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# An adaptable navigation strategy for Virtual Microscopy from mobile platforms

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ABSTRACT

Real integration of Virtual Microscopy with the pathologist service workflow requires the design of adaptable strategies for any hospital service to interact with a set of Whole Slide Images. Nowadays, mobile devices have the actual potential of supporting an online pervasive network of specialists working together. However, such devices are still very limited. This article introduces a novel highly adaptable strategy for streaming and visualizing WSI from mobile devices. The presented approach effectively exploits and extends the granularity of the JPEG2000 standard and integrates it with different strategies to achieve a lossless, loosely-coupled, decoder and platform independent implementation, adaptable to any interaction model. The performance was evaluated by two expert pathologists interacting with a set of 20 virtual slides. The method efficiently uses the available device resources: the memory usage did not exceed a 7% of the device capacity while the decoding times were smaller than the 200 ms per Region of Interest, i.e., a window of $256 \times 256$ pixels. This model is easily adaptable to other medical imaging scenarios.



## 1. Introduction

Virtual Microscopy (VM) may be thought of as a collection of techniques that facilitate a set of Whole Slide Images (WSIs) can be examined from any place and at any time. Typically, a histopathological specimen is digitized at the higher possible magnification to provide the pathologist with the required information for diagnostic, research, training or educational tasks [1]. During the last decade, the dynamic interpretation of WSIs has been integrated with many pathology activities such as teaching, research, digital archiving, teleconsultation, and quality assurance testing [2]. Different works have studied the viability and agreement of diagnoses by using WSIs, reporting promising results [3,2,4]. Recently, medical schools in the United States have introduced digital pathology courses and virtual slide laboratories, promoting a generation of pathology trainers who may prefer digital pathology imaging over the traditional hands-on light microscopy [5]. A large variety of technical solutions supported these studies, e.g., Aperio ImageScope [3], home systems such as U-DPS [2], DMetrix Digital Eyepiece [5] or WebScope [4], indicating little agreement has been so far accomplished.

Several technical and logistical barriers have delayed WSI becomes a widely accepted pathology modality [6]. A proper management of the number of files generated by a WSI demands large memory, processing and storage resources since the size of a WSI is typically on the order of gigabytes. Furthermore, since there is not a common image format for virtual slides, a large number of proprietary or vendor-specific formats has been constantly modified as long as new scanners have been introduced [7]. Standardization not only allows an user to perform certain functions in an optimal way, but it also offers quality guarantees, interoperability, independency from vendors and equipments, access to new technologies and possibilities to scale applications according to new requirements. A wider VM use will require full integration with laboratory information systems, seamless connectivity over broadband networks, efficient workstations, cost-effective storage solutions and standards-based informatics transactions for integrating information with WSI [5,6,8]. Lately, image quality improvements, smaller scan times and image-viewing browsers have converted digital pathology into an actual opportunity [6]. Overall, actual clinical scenarios require access to these files from any location, reason by which mobile devices might be considered as the support nodes of a VM network. However, such devices are still very resource limited [9] and, yet communication channels have remarkably improved, network bandwidths are frequently insufficient.

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This problem has been addressed using a variety of approaches, the most common consisting in constructing pyramidal data structures that deal with different image scales that are stored as independent files [10]. For a requested Region of Interest (RoI) to be displayed, a complex combination of pyramidal files must be composed and this is usually computationally expensive. These pyramidal approaches have been evaluated from a VM standpoint, HD View, Zoomify, Gigapan and Google Earth, reporting pleasant interaction experiences when navigating a single WSI from a conventional computer [10]. Nevertheless, these approaches might be very limited when displaying a WSI from a low resource mobile device since in such a case, applications should deal with variable storage requirements, low compatibility, high processing demand and poor adaptation to different displays. Likewise, limited devices may have trouble managing a large number of files since their cache space may be easily overflowed. Aperio [11], a commercially available software allows an user to pan and zoom in and out virtual slides, but this system is computationally very demanding and requires a powerful infrastructure. Similar approaches are OpenSlide [12], NYU Virtual Microscope [13] and Deep Zoom (formerly called Seadragon) [14], among them, Openslide is an open source library devised to display WSIs and is compatible with different image formats. The NYU Virtual Microscope uses the Google Maps API and Deep Zoom is part of the Microsoft Silverlight platform, a proprietary software with a very limited mobile version. These last three applications are based on a pyramidal structure and share the limitations aforementioned for mobile devices. A different approach was proposed by Hadwiger et al. who introduced a multi-resolution virtual memory that performs dynamic updates and deals with missing data [15]. This system is not based on any standard, uses the lossy JPEG version and was devised to display data at a full resolution, a bottleneck in limited devices.

