# Efficient Virtual Slide Telepathology Systems with JPEG2000

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## **ABSTRACT**

In the present paper we analyze the JPEG2000 standard and how to exploit all the offered powerful features to build efficient telepathology systems based on virtual slides. We also propose a fast method for stitching in the wavelet domain. Stitching is a process necessary in many virtual slide systems to generate only one composed image of a slide with a high resolution. The proposed method profits from the structure of the JPEG2000 images to carry out the process with the minimum memory consumption and computational load, obtaining a smoothed union without losing any detail.

# **INTRODUCTION**

Telepathology is the practice of the pathology at distance. A pathologist can make diagnostics by observing through a communication link the medical slides captured by a remote microscope. This way the localization of the pathologist and the medical slides are unbound. For example, diagnostics of pathologists from different centers can be compared and shared.

There are different kinds of telepathology systems, all of them commented in [1]. The first generation of these systems consists of the acquisition of the microscope image, either in real-time mode or in store-and-forward mode, and its sending to the pathologist. This can remotely manipulate the microscope to select the slide region to visualize, requiring a new acquisition whenever this region changes. In these systems the operator is always bound to the microscope, so any session requires using in an exclusive way this device. The use of the device is clearly inefficient and redundant.

The second generation of telepathology systems introduces the concept of virtual slide. Virtual slides are digitizations of complete slides, that are stored in a server for its later remotely inspection. A client/server architecture allows pathologists to navigate remotely through the virtual slides, simulating the working of a microscope. Different regions of the virtual slide can be observed, allowing to increase o decrease the zoom, without having to download the entire remote image. The server sends only the required data to see. Pathologists have in this way the sensation of working with a virtual remote microscope, with the difference that, in this case, the digitization is made in a previous step, of the whole slide. It is not necessary to reuse the microscope for the same slide. In [2] it is proposed a possible implementation of a system with these characteristics.

To obtain a digitization of the entire slide with the enough quality for a correct diagnostic, it must have, among other features, the appropriate resolution. Complying with this premise is not always possible with the available acquisition device. In many cases its resolution is not enough to cover the entire slide in order to digitize without losing detail. In these cases the slide is divided in contiguous regions in order that each region is digitized with the maximum resolution of the device. In a posterior step all the resulting images are joined in a stitching process, generating only one big image with the necessary detail.

The JPEG2000 still image compression standard is being imposed in the context of imaging medical systems, due to its powerful features. Telepathology systems are being favoured with the characteristics of this standard. For example, in [3] a new method for demosaicking microscope images based on this standard is proposed, showing how to integrate it within a telediagnosis system. The quality of the image compressed with JPEG2000 for the same bit-rate is quite higher than that offered by its predecessor, the JPEG standard, as it can be observed in [4]. This feature is essential in systems based on virtual slides.

JPEG2000 offers a high scalability, allowing a random access to the compressed bit-stream of the image, as well as its transmission by means of a quality progression. These features are specially interesting in the virtual slides context, allowing the server to extract regions of the images without recoding, and sending them adapting the communication to the available bandwidth. The JPIP protocol is defined within the same standard, designed to exploit at the maximum the features of this compression standard in remote browsing applications, as for example, telepathology virtual slide systems.

In the present paper the main features of the JPEG2000 standard are analyzed, as well as the JPIP protocol, showing how they can be used to build efficient telepathology virtual slide systems. It is also proposed a fast and simple method to construct virtual slides based on the stitching in the domain of the wavelet transform. With this method the necessary time and memory for the process are considerably reduced. Moreover, the image boundaries of the final montage appear quite smoothed without any additional processing or quality lost.

