User guide Cytomine version 1.0

(Version: 20160116)

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This document covers the main functionalities of our software. The software can be tested at http://demo.cytomine.be/ with one of these 3 accounts, using a modern web browsers (Google Chrome (preferred choice), Safari, Mozilla Firefox):

Username	Password	Role
jsnow	jsnow	User
clannister	clannister	User
estark	estark	User

The software can also be installed automatically on desktop/server computers using the procedure described in Section 6.1. In both cases, our installation procedure installs "toy data", namely five projects for testing main functionalities.

6.1 Installation

The automated installation procedure is described at: http://doc.cytomine.be/x/goCj
It basically requires the edition of a single configuration file (Bootstrap/configuration.sh) and the execution of a few command lines. The procedure will automatically create virtual environments (using Docker deployment system) for each Cytomine components and download, compile, and install all the required libraries, and start all servers. The whole process takes approximately 2 hours without user intervention. The web user interface is then directly accessible at the http://$CORE_URL$ location (e.g. http://demo.cytomine.be) using modern web browsers (we recommend using Google Chrome).

6.2 Usage (Cytomine-WebUI)

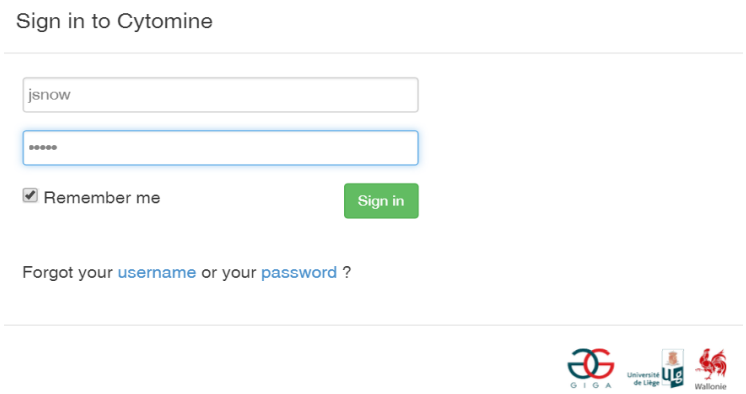
This guide explains how to:

- Visualize and annotate manually images
- Configure projects and manage users
- Upload new images
- Apply Cytomine-DataMining analysis modules and proofread them
- Perform textual search
- Follow online users
- Blind assessment (including IRIS: the Inter-observer study module)

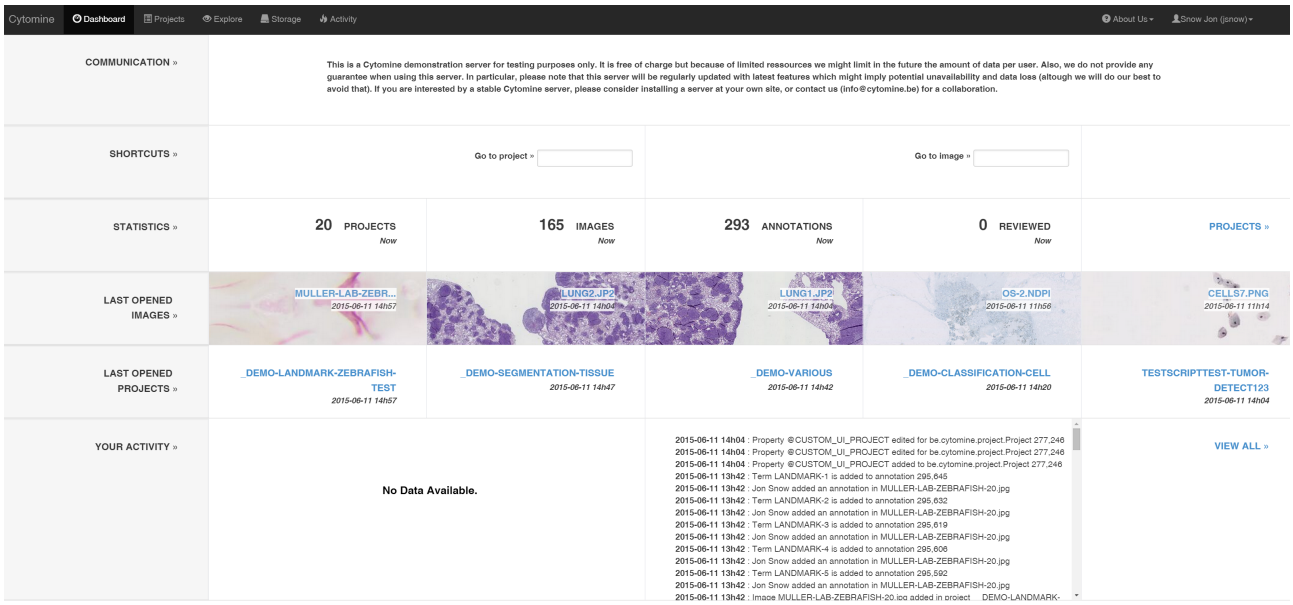
In this guide, we assume using the "jsnow" account.
Please refer to your web browser documentation for basic navigation operations (e.g. "F5" key might be useful to reload pages).

6.2.1 Visualization and manual annotations

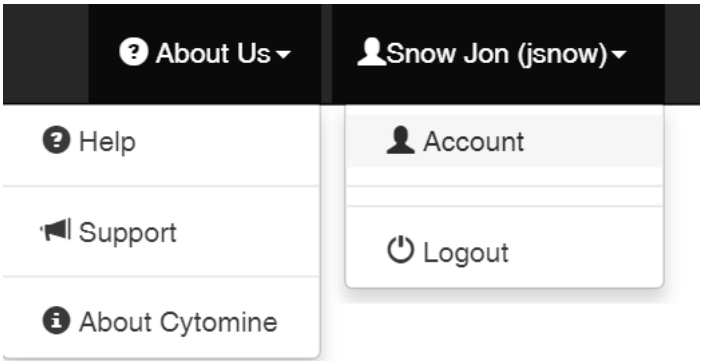
Users log into Cytomine using the login panel:



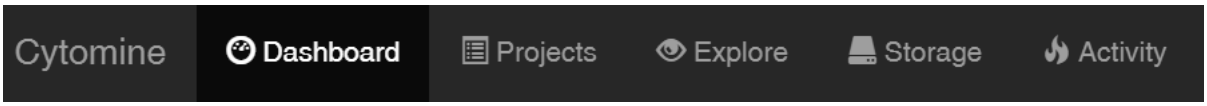
Once connected, the user has access to its user dashboard which summarizes global information (number of projects, images, annotations) and it also shows latest opened projects, images, and activities:



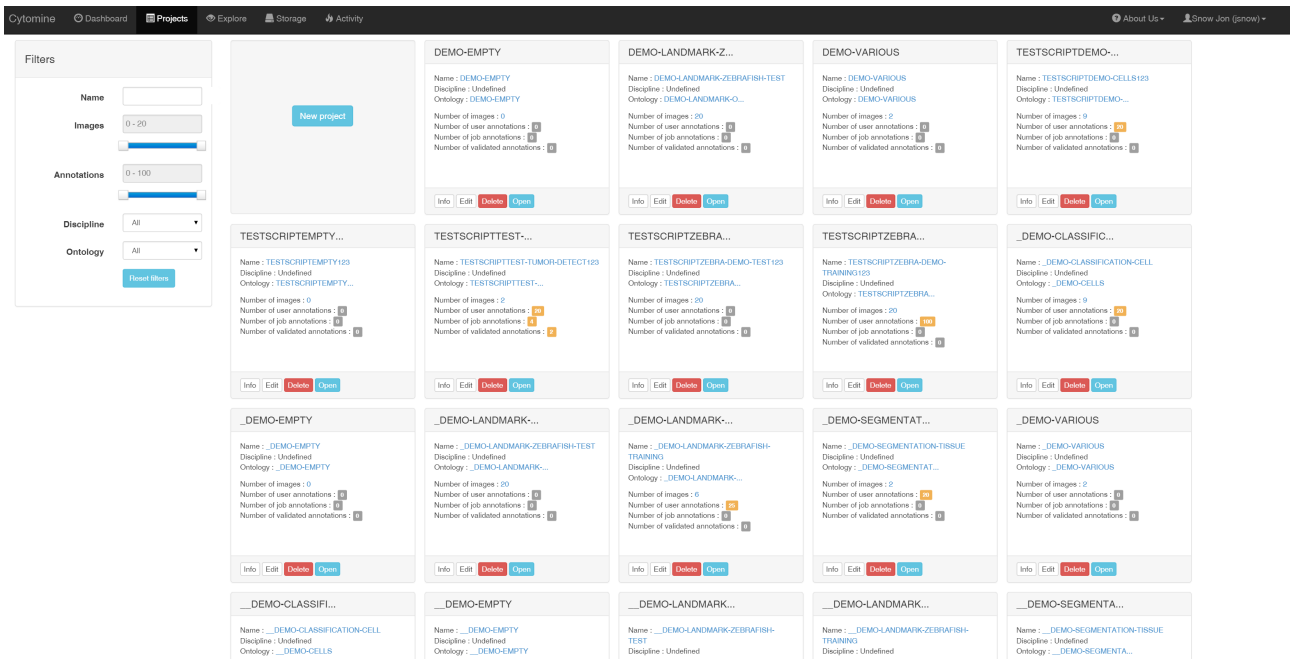
The menu on the top right (black bar) gives access to Account information (under the user name) where the user can change its password and get its public/private keys. The help sub-menu lists main shortcuts applicable when exploring images:



The menu on the top left (black bar) gives access to the User dashboard, the listing of Projects, the Storage panel (to upload new images through the web interface), and the Activity panel which summarizes latest user activities:

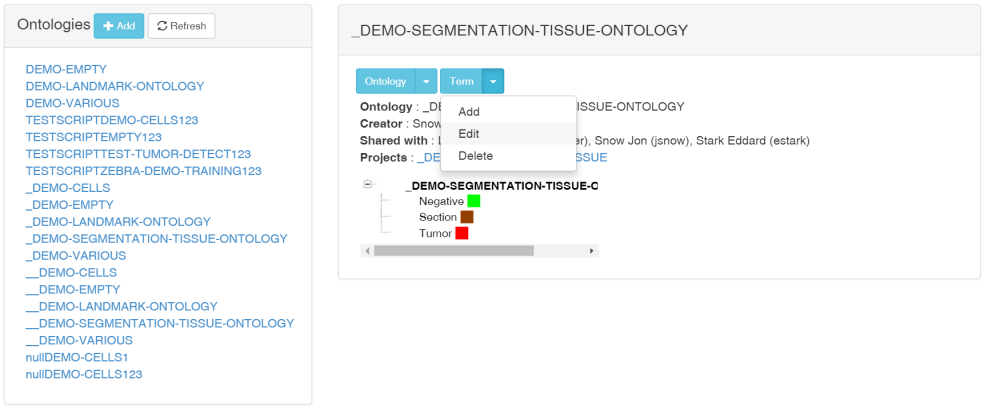


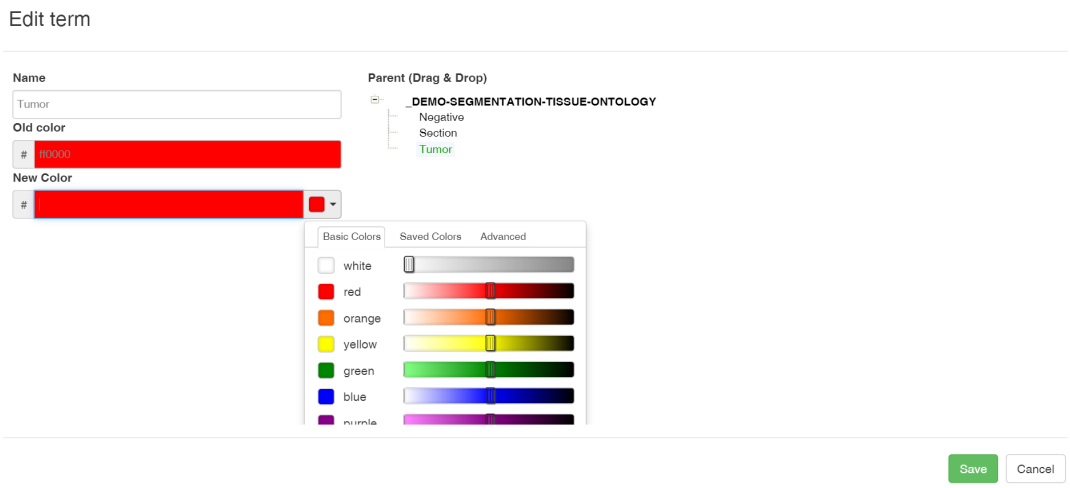
The project listing displays boxes where each box corresponds to a specific project. Project listing can be filtered (box at the top left) by names, number of annotations, images, disciplines, ontology names:



Clicking on the project name (e.g. _DEMO_SEGMENATION_TISSUE) or on the Open button will open the project and shows the Project dashboard with basic information (textual description on the top right, users currently online) and various statistics about the project (including number of images, annotations, various statistics of annotations by ontology terms, users, images, ...).

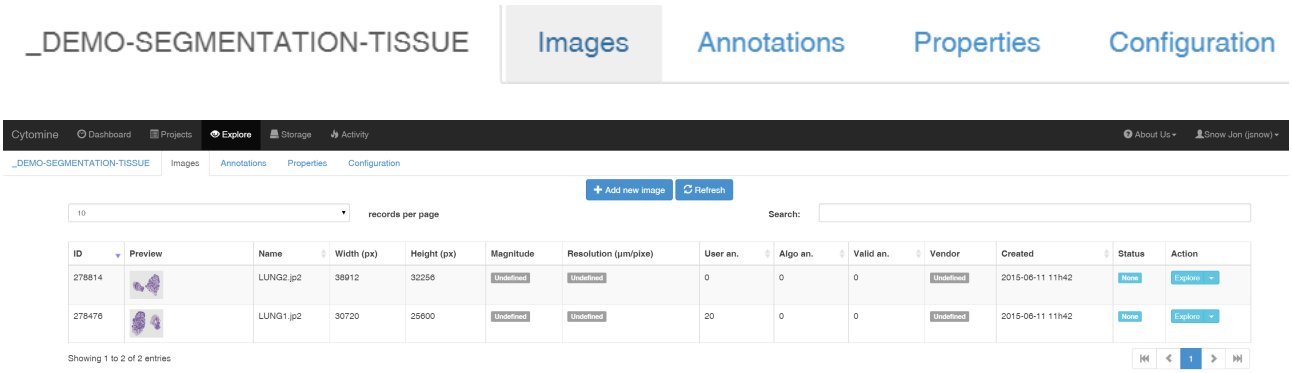
One key concept of Cytomine is the Ontology, a structured vocabulary of user-specified terms used for the semantic annotation of regions of interest in images. Each project has a single ontology. It can be either an existing ontology (it can be associated with the project when a user creates it) or a new ontology that can be edited online. Editing the ontology can be done by clicking on its name (first line under the project name) which opens the Ontology editor. The editor allows to rename the ontology, add/edit/delete terms from the ontology. In this "toy" project where life scientists are interested to quantify the sizes of tumor islets with respect to the size of tissue sections, the Ontology is simplified and has only three terms: Section (to delimit the tissue section, in brown), Tumor (for tumoral islets, in red), and Negative (for all other tissue substructures, in green):



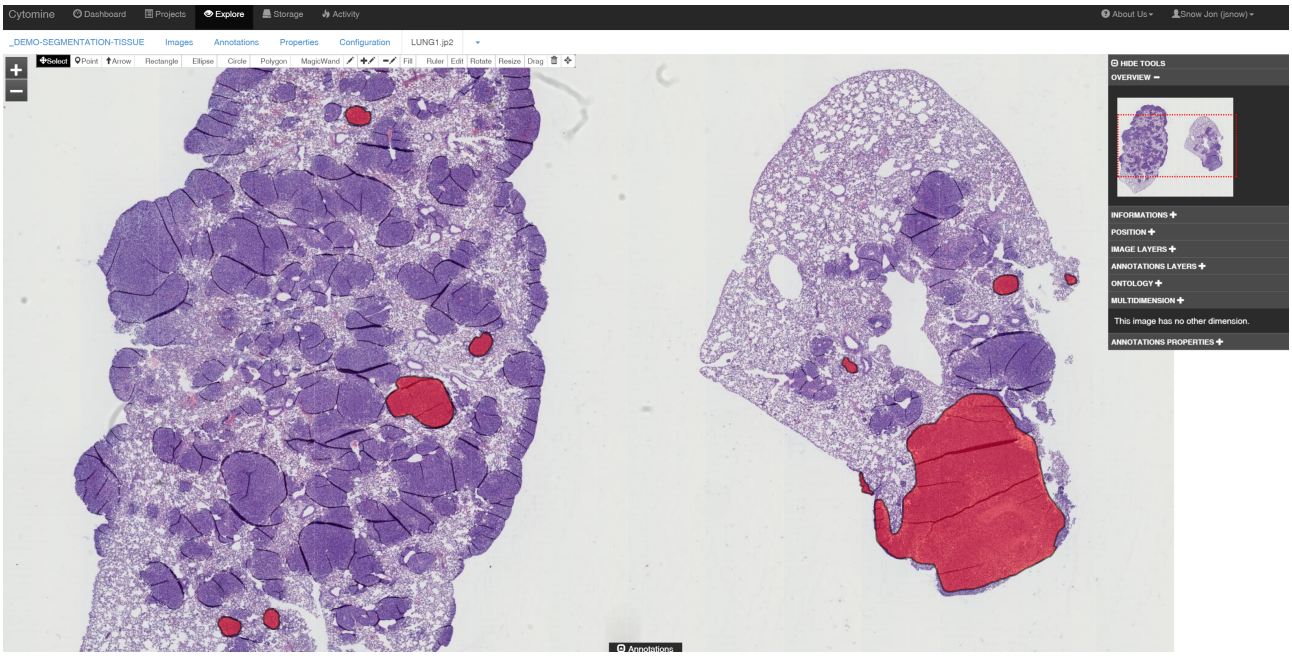


Once

the ontology is defined, one can start semantically annotating whole-slide images. It has to be noted that Term names and colors can be changed afterwards, only term identifiers are linked to annotations in the database. To start annotation, the user goes back to the Project dashboard and clicks on the "Images" tab which opens a page with the Image listing of this project:



This project contains only 2 images whose characteristics are listed. Image "LUNG1.jp2" already contains 20 user annotations. One can open the image by clicking on its thumbnail or on the blue Explore button at the right. Note that the arrow at the right of the Explore button gives access to supplementary information and operations (e.g. download the image, describe it, start reviewing it (see below), importing annotations from another project, ...). The explore view is then displayed.
It is a zoomable viewer for gigapixel images, with various tools for annotation. Note that multiple images can be opened in parallel, each one having its own tab. By default (this can be configured in the "Configuration" tab of the project), the viewer also displays current user's annotations (in red here, corresponding to the color of the Tumor term):



Annotations can be selected 

, edited, and drawn manually by using tools on the top bar:

It includes geometries such as:

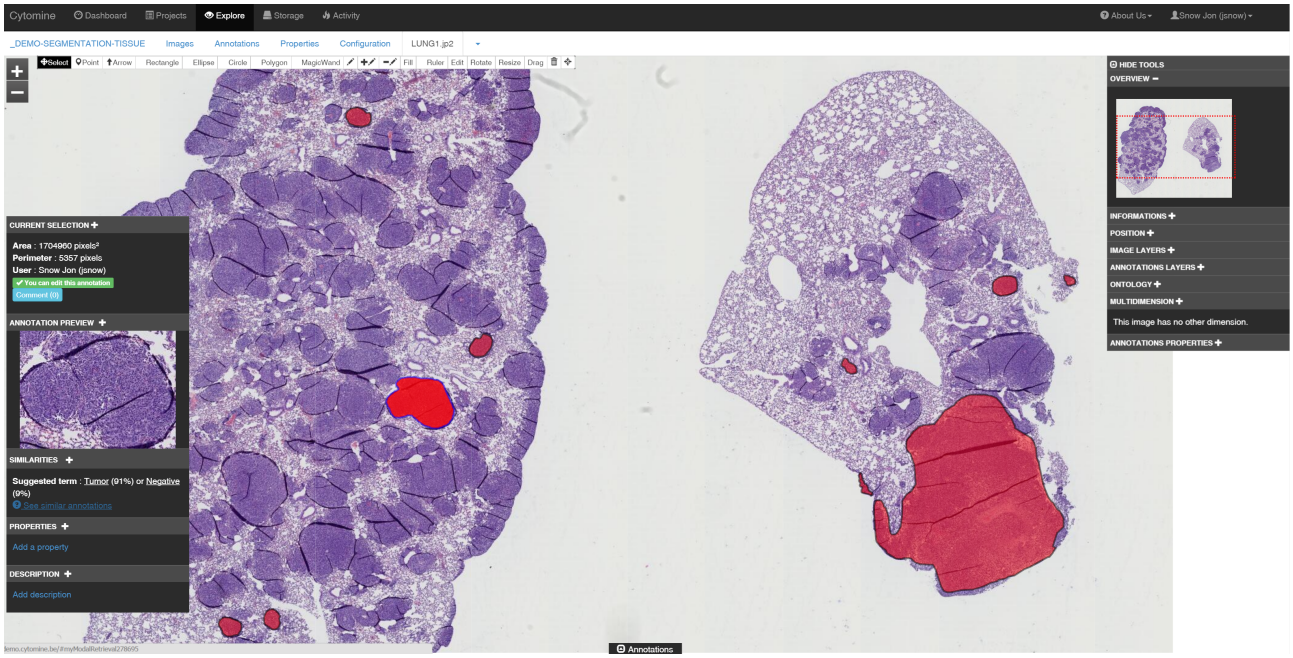
- Point, Rectangle, Ellipse, Circle, Polygon,

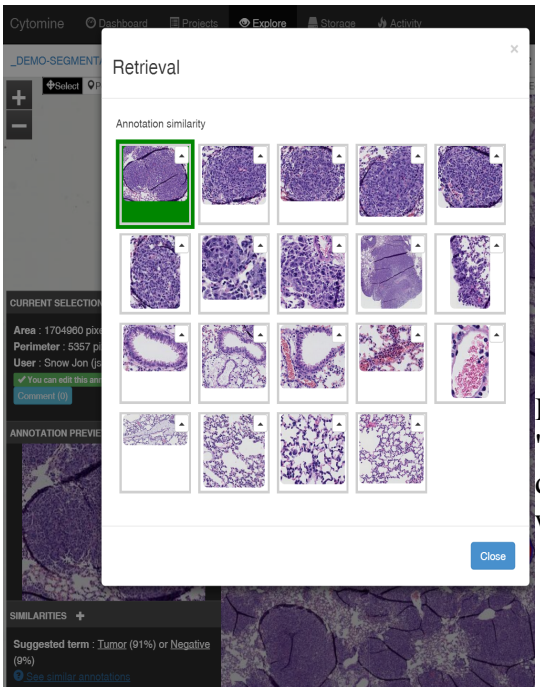
- Freehand
- Magic Wand (which parameters have to be configured in Project Configuration tab)

And operations such as:

- Rotate, Resize, Drag,
- Delete
- Fill
- Complement (performs the union of a new geometry with an intersecting, existing, geometry)
- Subtract (subtracts the intersection of a new geometry with existing geometry)

Selecting an annotation opens the Current Selection Annotation panel (at the bottom left) which gives basic information (e.g. annotation area based on image resolution) about the currently selected annotation and launch the content-based image retrieval algorithm. This algorithm suggests ontology terms based on visual similarity. The most similar annotations can be visualized by clicking on "See Similar Annotations" (they are ranked according to their computed similarity):

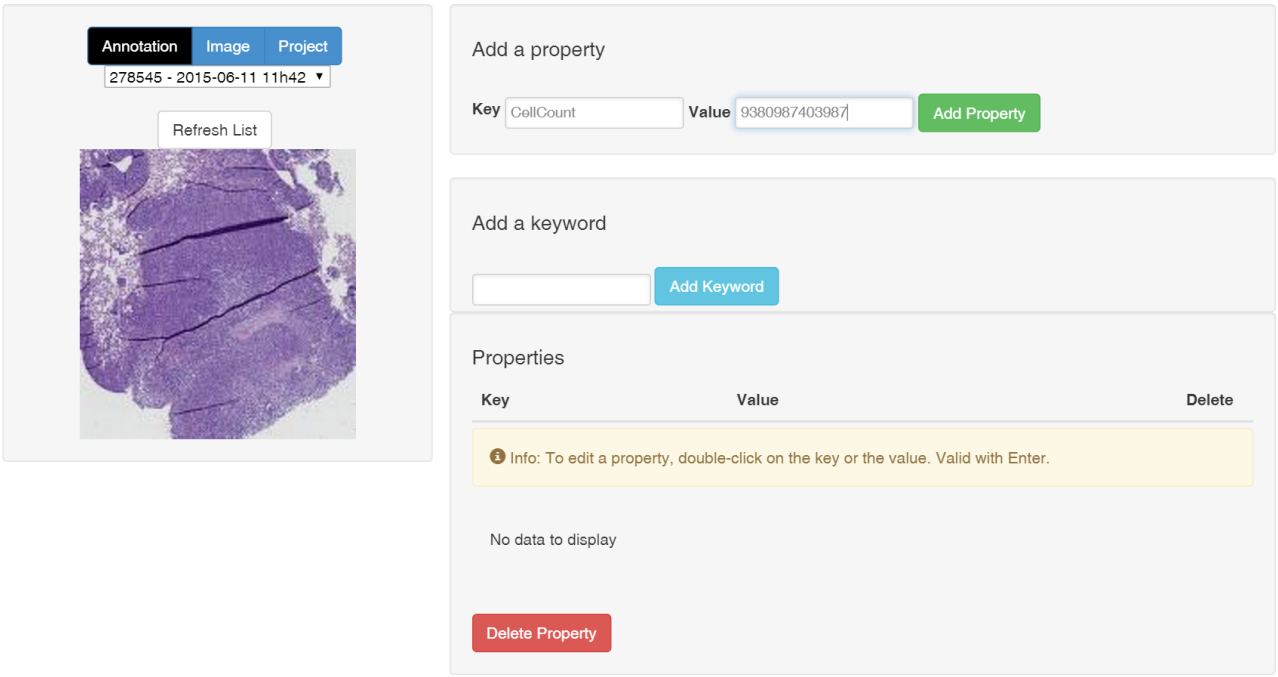




It is possible to click on these "similar" annotations to jump directly at their locations within their original image.

