Single Lens Off-Chip Cellphone Microscopy

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Abstract

Within the last few years, cellphone subscriptions have widely spread and now cover even the remotest parts of the planet. Adequate access to healthcare, however, is not widely available, especially in developing countries. We propose a new approach to converting cellphones into low-cost scientific devices for microscopy. Cellphone microscopes have the potential to revolutionize health-related screening and analysis for a variety of applications, including blood and water tests. Our optical system is more flexible than previously proposed mobile microscopes and allows for wide field of view panoramic imaging, the acquisition of parallax, and coded background illumination, which optically enhances the contrast of transparent and refractive specimens.

1. Introduction

Today, an estimated six billion cellphone subscriptions exist worldwide with about 70% of those in developing countries (www.itu.int/ict/statistics). However, developing countries often suffer from a lack of access to adequate healthcare, which is party due to the cost and training associated with high-tech scientific instruments required for medical analysis. We present a low-cost portable microscope that uses a cellphone camera and a simple, secondary lens that is placed on top of the specimen. As illustrated in Figure 1, our device can be used in the field, for instance to analyze water sources for potential contamination, and can either directly process the captured data or transmit it wirelessly for remote processing. Cellphone microscopes provide a unique opportunity to make disease diagnosis and healthcare accessible to everyone, even in remote and undeveloped parts of the world.

Starting in 2008, mobile computational photography has reached a tipping point and, largely due to the enabling capabilities of cellphone cameras, various approaches to cellphone microscopy have started to appear [11, 13, 1, 12, 16]. Based on their optical setup, these approaches can be categorized into three methodologies: on-chip analysis, off-chip clip-on methodology, and on-lens approaches.

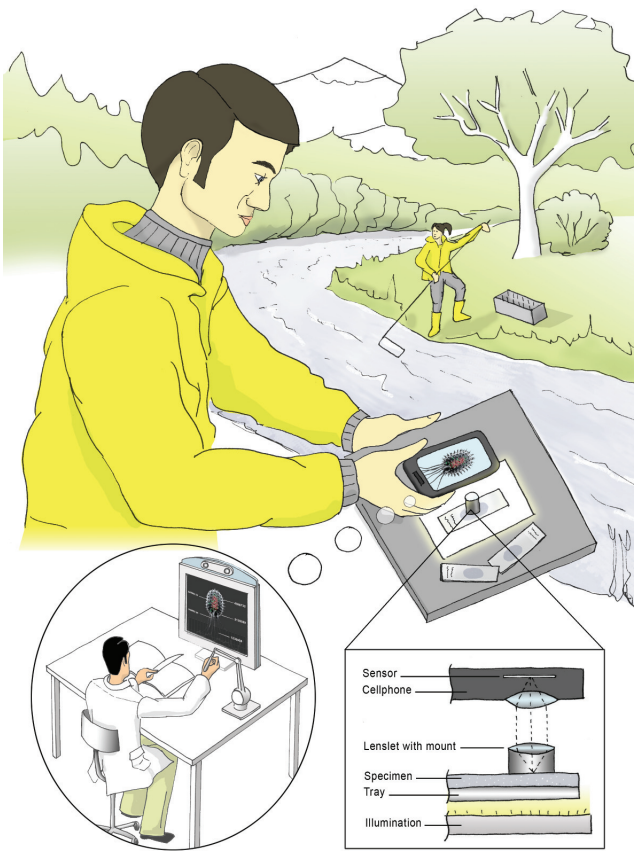

Figure 1. Illustration of our cellphone microscope in the field. The data captured by this versatile and low-cost platform can either be analyzed directly on the phone or remotely, for instance by a medical doctor in a hospital. Our prototype consists of a standard cellphone camera, a secondary lens on a mount that is directly placed on the microscopic sample, and background illumination, for instance provided by an LED.

The first category, "on-chip analysis", requires major, intrusive modifications to cellphone hardware [11, 13]. Furthermore, the associated holographic imaging requires standard photographs to be reconstructed from captured fringe patterns. The second approach, "off-chip clip-on", requires additional hardware attachments to be mounted on the cellphone [1, 16]. Due to the varying dimensions of different

Figure 2. Prototype microscope. A sample is rear-illuminated, in this case using a secondary cellphone display, and photographed using a cellphone camera. Optical magnification is achieved by mounting a small lenslet at its focal length to the sample.

cellphone models, however, a clip-on attachment usually only works with a specific model and also fixes the relative viewpoint of the specimen. The third methodology of cellphone microscopy can be described as an "on-lens" approach [12], where a refractive optical element is directly attached to the camera lens.

