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## CyTest – An Innovative Open-source Platform for Training and Testing in Cytopathology

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### Abstract

This paper describes an e-learning platform developed in the context of the European Project CyTest (2014-1-IT01-KA202-002607), dedicated to Cytological Training at European Standard through Telepathology. The main, and novel, feature of our system is the deep integration between virtual microscopy and the training system: images are not simply there to be seen but they are active parts of testing, supporting quantitative measurement of image comprehension, for instance by evaluating the identification of relevant cellular structures by the position of markers put by the student on the image. The solution we developed offers a complete tool for easy creation and interactive access to questions related to images and fully integrates the components of virtual microscopy and teaching, based on state-of-the-art instruments for digital pathology images management, as OMERO, and for training course distribution, as Moodle. The system can be easily extended to support histopathological diagnosis. The software is distributed as Open Source and available on GitHub.

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## 1. Introduction

Understanding of organ and tissue structure, at cellular level, is a basic requirement for Medical education and demonstration of histological and cytological slides at microscopes are part of the training in medical and biological courses, worldwide.

For various reasons, mainly economical, demonstrations at the microscope have in recent times become less practiced, and are encountering difficulties in many Universities (see Boyce, 2015).

The use of scanned images distributed and commented via Internet (s.c. Virtual Microscope) could overcome the difficulties and result in making histological and cytological examination more popular (see Dee, 2009). A proper setting would be to offer the functionality of a microscope via an interactive application, to be integrated within the Learning Management System of the University. Definite advantages would be the reduced economic cost (compared to the acquirement of several microscopes), the flexibility linked to the fact that students could practice Virtual Microscopy in times and places of preference and even the feeling that this approach could appear “cool” to young people, as compared to the technicality of managing a microscope, adjusting view and magnification, focusing etc... (as cited by Herrmann et al., 2015 and Ordi et al., 2015).

In order to reach the goal, and to build up a profitable learning approach, the setting should be user-friendly and allow examination of histological and cytological preparation at different magnification, the navigation being conducted by setting markers in combination with explanatory text within the images to directly point interesting areas or cells within the digital sample. Moreover, the teaching should not only be passive and interactive frames should be included. This is specifically critical in Cytopathology, where preparations are unique and not easily reproducible (as cited by Young, 1994 and Al-Janabi et al. 2011).

In this paper we will describe an Open-source e-learning platform, which supports bioimages sharing, with an integrated virtual microscopy capability, and enables remote and interactive training for cytologists. There are already works describing dedicated platforms mostly focused on associating digital pathology slides to categories like diseases or anatomical sites for both reference and e-learning where images are just displayed to be seen and no interaction with them is available (see Sinn, 2013). Other platforms make use of markers on the images to focus the attention of the students (see Rehatschek, 2011). With our work, we aimed to provide a new approach to obtain integration between the virtual microscopy and the training system, images are now an active part of the testing process allowing teachers to define new kinds of questions involving direct interaction by the students with the image.

## 2. Materials and Methods

The primary features of the e-learning platform we developed are bioimages management and cytologist training courses distribution: this section describes the implementation choices made to realize the infrastructure, illustrated in Fig. 1.

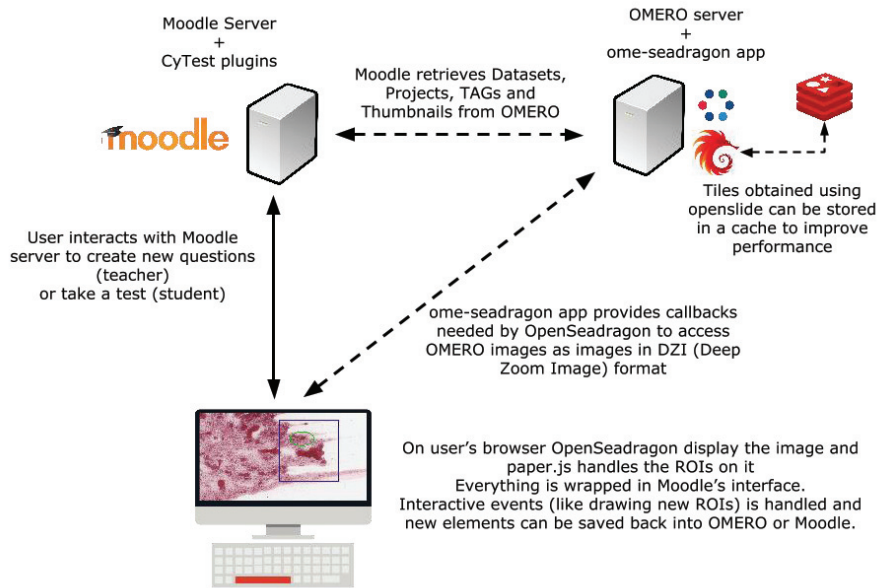


Fig. 1 - The e-learning platform architecture

### 2.1. Bioimages Management System

The infrastructure component devoted to digital pathology images management is based on:

- OME OMERO platform, an open source software “for visualization, management and analysis of biological microscope images”;
- *ome-seadragon*, the platform specialized viewer we developed.