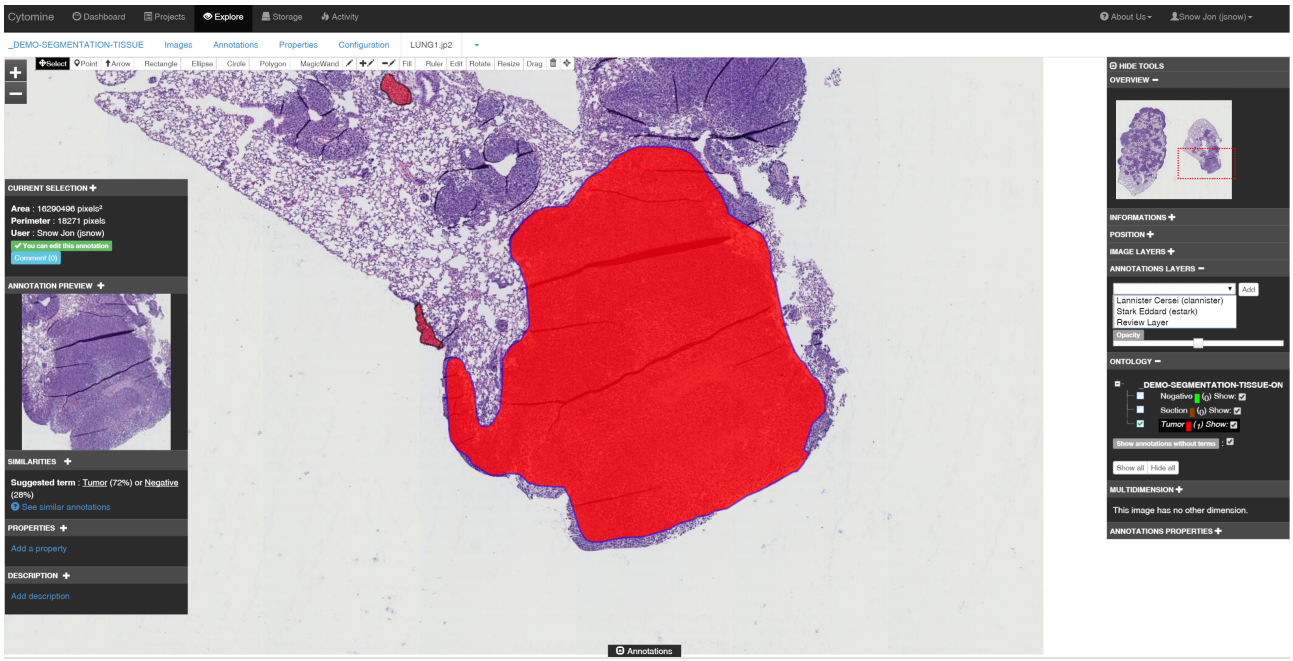
cytomine

Properties (key-value pairs) and keywords can be added to Annotations by clicking on the "Add property" link (at the bottom of the Current Selection panel).

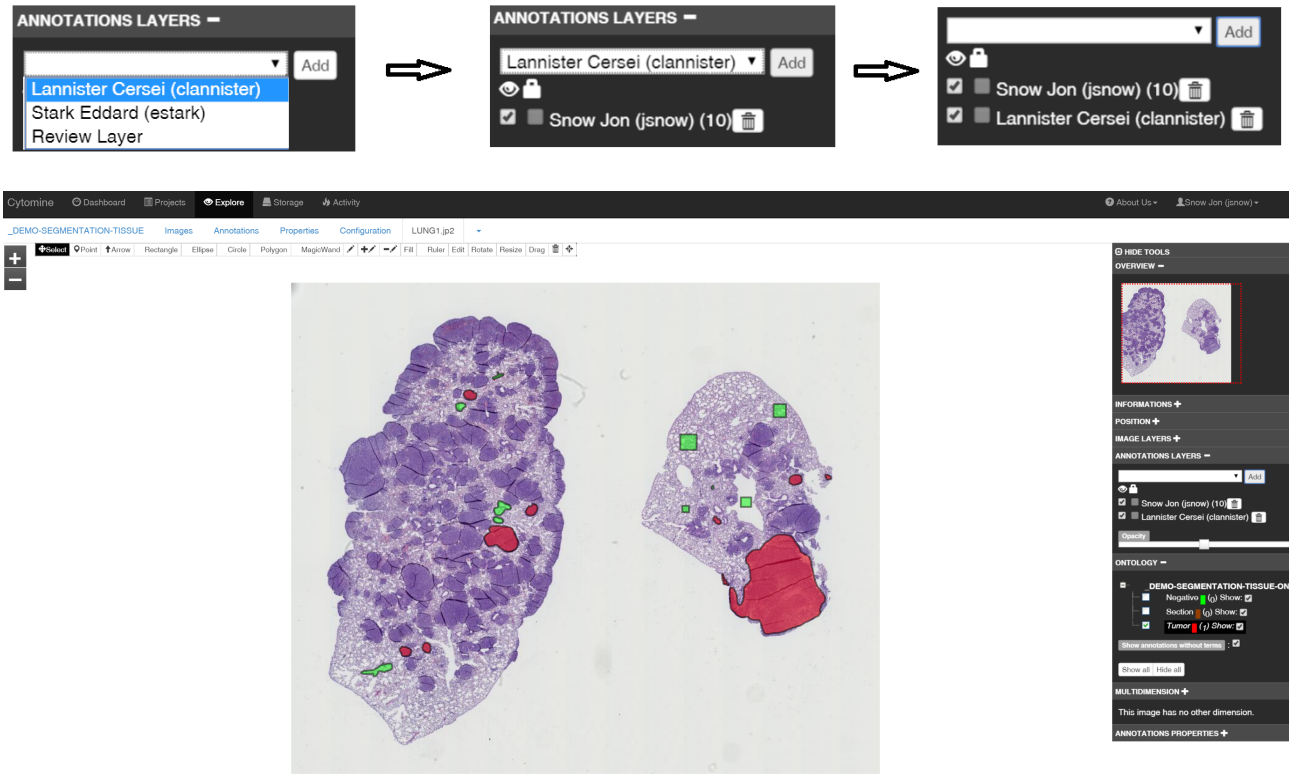


Rich text descriptions can also be added in a similar way as for Projects and Images.

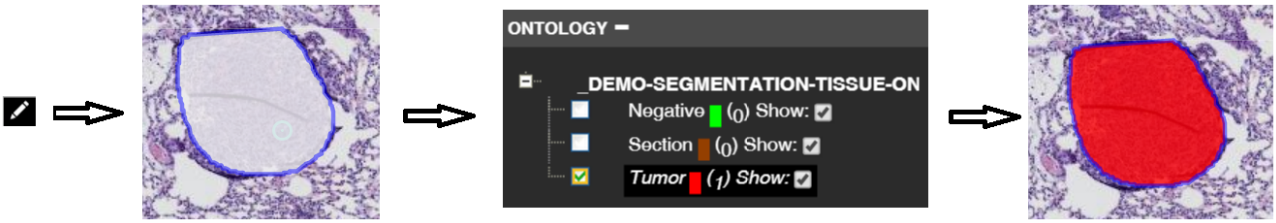
On the right side of the Explore view, the "Tools" panel can be activated to show an overview (thumbnail with red square corresponding to the active view), image information, image layers (which allow to apply on the fly image processing filter to tiles, see Configuration page of the project), annotation layers (containing user layers, userjob layers, and the review layer), ontology, and multi-dimensional browser.



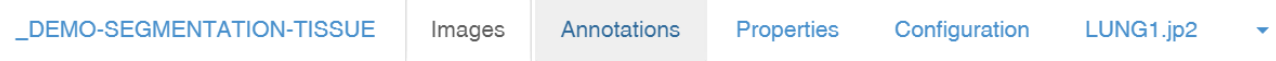
Selecting and adding another user layer will display its layer of annotations in the whole-slide images in addition to current user annotations (in this case, the user clannister only created annotations with the Negative term, in green):



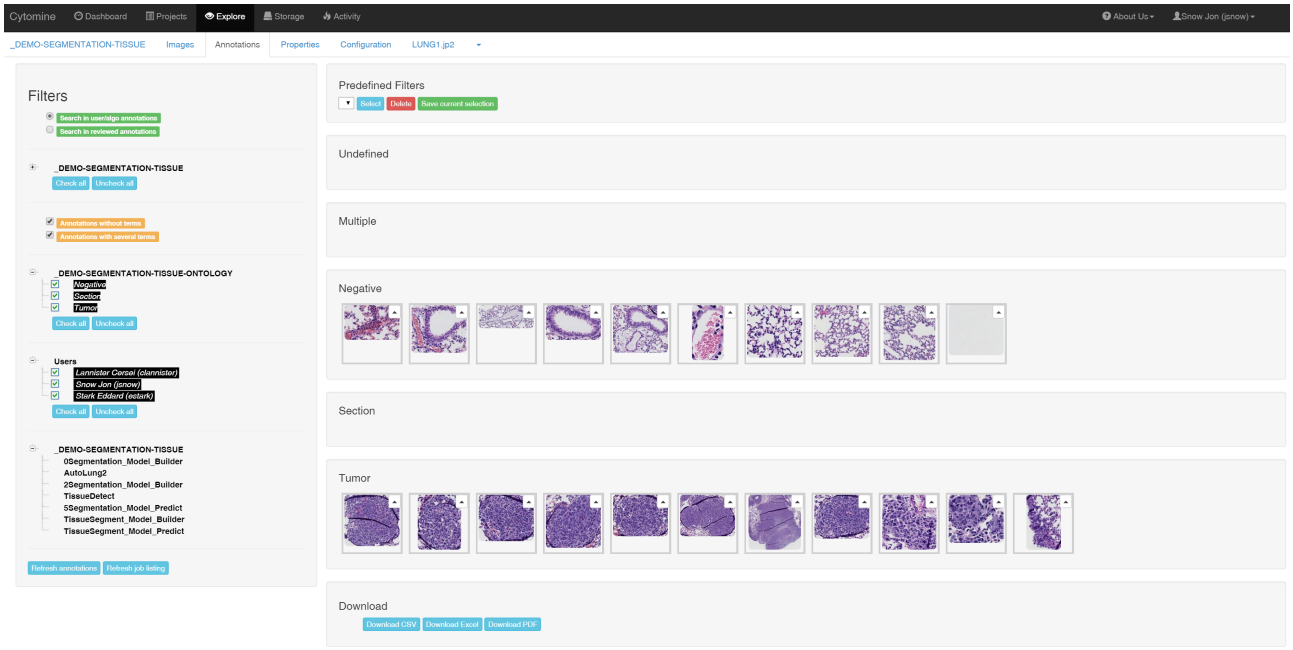
Multiple user annotations can then be displayed. A blinded mode allows to hide other user layers if needed (see Project Configuration page).
Adding an annotation requires the user to draw it, then eventually associate a term from the Ontology (the color of the Annotation thus changes):



All annotations created in a project are visible in filtered galleries in the Project Annotations tab:



Annotations can be filtered according to images they come from, terms from the Ontology, Users from the project and types (user/job/reviewed). Filters can be saved and reused later. The user can click on any of these annotations to jump to its actual location in whole slide images.
Annotation descriptions can be exported as tabular files containing annotation information (area, user who created them, direct link to it,...):



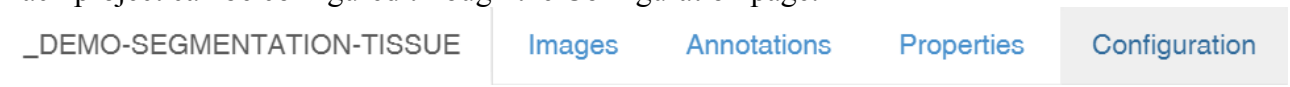
	A	B	C	D	E	F	G	H	I	J	K
1	Id	Area (micronsA^2)	Perimeter (mm)	X	Y	Image Id	Image Filename	User	Term	View annotation picture	View annotation on image
2	302661554624.0	2958.0	7046.116321532636	4725.001467744019	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/302661/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-302661	
3	278747175230.0	1594.0	7069.32970381784	6572.665609009112	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278747/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278747	
4	278734227312.0	1880.0	5960.75249290256	6380.173060228526	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278734/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278734	
5	278721253480.0	1946.0	12556.091504918204	13743.268818052706	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278721/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278721	
6	278708251696.0	1973.0	9331.685970376962	19742.053609645496	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278708/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278708	
7	278695.1704960.0	5357.0	11001.564964964966	12278.455655655656	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278695/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278695	
8	278682.71540.0	1605.0	10794.882024042494	20723.60314975305	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278682/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278682	
9	278669.162990.0	1568.0	8824.732830234983	19137.8159396282	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278669/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278669	
10	278656.434896.0	4195.0	4590.964963270912	5427.768220448107	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278656/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278656	
11	278643.129030.0	1419.0	10797.548818104317	13221.16981580511	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278643/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278643	
12	278630.373352.0	2724.0	10976.037383845094	13842.707636046769	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278630/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278630	
13	278617.14602.0	527.0	21993.5566817331	14925.346299593662	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278617/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278617	
14	278604.117600.0	1372.0	20585.0	13798.0	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278604/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278604	
15	278591.681792.0	3304.0	20730.0	17282.0	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278591/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278591	
16	278578443232.0	2664.0	25496.0	18924.0	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278578/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278578	
17	278564266760.0	2068.0	23736.0	14159.0	278476	LUNG1.jp2	clannister	Negative	http://demo.cytomine.be/api/annotation/278564/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278564	
18	278545.1.6290496E7	18271.0	25481.181634248584	9723.086243496413	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278545/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278545	
19	278532.279788.0	1982.0	26318.944643801737	15324.092674930067	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278532/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278532	
20	278519.96759.0	1279.0	22222.987084750086	13198.883933277524	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278519/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278519	
21	278506.57715.0	942.0	28014.469363828004	15463.15738254064 5	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278506/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278506	
22	278492.76746.0	1585.0	22618.569549137515	10065.900478421101	278476	LUNG1.jp2	jsnow	Tumor	http://demo.cytomine.be/api/annotation/278492/crop.png	http://demo.cytomine.be/#tabs-image-278366-278476-278492	

In addition to ontology terms, properties, keywords, and rich text descriptions, Comments can be associated to Annotations and send through e-mail to project's users (using e-mail addresses encoded in the User account). E-mails contain the textual comment and a direct link to the actual location of the annotation within its gigapixel image for direct visualization. The user has to click on the blue "Comment" button in the Current selection panel, then select recipients and then click on the green "Share" button:

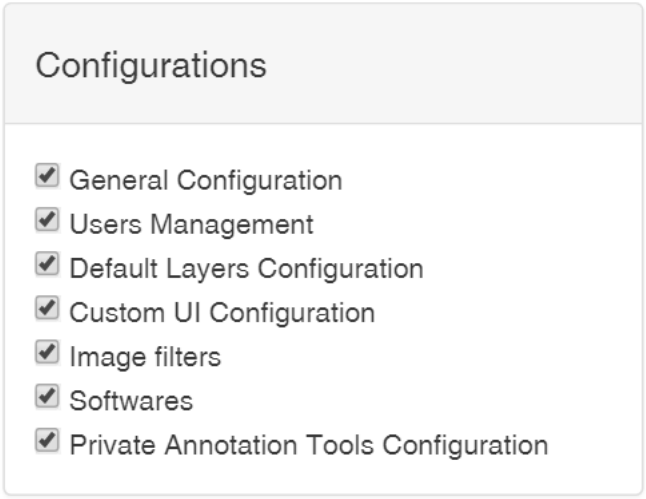
6.2.2 Project

configuration and user managment

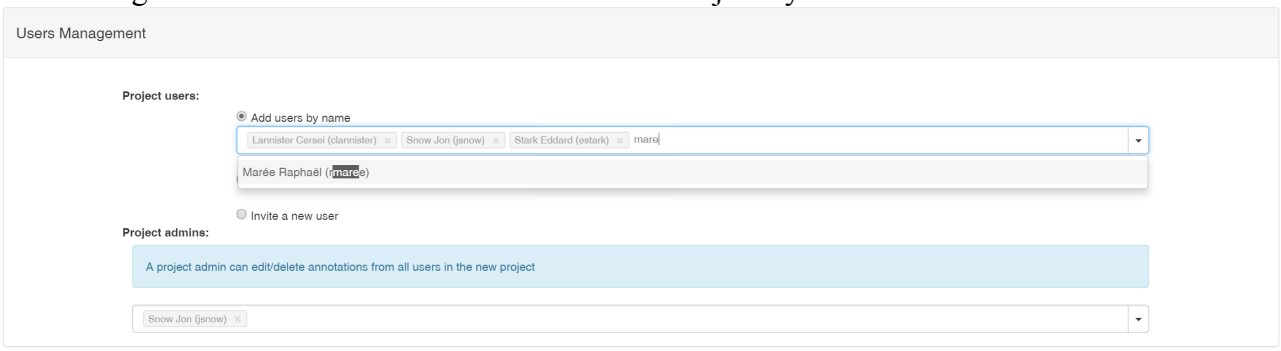
Each project can be configured through the Configuration page:



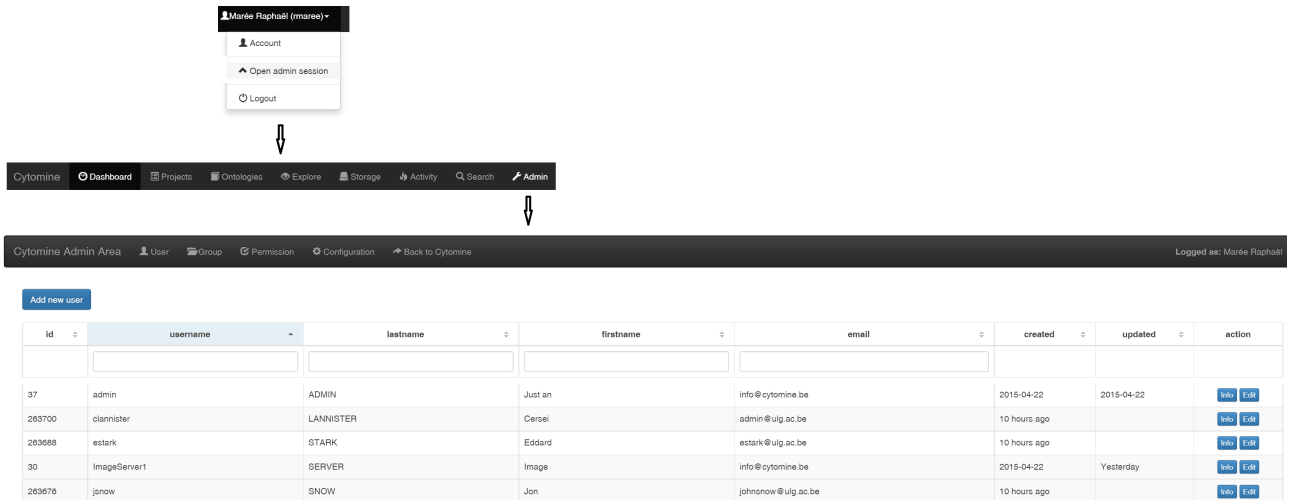
Admins of a project can configure all options including general configuration (e.g. blind mode which hides image names, enable/disable the content-based image retrieval algorithm,...), user management (add/delete users from this project), configure the default annotation layer in the Explore view, customize the user interface to enable/disable graphical tools and displayed information (such as the drawing tools and panels), the image filters (that can be applied on-the-fly to image tiles), the softwares to be associated (e.g. the Cytomine-DataMining modules or any other third-party softwares registered to the database), and some other visual configuration (e.g. the magic wand tolerance parameter or the size of Point annotations, configurable by a regular User).



An existing user in the database can be added to the Project by an admin.



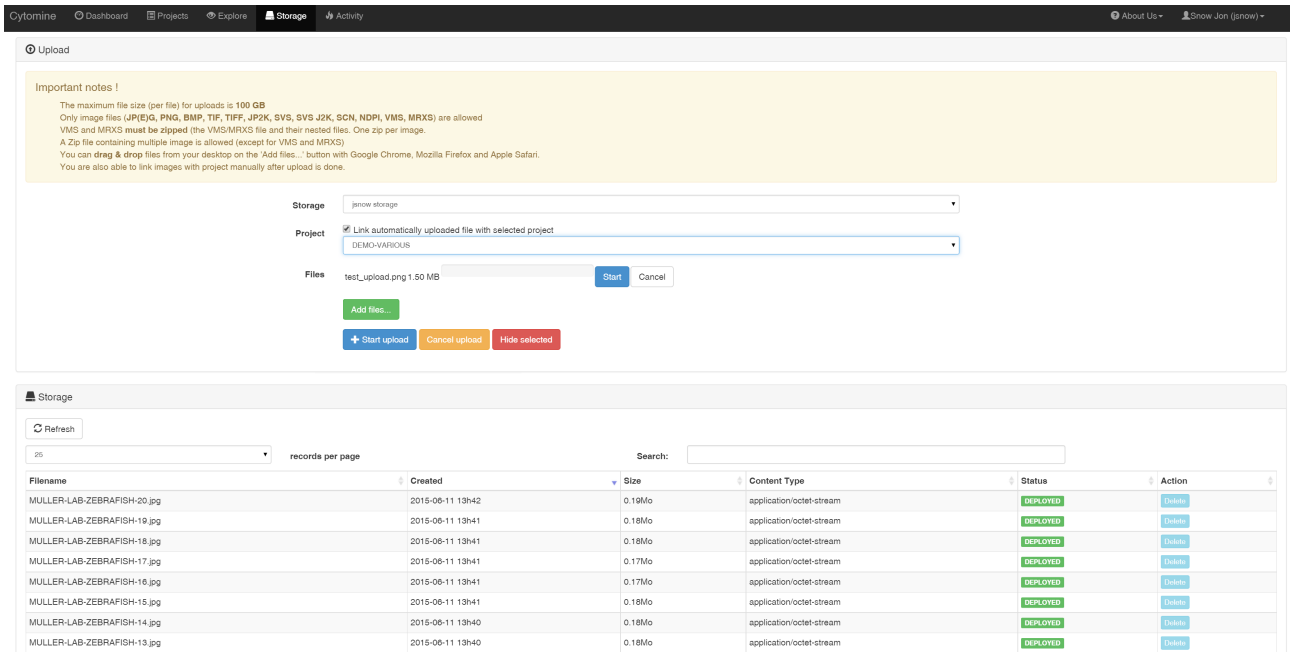
To add new user into the database through the web user interface, admins or super admins have to enter into the Cytomine admin area where the can add new user or edit existing ones (including their role):



Note: on our demo instance, we do not provide admin codes to avoid issues due to unintentional operations. If you install the software on your servers, an admin user will be created by our automated installation procedure (username/password is requested during installation).