In this paper, we introduce practical, low-cost, single lens off-chip computational microscopy using cellphone cameras. Our approach is unique in its optical design: a single lens is placed, separated by its focal length, on a microscopic sample and directly imaged from a detached camera phone, which allows different viewpoints of the sample to be recorded. We further demonstrate that an additional cell phone display can be used to provide structured background illumination, which optically enhances the contrast of the observed specimen. The focus of this paper is to make field microscopy practical and cost-effective at the same time. Our approach combines the following characteristics:

- **Cost-effective**: Only a single lens is required in addition to a cellphone camera.
- **Non-intrusive**: Our setup does not require intrusive modification of the phone.
- **Flexibility**: Our detached camera-lens configuration allows any camera to be used for microscopy.
- **Minimal computation**: We do not require extensive post-processing, as e.g. holographic approaches.
- **Computational illumination**: Using a second cellphone display as the background illumination allows enhanced microscopic images to be captured.

1.1. Overview of Benefits and Limitations

Cellphone-based microscopy is a well-explored area. We present a new, low-cost optical setup that, in addition to standard microscopic images (Sec. 4), allows for programmable background illumination (Sec. 4.3), wide field of view panoramic stitching (Sec. 4.1), and parallax acquisition (Sec. 4.2).

Parallax, however, is only observed in volumetric specimens captured from different camera positions. This information is essential for tomographic reconstructions [3] of three-dimensional microscopic samples and also provides the necessary data to assemble a light field from multiple photographs [2], which has been demonstrated to provide a flexible tool for microscopic imaging [4]. In this paper, we introduce a new optical configuration for off-chip cellphone-based microscopy and explore a variety of applications; we do not aim to reconstruct volumetric specimens or assemble full four-dimensional light fields.

We demonstrate that angular background illumination, provided by a secondary cellphone display, enables Schlieren imaging of microscopic samples. This effect has previously been explored in macroscopic environments [14] and enables the surfaces of refractive objects to be reconstructed [15]. We demonstrate that similar illumination patterns enhance the contrast of transparent, refractive samples by optically visualizing their refractive index gradients.

2. Related Work

Microscopy has been a fundamental tool of scientific imaging for centuries. A good introduction to optical setups and microscopy techniques can be found in the book by Murphy [7].

Cell Phone Microscopes have been explored within the last few years. Sungkyu et al. [11] and Tseng et al. [13] propose on-chip holographic microscopy using cellphone cameras. While successful in acquiring microscopic structures in the lower micrometer range, holographic miscoscopy requires significant hardware modifications of the cell phone. Any lenses integrated in the phone need to be removed and a custom attachement installed. This intrusive approach does not allow the camera to be used for other applications and constrains the imaging system to a specific device. Our setup is much more flexible by detaching the phone camera from the objective lens, thereby allowing any available cellphone to capture microscopic imagery. Furthermore, reconstructing images from interference patterns only allows for the acquitision of grayscale imagery [13] and is computationally expensive. In contrast, our design captures full color photographs and requires no post-processing.

Breslauer et al. [1] propose an off-chip cell phone microscope that is capable of imaging structures in the lower micrometer range. While successful in recording high-quality images, this setup requires a variety of optical elements, has a bulky form-factor, and is constrained to brightfield or uniform background illumination. Our design requires only a single additional lens and, combined with a secondary phone, provides structured background illumination that optically enhances transparent specimens.

Smith et al. [12] recently proposed to mount a ball lens on top of the cell phone camera lens. While resolutions comparable to those of alternative cell phone microscopes are achieved, the ball lens creates a spherical focal surface

that only allows small regions of any captured photograph to be in focus. While focus fusion can generate a fully focused image, multiple photographs with different focus settings need to be captured which does not allow for the capture of dynamic scenes. Our approach only requires a single photograph to acquire an all-focused image and provides a more flexible optical configuration, because it does not require any additional optical elements to be mounted on the camera itself.

A cell phone microscope that closely resembles our optical setup was recently proposed by Zhu et al. [16]. Here, a secondary lens was mounted directly in front of the camera lens to image a sample in a hardware clip-on attachment to the phone. As opposed to our design, the LED-based backlight does not allow for controlled illumination. Furthermore, the clip-on is customized for a specific cell phone model, whereas our detached setup can be recorded from any model.

Healthcare on Mobile Platforms has also been proposed for other applications, including the measurement of refractive index errors [8] and cataracts [9] of the human eye.

