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Liquid Lenses open new perspectives for Microscopy

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Abstract

The field of microscopy is now more developed than ever with a wide range of modalities such as fluorescence microscopy, OCT, and confocal microscopes, to name a few. Technical advances have significantly improved the image quality, size, and cost of such devices, thus making them available not only for industrial applications but also for researchers, universities, small laboratories and even the public.

Image resolution and quality is of the utmost importance to analyze data from the observed samples. Optical systems in microscopy have a short working distance and a large numerical aperture, resulting in a narrow depth of field and the need to systematically refocus on the sample under study. This paper describes how the use of liquid lenses can greatly improve the imaging capabilities of microscopy devices while overcoming the limitations of bulk, cost, and robustness of traditional systems.

Introduction to liquid lenses

Inspired by the functionality of a human eye, liquid lenses offer manufacturers and OEMs improved speed and reliability over mechanical solutions. The human eye can adjust its focus to the environment at incredibly fast speeds; similarly, Corning's liquid lenses emulate the eyes' fluid and adaptable characteristics to create a rapid response to variable circumstances. This process is made possible by a technology called electrowetting, which uses an electrical signal to manipulate a liquid solution into a workable lens.

Traditional mechanical solutions are limited in their ability to deliver sharp images continuously and reliably. Corning® Varioptic® Lenses (Figure 1) offer innovative solutions to complex optical challenges. Varioptic Lenses enable fast focus and micro-focus without moving parts. Traditional camera systems require moving parts which could begin to wear down and fail over the lifetime of the device. In comparison, liquid lenses function without the use of mechanically moving parts, eliminating much of the maintenance typically associated with vision systems.

Challenges in modern microscopy

In the field of microscopy there are today two main challenges:

- The first one concerns research microscopes that are built without constraints to observe the infinitely small. The challenge lies in the observation of nanoscopic samples scaling down to the atom level. Here, the size, cost and robustness of the equipment is not at stake and such devices are mainly used for research purposes.

- The second challenge lies in the continuous improvement of current microscopy setups regarding their general constraints: bulk, cost, weight, energy consumption, robustness, speed…

The primary concern in the field of microscopy is image quality. Without a proper image, it is impossible to extract any visual information from the sample. Microscopes often have a very short working distance in the range of a few millimeters with large numerical apertures to capture the maximum amount of light. This results in an extremely narrow depth of field. Focus is generally achieved by translating the optical system with mechanical parts or complex electronics to maximize sharpness on the sample or scan a 3D volume. The axial resolution (in depth) depends on the accuracy of the translation which requires bulky, expensive, and fragile mechanical parts. This goes against the global trend to build more compact and robust optical devices with equally good optical performances at an affordable price. Additionally, the energy and time required to move the entire optical stack is in the order of a few tens of seconds which adds up to minutes, hours or even days for the analysis of many samples.

A recent review on portable microscopes published in Microscopy Today1 highlights the growing need for simple and robust methods to capture images at the microscopic scale. According to this paper, the impact of climate change or the study of neglected tropical diseases for instance, has led scientists to carry out extensive studies in remote places such as Antarctica or the Amazon Rainforest. Out on the field, not only the image quality is at stake but the bulk, the durability and the energy consumption of microscopy device are also critical. There is a global trend for designing robust and compact portable microscopes that can be used anywhere outside a lab.

Liquid lens solution

Corning Varioptic Lenses are liquid lenses that enable autofocus with a single add-in element. With no mechanical moving parts, a liquid lens can endure hundreds of millions of cycles with low power consumption and at a speed unmatched by conventional actuators. Its robustness and accuracy in autofocus performance makes it well suited for any application requiring large scale autofocus such as 3D imaging or depth scanning for microscopy applications.
Liquid lenses can be integrated within an existing microscope setup by inserting it between the objective lens and the field lens or camera. Below is shown the addition of an A-58N0 on a x10 Nikon microscope objective lens. The light is going through the sample.

