DESIGN AND VALIDATION OF A LOW-COST TELEMICROSCOPY SYSTEM

Ignacio Prieto-Egido[1], Víctor García-Giganto[2], Alba González-Escalada[3] and Andrés Martínez-Fernández[1]
[1]*Department of Signal Theory and Communications, Rey Juan Carlos University, Fuenlabrada, Spain*
[2]*EHAS Foundation, Madrid, Spain*
[3]*Departments of Preventive Medicine and Public Health and Medical Immunology and Microbiology, Rey Juan Carlos University, Fuenlabrada Spain*

ABSTRACT

Microscopy is one of the main techniques in the diagnosis of diseases such as malaria, tuberculosis or diarrhoeal diseases. Diagnosis by microscopy requires specific knowledge and is usually performed by microbiology specialists. In health posts of rural areas of developing countries there are usually health technicians, who typically don't know to diagnose these target diseases. This paper presents the design and validation of a low-cost telemicroscopy system adapted to rural areas of developing countries. This system allows sharing the microscope image in real time, so that the specialist can lead the whole process and remotely provide a right diagnosis. The system uses a low-cost digital microscope camera to convert the microscope image to digital format, so any conventional microscope can be employed. The video streaming can be displayed directly on a web browser and the audio communication is established using VoIP. The system is implemented on a low-cost embedded system, Odroid-U3, and is based on open source software, so it can be easily replicated. A technical validation has been performed to check that the required bandwidth is lower than 500 kbps and that the video delay is below 1.5 seconds. The power consumption (including the local display system) is less than 15W and the total cost of the system is below $275. Finally, a preliminary clinical validation has been performed to prove that the system provides diagnose quality resolution.

KEYWORDS

Telemicroscopy, e-Health, telemedicine, rural areas of developing countries, open source software, embedded systems

1. INTRODUCTION

Rural areas of developing countries are characterised by a lack of resources, a low population density and a shortage of communication infrastructure. These facts, combined with a lack of trained health personnel, explain the difficulty in providing good health care in these areas. Primary health care is typically provided in health posts, where usually there is not a doctor but a health technician with basic knowledge of medicine. Some of the leading causes of infant mortality, like tuberculosis, malaria or diarrhoeal diseases (UNICEF et al. 2013), are diagnosed through the microscope. Nevertheless, using a microscope requires a specific knowledge that, generally, technicians don't have.

Microbiology specialists are usually found in hospitals, which are commonly located in urban areas. For this reason, the diagnosis of a microscope sample involves a high consumption of money and time: either the microscope samples or the patient need to be transferred from health posts to hospitals.

The expansion of wireless networks (WIMAX, WiLD, cellular) is helping to connect rural health posts with hospitals, improving coordination and data sharing. Several networks have been deployed successfully in rural areas of Peru, Colombia or India (Surana et al. 2008; Simo et al. 2006). These networks provide broadband connection (~1-2 Mbps) between health posts and hospitals. This makes it possible to offer e-Health services in order to improve the quality of health care, like the telestethoscopy system described in (Foche-Perez et al. 2012). In this context, a real-time telemicroscopy system that allows a specially trained doctor to connect the rural health posts would contribute to improve quality of health care. This work presents the design and implementation of a low cost telemicroscopy system adapted to the special requirements of rural areas of developing countries.

1.1 State of the Art

Telemicroscopy allows sharing the image of a microscope with remote users using the telecommunications networks. Thus, a medical technician can obtain remote assistance from a specialist, or a specialist can obtain a second opinion.

Sending the image of a microscope through a network requires the conversion of the image to a digital format (Hedvat 2010). This can be achieved by using a digital microscope, which directly performs the conversion. But rural health posts generally don't have this kind of microscopes, and their price is quite high. Lens-free systems are another option that use a digital optoelectronic sensor to obtain the image (Greenbaum et al. 2013; Greenbaum et al. 2012; Isikman et al. 2012). While this line of research is very active and will allow dispensing with the microscope in the future, this technology is still under development and not ready to be used in a widespread way. The most common form of converting the images of conventional analogue microscopes is by using digital microscope cameras. It is also possible to use the camera of conventional mobile phones, like explained in (Breslauer et al. 2009; Smith et al. 2011; Tuijn et al. 2011), but specific microscope cameras generally offer better quality and mechanical compatibility with microscope eyepiece lens. Thus, it is possible to utilise the existing microscopes and perform the image conversion at low cost.