Light Field Microscopy enhances traditional microscopy by allowing the viewpoint of captured images to be changed after the fact and three-dimensional volumetric microstructures to be reconstructed from a single photograph [4]. Furthermore, reflective light field illumination in microscopic environments has been shown to enhance captured image quality [5]. In contrast to prior light field microscopes, our system is low-cost and portable. We show that the data captured by our unique optical system contains parallax and could be assembled into a light field [2], allowing similar applications as light field microscopes.

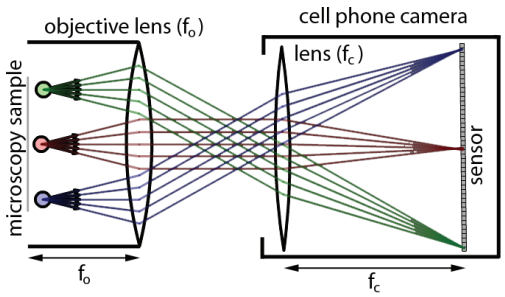

Figure 3. Schematic of our optical setup. An objective lens, separated by its focal length from the sample (left), is observed by a cellphone camera (right).

Computational Illumination has been explored in macroscopic environments to optically convert refraction caused by transparent media into observable changes of color and intensity [14] and reconstruct refractive objects from this information [15]. In a different application, bokeh codes or bokodes [6] have been used to create angular barcodes. Our approach exploits the bokeh effect for microscopic imaging; we demonstrate how structured illumination optically enhances the contrast of transparent microscopic specimens.

Lens Name "A x f"	Aperture "A"	Focal Length "f"	f/#	Numerical Aperture	Optical Magnification	Theoretical Resolution	Diffraction Limit
9x9	9 mm	9 mm	1	0.5	0.47X	2.59 µm	0.5 µm
6.25x7.5	6.25 mm	7.5 mm	1.2	0.42	0.57X	2.46 µm	0.60 µm
4x6	4 mm	6 mm	1.5	0.33	0.71X	1.97 µm	0.76 µm
1x0.6	1 mm	0.6 mm	0.6	0.83	7.13X	0.20 µm	0.30 µm

Table 1. List of all objective lenses used in our experiments along with the theoretically achieved resolution using an iPhone 4S and the diffraction limit of the optical system.

3. System Design

As illustrated in Figures 1 and 3, our cellphone camera consists of a rear-illuminated specimen, an objective lens, and a cellphone camera. The objective lens is mounted at its focal distance to the specimen and acts as a collimating lens for flat samples. The camera is focused at infinity to reimage the sample onto the sensor. Interestingly, the optical magnification M of the system is independent of the distance between camera and sample; it only depends on the ratio of the focal lengths of camera and objective lens:

$$M = \frac{f_c}{f_o}. \tag{1}$$

Due to our unique configuration, the camera can be freely moved around the objective lens so as to capture different viewpoints that can either be stitched into a wide field of view panorama (Sec. 4.1) or observe parallax (Sec. 4.2).

The theoretical resolution of the system is determined by the number of sensor pixels imaging the magnified specimen inside the camera. For all the experiments in this paper we use an iPhone 4S that provides a resolution of 3264×2448 pixels with a pitch of $1.4\mu m$ and a focal length of $f_c = 4.28mm$. We tested a number of different objective lenses, all being inexpensive singlets, that are listed in Table 1 along with their theoretical resolution. Practically, these simple lenslets exhibit chromatic aberrations and radial distortion, which lowers the achieved resolution by about an order of magnitude as compared to the theoretical limit (see Sec. 4).

The diffraction limit places an upper bound on the spatial resolution of any optical system. Given a wavelength λ, features with a diameter that is larger or equal to d can be resolved:

$$d = \frac{\lambda}{2NA}, \tag{2}$$

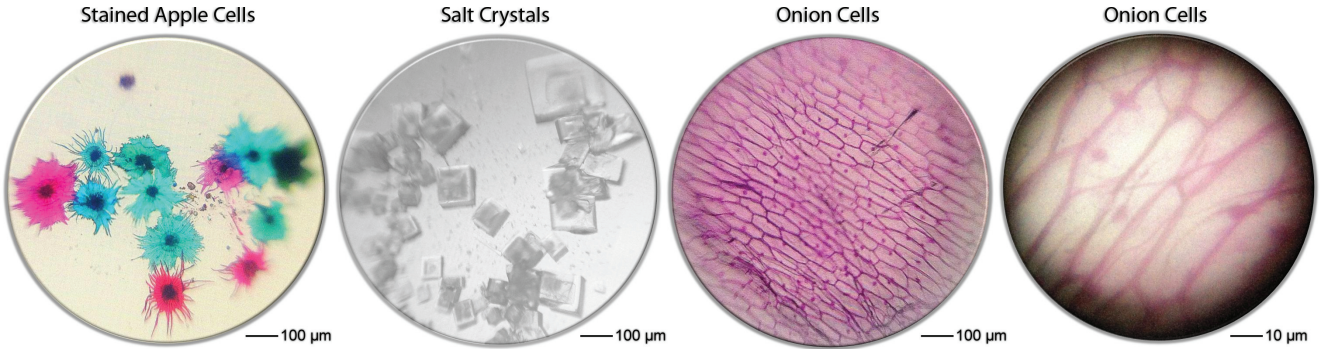

Figure 4. Microscopic images showing (from left) stained apple cells, sea salt crystals, and onion cells. These results are captured with an iPhone 4S camera using the 1×0.6 and 4×6 objective lenses listed in Table 1.

where NA is the numerical aperture of the system. With a paraxial assumption, the numerical aperture can be approximated as

$$NA \approx n\frac{D}{2f}. \tag{3}$$

The aperture size D and focal length f of a lens is usually known; we list the values for all lenses used in our experiments in Table 1. For specific diffraction limits in the table, we assume a wavelength of $\lambda = 500nm$ and a refractive index of air, i.e. $n \approx 1$. The f-number $N = f/D$ for each of the lenses is also listed in Table 1.

4. Results

We captured a variety of different microscopic specimens with our system. Three different examples are shown in Figure 4: stained apple cells, sea salt crystals, and onion cells. All of these examples were captured with an iPhone 4S camera; the right-most result is observed through the 1×0.6 objective lens listed in Table 1, the other results are photographed using the 4×6 objective lens. While individual cells are clearly visible, the inexpensive singlet lenses exhibit some aberration especially toward the outside of the photograph. These artifacts could be mitigated with aberration-corrected objective lenses, but increase the cost of the setup. As demonstrated in Figure 5, we can remove the blur computationally by stitching multiple frames into a panorama that only preserves the best-focused parts for overlapping regions.

4.1. Wide Field of View Panoramic Imaging

In contrast to other cellphone microscopes [1, 12, 16], our optical lens is not rigidly attached to the cellphone. This flexible configuration allows us to extend the field of view of the microscope by capturing multiple images from slightly different camera perspectives and merge them into a single panorama. An example of this method is shown in Figure 5. Here, the eye on the dollar bill is captured multiple times with the 6.25×7.5 objective lens; the resulting images are stitched together to form a single wide field of view panorama.

Figure 5. Panoramic imaging. While each photograph of our setup only covers a limited field of view, our unique optical setup allows us to combine multiple photographs into a wide field of view panorama as seen on the lower left. Due to the rear-illumination, the text on the other side of the bill is also visible in the panorama.

4.2. Parallax

Figure 6 demonstrates that three-dimensional specimens photographed from different perspectives exhibit parallax. This effect, however, is only observed for microscopic objects that extend in depth from the tray. We note that the parts of the scene that exhibit parallax are out of focus if the objective lens is focused on the tray. Nevertheless, the captured information is useful for tomographic reconstructions of volumetric specimen [4] and can be assembled into a light field [2].

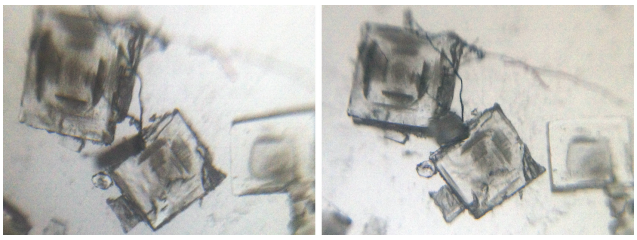

Figure 6. Two photographs of volumetric salt crystals taken from different perspectives demonstrating parallax between the views.

4.3. Computational Illumination

Conventional cellphone microscopes require either a coherent backlight [11, 13] or are only demonstrated with brightfield [1, 12] or darkfield illumination [16]. The pictures in Figure 2 show how our cellphone microscope can, as an alternative to uniform backlight, be illuminated by the display of a secondary phone. While such a setup increases the cost of the overall system, cellphones or other small displays are widely available, even in remote areas of the world. The display of the illumination device acts as a programmable light source and can implement a variety of structured illumination patterns.