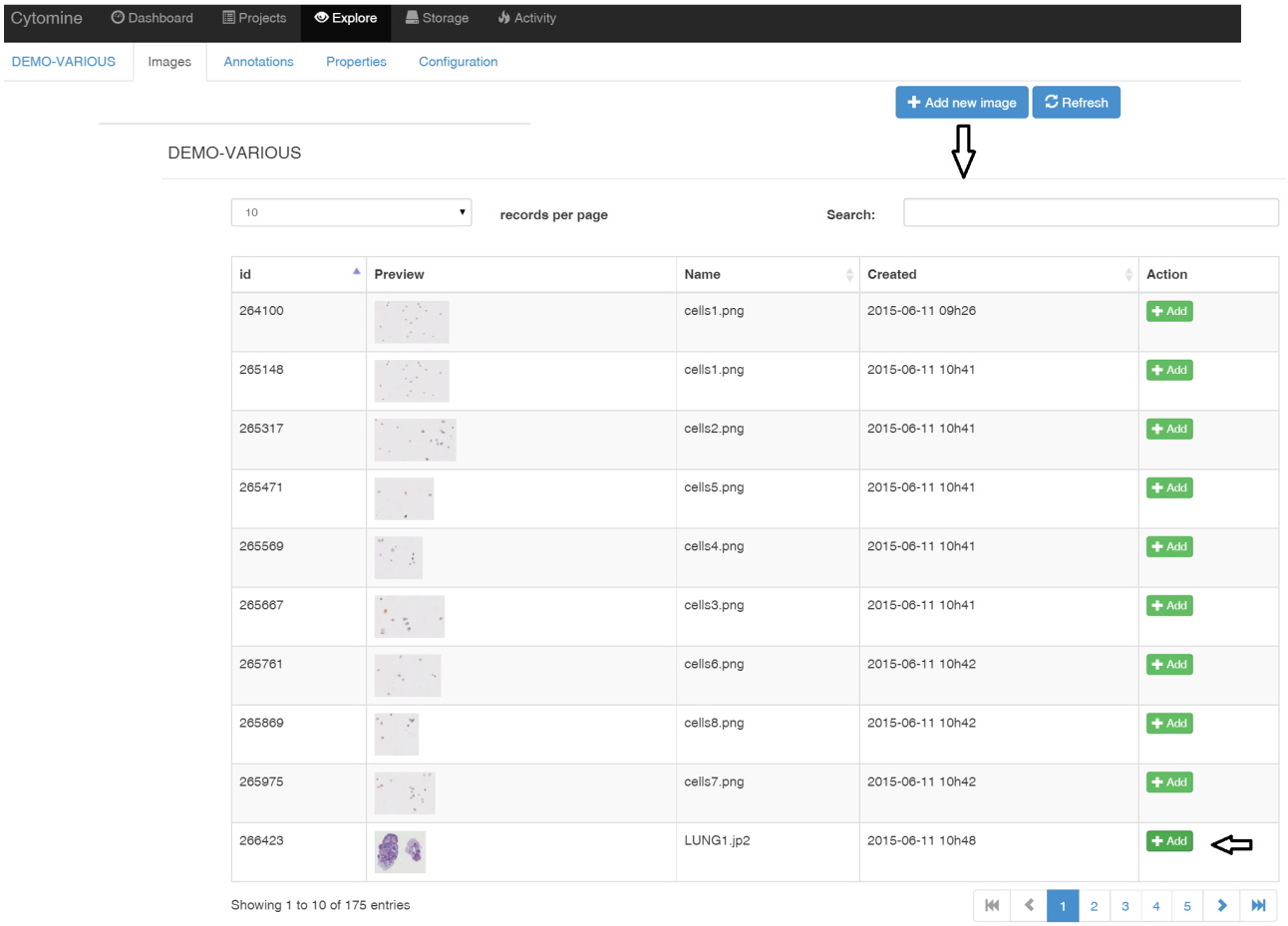
6.2.3 Upload and manage images

A user can upload images to its storage and then associate images to project(s). The user has to click on the "Storage" button (top black bar) to access the Storage panel where he can select (drag & drop or "Add files" dialog box) images from its local computer and link them automatically to a given project. If multiple files are to be uploaded, start upload will upload five of them in parallel:

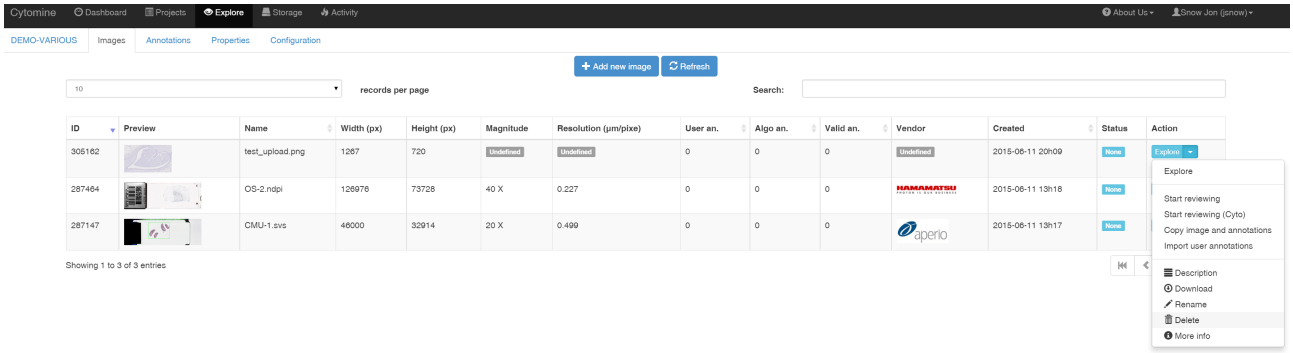


The bottom table lists all images uploaded to the Cytomine instance and their current status. Once it is "Deployed", an image will appear in the user storage and selected (if any) project image list. Some images require additional conversion steps (e.g. non-pyramidal TIFF, or multidimensional microscopy formats supported by Bio-Formats) and will take longer than natively supported formats. The uploaded image will also be available for other projects and the User can associate it

to another project through the "Add Image" (blue) button in the specific Project image list:



An image can be removed from a project through the "Delete image" option in the drop down list (Arrow at the right of the explore button):



6.2.4 Apply Cytomine-DataMining analysis modules and proofreading

Our Cytomine-DataMining analysis modules can be launched from Cytomine-WebUI. It has to be

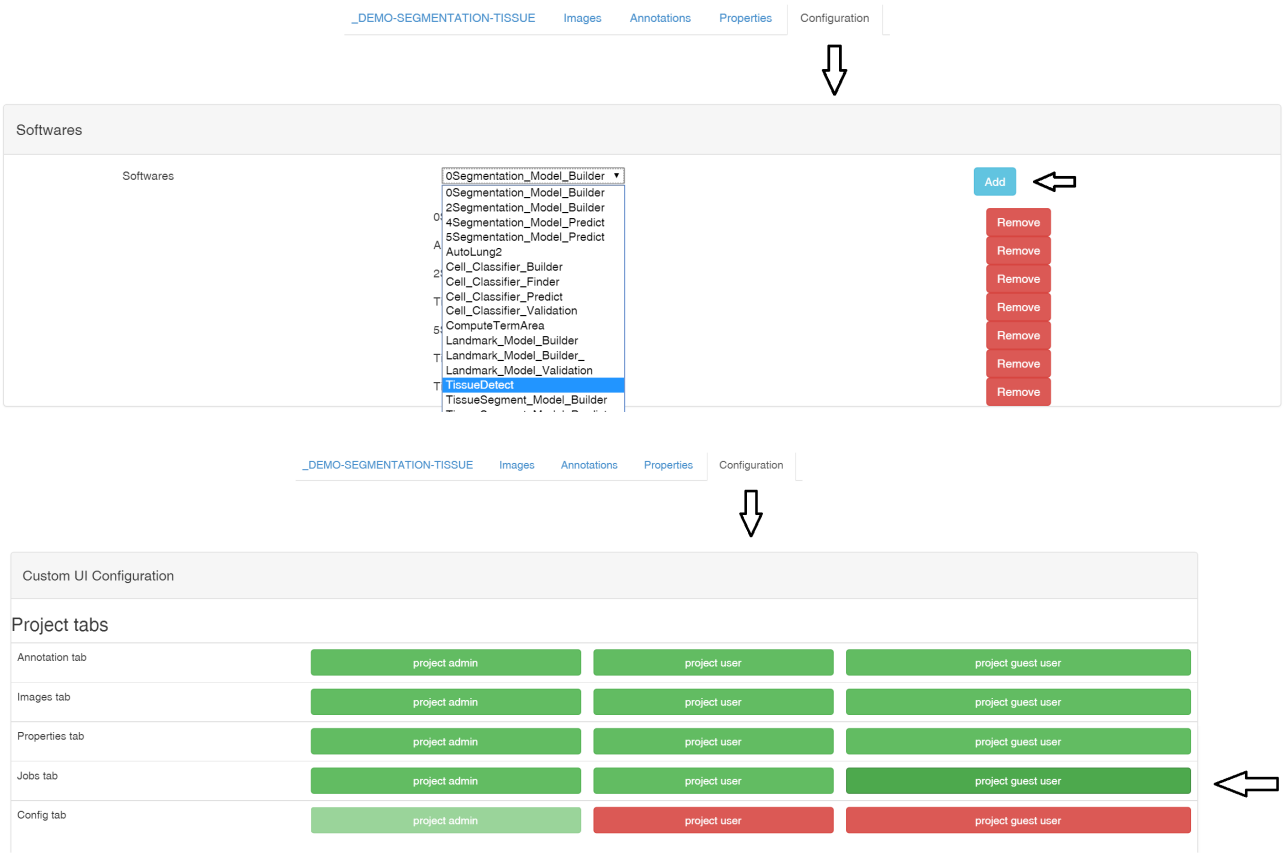
noted that other third-party modules can be similarly launched, provided they are registered as Software into the Cytomine-Core and described by a template of Software parameters.

Here we only illustrate the basic principles of these workflows on small ("toy") datasets. Obtaining satisfactory recognition performances on real-world applications depends on many factors including image variations (due to image acquisition and sample preparation protocols), and the quality and quantity of annotations provided for training. To obtain validated training sets by multiple experts, one might use the Inter-observer module (see below Section 6.2.5). Overall, our tool allows to rapidly prototype such applications by using our generic algorithms described in Supplementary Note 4. Additional research in machine learning and image analysis might produce algorithms better suited for specific applications. Our modules allow to build models by tree-based supervised learning, apply them on new images, edit results, and re-apply learning procedures based on enhanced training sets.

6.2.4.1 Tissue Detection and Semantic segmentation

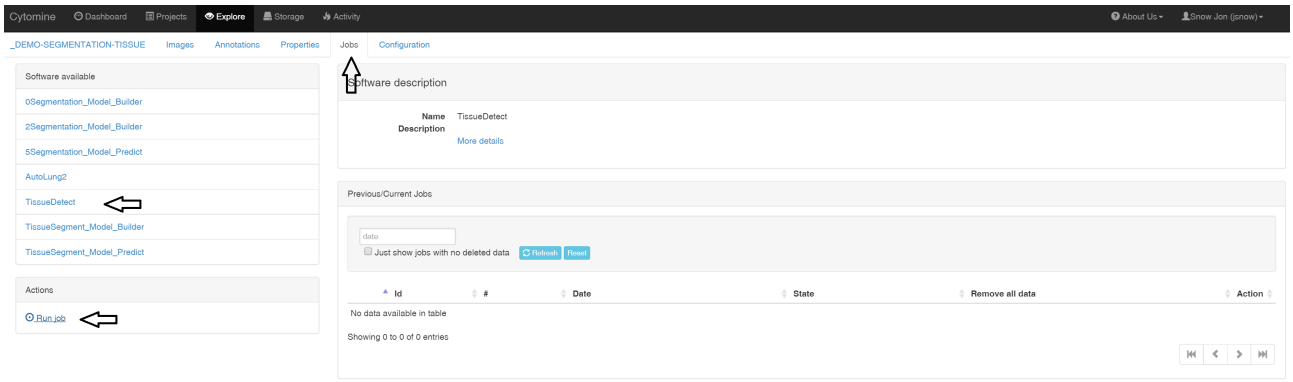
In this example, we want to quantify the size (area) of tumor islets with respect to section sizes in whole slide (gigapixel) images. In order to produce these quantification results, we will apply four registered softwares: a Tissue Section Detector, a Tumor detector learning procedure, a Tumor detector prediction procedure, and a final procedure to output statistics (ComputerTermArea). We use the toy project DEMO-SEGMENTATION-TISSUE.

The first step (if not already done) is to associate the Software to the Project in the Project Configuration page (bottom of the page), in our case we begin with the TissueDetect software:

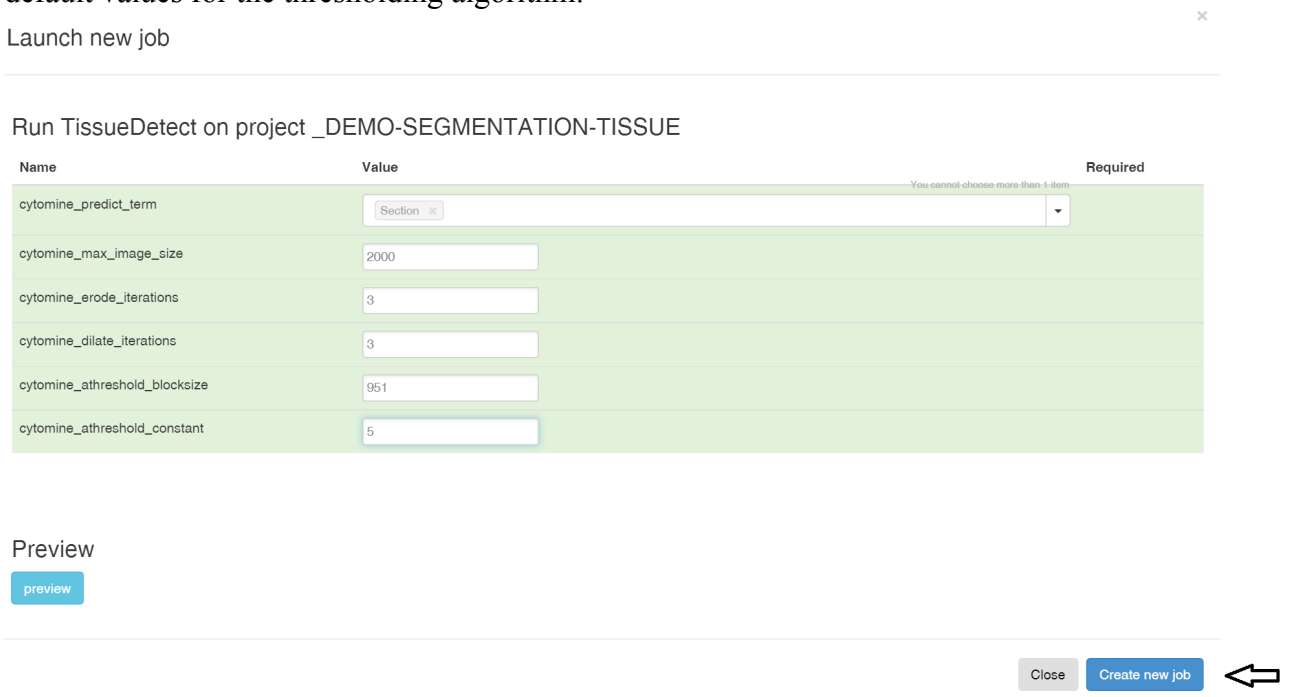


The user also has to activate (green) the "Jobs" tab in the "Custom UI" panel (if not already done):
Now let's consider the User wants to apply the "Detect Sample" analysis module to detect its tissue sections. The user first click on the "Jobs" tab of the project, then on the "TissueDetect" software,

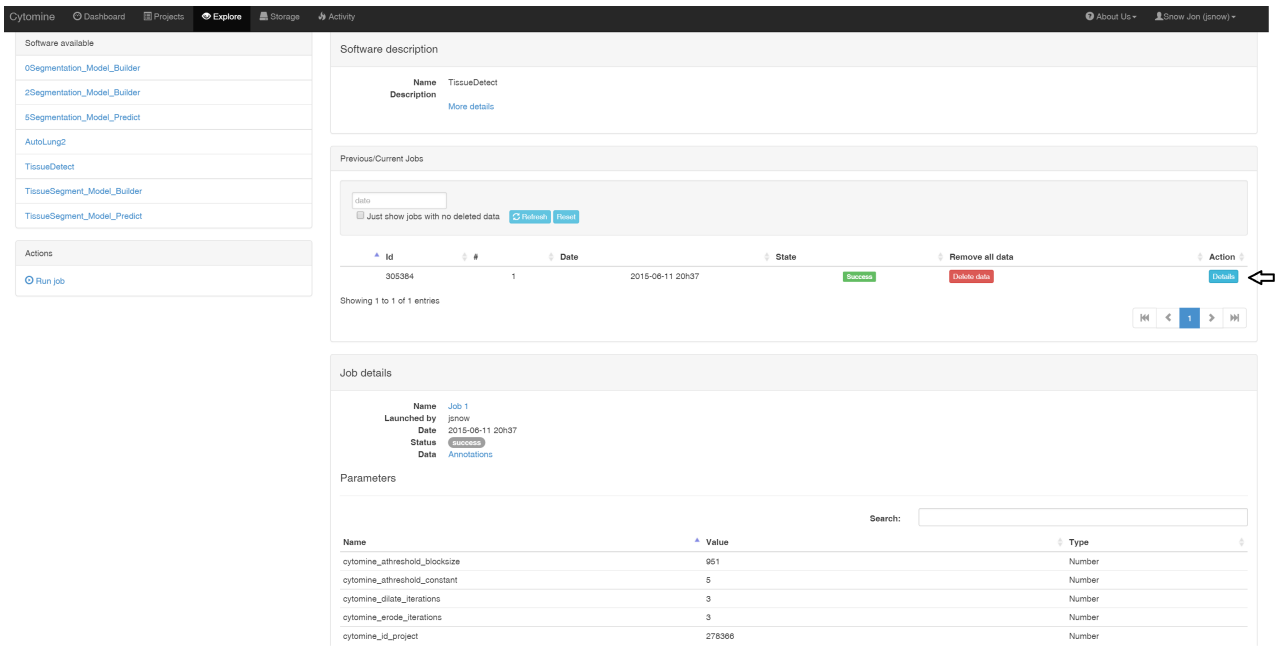
then on the "Run Job":



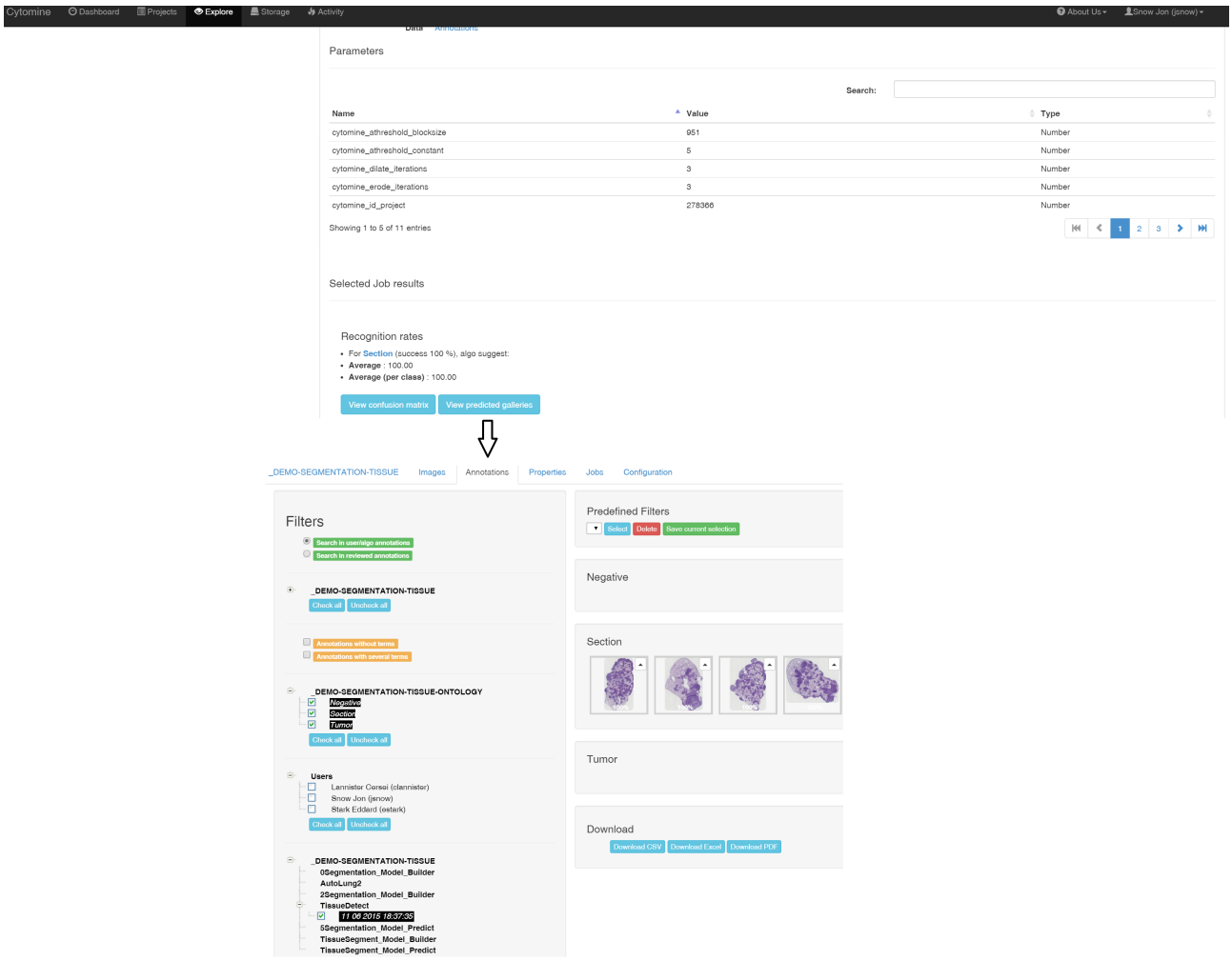
It opens a "Launch new job" dialog box to allow the User to configure the Software parameter values (the form is automatically build based on software parameter definition in the database). Here, we want to associate the term "Section" to objects detected by the procedure, and we keep default values for the thresholding algorithm:



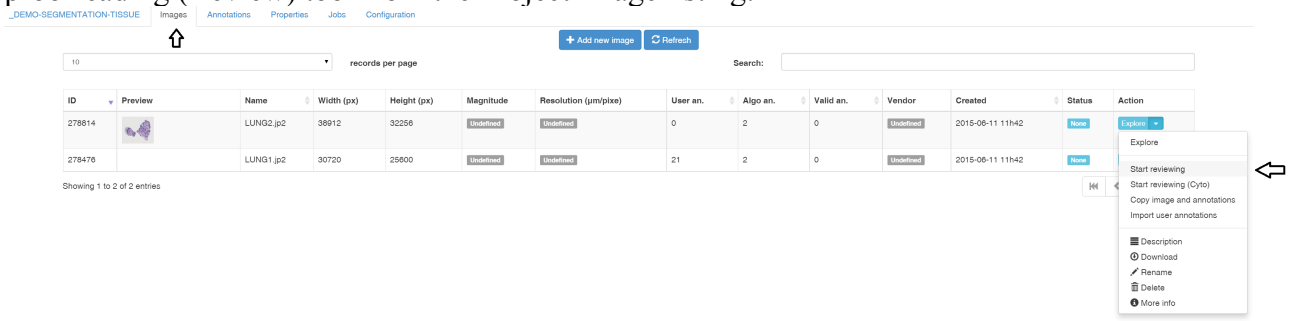
This will add an entry to the "Previous/Current jobs" panel. The job will be executed and Status is displayed and updated during execution. It can be seen by clicking on the "Details" blue button. This also displays parameter values of the running job:



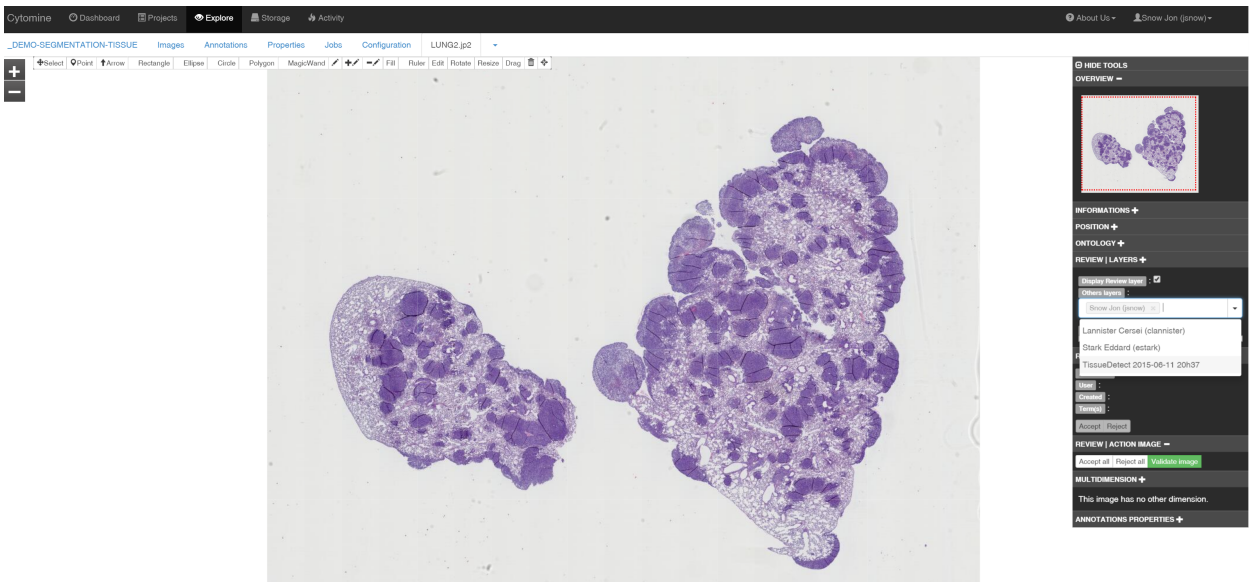
Once the job has reached the "Success" status (in roughly one minute for the two images of our toy project running on our demo instance), one can see (by scrolling down) the objects detected by this job by clicking on "View Predicted galleries" (blue button) that will open the Annotations tab with the filter corresponding to this UserJob. In our case, Sections of the lung are well detected automatically:



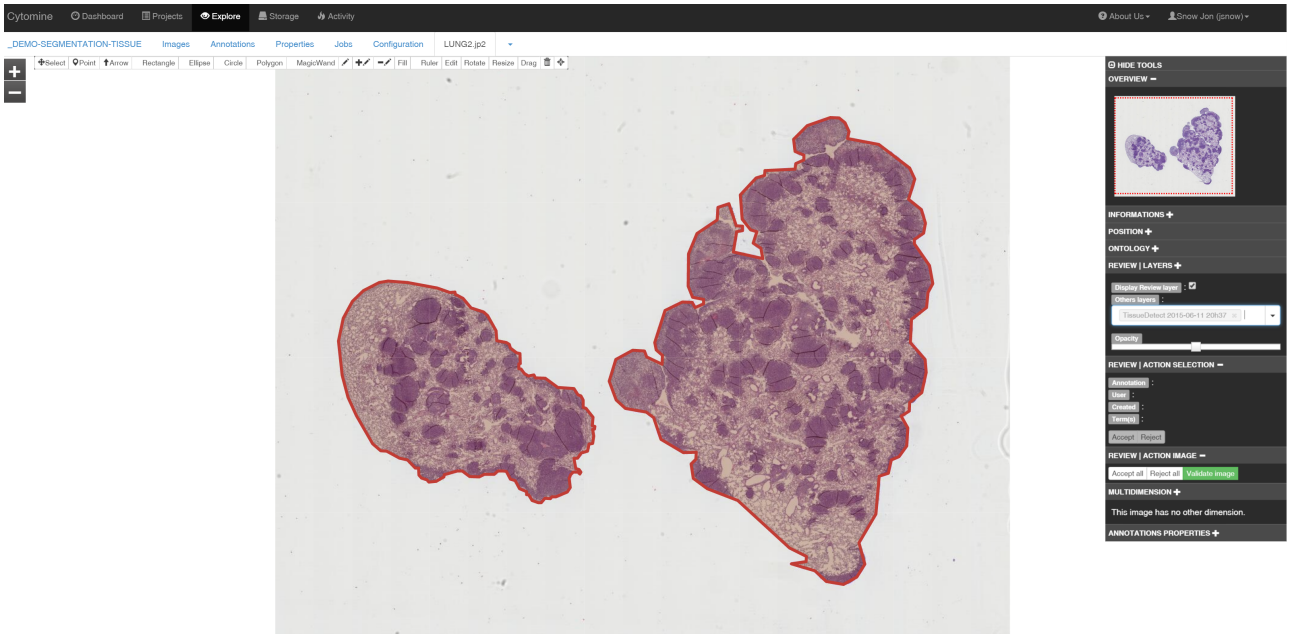
The user can then validate annotations produced by this module in all project images by using proofreading (Review) tool from the Project Image listing:



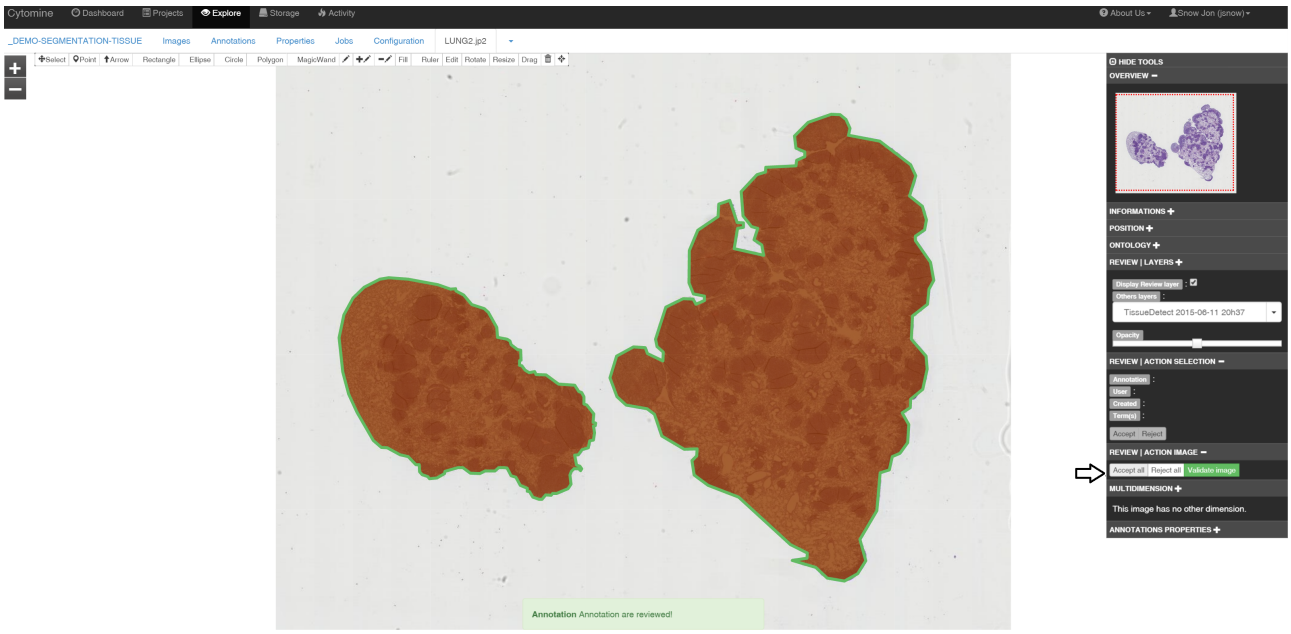
"Start reviewing" (using LUNG2 image) opens the Explore view with additional "Review" tools in the right Panel. The user can then first select the Job (or User) layer from which he wants to validate annotations:



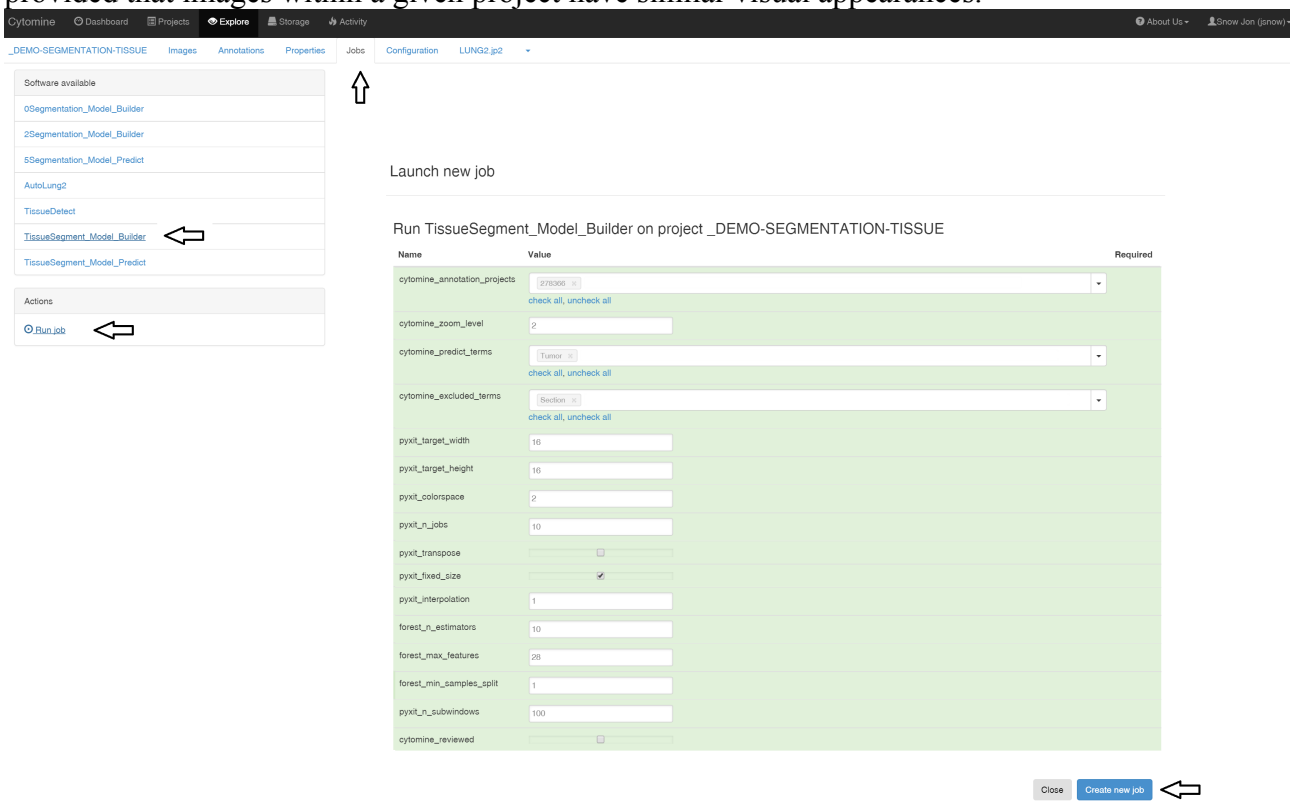
It displays the unvalidated annotations with a lighter opacity and red borders:



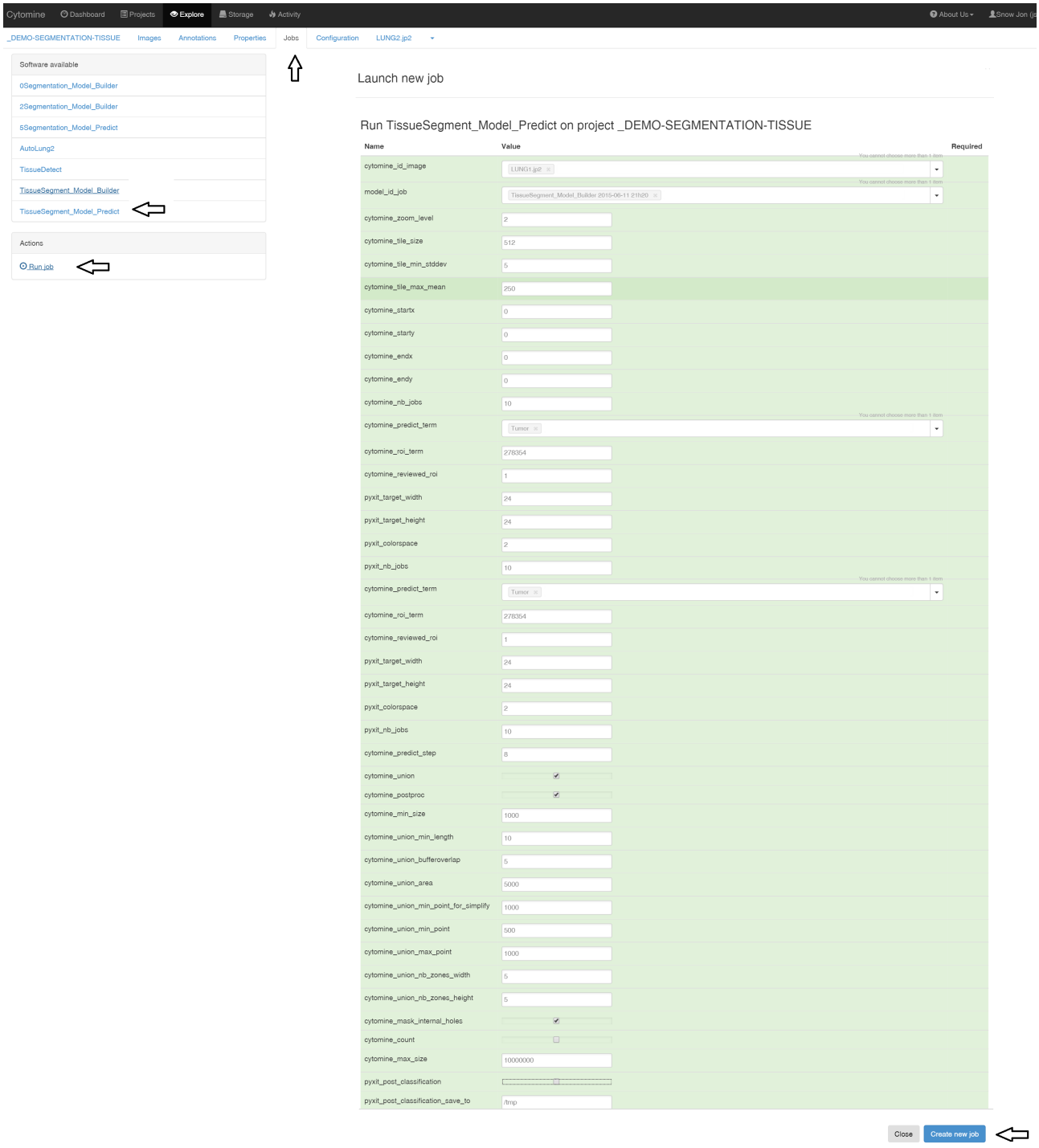
The user can then accept annotations one by one (by selecting the annotation, then click on "Accept" or press "A" on the keyboard) or all at one (by clicking on "Accept all"). Validated annotations are colored with the original color of the ontology Term and have green borders.
Concretely, these annotations are copied into the "Reviewed" annotations of that image:



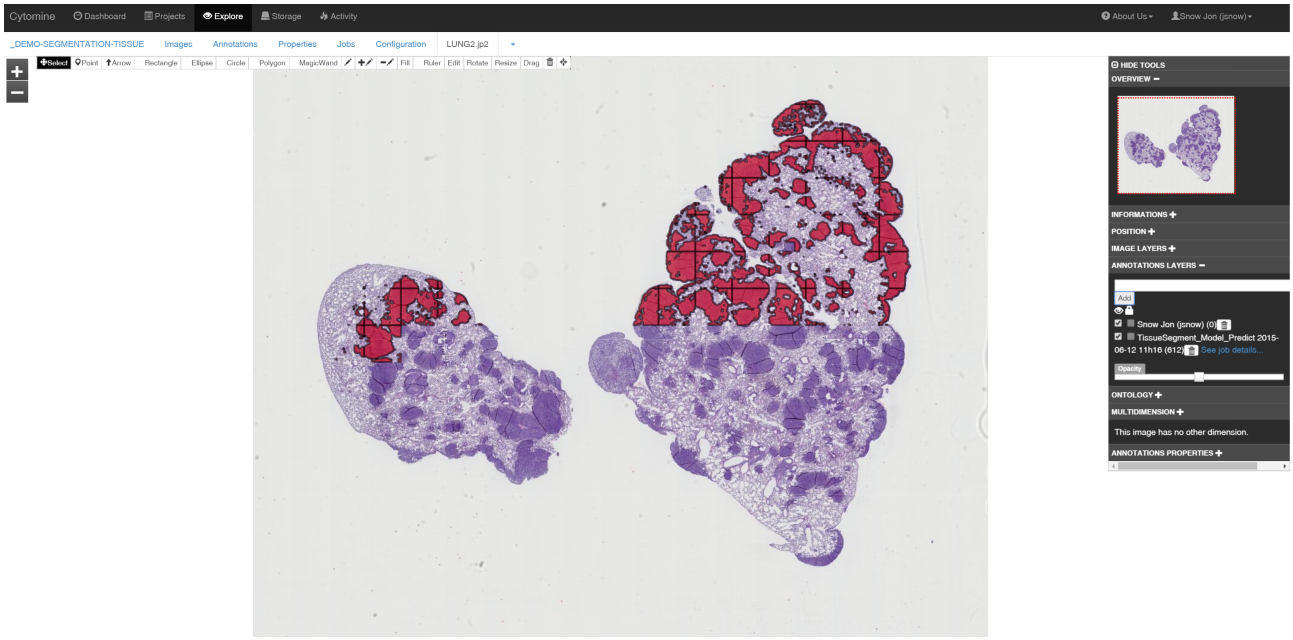
Once sections have been detected (e.g. to compute section Area), a typical application might be to detect tumor islets within them. For that, we use the Cytomine-DataMining Semantic Segmentation analysis module. We will exploit Tumor and Negative manual annotations to build a Tumor detection model, then we will use the model to segment whole slide images. As for the TissueDetect module, the software has to be added to the Project (if not already done) in the Project Configuration panel. Then the TissueSegmentModel_builder has to be run using appropriate parameter values (in our case select the current Project identifier to download annotations, the "Tumor" as predicted terms, the "Section" as excluded terms, and zoom level = 2). Learning is in general only performed once in a project (using annotations coming from this project or other ones), provided that images within a given project have similar visual appearances.



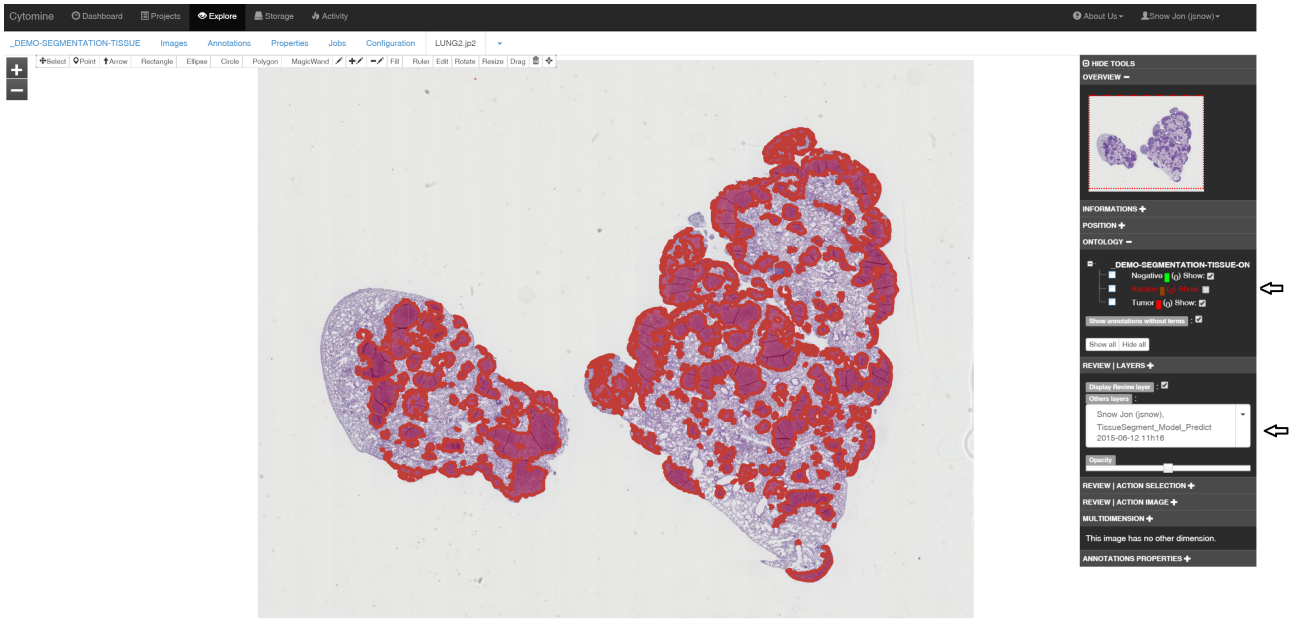
Once the Job reaches the "Success" status (in roughly one minute using our "toy" data on the demo instance), the Tumor detection model is ready to be applied to whole-slide images. The user then launch the TissueSegment_Prediction Job using appropriate parameter values (the image identifier, identifier of the TissueSegmentModel_builder job which created the model, the "Tumor" as predict term, the "Section" ROI term and activate the cytomine_reviewed_roi to only apply the model within validated Sections, zoom_level = 2):



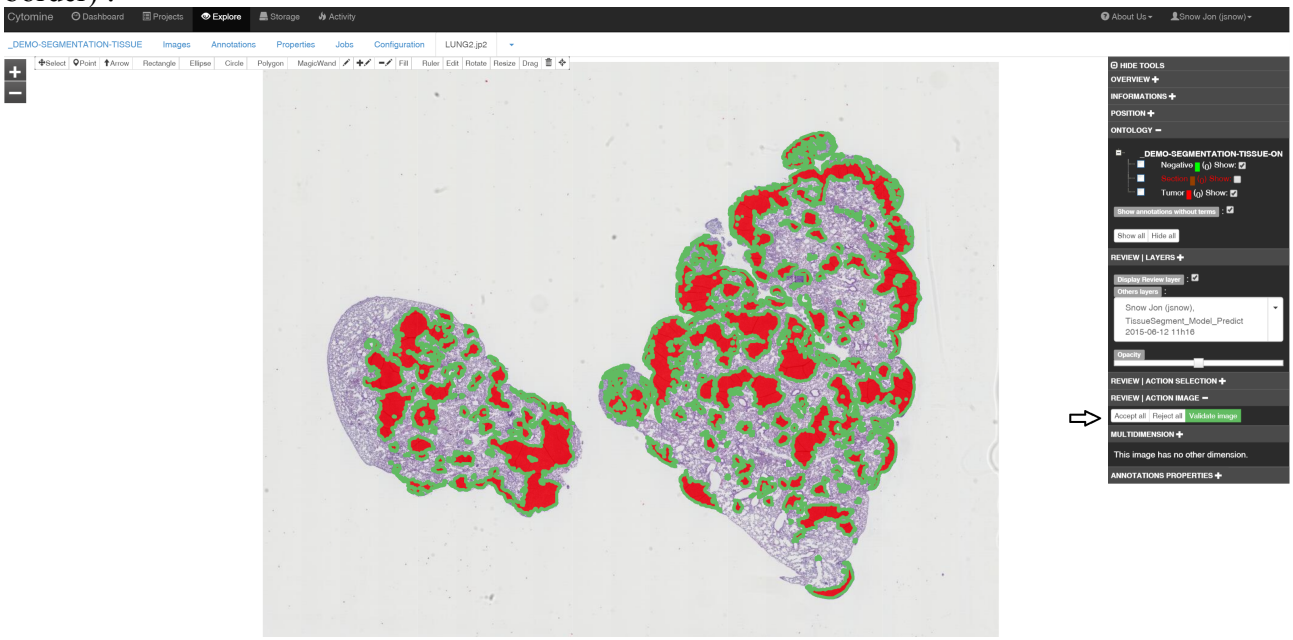
This procedure can take time (from minutes to hours) depending on model complexity, image sizes, resolution level, and allocated computing resources. It will create progressively annotations in tiles of the image. The process is running in the background and the user can perform other tasks meanwhile. The progress can be seen visually by opening the image and selecting in the "Annotation layer" tool the running Job, as illustrated below:



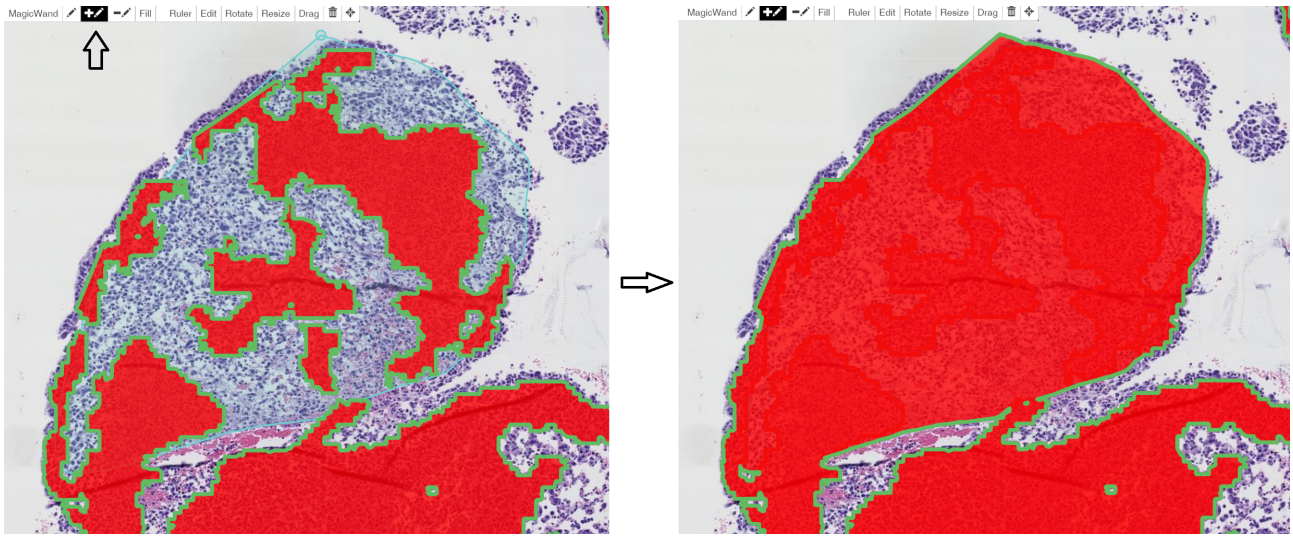
Then once all tiles are processed, the module will apply post-processing and an union procedure of all overlapping geometries. Once the whole process is done (it displays the "Success" status in the Job panel, it can take roughly 40 minutes to process this "toy" image on our demo instance), the user can review these tumor annotations using the same Reviewing procedure as for Tissue detection, by selecting the corresponding TissueSegment_Prediction job (the "Section" annotations can be hidden to ease reviewing by unselecting the box "Show" in the Ontology panel):