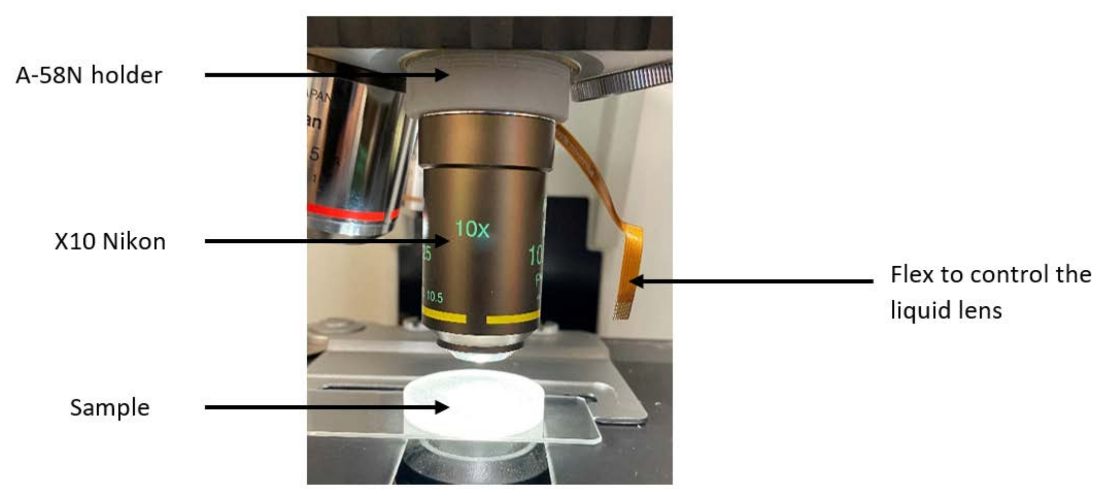

Figure 1 : Example of a liquid lens integration with a x10 Nikon® microscope objective

The images of an USAF target are shown below with and without a liquid lens coupled to a x10 Nikon® microscope objective for different imaging depths and no mechanical refocusing. The depth of field of this objective lens is 3µm and the working distance is 17.5mm. The benefit of the liquid lens is the fast electronic refocusing capability of the lens which can maximize sharpness without manual refocus.