#### JPEG2000 FOR VIRTUAL SLIDES

JPEG2000 is based on the dyadic DWT (Discrete Wavelet Transform). Figure 1 shows how the DWT decomposes an image in 1+3D spatial frequency subbands, where D is the number of analysis transform stages. The stage d generates four subbands  $LL_d$ ,  $HL_d$ ,  $LH_d$  and  $HH_d$ . L stands for the low-pass filter and H for the high-pass filter, and its position is associated to the direction of the filter (left when horizontally and right when vertically). Each stage d is applied to the  $LL_{d-1}$  subband, or the entire image when d=0. As it can be observed, applying D analysis stages a multiresolution representation of the image is generated, with D+1 different levels. Using the subbands  $LL_r$ ,  $HL_r$ ,  $LH_r$  and  $HH_r$ , the resolution level r can be reconstructed.

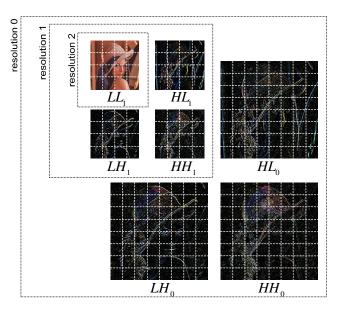


Figure 1. 2 DWT stages (3 resolution levels) applied to the *Lena* image, partitioned by code-blocks.

Each subband is divided into rectangular blocks called code-blocks which are independently coded and compressed. Code-blocks are collected in larger rectangular groups called precincts. The size of the code-blocks and the precincts determines the granularity for a later access to the compressed stream. This data organization is made for each image component.

The code-blocks are related to rectangular regions within each DWT subband but, the precincts are related to rectangular regions within each resolution level, in the image domain. For example, a precinct of the resolution level r would contain all the code-blocks belonging to the same spatial region, within the subbands  $HL_r$ ,  $LH_r$  and  $HH_r$  (or  $LL_{r-1}$  if r=D).

The compression process generates a list of concatenated packets. A packet includes an incremental contribution of all the code-blocks of a precinct. For each precinct there are as many packets as quality layers defined when compressing. The number of quality layers determines the scalability in quality.

The standard is organized in several parts. Part 1 [5] describes the compression system and how to build the simplest code-stream. This code-stream contains the packets generated by the image compression process and additional information. The simplest JPEG2000 image file format contains a code-stream, without any other addition. In this Part of the standard a more complex image file format is also defined, allowing to include any user metadata information. This is specially exploitable in telepathology systems. For example, in [6] it is proposed to include patient XML data within the same image file of the digitalized slide.

Part 9 [7] covers the definition of a new protocol, JPIP (JPeg2000 Interactive Protocol), as well as a framework to develop systems for remote browsing of JPEG2000 images. Figure 2 shows a representation of the client/server structure proposed for this new protocol.

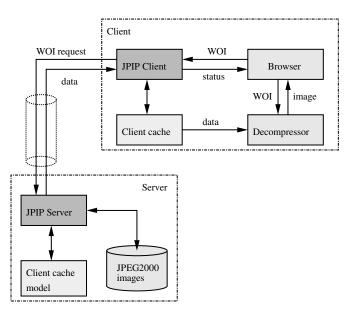


Figure 2. Client/server structure proposed for the JPIP protocol.

On the client side, the user specifies a WOI (Window Of Interest) using the application browser. The WOI defines the region of the remote image that the user wants to see. This WOI is passed to the JPIP client module and the decompressor module. The first one manages the communication with the server, elaborating the corresponding request and reading the response from the server. When the information is read, it is stored in the internal cache. The decompressor module will gather the required cache information to reconstruct the WOI image, which will be shown to the user by the browser module. When the JPIP server receives a client request for a specific WOI, it reads the associated image extracting the appropriate information which must be

sent to the client in order to reconstruct the requested WOI. Thanks to the high scalability offered by JPEG2000, this extraction can be done with a minimum of computational load. The server optionally maintains a model of the client cache that is used to avoid resending redundant information to the client.

All the commented features offered by the JPEG2000 standard allow to build highly efficient telepathology systems based on virtual slides. All the images would be compressed with this standard. The image files can be used independently, without being included within any other more complex file. As advantage it is possible to include any associated metada, as it is proposed in [6], and retrieve it with any common JPIP client, independently of the metadata format. The compression of the images would be done in order to obtain a good scalability, configuring a large number of quality layers and a small size for precincts. In this way the server can extract more exactly only the required data and send it adapting the communication to the existent bandwidth. The pathologist can inspect remotely the images using a JPIP client, so the architecture simulates a perfect virtual microscope.