When most of the annotations are correct, we recommend to use the "Accept all" operations that will validate all annotations at once (they now take visually the original term color and have a green border) :

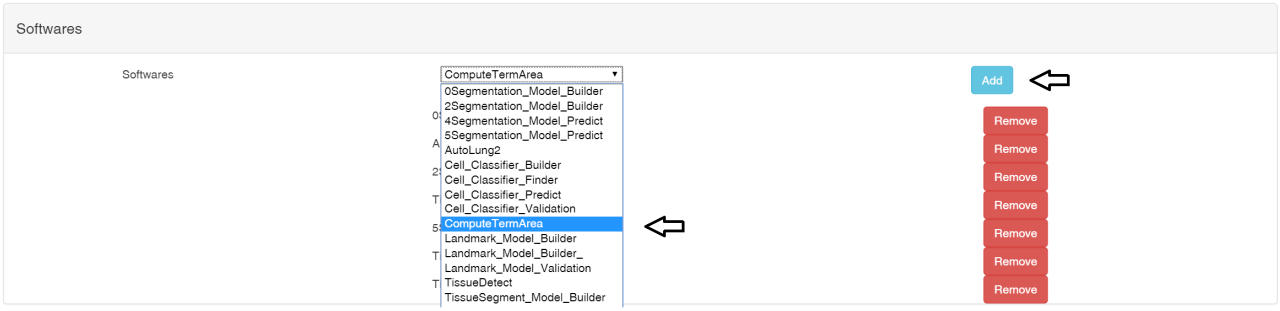


If annotations are not satisfactory at all, we recommend to annotate manually more examples (corresponding to observed predictions errors) and re-train a model. If only some annotations do not fit well the regions of interest (e.g. it misses portions of several tumor islets), the user can use proofreading tools to edit their geometries (or reject objects, e.g. tissue subtypes that are not tumor islets). Using the "t" keyboard or the "Display review layer" checkbox, the user can switch the display of the review layer for further inspection to look at the original tissue, and refine tumor contours using +/-/Fill polygon operations (+ operates an union of the draw polygon with the reviewed polygon, - subtract it):

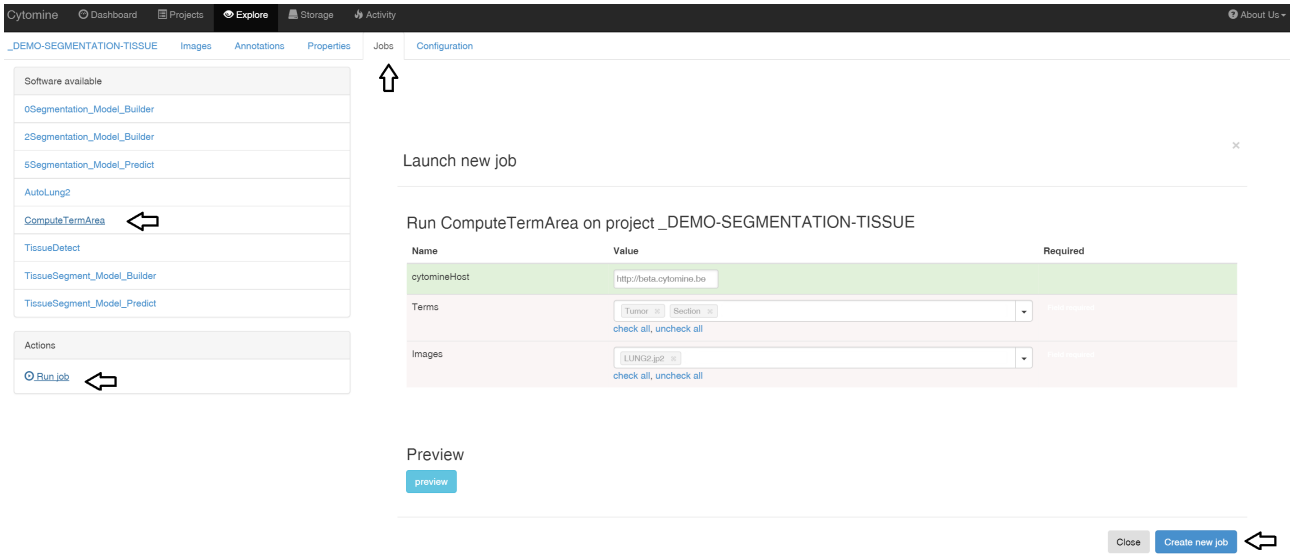


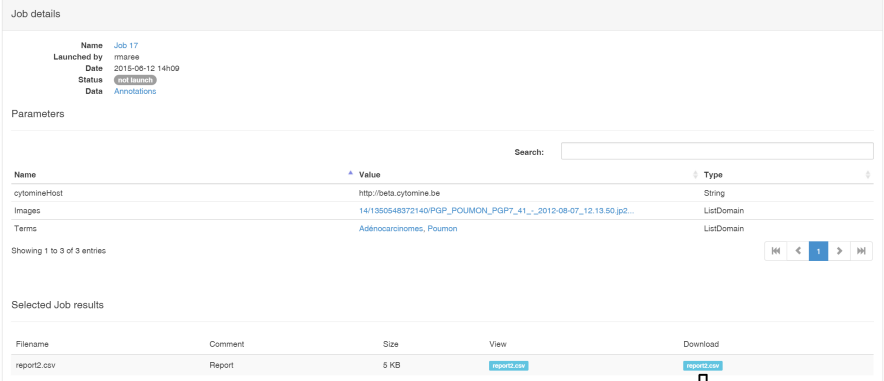
Once the whole image is proofread, the user has to Validate the image (green button) in the right Tool panel:

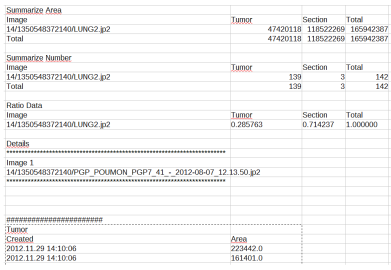
Now, it is possible to use the "ComputerTermArea" software to generate statistics about Section and Tumor area and ratios. Add the software to the project (once) in the Project configuration Panel, and run the Job:



Then run the job, select "Tumor" and "Section" as Terms, and your image, in order to generate and download a CSV file with statistics:





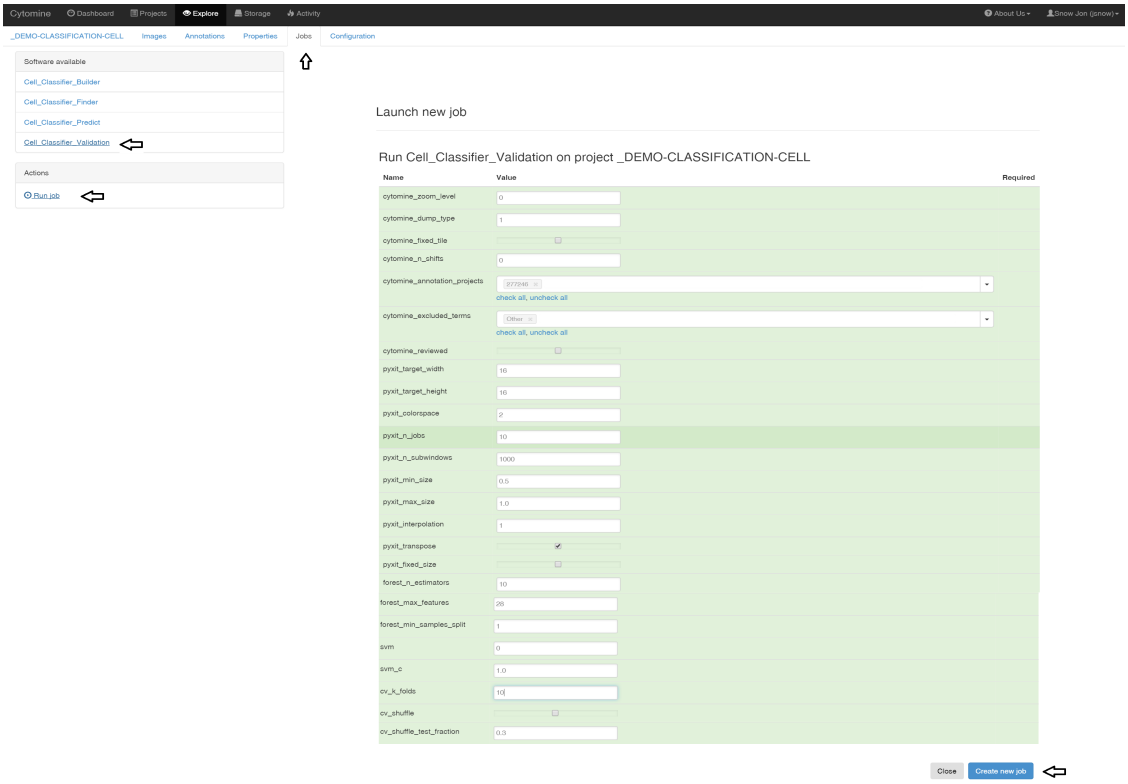


cytomine

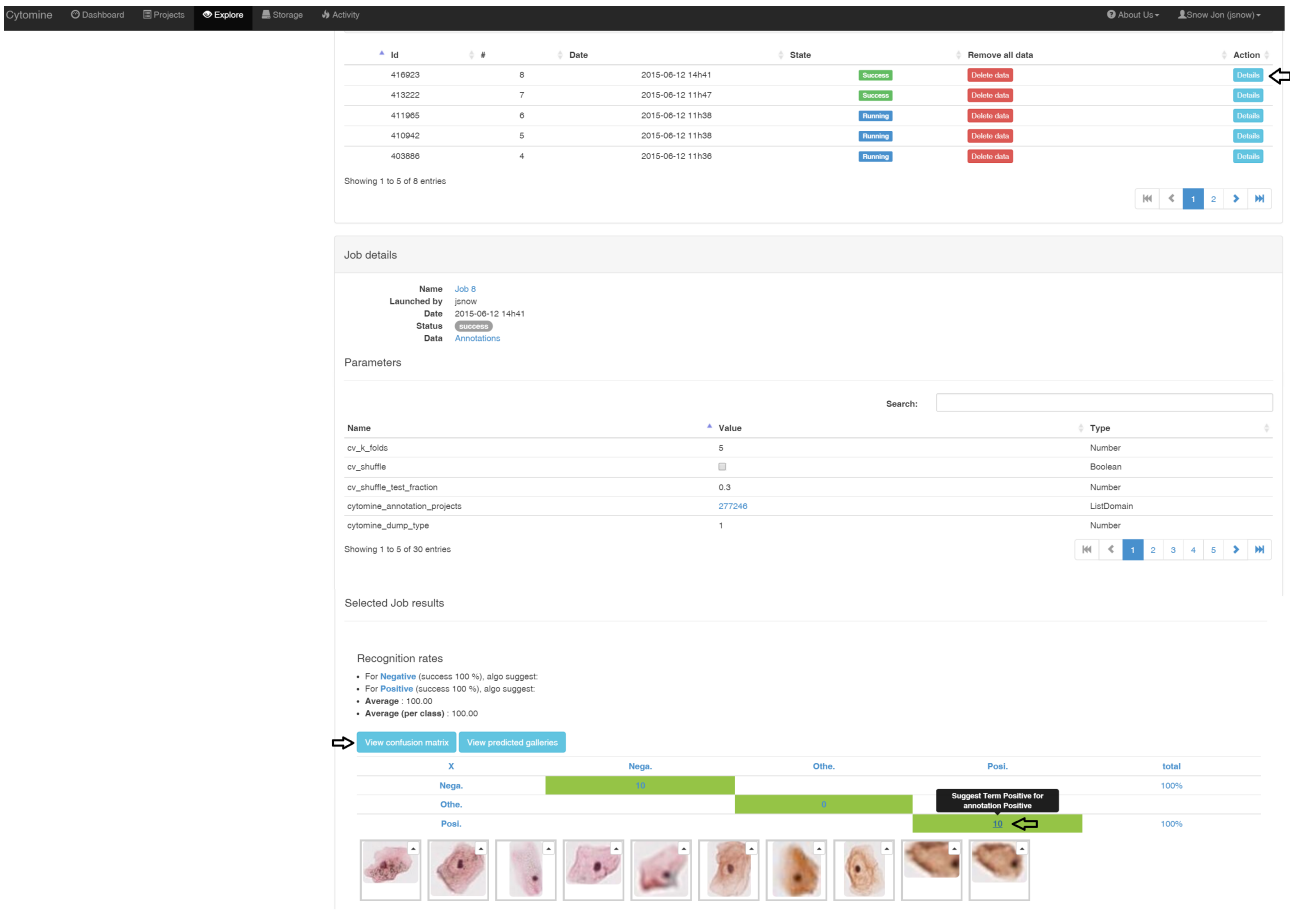
6.2.4.2 Object detection and classification

In this guide, we explain how to apply an object finder procedure followed by an object classification step, e.g. to classify positive and negative cells in cytology images. This example uses four softwares from the Cytomine-DataMining analysis modules: classification validation, classification model builder, object finder, and classification prediction. The provided "toy" demo project (DEMO-CLASSIFICATION-CELL) contains two main classes of cells (10 positive in red, 10 negative in blue). The goal is to build a workflow to detect and classify these cells automatically.

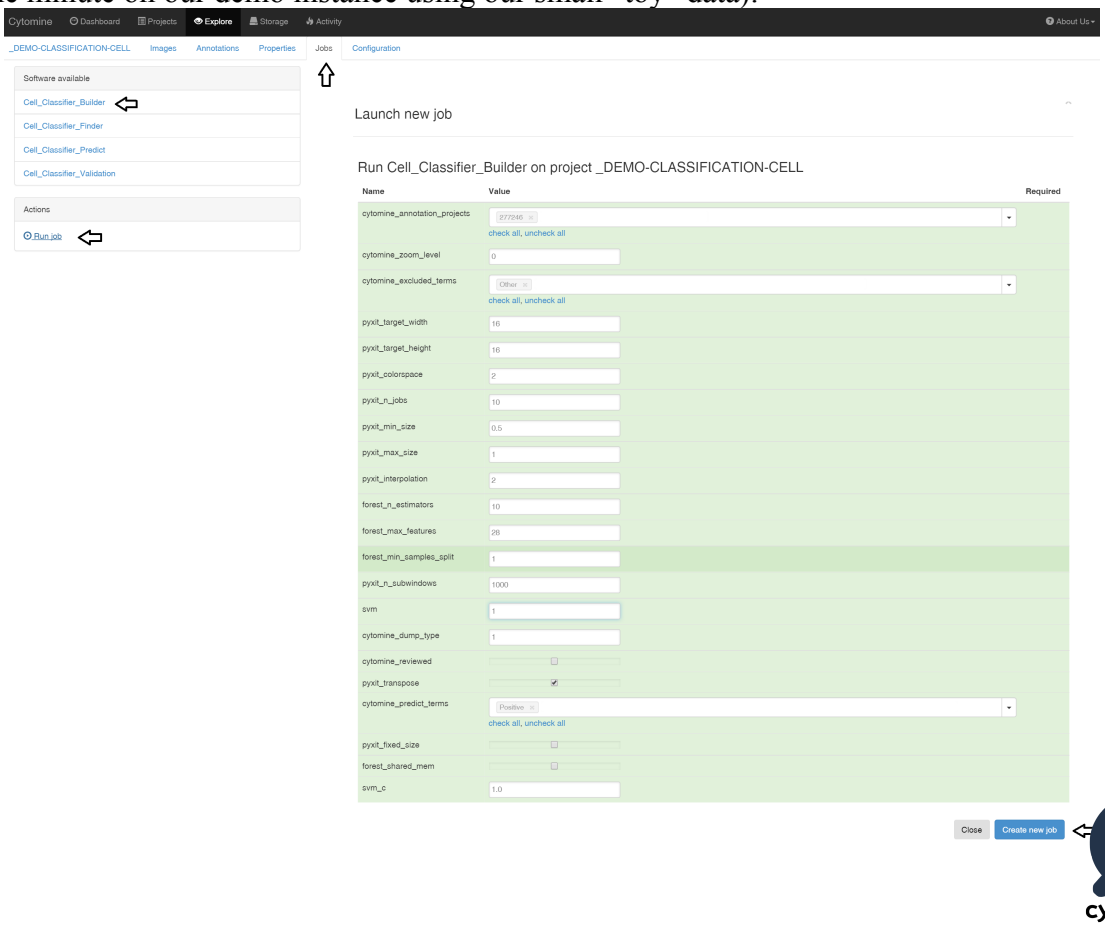
First, the classification validation module allows to evaluate by cross-validation classification performances of the image classification algorithm, given its parameter values and manual annotations with semantic terms. It is launched as other modules through the Jobs panel of the Project:



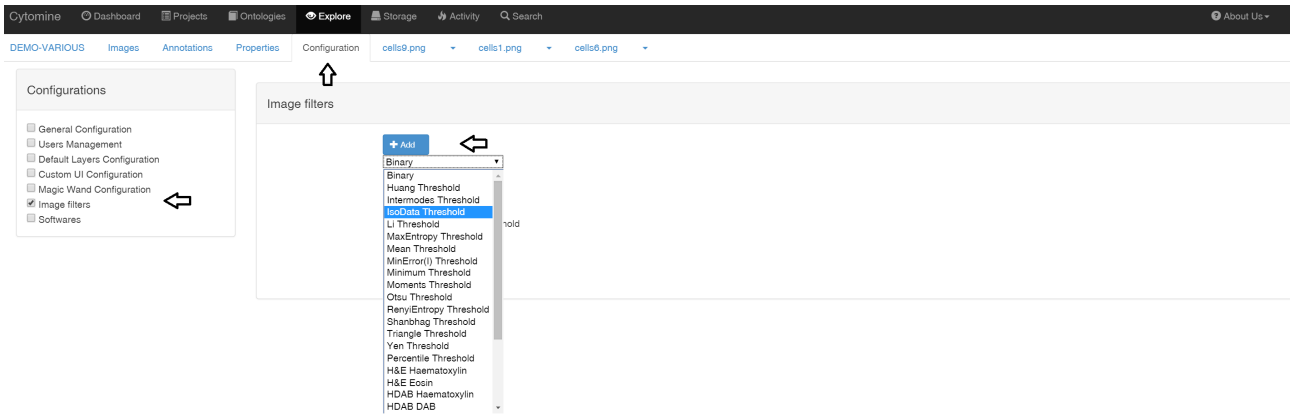
Once the process reaches the "Success" state, it is possible to view recognition rates, misclassified objects, and an interactive confusion matrix of the classifier in the Job Details (click on the Blue "Details" button, then scroll down and click on the blue "View confusion matrix"). It is possible to click on the confusion matrix numbers to view galleries of cell classifications. In our example, the classifier reaches 100% recognition rate for both cell types:

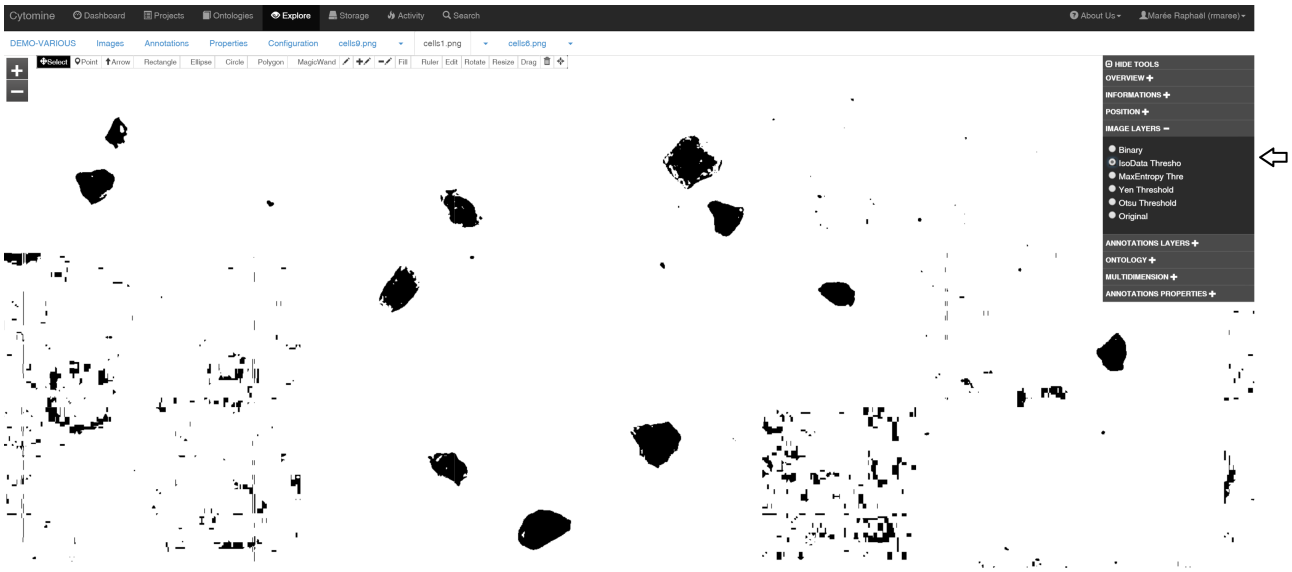


The classification validation module only evaluates classification models without saving them. Once satisfactory results are obtained, the user can build with corresponding parameter values and save a classification model by using the classification model builder module. It will save a model on the processing server that can be later reused by the classification prediction module (it takes less than one minute on our demo instance using our small "toy" data):

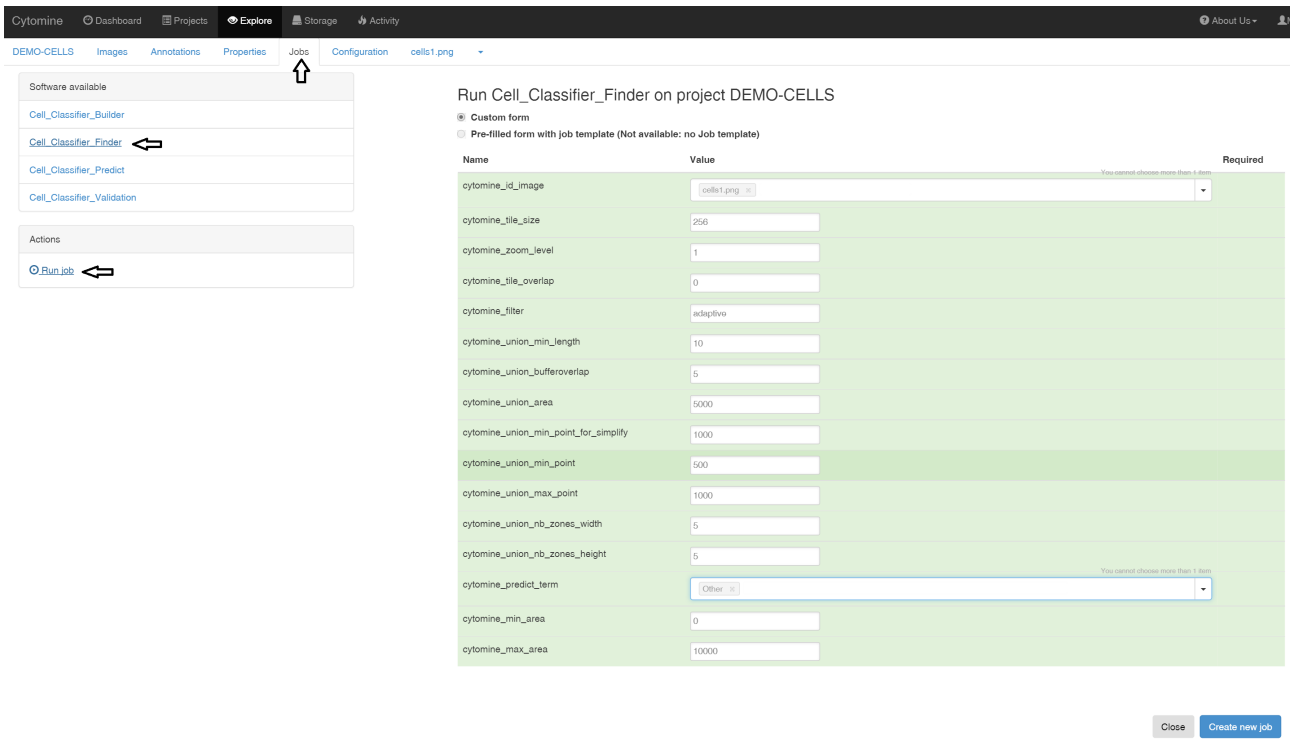


Now it is possible to apply this model to classify annotations of an image. We thus need before to apply an object finder to the image to create annotations corresponding to candidate objects. To ease the choice of a thresholding algorithm, it is first possible to apply standard algorithms on-the-fly, tile per tile, in the Cytomine-WebUI image explore view. The user needs first to add the image layer (in the Project Configuration panel), then apply it using the "Image Layers" panel at the right of the image Explore view:

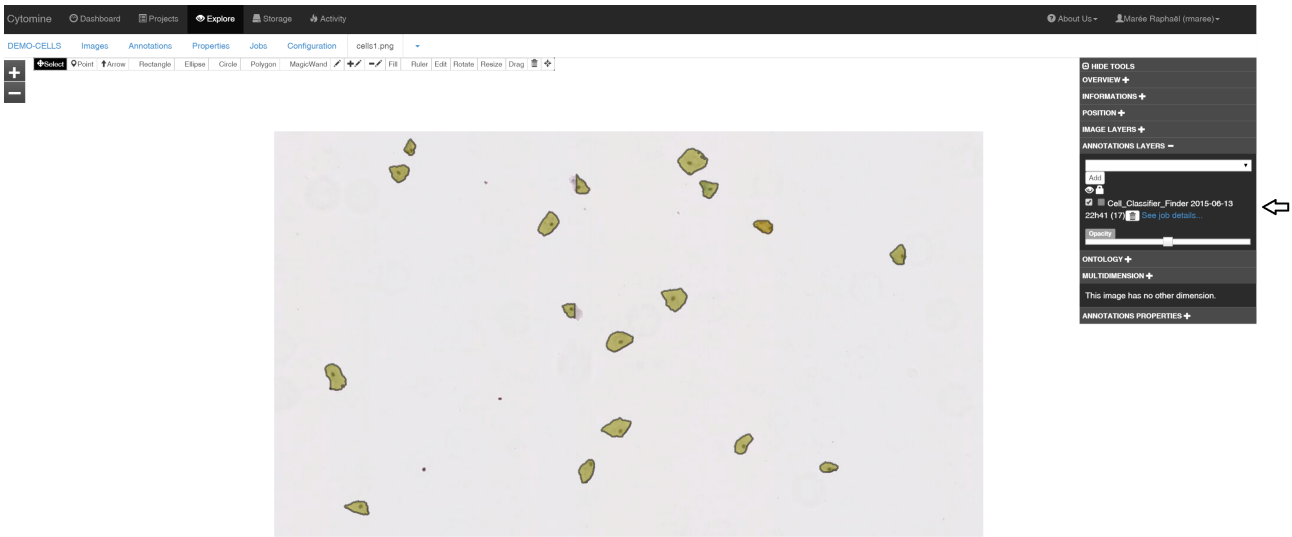




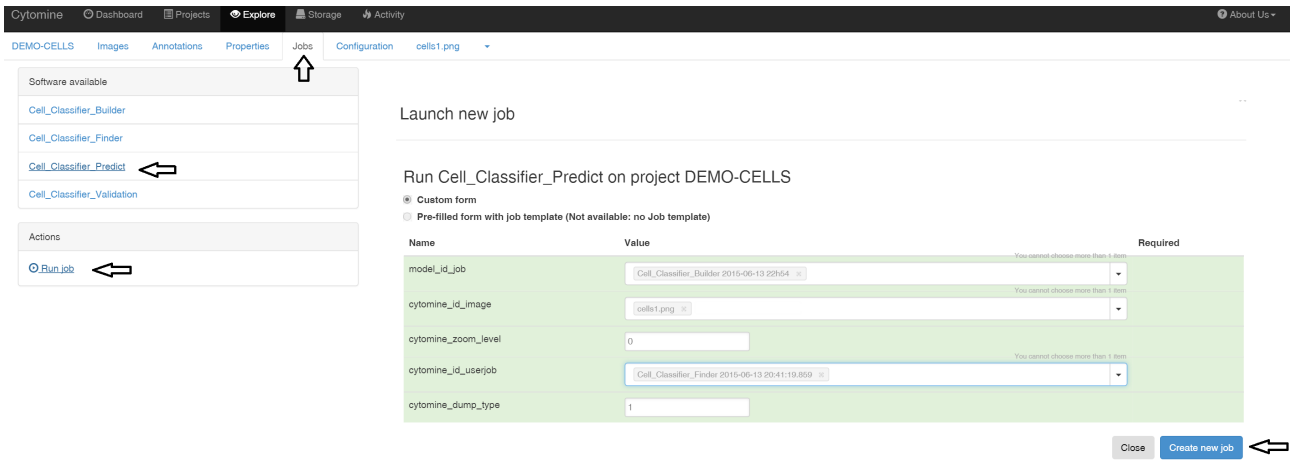
To apply the Object finder module on an image to create annotations, the user needs to add the software to the project (once), then launch it. It will create annotation objects in the corresponding job layer (here we use zoom level=1 and adaptive thresholding algorithm on cells1 image):



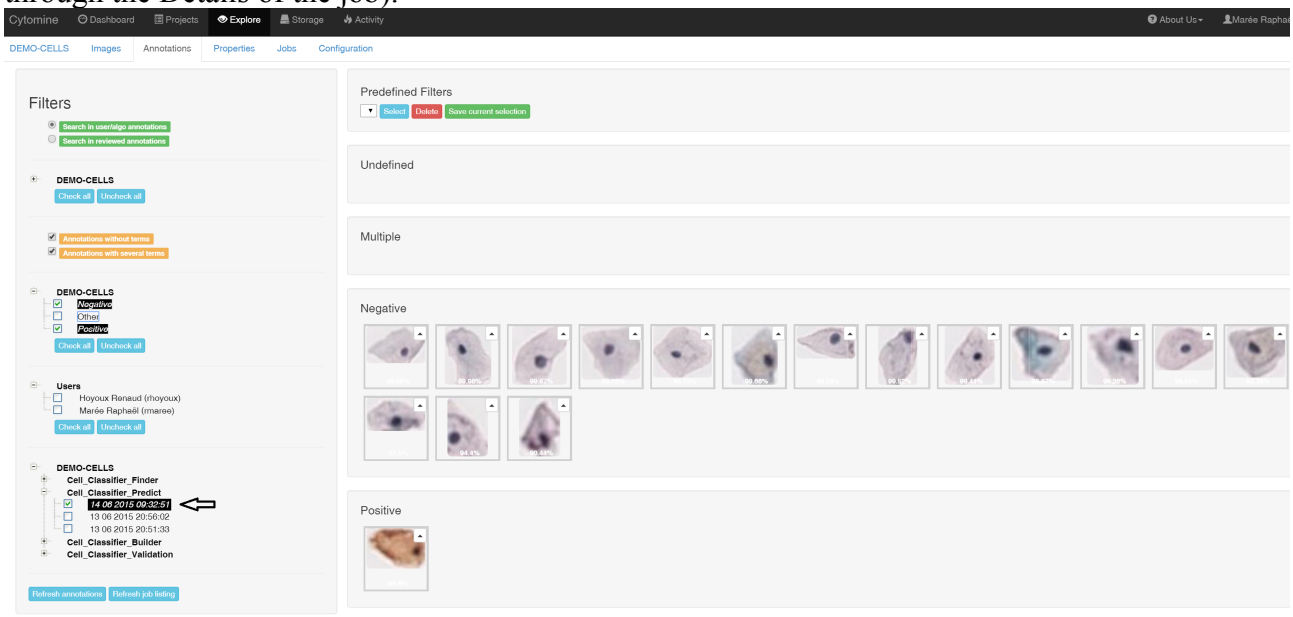
Once the job has reached its "Success" (less than one minute for one image on our demo instance) status, detected objects can be seen in "View predicted galleries" (blue button in the "Details" of the job) or directly in the Explore view of that image:



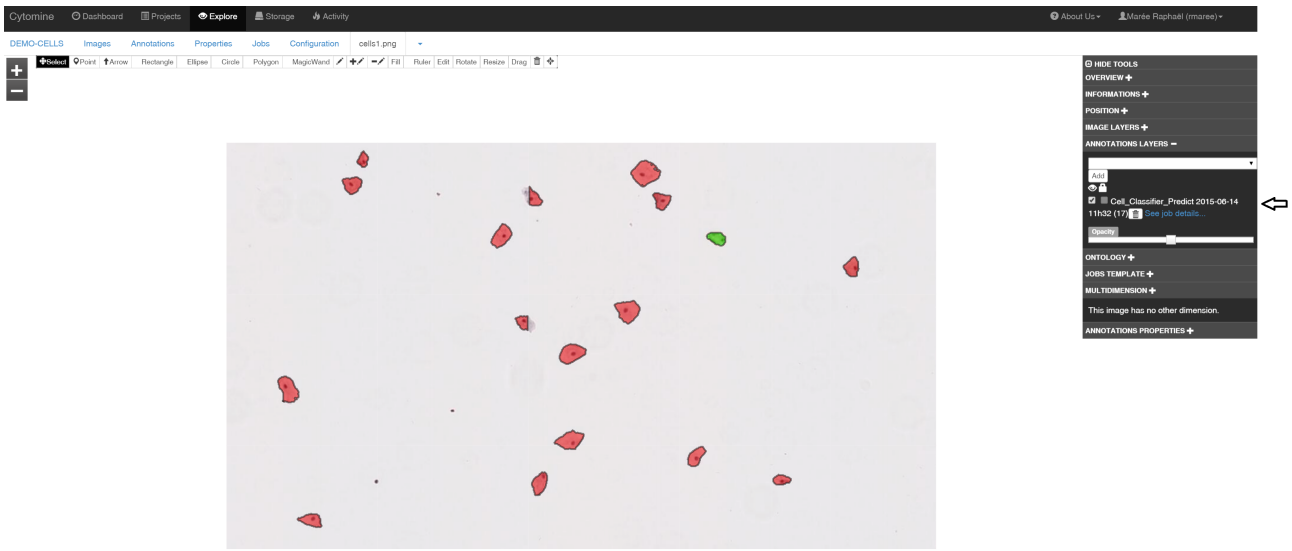
Now, we can apply a classifier to these detected objects in the image, by launching the classification prediction module (Cell_Classifier_Model_Predict), using the previously built classifier model, and the previously found candidate annotations (using the identifier of the job which generated these objects):



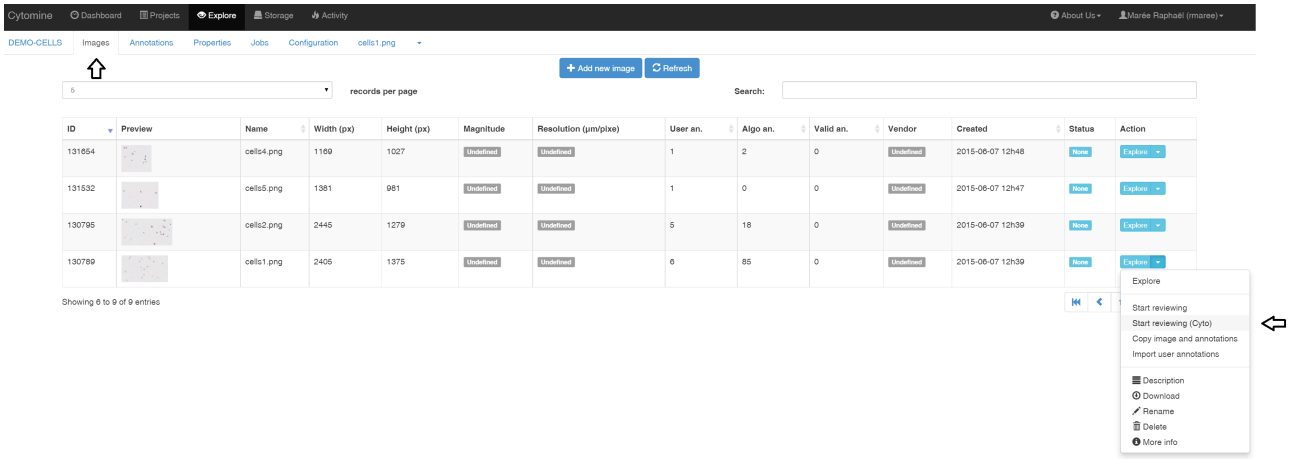
Once the classifier has reach its "Success" status (it takes less than one minute on our demo instance using annotations detected in cells1.png image), it is possible to visualize its classifications (as another job layer, either in the Explore view, or as "Predicted galleries" in the Annotation tab through the Details of the job).



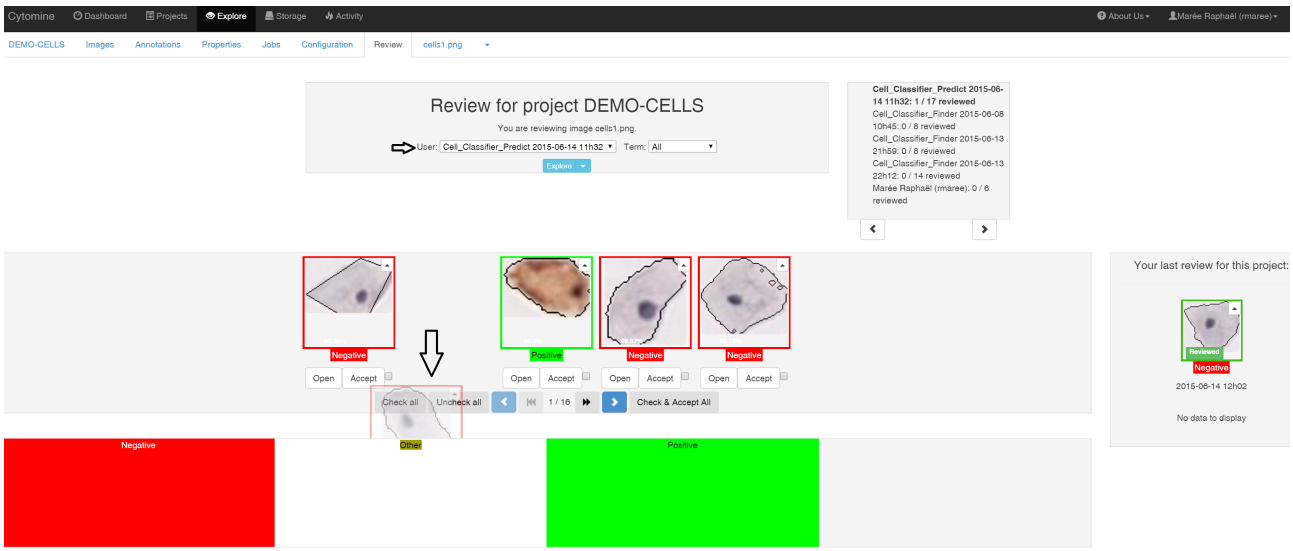
In this toy example, the classifier perfectly classifies cells (one positive in green, others negative).



As in the tissue detection application, these annotations can be reviewed by an expert. We have developed a specific "Review (Objects)" module to review object classifications in a more efficient way. It can be launched from the Project image listing:



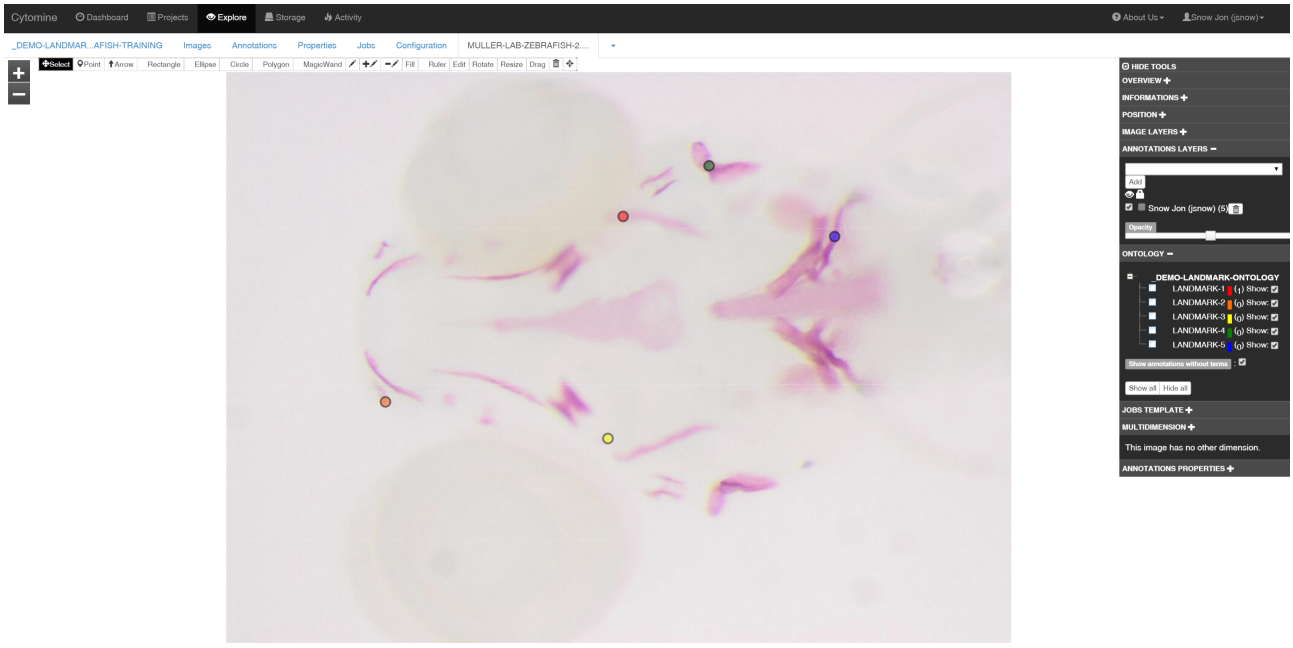
This module allows to select a user/job layer and displays galleries of its predictions (using pagination across all annotations). The user can then either accept these classifications, or correct them by drag'n'drop into visual boxes corresponding to the correct term. Validated and corrected annotations are copied to the Review layer of that image.



6.2.4.3 Landmark detection

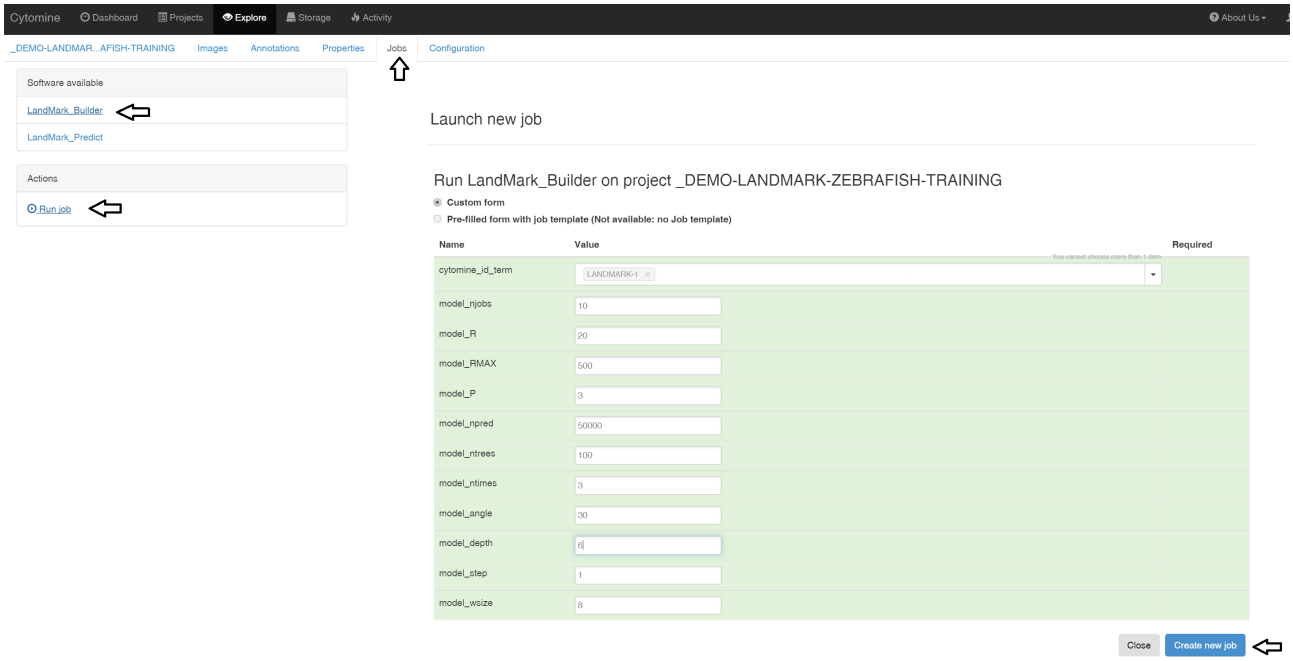
In this guide, we explain how to use the landmark detection module on a "toy" dataset of Zebrafish embryo images. This example uses two softwares from the Cytomine-DataMining analysis modules: Landmark_Builder and Landmark_Predict. The provided "toy" demo project (DEMO-LANDMARK-ZEBRAFISH) contains five landmarks for 20 images, and 10 unlabelled images. The goal is to build a workflow to detect these landmarks automatically in the unlabelled images.

This module uses examples of landmarks positioned in images to build landmark recognition models. Here is an example of 5 manual landmarks on Zebrafish alizarin red images:

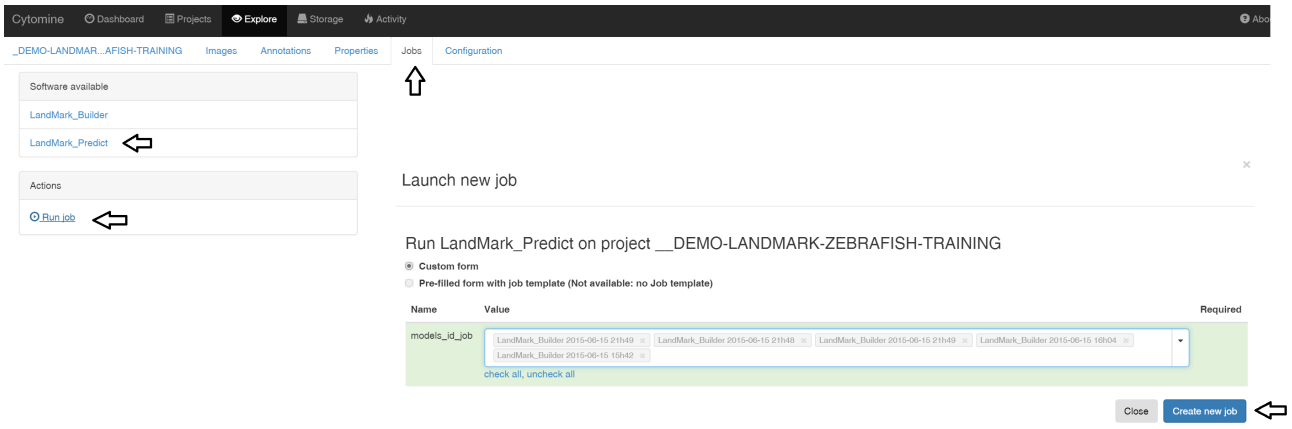


As previously, to launch the learning procedure, the user first needs to add the software Landmark_Model_Builder to its project (if not alreay done) in the Project Configuration panel:

Then, it launches the training algorithm (the algorithm will use all landmark UserAnnotations from images of this project):

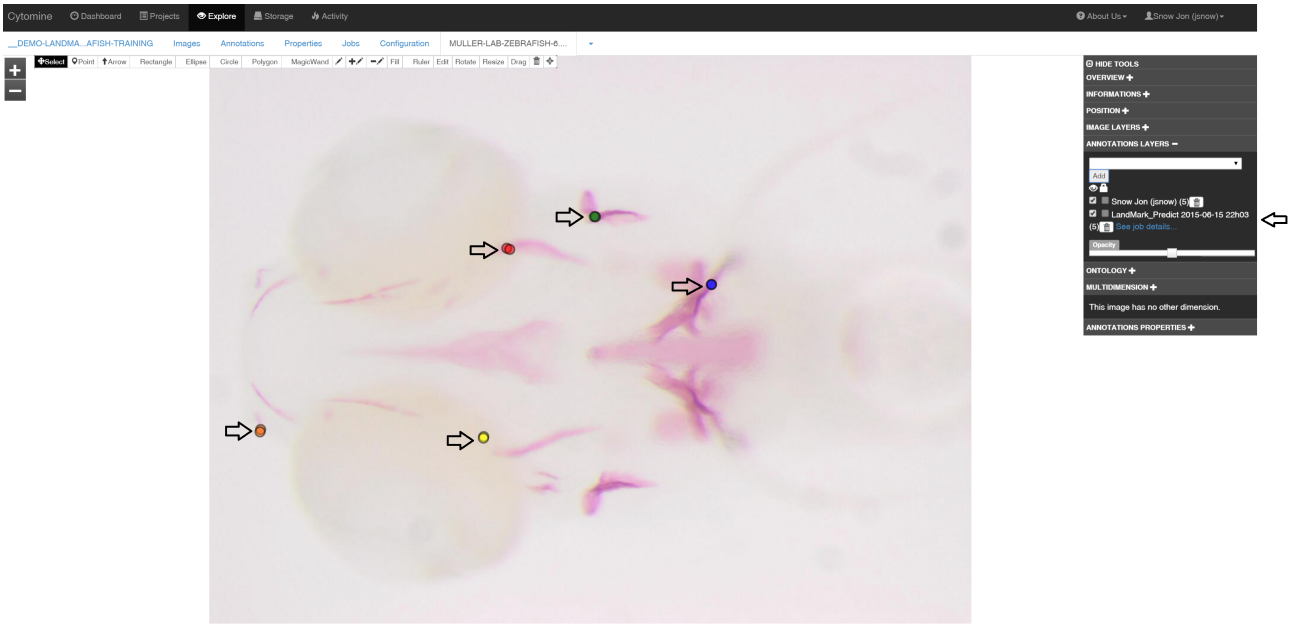


This procedure will generate a model to detect a single landmark. If multiple landmarks have to be detected, the training procedure should be repeated for other landmarks. Once a job has reached the "Success" status (it takes roughly 5 minutes per landmark on our demo instance with default parameter values), its model can be used to predict landmarks in other images. In this guide, we created models for landmark_1 to landmark_5 using 20 manually annotated images.
Applying models to predict landmarks is done by launching the Landmark_Model_Predict module and by selecting the previously build models:

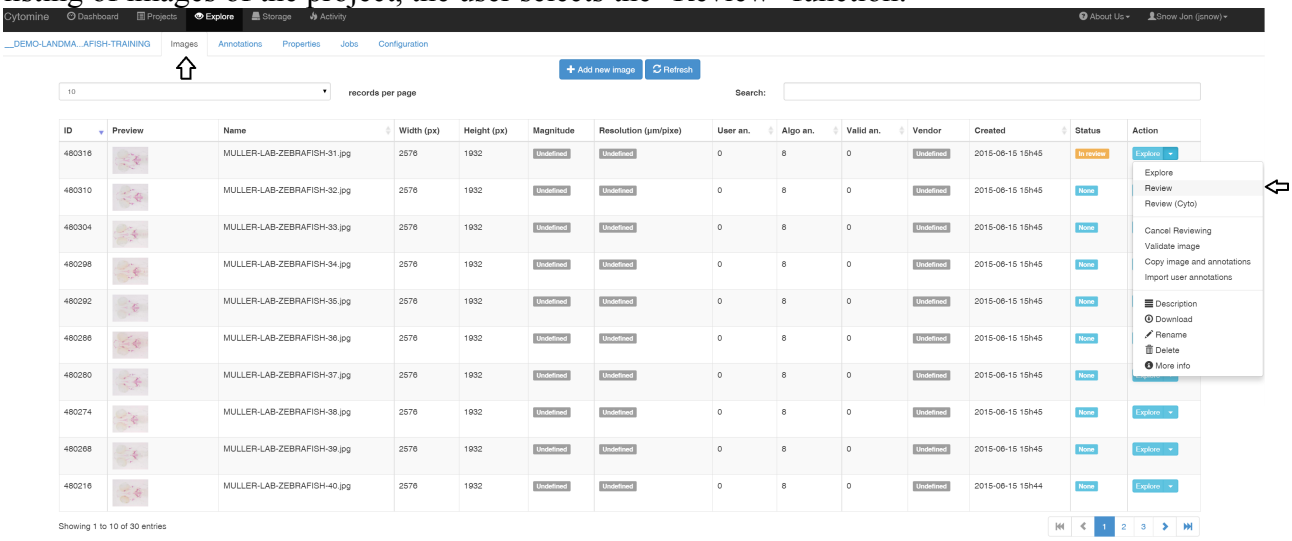


In our case, it will create Point annotations corresponding to the five predicted landmark positions in all 30 project images (it takes roughly 12 minutes on our demo instance with default parameter

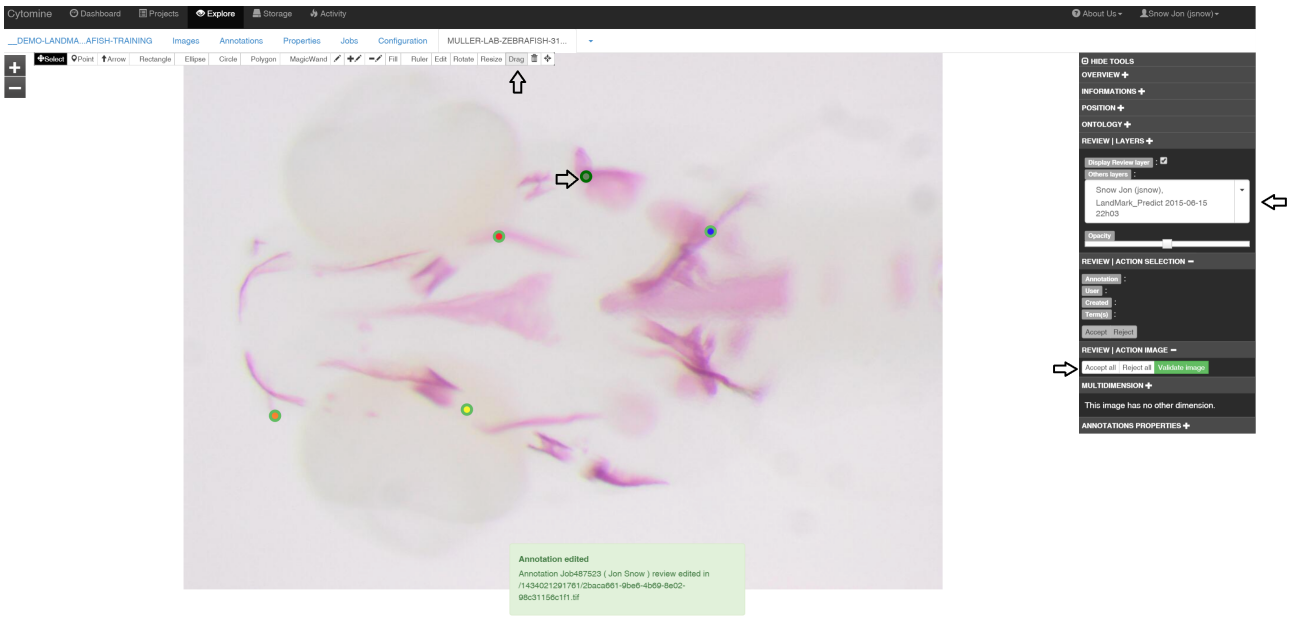
values). Here we illustrate predictions for a training image (the Figure shows both manual and predicted landmarks to assess position precision, one can observe slight shifts only) and an unlablled image for which no manual annotation was provided for training the model:



As with other modules, the user can now proofread these detections on new images. From the listing of images of the project, the user selects the "Review" function:



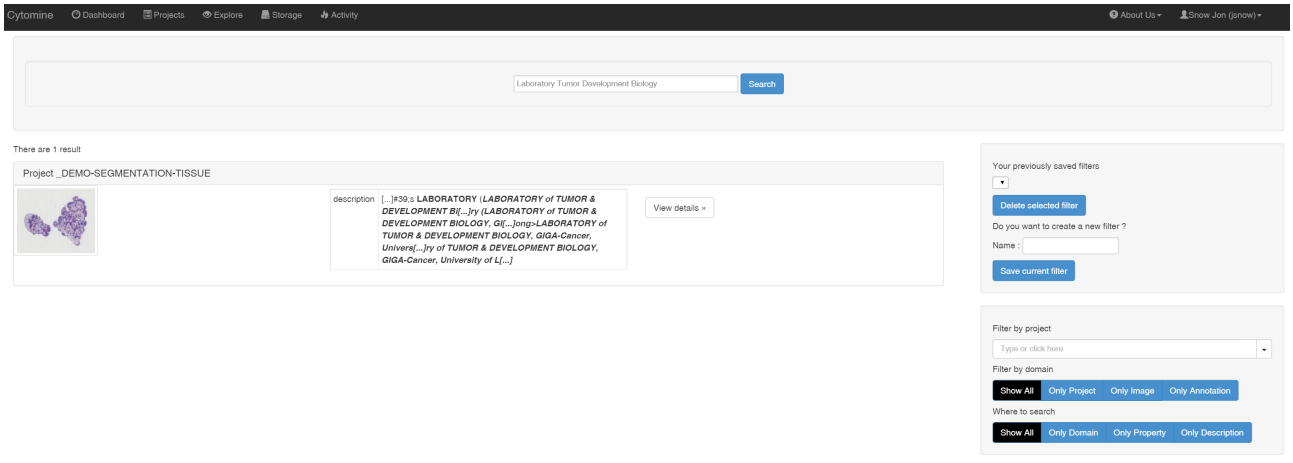
It opens the image in the Explore view with reviewing tools activated. The user first selects the UserJob layer in the right panel. When most of the landmarks are well detected, we recommend to use the "Accept all" function (Points now have a green border) and then use the "Drag" tool (click on the landmark to edit) to move landmarks that are not well detected only:



Once all landmarks are well positioned, the user validates the image (green button). Reviewed landmark positions can later be exported to derive morphometric measurements.

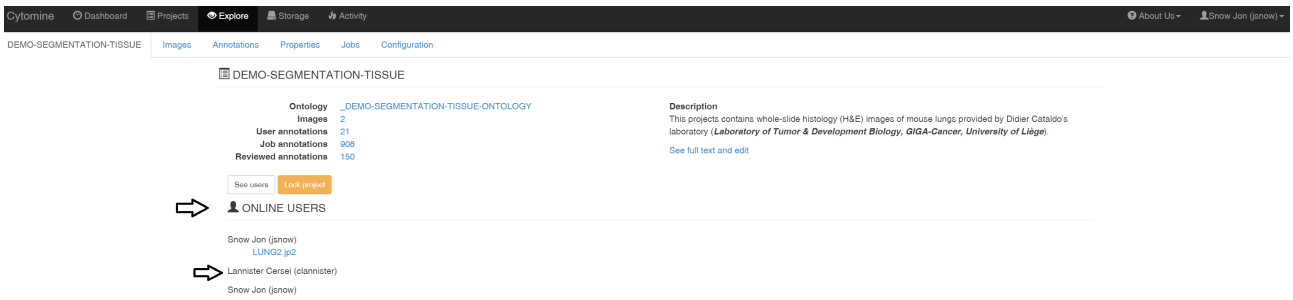
6.2.5 Textual search

In addition to content-based image searching and user interface tools to filter annotation based on semantic terms, it is possible to perform textual searches through Cytomine-WebUI using http://demo.cytomine.be/#search-
Searching will be performed across data entities (projects, images, annotations, domains, properties, descriptions) that are accessible by the user. In the example below, the user looks for "Laboratory Tumor Development Biology" and the search engine displays a project that contains these words in its description:

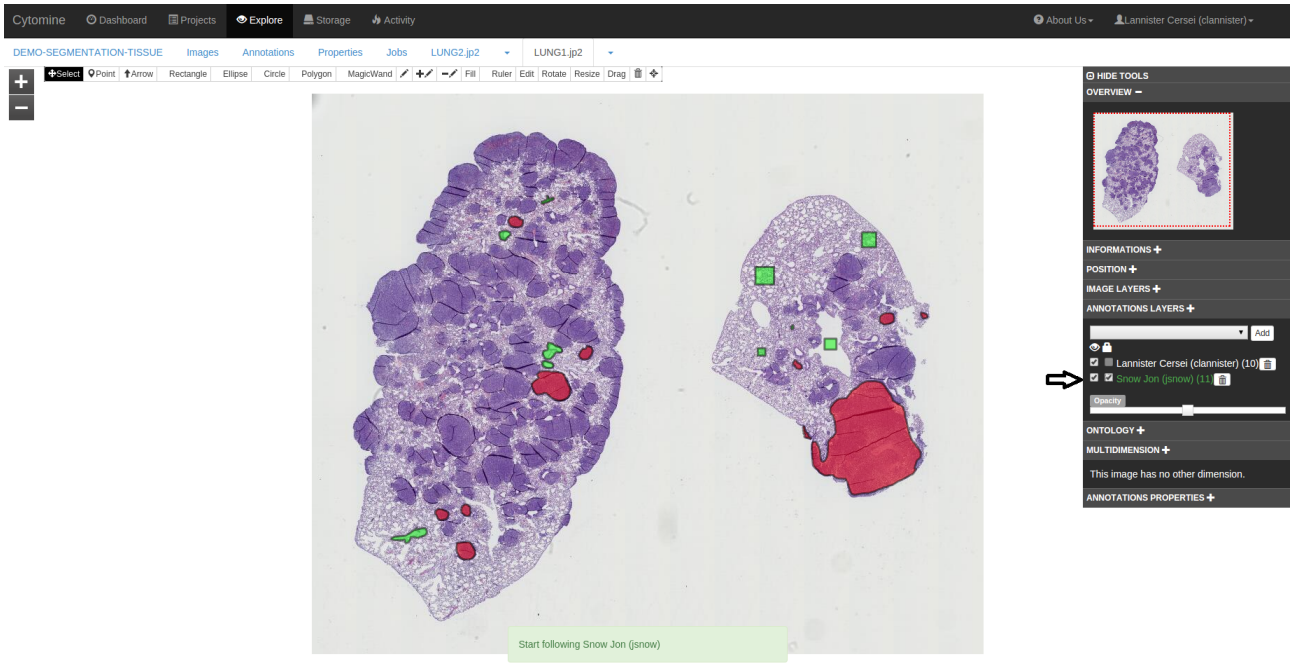


6.2.6 Online users

Cytomine can perform the tracking of all user activites (user positions in images are stored in the database) that e.g. allows multiple users to follow remotely another user observation paths and actions. Online users appear in the project dashboard, and in the Explore Annotation layers panel.



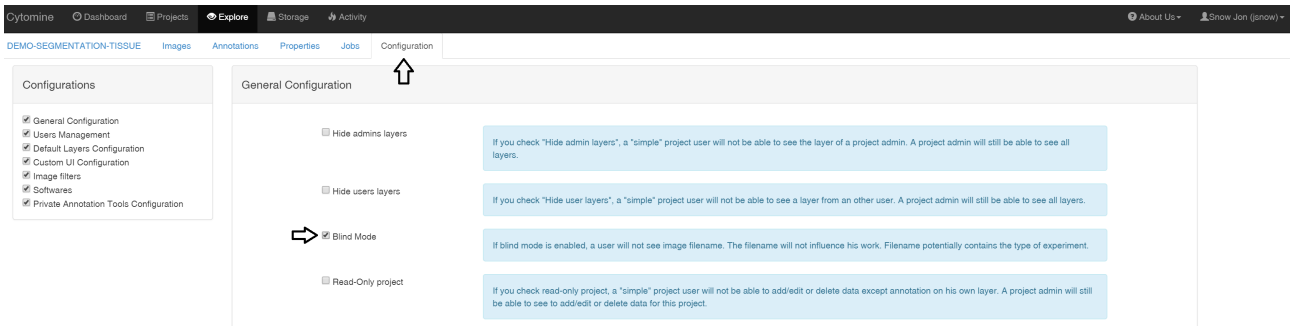
It is possible to follow another online user (in green) by checking the closest box next to the user name. Once the followed user moves in the gigapixel image or creates an annotation, the following user explore view will move to the same position and display novel annotations. Geographically distributed users can thus discuss remotely in front of the same image areas (using e.g. instant messaging or phone calls).

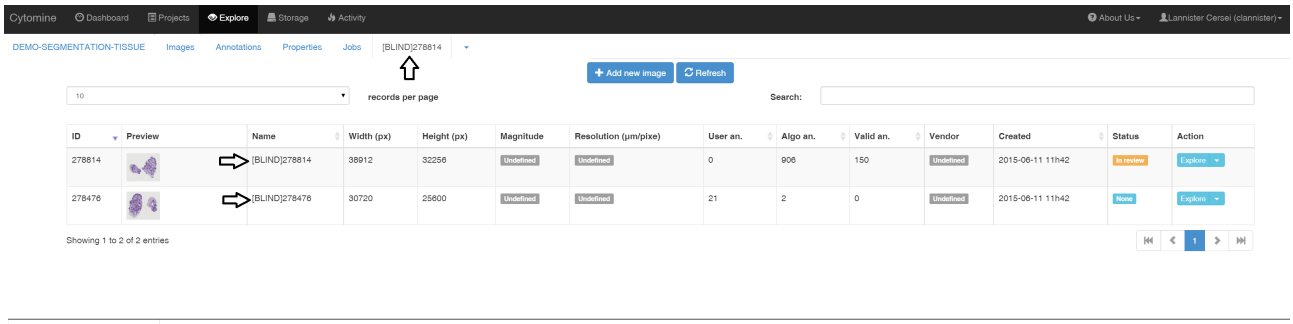


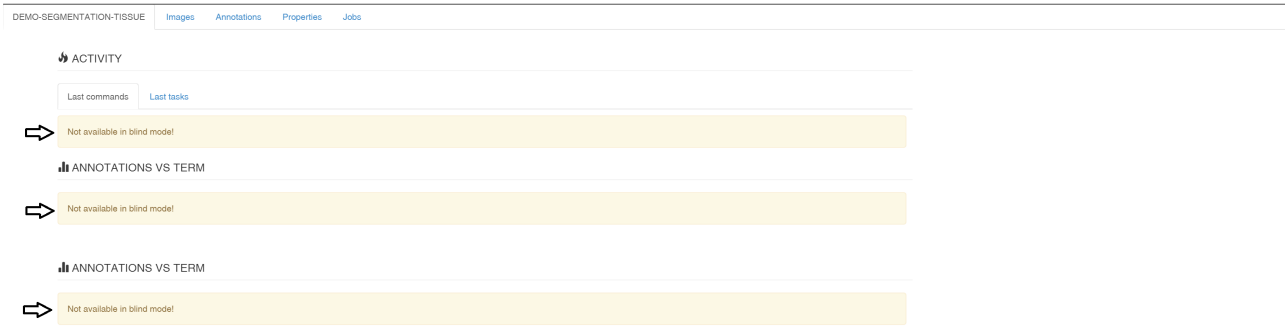
6.2.7 Blind assessment

6.2.7.1 Blind configuration

Cytomine has a blind mode that can be activated by administrators of a project in its Configuration Panel. This option will hide (for non-admin users) in Cytomine-WebUI image names (in the Image listing, the Explore view, …) so that the user quantifying experimental outcomes is blinded to the experimental setting that might appear in original filenames. This option also hides user activities and annotation statistics. This option might be used to reduce bias in analyzing imaging data.







6.2.7.2 Cytomine-IRIS: Measuring Inter-observer Reliability

In contrast to the intentionally collaborative nature of the Cytomine-Core and Cytomine-WebUI annotation modules, Cytomine-IRIS, the inter-observer reliability study module, provides an intuitive web interface for blind assessment of annotations. It is based on the public Cytomine REST API described in section 6.3 to leverage existing Cytomine backend functionality like project and user management, or annotation services for manipulating ontology terms of annotations. On the other hand, it provides a completely decoupled user interface. In addition to the basic project configuration done using the regular Cytomine-WebUI, particular projects and images can be disabled per user on IRIS, such that for example within existing projects only few images are used for assessing the inter-observer reliability among particular users.

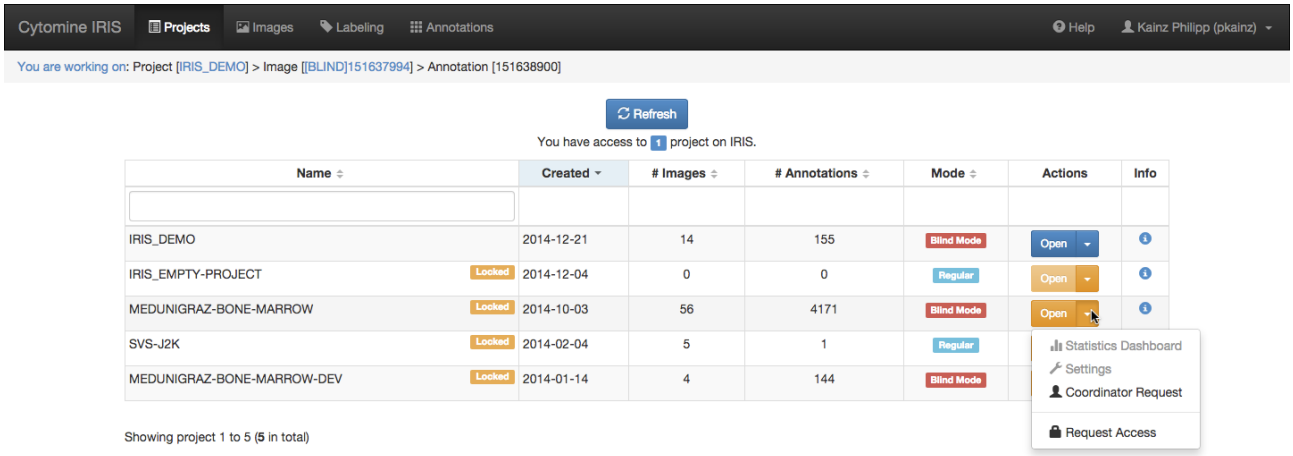
IRIS Installation

Since Cytomine-IRIS is an additional module, multiple instances of IRIS running on different servers can be connected to a single Cytomine-Core server. Thus, the installation of IRIS differs a bit and is detailed on https://github.com/cytomine/Cytomine-IRIS.

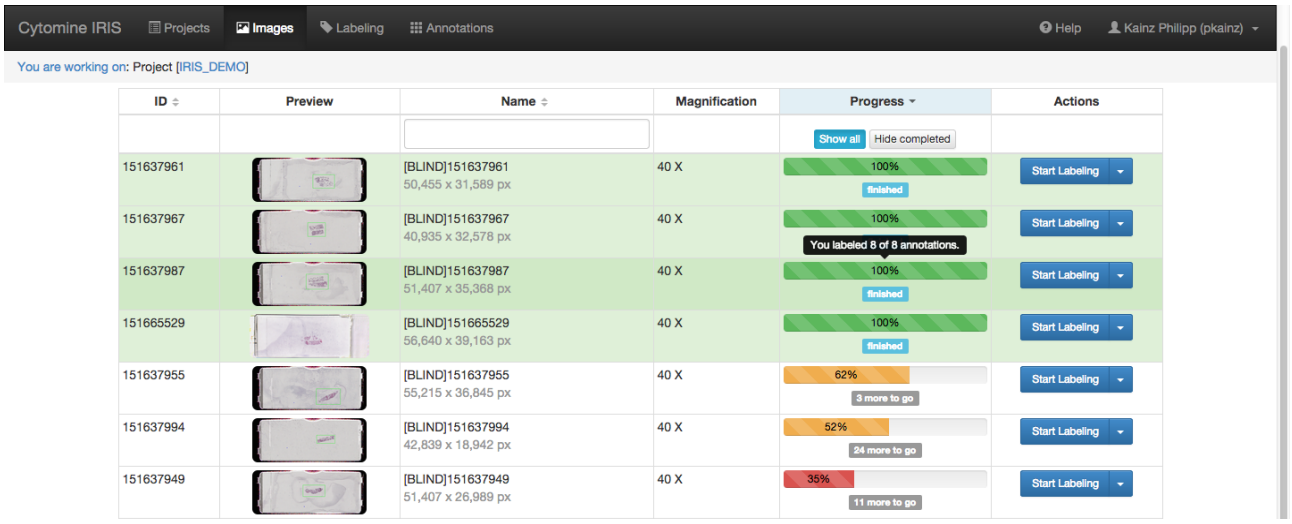
In contrast to previous sections, this user guide is based on larger dataset not yet publicly available and therefore it is not directly reproducible on our demo instance (http://demo-iris.cytomine.be/iris/index.html#/) but main functions are presented here to allow users to apply these concepts on a reduced "toy" dataset or on their own data.