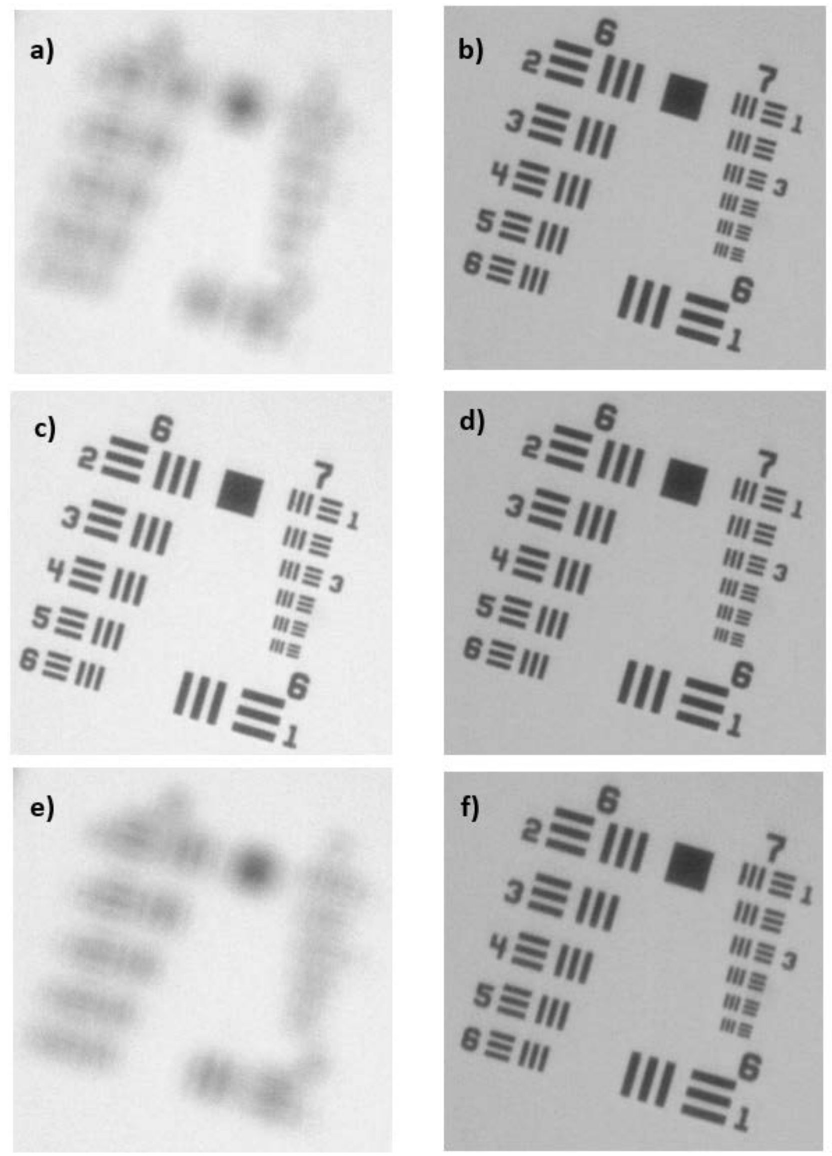

Figure 2 : Images obtained with a 10x microscope objective (depth of field 3µm and working distance 17.5mm). On the left are images acquired without the liquid lens. On the right, an autofocus was performed using the liquid lens. a) and b) At -0.5mm in depth c) and d) At 0mm in depth (focus initially optimized at this position) e) and f) at +0.5mm in depth.

Use case 1 : Red blood cell imaging for sickle cells detection

Red blood cell imaging is used to monitor chronic diseases, prevent cardiogenic and septic shocks or study hemopathology. Blood samples are easy to collect but not as easily analyzed at the cell level due to the small size of the blood's components. A red blood cell typically measures 7µm which requires a significant magnification to be imaged.

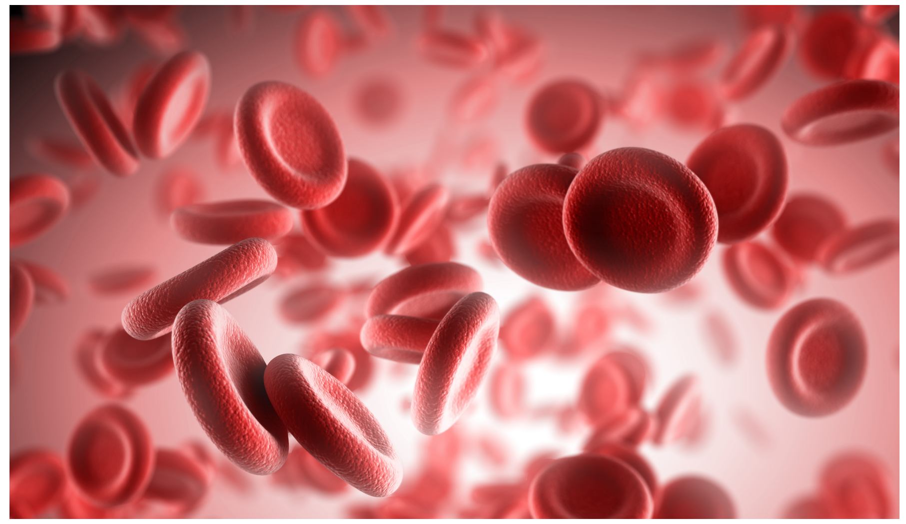

Figure 3 : Representation of red blood cells.

In this use case we observe red blood cells with different setups that use a liquid lens. The first is using a x40 Nikon® objective lens on a microscope together with a A-58N0 liquid lens in add-on at the back of the objective lens. Thanks to a closed loop auto-focus algorithm, which maximizes the sharpness score of an image iteratively, the liquid lens allows to fine-tune the focus on the biological sample without any translation platform.