There are two main modes for performing a telemicroscopy session: store-and-forward or real-time. In store-and-forward telemicroscopy, digital images and video are captured and stored locally, and sometime later they are sent to the specialist. This mode has low connection requirements, and it can operate even by sending MMS (Bellina & Missoni 2009). But, by contrast, it requires that the health technician has enough knowledge to properly focus the sample and identify the regions of interest. Besides, interaction between technician and specialist is very restricted, which slows down the process of diagnosis. For this reason, this research will focus on the development of a real-time telemicroscopy solution.

Real-time telemicroscopy allows instantaneous video and voice interaction between technician and specialist. In this mode, technicians are not required to have a deep knowledge because specialists will lead the process of diagnosis. The major disadvantage is that a stable connection is needed in order to allow live video streaming. A successful case of real-time telemicroscopy is described in (Thompson et al. 2011), but the high cost of the system proposed makes it unsuitable for rural areas of developing countries. This is why this work searches for a low cost solution.

1.2 Aim

The main objective of this research is the design, implementation and evaluation of a low-cost real-time telemicroscopy system adapted to the special requirements of rural areas of developing countries. The system must meet the following requirements:

- Provide enough image quality (according to the criteria of specialists) to allow diagnosis of, at least, the following diseases: tuberculosis, malaria, diarrhoeal diseases and vaginal swabs.
- Allow real-time displaying of the microscope image both locally and remotely.
- Establish a voice communication between technicians and specialists.

In addition, the system must meet the following technical requirements:

- Keep the video delay below 1.5 seconds.
- Require a maximum bandwidth of 500 kbps.
- Need low power resources, below 15W (including the local display system).
- Have total cost no more than $275.
- Use as much as possible open source tools in order to facilitate the adaptation and dissemination.

2. METHODS

The research process is divided into three phases: design, implementation and evaluation. An expert microbiologist will verify that the diagnostic quality is maintained along the three stages. The steps in each phase are described below:

In the design phase:

1. Identification of the most relevant parameters of digital microscope cameras.
2. Review of cameras and selection of one that meets the image quality requirements at low cost.
3. Selection of a live video streaming system and specification of all its components: display technology, video container format, video codec, and transport and application protocols.
4. Design of the telemicroscopy software and test of the whole system on a personal computer.

In the implementation phase:

1. Review of embedded systems with focus on processor capabilities, software compatibility, power consumption and price.
2. Selection of an embedded system that supports a video streaming with the image quality requirements defined by the expert microbiologist.

In the evaluation phase:

1. Technical validation in a laboratory environment to check that the system meets the requirements of delay and bandwidth.
2. Preliminary clinical validation where three expert microbiologists will verify that remote diagnosis is equivalent to direct diagnosis with ten samples of each disease.

3. RESULTS

The results obtained in each stage of the research are detailed below.

3.1 System Design

For the system design the image acquisition system was first selected, then the video streaming system was chosen, and finally a software application was developed to integrate all components in one device.

3.1.1 Characterisation of Digital Microscope Cameras

For image acquisition a microscope camera will be employed. The objective of the camera is to provide an image with sufficient quality so that the specialist can make the diagnosis. The most relevant parameters are:

- **Sensor size (chip) –** The camera sensor size determines the field size that is viewed through the camera. The field area is significantly lower that the covered directly by the eyepiece lens: in a typical scenario, the eyepiece lens diameter might be 18mm (255 mm^2) and the sensor size might be 5.7x4.3mm (25mm^2). The difference between these areas is considerable.
- **Image size (resolution) –** Currently there are cameras whose resolution can reach, and even exceed, 10 megapixels. However, using such a high resolution is sometimes useless as it is possible to maintain diagnostic quality using lower resolutions. The lowest resolution that provides diagnostic quality will depend on the disease being diagnosed as each disease requires a different level of detail. It is also important to consider the number of images per second that the camera provides. This number should be high enough to allow identification of parasites even when the image is moving.
- **Software compatibility –** Application software development will be based on GNU/Linux. For this reason, cameras should be compatible with video4linux2 driver, which controls all video devices connected to the system. Sometimes manufacturers provide their own drives for GNU/Linux.