VM demands highly flexible, efficient, manufacturer independent and standard-based tools [7,16]. An alternative to the artificial pyramidal approach is the JPEG2000 standard, founded on the concept of making available any piece of required information, i.e., a particular spatial region at any desired quality and magnification. The standard appears to be flexible enough as to address the issue of streaming and visualizing demanding content in mobile devices [17], such as WSIs. This standard was smartly conceived to be granular, i.e., an image can be decomposed and compressed in small independent parts (grains) of information at different levels of magnification, several degrees of quality and independent spatial representation, facilitating a separated access and process of specific regions of the image, while also supporting large file sizes and a larger dynamic range of the pixel representation [18]. In addition, by the JPIP (JPEG2000 Interactive Protocol) standard, the client may demand specific RoIs from the server, instead of remotely accessing the whole JPEG2000 content [19]. Nevertheless, the JPEG2000 standard complexity may make it very expensive in computational terms [7] and therefore unrealistic at supporting a VM network. Basically, data allocation can be an actual burden of the navigation while the decoding process may be on the order of 2–5 s, even when decoding a small VS of $9000 \times 12{,}000$ pixels. There exist some applications using different JPEG2000 implementations, all of them decompressing data at the server side and leaving to the client a purely passive role at receiving the raw decoded information to be displayed, for instance IIPImage [20], Djatoka [21], JVSMicroscope [7] and Web Microscope [22], being the latter a reference in certain academic and clinical institutions. This strategy throws away the JPEG2000 high compression rates since only uncompressed data are transmitted and ignores the potential processing improvement at the client side. Other works have explored the JPEG2000 as an interaction tool for VM by modifying the decoder implementation, retrieving and decompressing specific portions of the codestream [23–25], unfortunately, this tightly-coupled solution could be hardly extended to different platforms. Finally, Rosenbaum et al. proposed to send only the RoI encoded information and to complete the missing codestream (untransmitted) at the client side with a pre-defined template [17], but then the decompression times result equivalent because of the size of data.

This work introduces an adaptable and low computational cost VM framework that exploits the JPEG2000 potentiality at both the server and client sides. The possibility of meeting any requirement, i.e., any spatial region at any size, with a desired magnification and quality, makes this proposal adaptable to new scenarios, in particular to the training and educational VM. In that case, a group of pathologists or students, might simultaneously access the same WSI and therefore saturate the network. The main contributions of this work are:

- Unlike most existent solutions, this strategy has been devised to maximally exploit the processing resources at both the client and the server so the server sends compressed data and the client decompresses data, even under very limited computational capacity.
- A smart decoding strategy addressed to construct any RoI by setting the requested region to an image which can then be decompressed by any standard decoder.
- A flexible and scalable data management strategy that efficiently retrieves JPEG2000 compressed data at the server side, independently of the image size, by a coupled designed meta level index file.
- A loosely-coupled architecture, web service oriented, providing functionalities that support interoperable and standard interaction over the network. This highly adaptable architecture adjusts the content to the user requirements, the device capacity and the network bandwidth, while it offers a progressive lossless visualization.

## 2. Materials and methods

### 2.1. JPEG2000 overview

JPEG2000 is a highly flexible image coding standard that optimizes interaction with compressed data [26,27]. A key feature of this standard is that it encodes multiple resolution levels and quality layers. Resolution is related with the number of pixels that are needed to ensure that, at a particular image size, the displayed information is maximum. In contrast, the quality is a function of the number of bits that are used to represent a pixel. Resolution flexibility implies that an image can be retrieved at a low resolution (a small version of the image) and can be enlarged (by a factor of two) by adding the missing data and only these data [28]. The quality is connected with the concept of progressive user interaction and consists in displaying a very basic version of the image, with few details, that are progressively added as long as the user demands more information, until reaching a full lossless visualization, if needed [28].

The JPEG2000 norm is based on the Discrete Wavelet Transform (DWT) and the Embedded Block Coding with Optimal Truncation (EBCOT), both endowing the data representation with high granularity [29] (see Fig. 1). The DWT decomposes the input image into frequency subbands, producing a natural multi-resolution decomposition, with basically two wavelets: the Daubechies 9-7 for lossy compression, and the reversible Daubechies 5-3 for lossless compression [30]. The DWT image is divided into tiles that allow random access to spatial regions with different frequential information. The EBCOT compresses the image into small blocks (code-blocks) that encode the DWT coefficients of each subband. Each of the codeblocks, composed of a set of bit-planes, is ordered