OMERO (see Allan et al., 2012) has been chosen since it can handle a wide range of bioimages formats, it supports image metadata management and it can be easily extended. OMERO, in fact, is compatible with more than 140 different image formats with an almost complete coverage of the digital pathology ones and natively offers the possibility of storing meta-information, like classification TAGs or Regions of interest (ROI) associated to an image. The access to the images can be both via a Java client (OMERO.insight) and via a web application (OMERO.web). OMERO is a de-facto reference system for bioimages management in research with thousands of running installations worldwide.

To simplify the integration of the images stored within OMERO into an external web system we developed a specialized web application, *ome-seadragon*. It's based on the OpenSeadragon viewer (version 2.1.0, 2015), an open-source viewer for high resolution images like the ones produced by a digital pathology scanner, and an overlay system developed using paper.js (version 0.9.25, 2015), a javascript library for vectorial graphic on web, to handle ROIs defined on the image. Our web application acts like a middleware between OMERO.server and our viewer and converts images to DZI (Deep Zoom Image) format, an XML specification defined and maintained by Microsoft (see file format overview in Microsoft's Developer Network website), using the openslide library (version 3.4.1, 2015). Fast access to the tiles produced by openslide can be optionally provided enabling a cache mechanism, developed using redis (version 3.0, 2016) as backend.

The server-side application of *ome-seadragon* exports the default URLs used by an OpenSeadragon viewer that wants to display a DZI image. The client-side part of the application is basically a Javascript API that can be used to easily create an instance of the viewer and place over it an overlay where shapes retrieved from OMERO (the ROIs) are drawn using the paper.js library.

Our Javascript API handles the proper conversions needed to adapt a paper.js canvas over the image viewer and bind the two elements in order to handle events propagation (for example, a zoom on the OpenSeadragon viewer will be extended to the paper.js canvas). The client also provides a set of tools that will enable users to define new ROIs on the image and save them on a third-party system.

## 2.2. Training Course Distribution

The component supporting training course distribution is based on Moodle (Modular Object-Oriented Dynamic Learning Environment) (version 2.9, 2015), an open source platform for the creation of personalized learning management system. Moodle is adopted by a vast number of academic institutions and enterprises and provides a set of tools to design training environments that are robust, secure, modular and highly customizable.

We developed a set of Moodle plugins to obtain proper integration with OMERO and to add new types of questions based on images. As an example, some customized modules enable the access to OMERO images as if they were in a standard Moodle repository. Using these components, teachers can navigate OMERO repository by Datasets and Projects and by the TAGs used to classify images, as shown in Fig. 2.

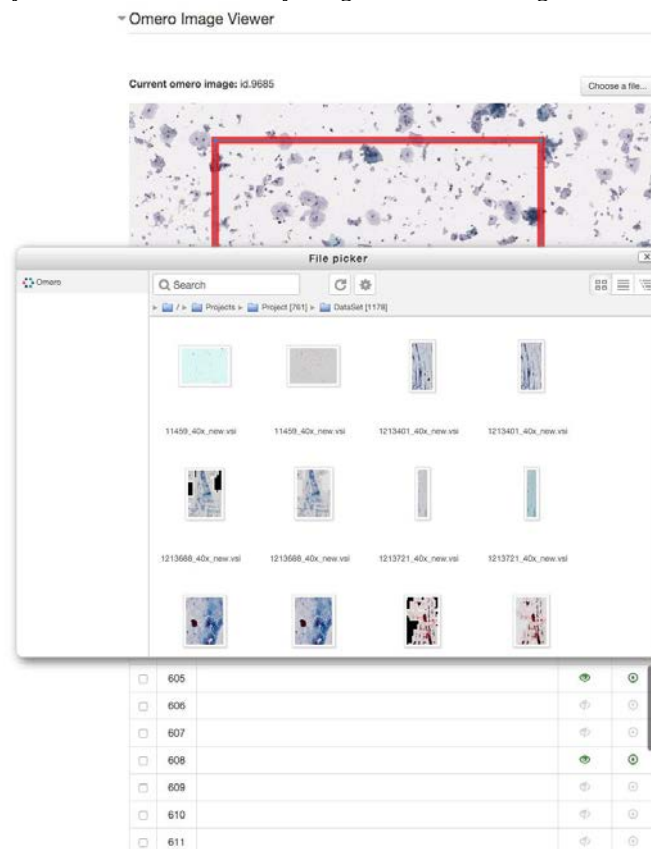


Fig. 2 - Navigation in OMERO repository for images selection during question preparation