3.1.2 Selection of the Camera

Commercial cameras have prices ranging from 30 dollars to thousands of dollars. With the purpose of reducing system cost, a low cost model will be evaluated, the Celestron 44421, selected because it provides the image quality required by the system. Also, a mid-range camera, Moticam 1SP, and a high-end camera, Moticam 5, have been selected and evaluated in order to compare the Celestron 44421 versus other cameras with higher performance.

- **Celestron 44421** – It is a low cost camera with estimated price of 30 dollars. Its chip size is 5 x 3.75 mm and its top resolution is 2MP. It is compatible with video4linux2 driver.

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- **Moticam 1SP** – It costs approximately 350 dollars. Its chip size is 4.8 x 3.6 mm and its top resolution is 1.3MP. It has its own drivers for Windows and Linux.
- **Moticam 5** – This camera costs approximately 900 dollars. Its chip size is 5.7 x 4.3 mm and its top resolution is 5MP. It has its own drivers for Windows and Linux.

In order to determine the minimum resolution that offers diagnostic quality, a sample for every disease was observed. Expert microbiologists determined that 0.3MP was the minimum resolution. There are no significant differences in quality between the images obtained by the three cameras, therefore, the Celestron 44421 is chosen due to its significantly lower price. Figure 1 shows two images obtained with this camera at 0.3MP for malaria (left side) and tuberculosis (right side). In both of them parasites can be clearly identified.

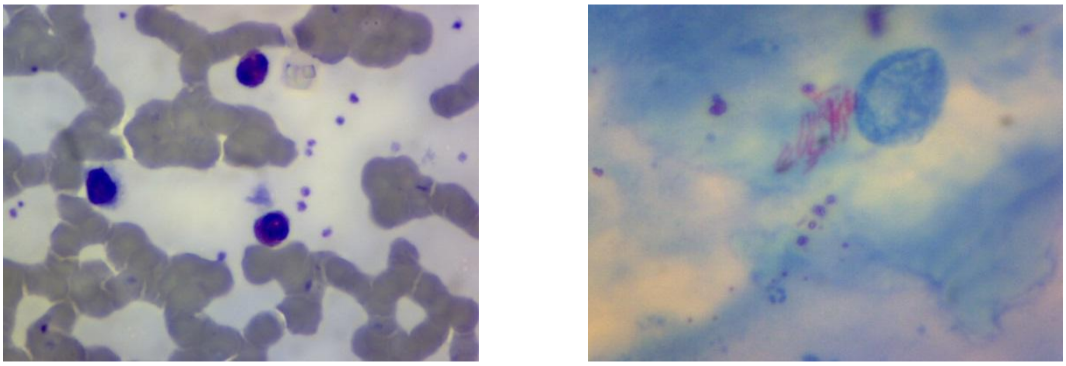

Figure 1. Microscope image at 0.3MP. Celestron 44421

3.1.3 Selection of the Video Streaming

One of the system requirements is that remote specialists can view the video without installing any additional software in their computers. Currently, the easiest way to achieve it is by using a web browser because they are usually installed in every computer and their performance barely varies between most common operative systems (Windows, GNU/Linux, iOS). In the following paragraphs the whole streaming system will be defined: first, the video playback technology; second, the video container format; third, the video codec; and finally, the transport and application protocols.