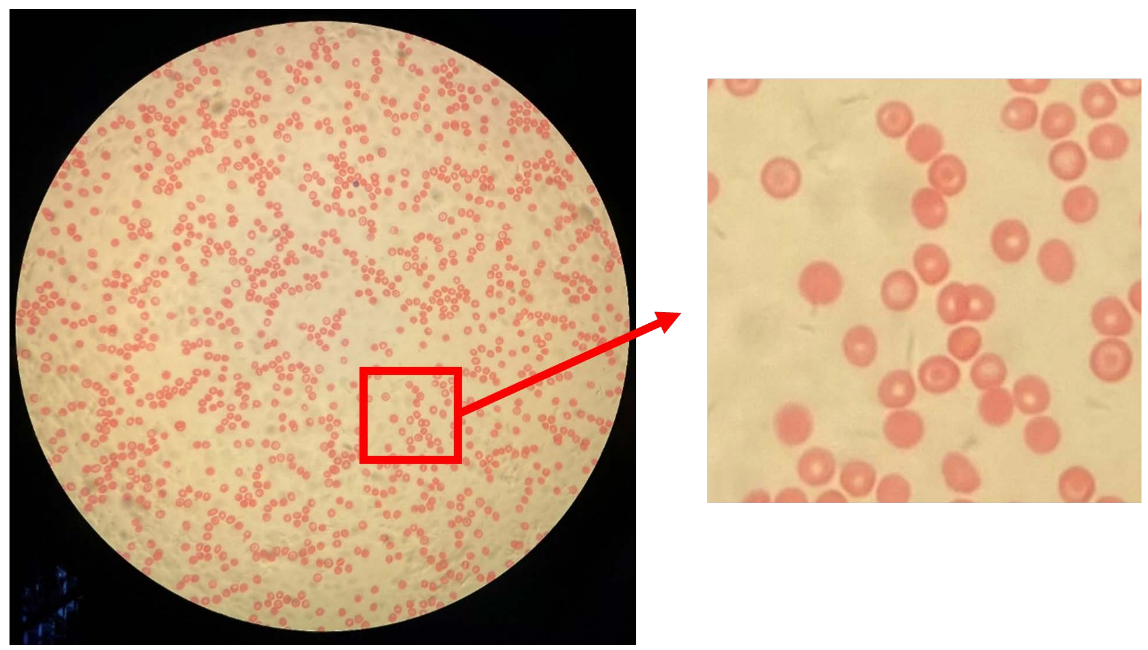

Figure 4 : Image of a sample of blood under a x40 microscope objective coupled with an A-58N0 liquid lens (left) and zoom on red blood cells (right).

For this use case, a translation of 30 µm in the depth axis corresponds to a shift in optical power of the liquid lens of 10 diopters. The depth of field for this microscope objective is 1µm which corresponds to 0.33 diopters of the liquid lens. The expected response time for this lens with this depth of field is around 80ms (optimized). On average, the autofocus algorithm records and analyzes 10 images before reaching the best focus. The time to focus for this use case is about 1s.

The process of extracting the sharpest image can be accelerated by using the V-sweep function of the A-PE series dedicated to Corning® Varioptic® Lenses. This function allows the user to program a ramp of voltage to sweep the entire optical power range. Because there is no transient aberrations for the liquid lens, images can be captured quickly and analyzed in post-processing to extract the best focus.

The ramp can be tuned to any use-case: the user defines the upper and lower boundaries for the voltage as well as the size of steps and their timing. We estimate that the V-sweep function allows to extract the best focus image up to 5 times faster than with a standard autofocus algorithm. For the RBC imaging example presented above, the corresponding V-sweep function could be implemented over 200ms provided that the sensor can acquire images fast enough (minimum 150fps for this use-case).
Thanks to the focus capability of the liquid lens, it is easy to count red blood cells and analyze their shape efficiently. This compact and cost-effective solution can also be used to observe sickle cells (drepanocytes).