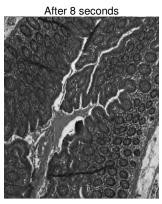


Figure 3. Tissue reconstruction at two different instants of time.

With the aim to give a little example of the performance of JPEG2000, we have used a JPIP client/server architecture to explore a remote image through a communication channel with a bandwidth limited to 4 KB/s (like an old modem). The image, about a medical tissue, has a resolution of 2618×1787 and a compressed size bigger than 2 MB. In Figure 3 two reconstructions of a WOI of 700×700, at two different instants of time, have been shown. As it can be observed, after only 2 seconds the user can decide if the WOI is the required one or not. And, after 6 seconds more, the user can observe a high quality reconstruction.

There are different JPEG2000 software packages, with support for JPIP, commercial as well as non-commercial, like for example Kakadu [8] or 2KAN [9]. The first one has been used in this work to develop the examples and evaluation experiments. These software packages allow to develop quickly JPIP client/server architectures that, with some additional modifications, could be fine virtual slide telepathology systems.

#### STITCHING IN THE DWT DOMAIN

In the previous Section it has been possible to observe that the JPEG2000 standard offers all the necessary features to create telepathology systems based on virtual slides, and furthermore these systems can achieve a high efficiency. There is also other aspect in the context of the virtual slides that can be considerably improved using JPEG2000: the stitching of images.

Virtual slides are created as a composition of a set of microscope images that contain information about contiguous areas of an entire slide. This composition or stitching consists basically of three global steps: i) unification, ii) search of the matching regions, and iii) union. In the first step the possible geometric distortion of the images is corrected in order to be able to join all the images in the same plane. The possible differences of illumination between the images, like for example the vignetting, are also corrected. In the second step the existent common regions between the images are searched, determining how to join them. Finally, in the last step, all the images are stitched, including a blending process too, smoothing the borders of the unions.

The more heterogeneous are the images to join the more complex are these three steps. In the concrete case of the images acquired with a microscope, in general, there is quite homogeneity between them. The geometric distortion is not common, and if it appears it can be identified and corrected independently in each image. The possible illumination differences or vignetting can be also corrected independently. The search of the matching regions consists of finding simple overlappings between the images, as translation displacements. The stitching process is applied using rectilinear borders.

The stitching process for generating virtual slides has less complexity than the process for generating other kinds of mosaic images, like for examples panoramas. In [10] the high complexity necessary of an automatic stitching method for panoramic images can be observed. The generation of virtual slides, as an image composition, does not require to take into account all the parameters and possibilities assumed in this work. This characteristic allows to develop efficient and fast automatic stitching methods. Next a new method that exploits the features of the JPEG2000 standard is proposed.

Here in after we assume that the acquired microscope images are initially processed, during the unification step, and after that they are compressed with JPEG2000, all of them with the same compression parameters (resolution levels, quality layers, etc.).

It is necessary to configure the compressor so that the precincts have the same spatial influence in each resolution level, as it is proposed in [11]. A certain precinct size for the resolution level 0 is chosen, and this is divided by 2 successively for the followings levels.

Thus, for each resolution level r, the precinct would have a size of  $p_{x,r}$  (width) and  $p_{y,r}$  (height) so that:

$$p_{x,r} = \frac{p_{x,r-1}}{2}$$
  $p_{y,r} = \frac{p_{y,r-1}}{2}$ 

This allows to access to the code-stream of the images with a finer granularity and to merge them without recoding when it was possible.

Due to the multiresolution representation of the compressed content of the JPEG2000 images, the second step of the stitching process can be made in two different hierarchical substeps, initial search and refinement, without having to decompress the entire contents. A graphic example of the search of the matching regions between two images can be observed in Figure 4. For the initial search, it is necessary to decompress only the smallest resolution level. After finding the matching regions, they are decompressed, using the biggest resolution level, to refine the precision. In this way a considerable amount of memory and computational load is saved.

