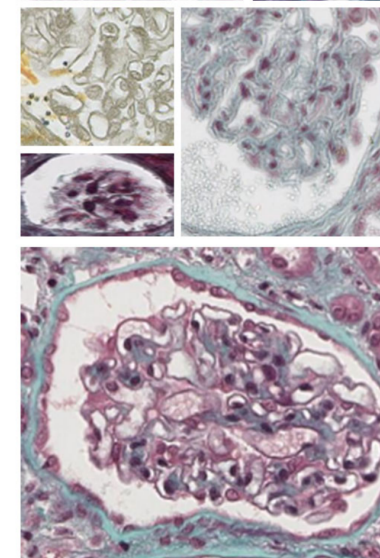
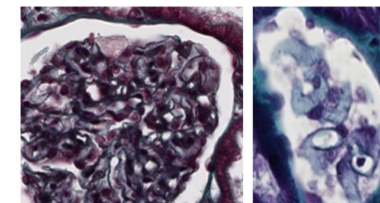
Current challenges: algorithm robustness



Ongoing evaluation on > 1000 slides (one lab)



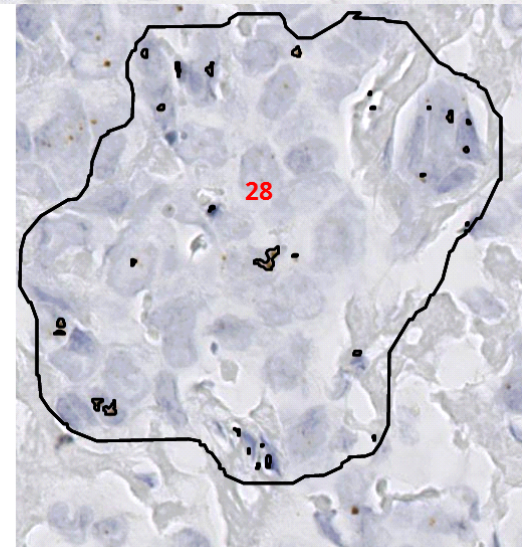
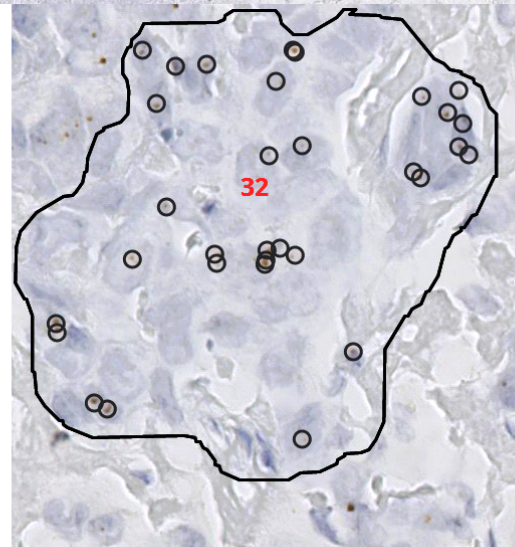
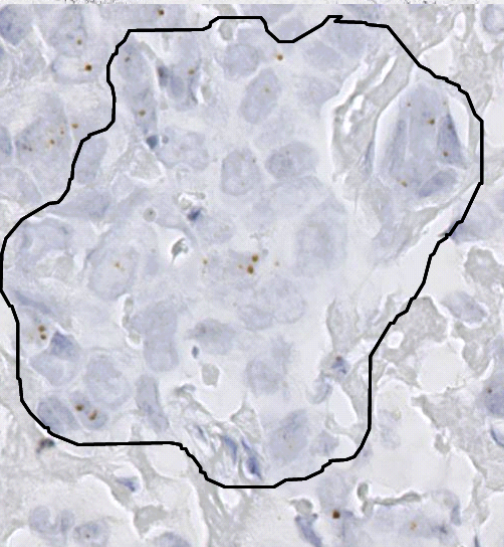
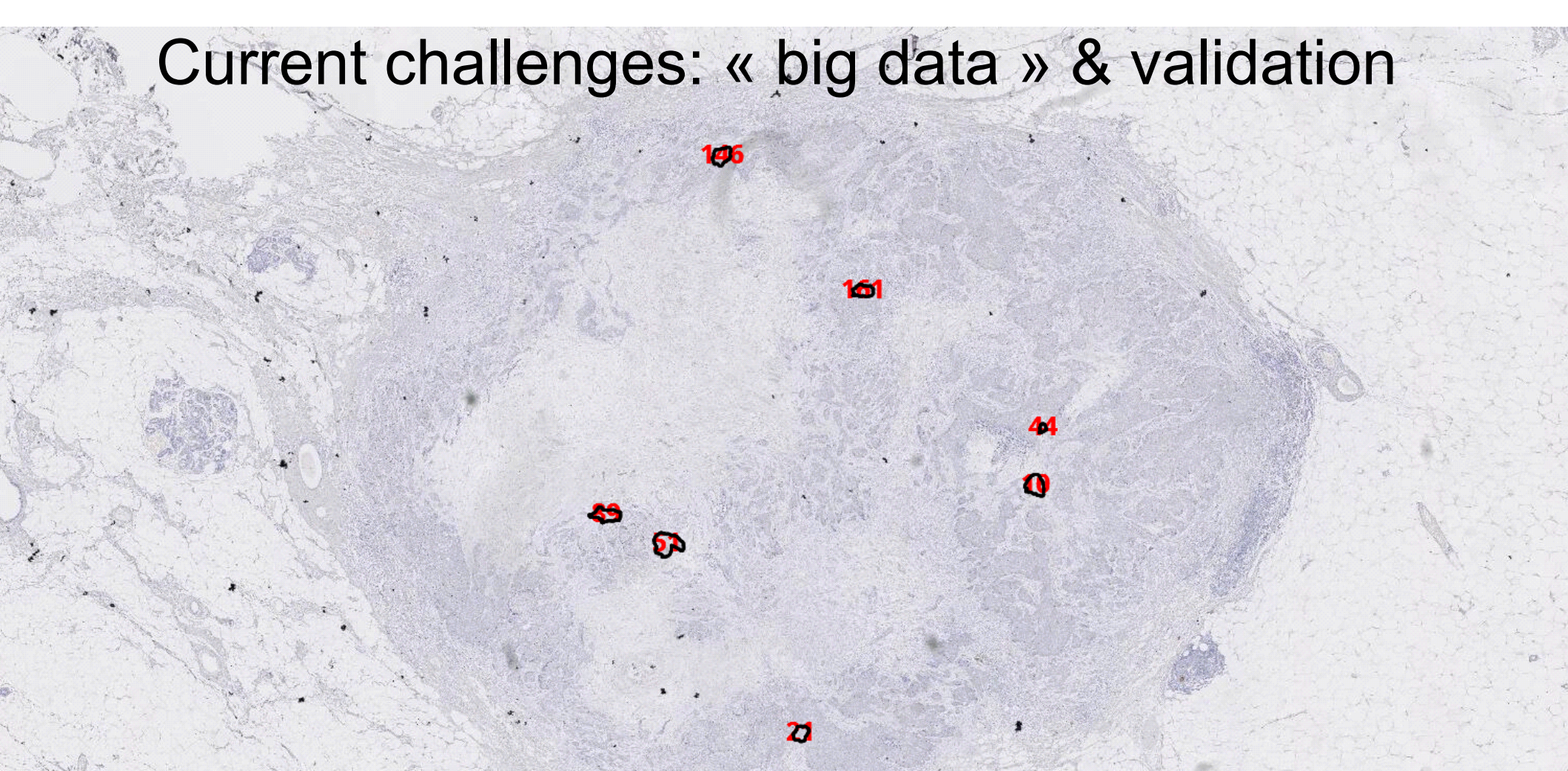
Non-glomerular Structures (Class 0)