Organisms in the microscopic world are often translucent and refractive and, as a result, are generally difficult to observe. Phase contrast microscopy, such as Zernike phase contrast and differential interference contrast (DIC), are common approaches to increase the contrast of translucent materials or cells, but require coherent light and complex optical setups. We demonstrate in Figure 7 that the incoherent illumination provided by a cellphone display can optically enhance the contrast of transparent refractive samples. Following Wetzstein et al. [14], we display an intensity gradient on a region of the display, place a lens at its focal distance on top of the screen and position the specimen with the objective lens on top of that. The first lens converts the spatial intensity gradient into an angular illumination gradient and the second lens magnifies the specimen for the cellphone camera.

As seen in Figure 7 (left), broken pieces of glass are barely visible under brightfield illumination. The Schlieren setup uses an angular intensity gradient to optically visualize the refractive index gradients of the glass pieces, thereby amplifying the contrast in the scene. As demonstrated for macroscopic phenomena [15], angularly-varying illumination encodes sufficient information to reconstruct the surfaces of refractive objects under certain conditions.

4.4. Evaluation

We evaluate the resolution of our system by photographing a 100 lines per inch (lpi) Ronchi ruling (see Fig. 8). These rulings are commonly used to test the optical resolution of microscopes. Individual lines, each one being 5 microns in width, are clearly visible. This result was captured with an iPhone 4S camera and the 1×0.6 objective lens listed in Table 1. The 10 μm bar on the lower right of Figure 8 covers about 50 pixels on the camera sensor; the resolution, however, is limited by the inexpensive optical elements and is an order of magnitude lower than the diffraction limit and the theoretical resolution discussed in Table 8.

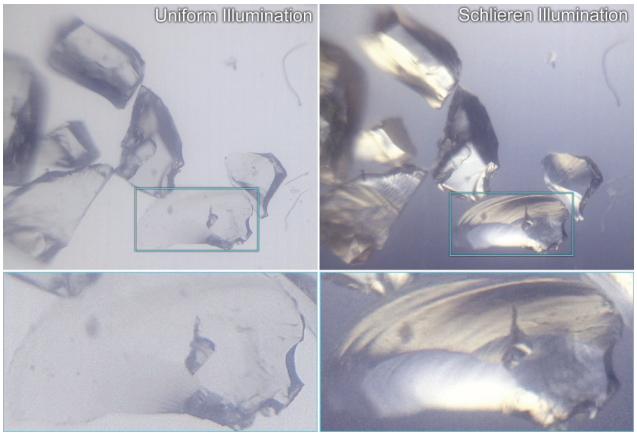

Figure 7. Schlieren imaging. Bits of broken glass are photographed with uniform background illumination (left) and with an angular intensity gradient (right, [14]). The gradient illumination enhances the contrast of the refractive structures by optically encoding their refractive index gradients in intensity variations.

5. Discussion and Conclusion

In summary, we have presented a new approach for low-cost cellphone-based microscopy. The proposed optical setup decouples the objective lens from the cellphone camera allowing for wide field of view panoramic imaging and the observation of parallax. We also demonstrate how controlled background illumination enhances the contrast of refractive transparent specimen and evaluate the optical resolution of the system.

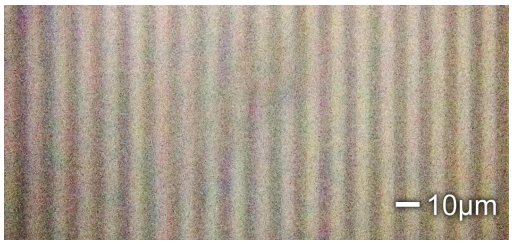

Figure 8. Photograph of a 100 lpi Ronchi ruling. The proposed system can resolve structures in the lower nanometer range, which is comparable to alternative cellphone microscope architectures.

5.1. Future Work

We would like to experiment with more sophisticated structured background illumination and reconstruct refractive [15] and volumetric [4] samples. Although the achieved quality is clearly good enough to distinguish apple and onion cells, we would like to implement automatic cell counting and classification, for instance using CellC [10], which is helpful for classifying diseases in blood or urine samples.

5.2. Conclusion

Cellphones are widely available, especially in developing parts of the world. We demonstrate that these ubiquitous devices can be converted into scientific instruments for microscopic imaging. Equipped with wireless network connections, cellphones also allow the transmission of recorded data for remote analysis or statistical inference. The work presented in this paper has the potential to make disease diagnosis and screening accessible in parts of the world that have no adequate access to healthcare.

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