Video playback in web browsers can be performed, mainly, in two ways: through the use of HTML5 video tag or through an embedded flash player. HTML5 is likely to become the standard for video playback on the web, but currently its implementation relies on each browser. Three formats can be used (mp4, WebM, Ogg) but any of them is currently supported at the same time by the most important browsers (Internet Explorer, Chrome, Firefox, Safari). On the other hand, flash playback requires the installation of a plugin, which it is not a real problem because this plugin is usually installed on all browser or it can be installed easily and free. This is why flash is finally selected as video playback technology.

Once flash has been chosen, the next election is the video container format. The main formats accepted by flash are F4V and FLV. Due to its internal structure, F4V is suitable for "video on demand" and presents some implementation challenges to be used as "live streaming". For its part, FLV has been for many years the preferred format for video streaming over the Internet. Although HTML5 is likely to substitute flash as the standard playback technology in the future, FLV currently offers solid performance and great compatibility, so it will be adopted as the container format.

The election of FLV limits the number of possible video codecs. The main codecs accepted by FLV are Sorenson Spark, On2 TrueMotion VP6 and H.264. Sorenson Spark codec is subject to licensing fees, so its use is not considered. Meanwhile, On2 TrueMotion VP6 remains unsupported since the release of VP8 as open source. It was decided to use H.264 due to this reason and other ones: first, its use is permitted for non-commercial applications; second, it is the most advanced codec of these three ones, including innovative techniques such as the reference to multiple images and the use of sub-macroblocks for motion estimation and compensation; and third, because there are solid open source tools for H.264 encoding. The implementation will be performed by the open source tool Ffmpeg together with the library x264.

The distribution of multimedia content in real-time has two main challenges: to achieve low delay and ensure the integrity of the video. Transport and application protocols have a very important role in this. Regarding the transport protocols, TCP protocol includes mechanisms in order to ensure packet arrival and video integrity. These mechanisms introduce an additional delay on video playback, which sometimes can be annoying. For this reason, it is generally recommended the use of UDP for applications that require low delay. But UDP does not ensure packet arrival, which can become a major problem when a video codec is used, since the loss of headers or keyframes can lead to image distortion for several seconds. In a microscopy application is more important to ensure packet arrival than to keep a low delay. Image distortion, even for a short period of time, can cause the loss of important fields of the sample. For this reason, TCP is selected as transport protocol. Regarding the application protocol, there is a specific protocol for video distribution between a server and a flash player, RTMP (Real Time Messaging Protocol). This protocol is owned by Adobe, which has released a version of the specification for public use (2009). It uses TCP as transport protocol, maintains persistent connections between client and server, and achieves low delay communication thanks to low overhead of headers. It was decided to use RTMP as application protocol and implement it using the open source software Crtmpserver.

3.1.4 Software Design

Finally, an application has been developed in order to integrate the above components and to add functionality for image edition and management. The program is written in JAVA using Ant (Apache License v2) as build tool and has been released under GNU PGL v3 license.

The program makes use of the software ImageJ (public domain). This software includes tools for managing the captured images, pointing out the regions of interest and writing comments over the image. This can be really useful for image sharing between medical personnel when it is not possible to establish a real-time communication, or when the technician has enough knowledge to identify the regions of interest.

Video codification is performed by the software Ffmpeg (GNU GPL v3). This software uses the video4linux2 library (GNU GPL) to communicate with the camera and the x264 library (GNU GPL v3) to encode the video in H.264 format.

Video distribution is performed by the server Crtmpserver (GNU GPL v3). This server accepts a video streaming from Ffmpeg and delivers it to clients in FLV format using the RTMP protocol. Video playback in web browsers is performed by the web player Flowplayer (GNU GPL v3).

Lastly, the voice communication is done by the Ekiga softphone (GNU GPL). It uses the open source audio codec Speex at a sample rate of 8 kHz.

3.2 Implementation

After confirming that the system design met the required functionality when implemented on a personal computer, we proceed to find a low cost embedded system to replace it.