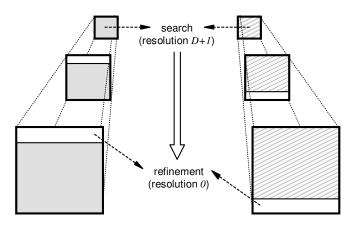


Figure 4. Scheme of the proposed two-steps search method.

In JPEG2000 the colour images are not usually compressed using the classic RGB components, but a transform is performed in order to generate other colour representations that allow bigger compression ratios. In these colour representations there is a component with the luminance content of the image. This component can be used to carry out the searching process, without having to decompress the rest of the image components.

Once the matching areas are found precisely, the joining process is made in the DWT domain. This implies to make a multiresolution stitching, as it appears in the example of Figure 5. From each subband from each resolution level the regions to join are extracted. For example, if the region to extract of an image is defined by (x, y, w, h), horizontal and vertical position and width and height, respectively, it would be necessary to extract the regions:

$$\left(\frac{x}{2^{(r+1)}}, \frac{y}{2^{(r+1)}}, \frac{w}{2^{(r+1)}}, \frac{h}{2^{(r+1)}}\right)$$

from the subbands  $LL_r$ ,  $HL_r$ ,  $LH_r$  and  $HH_r$  for  $r = \{0...D-1\}$ . Then the regions associated to the same subband, from each image, are joined. The final global result would be conceptually the same that the result of a DWT transform of the direct union of the images. Notice that the number of resolution levels of the result is the same that the number of resolution levels chosen when compressing the images.

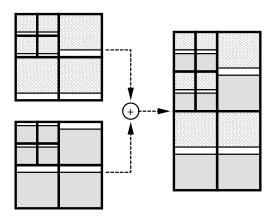


Figure 5. Example of the stitching process in the DWT domain.

There are two main advantages when the stitching process is made in the wavelet domain: i) the computation time is reduced and ii) the union borders are smoothed. The first advantage is given since the inverse DWT of each image to join and the DWT of the composed result is avoided.

Due to the properties of the frequential domain in which the stitching is made, the high frequencies of the union borders are reduced. This means that these borders are naturally smoothed in the image reconstruction. The more resolution levels are used, the more smoothed become the borders. The smoothness is even more efficient than other methods that are performed in the image domain, since these ones usually affect to the entire image, losing information. Carrying out the stitching process as here is proposed, only the union borders are smoothed, without affecting the rest of the content.

Since a smooth postprocessing is usually necessary when the virtual slide is composed, with the proposed stitching method would avoid this associated computation load.

The regions are joined in the wavelet domain but by means of the image precincts, since they are the basic organization unit when accessing to the code-stream content. Profiting that each precinct is compressed independently of the rest, we have not to recode all of them when joining the images. It is necessary to recode

only those precincts unaligned with the global precinct grid of the final composed result.

Notice that the final result, that is, the virtual slide composed after stitching all the images, has a global precinct organization that defines a grid for each resolution level. Every region to join has a specific position and size within this grid. The precincts of the regions that are not aligned with this grid need to be recoded in order to comply with the global organization. If the position of the region is not aligned, then all of their precincts will need to be recoded. If the position is aligned, probably only the precincts of the borders would need to be recoded.

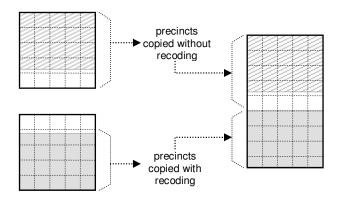


Figure 6. Example of how to join two regions within a resolution level.

Figure 6 shows a little example of how to join two different regions within a specific resolution level. As it can be observed the result image has a specific grid organization. The top region is completely aligned with this grid, so all their precincts can be copied without recoding at all. Nevertheless, the bottom region is not aligned, so all their precincts need to be recoded, that is, they are decompressed and their contents are aligned with the global grid and compressed again.