Glomeruli (Class 1)

(Marée et al., ISBI 2016)

Current challenges: « big data » & validation



cyt@mine summary :

- **Free and Open-source**
- **Easy installation procedure**



(check www.cytomine.be)

- **General-purpose** using generic software design, web services, user-defined ontologies and machine learning for semantic annotation
- Fosters **collaboration** between life scientists, pathologists, teachers, and computer scientists. Eases big image management for image analysts.
- Not universal but...
 - Many potential direct applications
(J. Pathol, Oncotarget, BMC Cancer, Am J Transl Res, PLoS ONE,...)
 - **Fully extensible...**
 - **Please contribute:** <http://github.com/cytomine/>
- Permissive licence + cooperative with social economy goals



Acknowledgments

- Systems and Modeling (Montefiore Institute / GIGA-Research @ ULG):
 - Cytomine core development : Renaud Hoyoux, Loïc Rollus, Benjamin Stévens
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Pierre Geurts, Louis Wehenkel
- Other collaborators :
 - GIGA/ULG : Didier Cataldo, Natacha Rocks, Fabienne Perin, Christine Fink,
Valérie Defaweux, Pascale Quatresooz
 - Students : Julien Confetti, Pierre Ansen, Olivier Caubo, Antoine Deblire
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 - ULB : Isabelle Salmon, Caroline Degand, Xavier Moles Lopez, Nicky D'Haene.
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- **CYTOMINE** (2010-2016) n° 1017072
- **SMASH** (2012-2014) n° 1217606
- **HISTOWEB** (2014-2017) n° 1017072

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- Machine learning, image analysis
- Spatial or graph-based methods for high-level feature extraction
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- Mass cytometry, and other spectroscopy techniques
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Saturday September 3, 2016

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