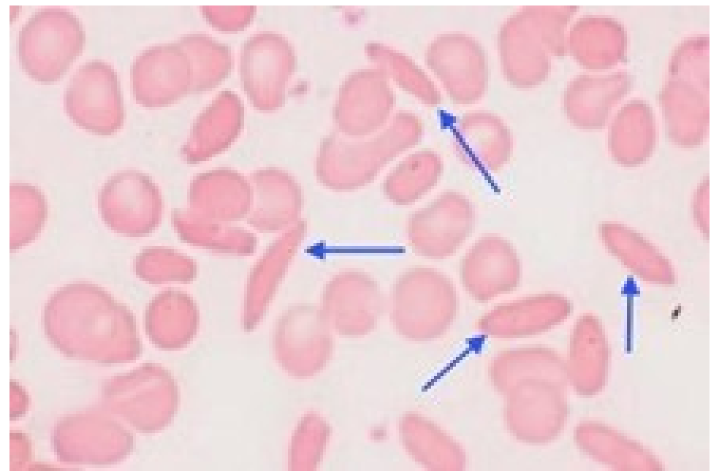

Figure 5 : Blood sample showing sickle cells (shown by blue arrows).

Use case 2 : Spore analysis by Scanit technologies

Scanit is a US-based company that developed a device to address a critical need in agriculture by physically detecting airborne pathogens before infestation. The company's solution captures airborne pathogen spores and uses a liquid lens-based microscope to inspect and classify the pathogens. This can help farmers and growers take necessary precautions or preventive actions to help minimize yield losses, optimize pest management practices, and control the efficacy of their actions on their crops.

Figure 6 : Scanit technology device installed in an indoor flower culture (left) in vineyards (center) and cornfields (left)

Scanit's technology relies on the capture of microscopic particles on an adhesive black media which is analyzed with a liquid lens-based dark field microscope under white and UV fluorescent lighting as shown on Figure 8. Each pathogen has a unique signature that can be identified using a machine learning algorithm. The embedded intelligence analyzes microscopic information at the pixel level such as color and light intensity but also macroscopic cues such as the particle morphology, texture, and light frequency.

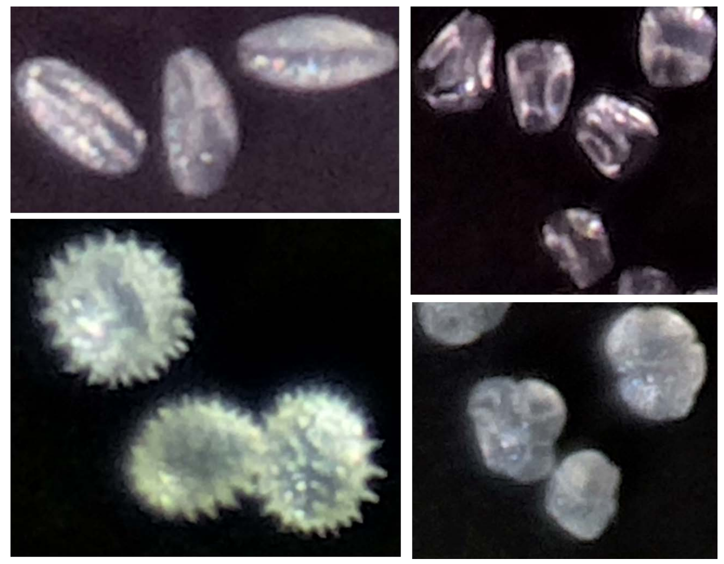

Figure 7 : Examples of allergenic pollens and spore captured using a liquid lens-based microscope.

The image quality of the samples is of the utmost importance since their identification relies on the comparison of the data collected to a reference dataset. Liquid lenses help achieve optimal image sharpness and provide useful information for the post-processing analysis.

Once all the information has been collected, a decision-tree regression algorithm classifies the particles based on the data previously gathered by the trained AI.

Liquid lenses are compact and extremely robust to harsh environmental conditions. Additionally, they have a lifetime of more than several hundred million cycles and are extremely power efficient compared to similar autofocus solutions (<1mW for the lens itself). All this makes them ideal candidates for embedded devices in need of autofocus that are used in remote locations.

Solutions from Corning® Varioptic® Lenses

Varioptic offers off-the-shelf solutions for microscopy applications. The D-u-25H0-075-03 is based on a reversed 7.5mm focal length S-mount module. Its resolving power is 1.2µm with a magnification comprised between x2 and x5 depending on the length of the back focal. Thanks to the variable focus capability of the liquid lens, the imaging depth ranges between 1,5 and 2mm. This allows the user to scan through a sample and image a complete 3D volume. The second kit is based on a reversed 16mm C-mount module. Its resolution is 2.2µm with a magnification ranging between x3.4 to x6.4 depending on back focal length.