3.2.1 Review of Embedded Systems

The use of an embedded system instead of a personal computer pursues two of the system requirements. On the one hand, it allows a reduction in the price of the system since these devices have a significantly lower cost than conventional computers. On the other hand, it matches the low power consumption requirements since these devices are designed to consume 5-10 W approximately. Also, a reduction in size is achieved. Currently there are devices with similar features to a midrange computer for a very low price (< $100).

The most important parameters are:

- **Processor:** generally, all these devices have a processor with ARM instruction set. They are typically found in smartphones and tablets due to their low power consumption.
- **Software compatibility:** software compatibility with ARM architecture is continually developing. The most common operative systems on these devices are Linux and Android. In many cases, the hardware manufacturers are responsible for generating and maintaining the different SO versions, so that the existence of a community of developers and users is vital.
- **Price:** currently the price can vary from $25 for a low-end device to some hundreds of dollars for a high-end device.

With the purpose of covering a wide range of processor power, six different low cost devices have been selected and tested. The list ordered from lowest to highest processor power is: Raspberry Pi, BeagleBone Black, A20 OLinuXino, MK802IIIS, MK802IV-LE and Odroid-U3. Table 1 shows a summary of their features.

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Table 1. Summary of embedded systems

Device	Processor	RAM	Power consumption (max)	Estimated price*
(1) Raspberry Pi	700 MHz	512 MB	5W	$35
(2) BeagleBone Black	1 GHz	512 MB	10W	$45
(3) A20 OLinuXino	Dual Core 1 GHz	1 GB	4.8W	$75
(4) MK802IIIS	Dual Core 1.6 GHz	1 GB	10W	$50
(5) MK802IV – LE	Quad Core 1.6 GHz	2 GB	10W	$125
(6) Odroid-U3	Quad Core 1.7 GHz	2 GB	10W	$65

*It does not include taxes or shipping.

3.2.2 Selection of the Embedded System

The devices were subjected to a test of video coding with the parameters defined by the expert microbiologists. The following results were obtained: the devices (1) and (2) did not have enough processor power; the device (3) reached its performance limit, causing the system to became slow and unwieldy; the devices (4) and (5) showed problems of software compatibility between Ffmpeg and v4l2 library; and the device (6) was the only one that offered enough processor power and software compatibility with all the components. Therefore, Odroid-U3 was selected as the embedded system.

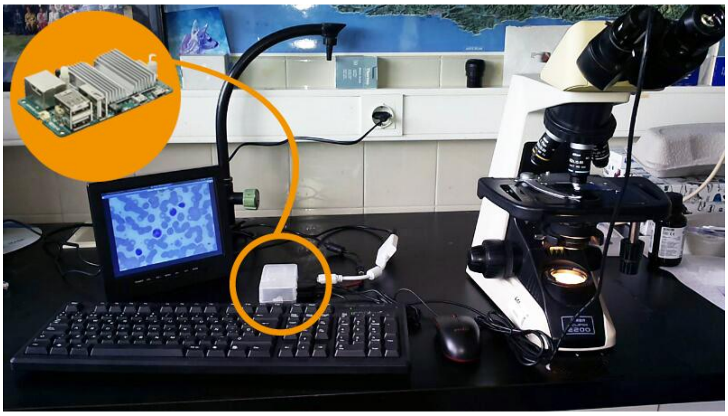

Figure 2. Telemicroscopy system with a detail of Odroid-U3

3.3 Evaluation

3.3.1 Technical Validation

The technical validation has been performed in a laboratory environment and in the presence of expert microbiologists. The telemicroscopy system has been connected to a laptop HP envy m6 through an Ethernet network cable without any external traffic. With the aim of ensuring that the measurement environment does not impose any limitation, it has been verified that the delay between the two devices is negligible (< 1ms) and that the available bandwidth is high enough (> 80 Mbps).

Bandwidth occupied test - This test aims to determine the minimum bandwidth of the streaming that ensures the diagnostic quality. As a starting point, the following coding parameters were used:

- Resolution: 640 x 480 pixels
- Frames per second: 10
- Profile H.264: High
- Group of pictures: 60
- Other settings: x264 tune for low latency

The encoder accepts the target bitrate as an input parameter. This parameter is directly related to the quality of the video. In order to know the minimum bitrate that offers diagnostic quality, the expert microbiologists evaluated a video streaming with several target bitrates: 2Mbps, 1Mbps, 512kbps, 384kbps, 256kbps, 192kbps y 128kbps. They determined that 256kbps was the minimum bitrate that still provides enough quality to clearly diagnose the target diseases.