The current version of the system supports two different types of questions:

- **questions with answer based on images** (Fig. 3): images are displayed only as a reference for the question. Teacher must only choose which image and, optionally, ROIs will be displayed; students could have controls to navigate the image;
- **questions based on answers given interactively on images** (Fig. 4 and Fig.5): answers must be given as markers on the images. Teacher must choose an image and a set of related ROIs; the ROIs are then divided in two groups: those that can be displayed as a guide for the student, and those that identify regions of the image that are considered by the teacher as good possible answers; students won't see the latter type of ROIs but only the "guide type". Students can drop one or more marks (the teacher can set this limit) on the image and the Moodle plugin will calculate the score based on the position of the markers with respect to the ROIs selected by the teacher.



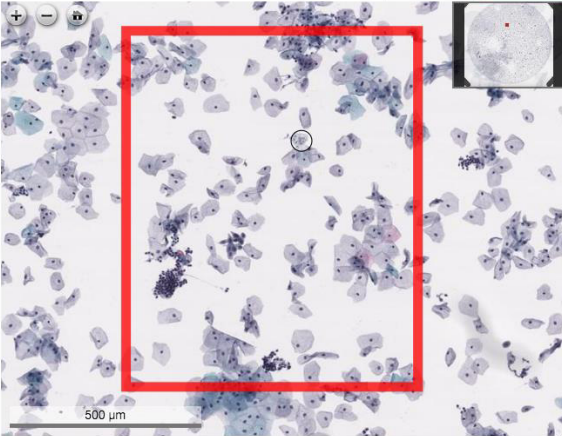
Fig. 3 - Multiple choice question example

**Question 1**  
Not yet answered  
Marked out of 1.00

58 years old. Thin Prep

Please click on the cells diagnostic of ASC-US in the red-squared area. (1 click)

+ Add Edit Clear



(x,y): 44129.099993099, 22640.544843915

\* Focus Areas:

\* Your markers: Marker 1

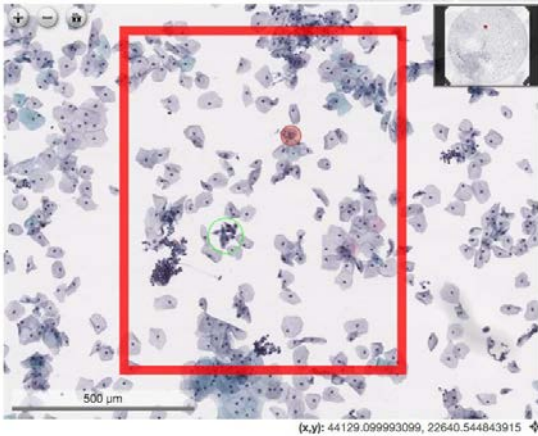
Fig. 4 - Interactive question example: the student answers the question adding a marker in the focus area inside the rectangle

**Question 1**  
Incorrect  
Mark 0.00 out of 1.00

58 years old. Thin Prep

Please click on the cells diagnostic of ASC-US in the red-squared area. (1 click)

+ Add Edit Clear



(x,y): 44129.099993099, 22640.544843915

\* Focus Areas:

\* Your markers: Marker 1

The set of ROIs (Regions Of Interest) of this question is:

- [896]

Fig.5 – Interactive question example: the correct answer is displayed as a feedback for the student

### 3. Results

The result of our work is a web platform for virtual microscopy images -- and bioimages in general -- distribution and e-learning specialized for cytologists. The platform is currently being populated, there are currently many hundreds of images, the CyTest system will be distributed for validation by October 2016. All the software is available as Open Source and the source code can be downloaded from GitHub.

Moodle and OMERO are the core technologies for the platform developed: the Moodle server provides access to the training system and acts as a gateway to images and meta-information on them (like ROIs and classification TAGs); the OMERO server and the ome-seadragon web application are the components that actually manage and store data related to the images.

The system enables students to take classes and tests and teachers to easily create personalized courses, inventing questions based on the images previously loaded and annotated and aggregating them in quizzes to enrich the Question Bank.

### 4. Conclusions

The main, and novel, feature of our system is the deep integration between virtual microscopy and the training system: images are not simply there to be seen but they are active parts of testing, supporting quantitative measurement of image comprehension, for instance by evaluating the identification of relevant cellular structures by the position of markers put by the student on the image.

The system has been developed in the context of the European Project CyTest, focused on Cytological Training at European Standard through Telepathology (2014-1-IT01-KA202-002607). The final goal of this Project is to provide, in collaboration with the European Federation of Cytological Societies, an easy approach for teaching, testing and quality assessment of Cytopathology. The platform can also be considered as a basis to realize an e-QUATE (Quality Assurance, Training and Examinations committee) test at European level (see Branca et al., 2000).

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