D-u-25H0-075-03

F# 2.9
Max object size : 7.2 mm
Object res. for pixel res. : 1.2 µm

	x2	x3	x5
MBFL (mm)	15	22	37
W.D (mm)	7.8	6.4	5.4
ΔWD (mm)	1.85	1.58	1.41

Figure 8 : D-u-25H0-075-03 development kit provided by Corning® Varioptic®

D-u-39N0-160

F# 2.8
Max object size : 3.7 mm
Object res. for pixel res. : 2.2 µm

	X3.4	X4.6	X6.4
MBFL (mm)	17.5	37.5	67.5
W.D (mm)	15	14	13
ΔWD (mm)	4	4	4

Figure 9 : D-u-39N0-160 development kit provided by Corning® Varioptic®

Sample images obtained with Corning® Varioptic® microscopy kits

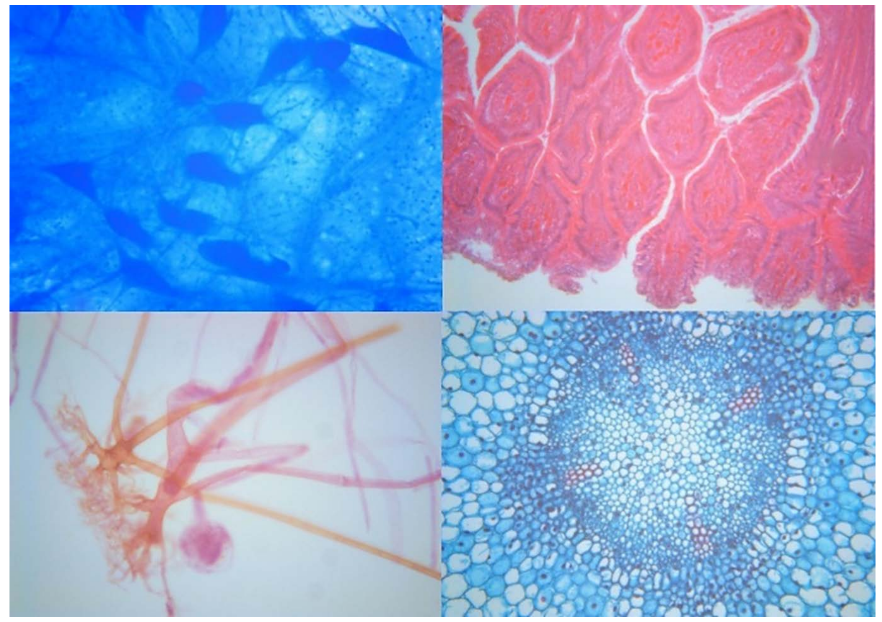

Figure 10 : a) Image of neuron cells b) Image of muscular cells c) Image of a fungi d) Image a rhizome.

Conclusion

The applications and modalities in microscopy are extremely diverse but the need to focus on the sample or object under study is recurrent. The narrow depth of field of these systems are inherent to the way they are designed:

- The working distance is short due to the small size of the samples
- The numerical aperture is large to maximize the light input
- The pixel size of the sensor is small to maximize image resolution

Consequently, auto-focus is essential to form an image sharp enough to analyze the data at the microscopic scale. To overcome the bulk, fragility and cost of traditional systems that use mechanical actuators, liquid lenses allow the user to automatically adjust the optical power of a single optical component to refocus on the object.

As scientists move research out of brick-and-mortar laboratories, transporting the necessary equipment on the field becomes a real challenge. Embedded devices have been emerging in the past decade and their importance is growing by the day. Microscopes are an example, but other embedded imaging technologies also rely on auto-focus to capture images. Corning® Varioptic® provide a low-cost, high-quality solution for imaging applications in need of variable optical power.

References

1. A. Monk, “Portable Microscopes for Scientific Publications” in Microscopy Today, 29(2), 16-19 (2021)

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