Nevertheless, the actual bandwidth used by the application is higher than 256kbps due to the protocols overhead. The actual bandwidth has been measured using the “ifconfig” Linux tool for a period of 30 minutes. The result is shown in Table 2.

Lastly, it should be considered the traffic generated by the voice communication. This communication is established through the softphone Ekiga with the audio codec Speex at a sample rate of 8 kHz, which generates traffic of 40kbps in both ways. It has been established that the correct performance of the application is guaranteed when the available bandwidth is 500kbps.

Video delay test - This test aims to measure the delay of video playback in the specialist's computer. In the test environment, there is no external traffic and the available bandwidth has been limited to 500 kbps.

A good way to determine the exact moment when an event occurs is to register the event with a clock. In this test, the microscope image has been replaced by a clock with millisecond precision. For that, the computer clock has been employed so that both clocks can be displayed in the same screen: on one side, the computer clock unchanged; on the other, the clock image captured, encoded and delivered by the Odroid-U3.

The test was carried out for 30 minutes and measures have been taken every minute. The result is shown in Table 2.

Table 2. Summary of measurements

Measurement	Mean value	Max value	Min value
Bandwidth	275 kbps	323 kbps	236 kbps
Video delay	1.35 seconds	1.45 seconds	1.24 seconds

3.3.2 Clinical Validation

The sample set for the clinical validation is composed of: 100 samples of faeces (concentrated and extended) for the diagnosis of intestinal parasites, 90 vaginal swabs for the diagnosis of thrush and bacterial vaginosis, 50 respiratory samples for the diagnosis of tuberculosis and 100 samples of thick blood film together with 100 samples of thin blood film for the diagnosis of malaria.

First, the diagnosis of the samples was performed using directly a bright field microscopy and following the standard procedure. The value of this diagnosis was established as the reference to validate the system. Then, the diagnosis of the samples was performed using the telemicroscopy system.

In this preliminary clinical validation, 10 samples of each type were visualised using both methods and no difference was observed in either the image quality or the diagnostic value.

4. DISCUSSION OF RESULTS

The results show that the telemicroscopy system is really useful to consult doubts and ask for second opinions. The communication between the technician and the specialist is fluent and the video delay (~1.3 seconds) is not a barrier.

The main problem of the system is related to the size of the field observed through the microscope camera. The area relation between this field and the one observed directly through the eyepiece is about 1:15. The camera only covers a small portion of the field, which significantly increases the time required to observe the same area. This is a widespread problem due to the small size of the sensors of commercial microscope cameras. If we add the interaction delay between the technician and the specialist, the session time becomes high depending on the disease and the number of fields to observe.

The preliminary clinical validation confirmed that the work is going in the right direction. However, it is necessary to perform a detailed clinical validation in order to obtain statistically significant results.

Lastly, it is important to highlight the interesting educational applications of the system. It can be used in classrooms with shortage of microscopes or even in online training sessions.

5. CONCLUSION AND FURTHER WORK

This work demonstrates that it is possible to have a low cost telemicroscopy system adapted to rural areas of developing countries. The total power consumption is reduced to less than 15W through the use of an embedded system. Also, the correct operation of the system is ensured when having a bandwidth of 500 kbps. The system is based, as much as possible, on open source tools so that it can be easily replicated.

Once the system has passed the detailed clinical validation, the last step will consist in a pilot in a rural area of a developing country. The selected area is the WiLD network deployed on the Napo River that connects 16 health posts with the Iquitos Regional Hospital in Peru (Rey-Moreno et al. 2011). The system will be installed in 6 health posts and the technicians will be trained in the sample preparation for the target diseases and the use of the application for a remote diagnose.

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