Annotation Labeling and Reviewing

The structure of a standard Cytomine project is reflected in the workflow of IRIS: once a user logs into IRIS, a list of available projects is shown, where particular projects may be disabled just for this IRIS instance. In order to start labeling, the user opens a project and views a list of available images which contain the annotations:

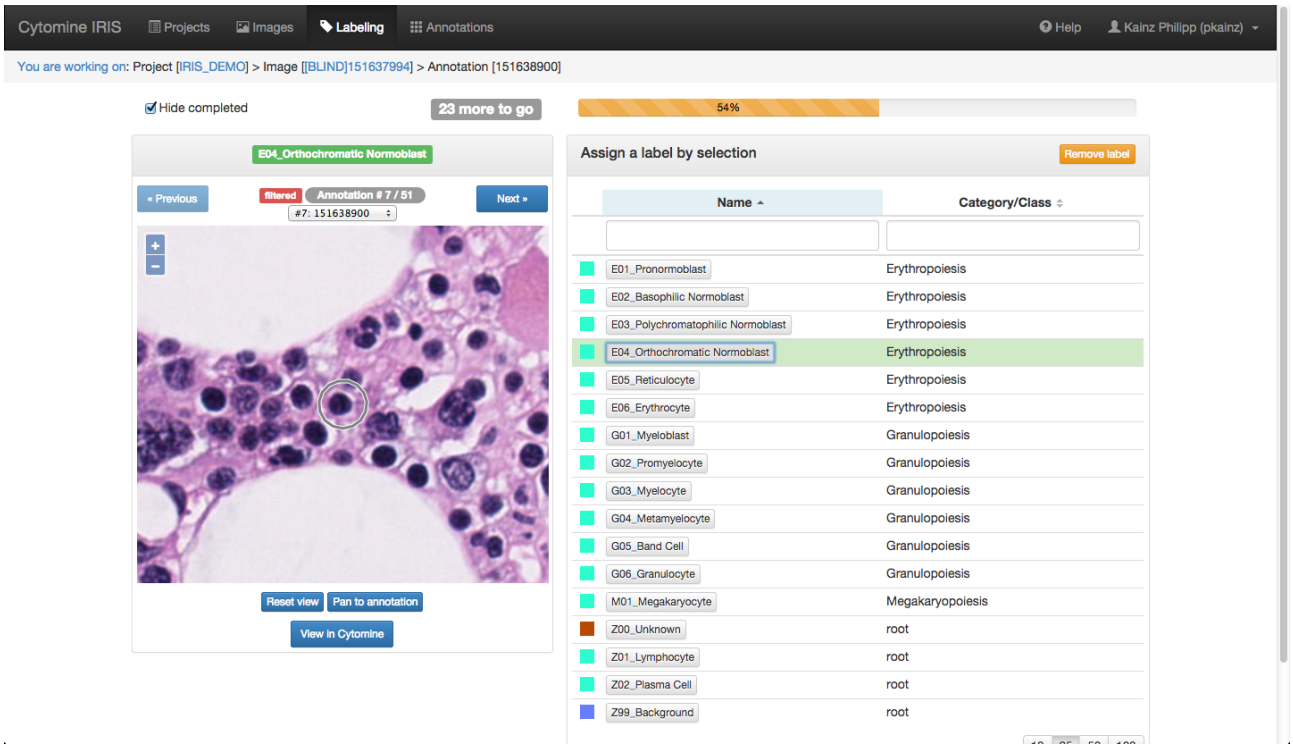


The image table also reflects the overall labeling progress within each image and provides functions for sorting and filtering. For example, this enables the user to filter out all images, where annotations are left to be labeled. This is particularly useful in situations where the study protocol requires all users to label all annotations, or when there are lots of images in a project.

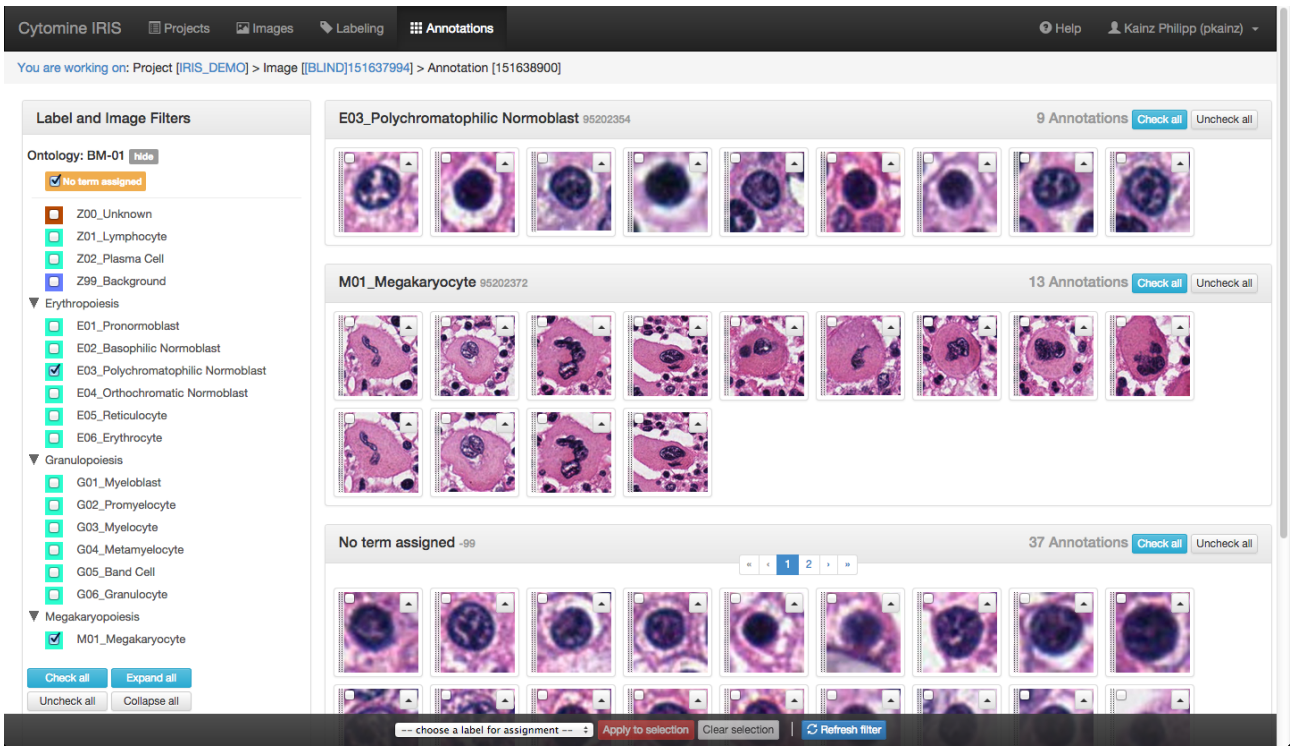


The annotation labeling can be performed per image in a dedicated view by selecting "Start Labeling" from the rightmost column. Image zooming and panning is available like in the main Cytomine-WebUI, allowing proper exploration of the image context of an annotation in order to

make an informed decision about the label. The user can hide annotations where a label already exists and thus just navigates through unlabeled annotations, while their order is preserved.
Navigation among annotations can be done either using the buttons above the image view or by pressing the keys “n” for the next, or “p” for the previous annotation. A label is assigned by simply selecting the term in the table on the right hand side, which is basically a flat representation of a possible hierarchical ontology:



It is convenient to view annotations in a gallery-like view per ontology term, which can be done by selecting “Annotations” from the menu bar at the top. This enables users to visually filter out outliers that do not comply e.g. with the appearance of the majority of annotations having the same label. Moreover, the gallery can display annotations across different images in a project and provides several methods to correct the label either directly or by navigating to the labeling view, if more context around the annotation is required. Multiple objects can also be re-assigned labels at once, which drastically reduces the time of manually navigating to the corresponding images and finding these annotations in the labeling view.



IRIS Sessions

In some scenarios, a single image may contain hundreds of annotations that sometimes cannot be assessed at once. Finding the exact annotation to continue is tedious and thus, IRIS preserves the current status of labeling across logins in sessions, such that the user can continue labeling at the exact same point where the application has been left last time. This can be done by simply going to any IRIS page and clicking on the current image name below the menu bar, or pressing the “r” key on the keyboard, which takes the user back to the labeling view in order to resume the labeling.

Interface Documentation: Help Pages

Each view in IRIS has a dedicated help page that is accessible from the main menu bar (top right corner) or by pressing the “h” key. The pages contain instructions on how to handle the interface.

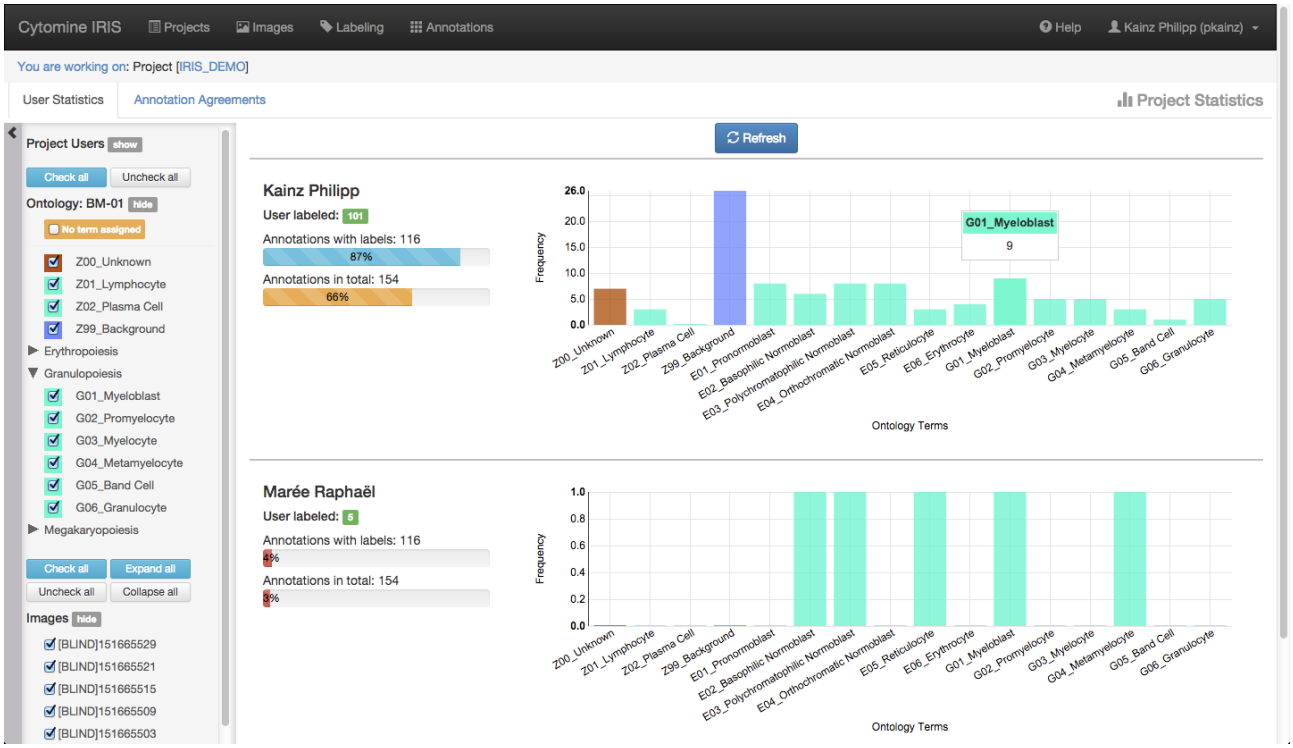
IRIS Project Coordination

The standard Cytomine user management is extended in IRIS by granting special rights to particular users: the IRIS project coordinators. Each user can request to become a project coordinator and they are authorized once as such by the administrator of the IRIS instance. Coordinators are able to view and visualize project statistics such as histograms of assigned ontology terms for all users or annotation agreements. Each of these visualizations also comes with a variety of filters for particular users, ontology terms and images. Moreover, they can manage project and image access settings for all users and authorize other users to become a project coordinator. Communication among access request and authorization is handled via email, using the email address encoded in the Cytomine User Account page.

Dashboard: User Statistics

The distribution of assigned terms can be evaluated for one or more users in the Statistics Dashboard of each project from the project table (project coordinators). This enables a quick

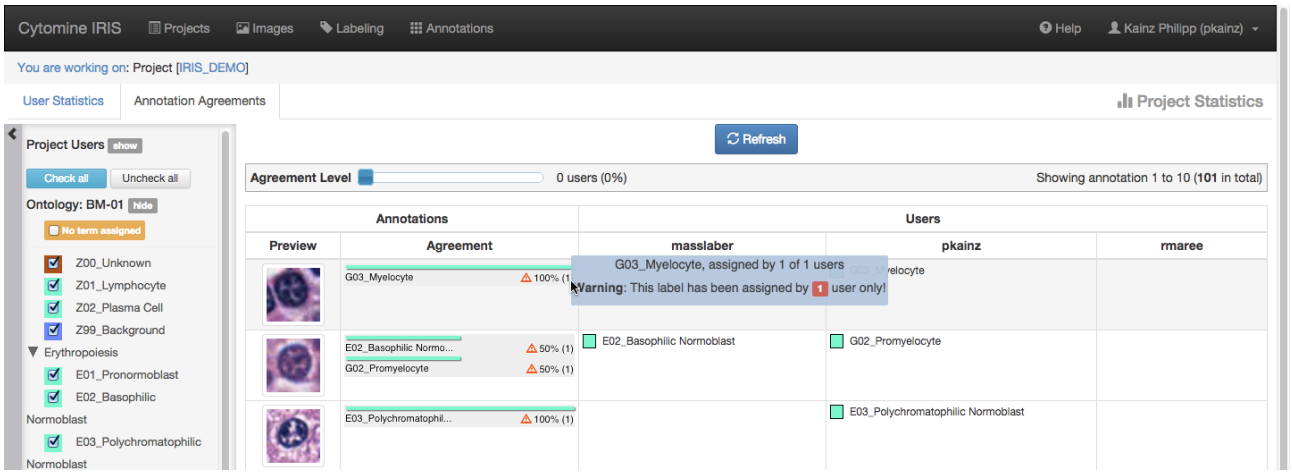
examination, for example, of whether one or more users are biased towards assigning a particular label. This also gives a clear picture of how many terms have already been assigned by the users with respect to the total number of assigned terms and the total number of available annotations.



The coordinator can combine several filters (users, ontology terms, images) to meet the current requirements of the query.

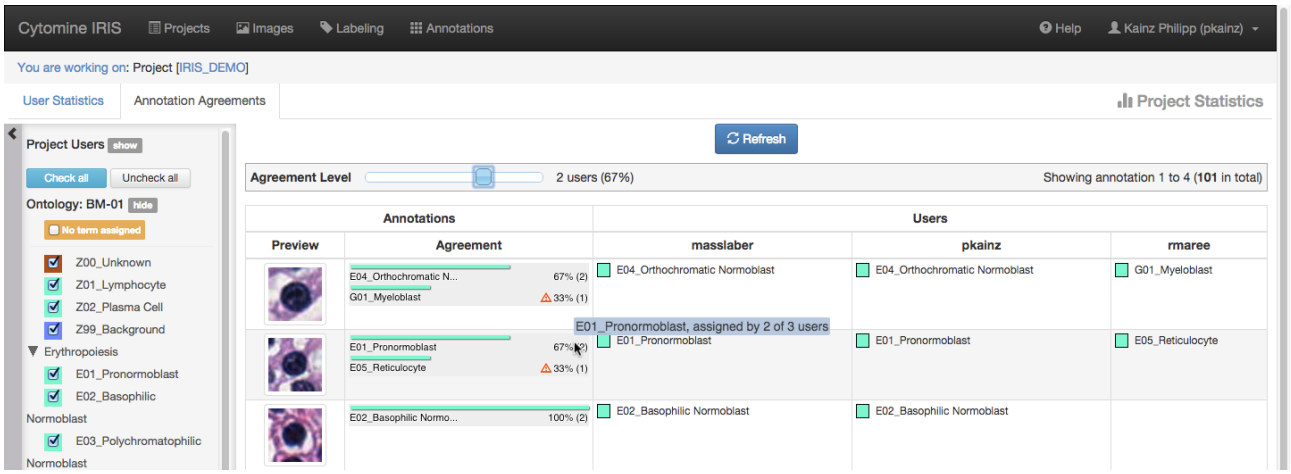
Dashboard: Observer Agreements per Annotation

Inter-observer variability of labeled annotations can be visualized in the Statistics Dashboard of a project by selecting the tab titled “Annotation Agreements”.



From the filter panel on the left hand side, a coordinator can construct the query and a list of annotations is shown. In addition, this result list can be filtered by annotation agreements using the “Agreement Level” slider at the top of the list. This slider's maximum value corresponds to the total

number of observers that assigned any label in the query. So if the slider is moved to the right, the agreement level increases and filters out annotations, where at least *n* or more observers are agreeing on one or more terms. Moving it to the right usually shrinks the list and hence all annotations in the smaller list have a higher level of inter-observer agreement.



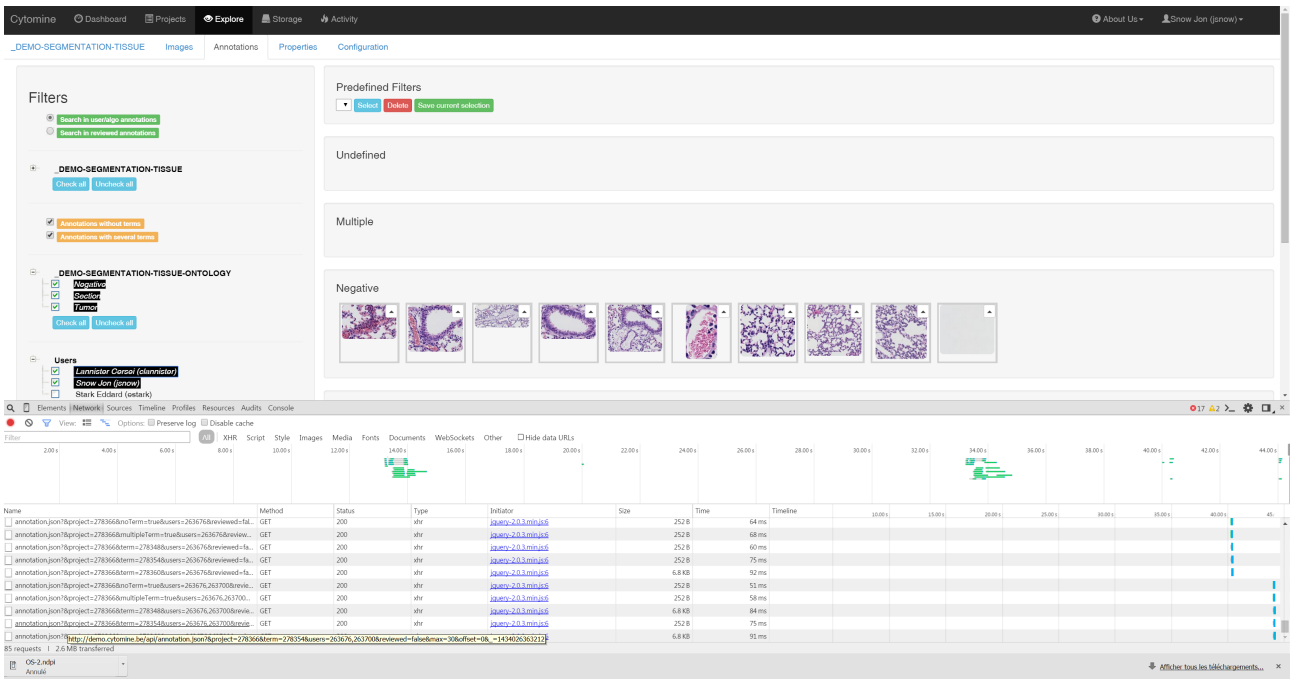
6.3 Usage (API documentation)

Cytomine documentation is available on http://doc.cytomine.be/
A documented RESTful API is continuoulsy updated and accessible online at
http://demo.cytomine.be/restApiDoc/?doc_url=http://demo.cytomine.be/restApiDoc/api#
If you install your own Cytomine instance, this documentation is also automatically installed on your server by our automated installation procedure and then available at:
http://$CORE_URL$/restApiDoc/?doc_url=http://$CORE_URL$/restApiDoc/api#

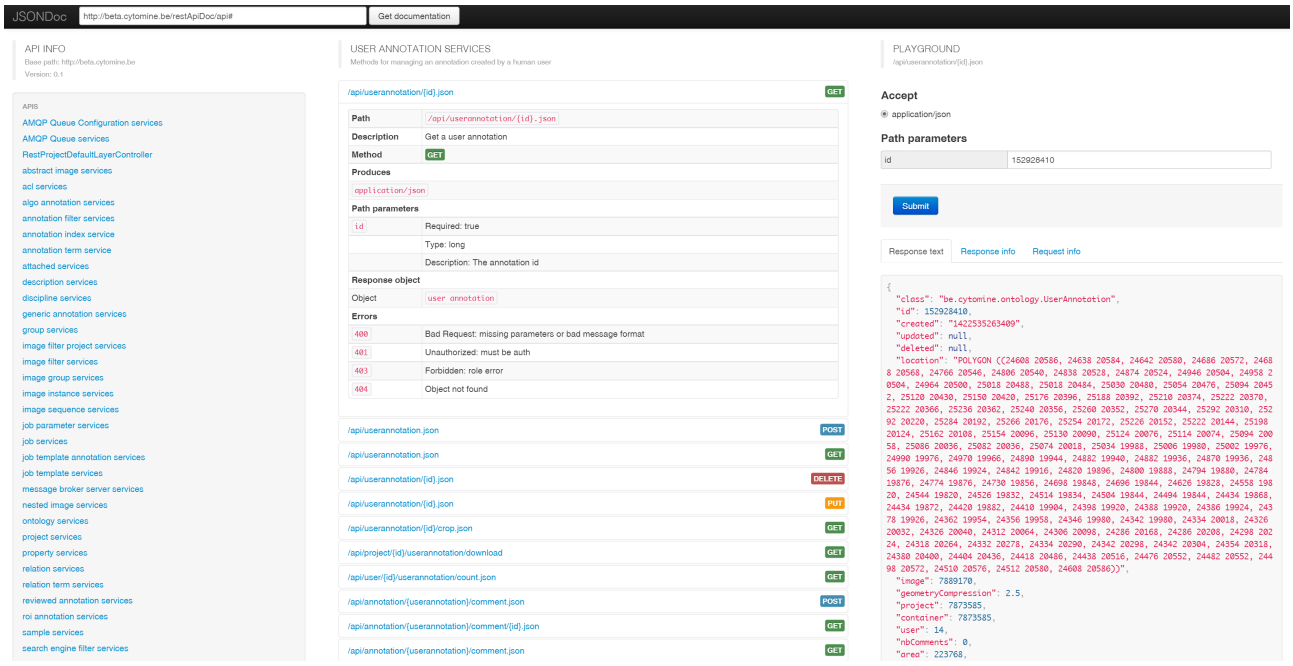
This API is used both by Cytomine-WebUI (including Cytomine-IRIS) and Cytomine-DataMining analysis modules. It can also be used by third-party software. Code examples that encapsulate http requests in Java and Python are provided here:

- https://github.com/cytomine/Cytomine-java-client/tree/master/src/main/java/be/cytomine/client/sample
- https://github.com/cytomine/Cytomine-python-client/tree/master/client/examples

Web users can inspect communications between their web browser and Cytomine components through the "Network" tab in the "Inspect Element" (Google Chrome)/"Inspector" (Mozilla Firefox) module of their web browser:



In addition, the API online documentation includes a "Playground" for each web service that allows the user to test server responses according to user input (e.g. here we use the service to get annotation description given an annotation identifier):



The following table give some examples of URLs to export data (using jsnow username account on demo.cytomine.be):

URL example	**Description**
http://demo.cytomine.be/api/user.json	List of users (JSON)
http://demo.cytomine.be/api/user/263676.json	Description of a specific user (JSON)
http://demo.cytomine.be/api/project.json	List of projects (JSON)
http://demo.cytomine.be/api/project/528050.json	Descrpition of a specific project (JSON)
http://demo.cytomine.be/api/project/528050/imageinstance.json	List of images in a specific project (JSON)
http://demo.cytomine.be/api/imageinstance/528460.json	Description of a specific image (JSON)
http://demo.cytomine.be/api/abstractimage/528120/thumb.png?maxSize=1024	Thumbnail of a specific image (PNG)
http://demo.cytomine.be/api/annotation.json?&project=528050	List of annotations in a specific project (JSON)
http://demo.cytomine.be/api/annotation.json?&project=528050&term=528044&users=263676&images=528132	List of annotations of a specific ontology term, in a specific project, for a specific user (human or userjob), in a specific image (JSON)
http://demo.cytomine.be/api/annotation/528401.json	Description of a specific annotation (JSON)
http://demo.cytomine.be/api/userannotation/528401/crop.png	Crop image of a specific annotation (PNG)
http://demo.cytomine.be/api/userannotation/528401/crop.png?increaseArea=2	Crop image of a specific annotation (PNG) with context
http://demo.cytomine.be/api/userannotation/528401/crop.png?zoom=2	Crop image of a specific annotation at zoom level 2 (PNG)
http://demo.cytomine.be/api/userannotation/528401/crop.png?zoom=2&mask=true	Crop binary mask of a specific annotation at zoom level 2 (PNG)
http://demo.cytomine.be/api/userannotation/528401/crop.png?zoom=2&alphaMask=true	Crop alpha mask of a specific annotation at zoom level 2 (PNG)
http://demo.cytomine.be/api/imageinstance/528460/window-23181-14285-1000-1000.png	Tile of size 1000x1000 at a specific location (23181,14285) in a specific image (PNG)
http://demo.cytomine.be/api/imageinstance/528460/window-23181-14285-1000-1000.png?mask=true&review=true&terms=528044	Tile reviewed mask of size 1000x1000 at a specific location (23181,14285) for a specific ontogy term in a specific image (PNG)
http://demo.cytomine.be/api/job/1939560.json	Description of a specific job (JSON) including software parameter values