Joining the regions in this way allows to save a considerable amount of computation load and memory consumption, depending of the overlapping degree of the images

#### **EVALUATION**

In order to evaluate the proposed stitching method, we have obtained the necessary time to stitch each pair of images of two different sets. Neither the algorithm to select the pair of images nor the associated time is evaluated in this paper, since this is already well covered in other works, like [12] or [13]. The main goal of the experiments is to evaluate the performance of the stitching method, exploiting the features of the JPEG2000.

This time is compared to the obtained one using a classical method that consists of searching and joining in the image domain. Each pair of images would be

completely decompressed, processed, and compressed again.

The used search algorithm, for the two methods to compare, is based on finding the phase correlation between each pair of images. We have assumed that the images are homogeneous and geometrically compatibles. Every image can be expressed as a displacement of another. For the proposed method the phase correlation has been calculated for the lowest resolution level and has been refined in the highest one.

As it is used in [12] as well in [14] the Normalized Cross Correlation coefficient has been used to obtain the phase correlation. This coefficient is calculated with:

$$NCC = \frac{\sum (u - \overline{u})(v - \overline{v})}{\sqrt{\sum (u - \overline{u})^2 \sum (v - \overline{v})^2}}$$

where u and v are the images of the pair to stitch, and  $\overline{u}$  and  $\overline{v}$  their respective means. This calculus can be performed faster by means of the Fast Fourier Transform, and thereby the phase correlation would consist of looking for the peaks of:

$$F^{-1}\left\{rac{U{\cdot}V^*}{\left|U{\cdot}V^*
ight|}
ight\}$$

where  $U = F\{u\}$  and  $V = F\{v\}$ , F is the Fourier transform, and the asterisk stands for the conjugate.

The first image set (A) contains 36 images with a size of 2618 X 1787. The other image set (B) contains 25 images with a size of 3272 X 2469. Each image set is associated to a complete virtual slide, obtained from a microscope.

All the images have been compressed with JPEG2000 using these compression parameters:

Resolution levels: 6

Quality layers: 10

Code-block size: 64×64

## **RESULTS**

In Table 1 we have shown the average time percentage of the proposed stitching method in relation to the average time required for the classical method.

It is clear that exploiting the JPEG2000 features it is possible to reduce significantly the computation time of the stitching process. The virtual slide construction can

be performed quickly and with the minimum resource requirements.

In Figure 7 a detail of a union border is shown, comparing the result of the proposed method to the result of a simple method (simply join without smooth postprocessing).

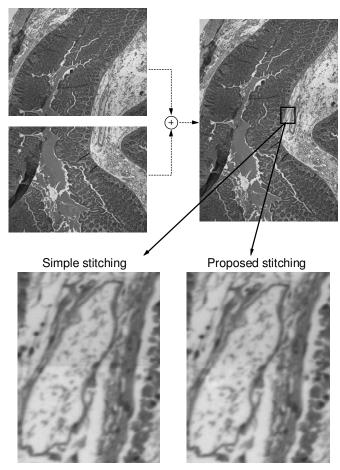


Figure 7. Comparison of the simple stitching and the proposed stitching.

The proposed stitching method can improve considerably the result, smoothing the union border without losing information. This border is noticeable due to, although the images are quite homogeneous, the illumination is not completely perfect.

Image set	Number of images	Image size	Time percentage
Α	36	2618×1787	1.05%
В	25	3272×2469	0.38%

Table 1. Average time percentage for the proposed stitching method in relation to the simple stitching method.

#### CONCLUSIONS

In this paper the main features of the JPEG2000 standard have been analyzed in order to exploit them to build highly efficient telepathology systems based on virtual slides.

A new automatic stitching method has been also proposed, based specially on the structure of this standard. This method reduces at the maximum the requirements of computation load and memory. Moreover, using this stitching method, the union borders are automatically smoothed without losing information.

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