NEXT-GEN PHOTONICS INSTRUMENTS FOR BIOIMAGING AND SPECTROSCOPY

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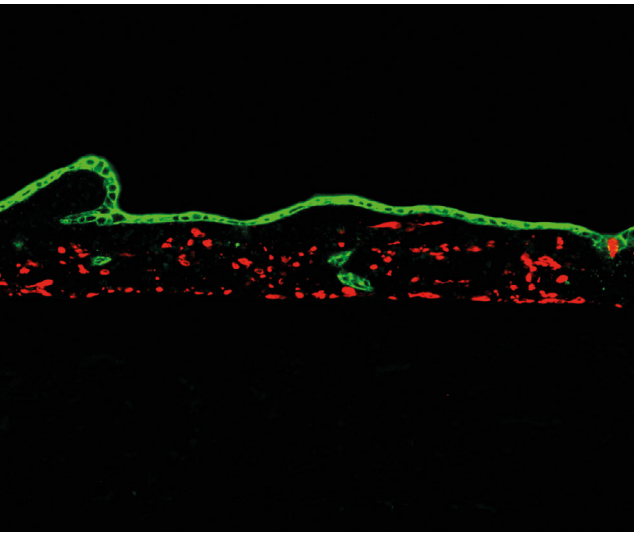

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Photonics has revolutionized the life sciences by providing powerful, non-invasive tools for observing, measuring, and manipulating biological systems with exceptional precision and sensitivity. Imaging techniques such as optical microscopy, fluorescence imaging or optical coherence tomography enable researchers and clinicians to study cells, tissues, and molecular interactions in real time and in their natural environments. And spectroscopy of biological samples enables the non-invasive investigation of molecular composition, structure, and dynamics within cells, tissues, and biofluids. These technologies are essential for early disease diagnosis, drug development, neuroscience, genomics, and personalized medicine.

Recent advances in photonics are pushing the boundaries of what's possible in bioimaging and spectroscopic analysis of biological samples. New developments in light sources and detectors are opening exciting frontiers in sensitivity, speed, and spectral coverage. The latest LEDs technologies bring greater flexibility, brightness, and depth performance to bioimaging and spectroscopic tools, enabling new capabilities in noninvasive diagnostics, functional imaging, and real-time molecular sensing. Quantum dots detectors, along with enhanced readout electronics and integrated multiplexing, are and exciting development which enables the next-generation of imaging systems to capture weak signals and resolve fast dynamics. And the most recent optical components are being tailored to biological samples and to optimize the illumination and the performance of the imaging systems.

NEW DEVELOPMENTS IN FLUORESCENCE MICROSCOPY

Fluorescence microscopy is a cornerstone of modern biological and biomedical research. This technology offers unparalleled sensitivity and specificity for visualizing structures and processes within cells and tissues. By tagging molecules with fluorescent markers, researchers can observe the localization, dynamics, and interactions of proteins, nucleic acids, and other biomolecules in real time, often at the single-molecule level. This ability to illuminate specific

components within complex biological systems has transformed our understanding of cellular function, disease mechanisms, and developmental biology.

Light sources are a critical component of fluorescence microscopy, as they provide the excitation energy required to stimulate fluorophores and generate the emitted fluorescence signal. The choice of light source directly influences the brightness, resolution, and sensitivity of the imaging system. Modern fluorescence microscopes increasingly use LEDs as light sources due to their long lifetimes, low power consumption, and rapid switching between wavelengths, making them ideal for routine and multi-color imaging. Compared to mercury and metal halide lamps traditionally used for widefield fluorescence, LEDs offer many advantages for automated systems.

The UK based company CoolLED designs and manufactures cutting-edge LED illumination systems for these applications. They have developed powerful, stable and customisable multi-spectral solutions for manufacturers of automated fluorescence systems. Their ultra-bright illumination with high-speed TTL triggering increases imaging speed, boosting throughput which is especially valuable for high-content screening. Slide scanning also benefits where homogeneous illumination is critical for high-quality image stitching, so image acquisition is both fast and high quality.

The need for deeper tissue penetration, reduced background autofluorescence and improved photostability has driven the development of fluorescent dyes in the red to nearinfrared (NIR) spectral region. Some examples are the stabilized boreniumion dye, which emits in the red/NIR region and remains stable in air, or the optimized redabsorbing rhodamine derivatives, which can improve brightness and spectral tuning in the red region. For these new dyes, the wavelengths range 340-850 nm of the CoolLED's solutions allows them to cover the full range of fluorophore needs.

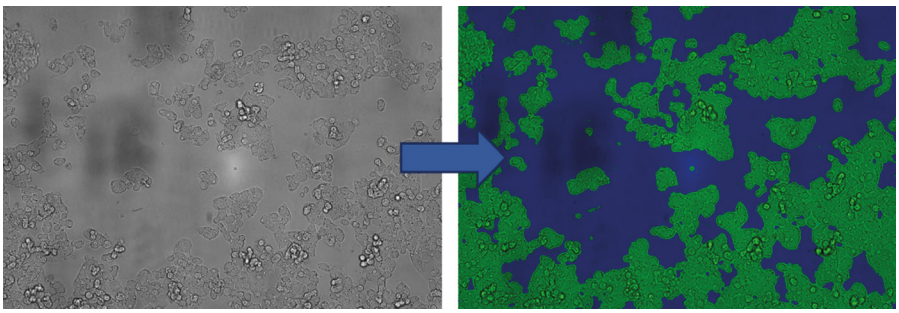


Figure 1: Cell confluence measurement. Left, raw image from the incubator; right, AI processed false color image (Source: Opto GmbH).

THE ROLE OF CALIBRATION TARGETS

High-end fluorescence microscopes often require the use of calibration targets for reproducible x/y/z positioning and sensitivity. They are essential tools for ensuring the accuracy, consistency, and reproducibility of imaging data across different instruments and serve as reference standards to assess key imaging parameters such as spatial resolution, intensity uniformity, spectral alignment, and chromatic aberration. As fluorescence microscopy becomes more complex, reliable calibration becomes increasingly critical for validating results and meeting rigorous standards in different biomedical applications.

Figure 2: LED source for fluorescence microscopy (Source: CoolLED).©

Calibration targets traditionally consisted of reservoirs of fluorescent liquids, doped specialty glass or colored beads. The recent developments in broadband photoluminescent coatings have shown very interesting advantages. These engineered thin-film or substrate-embedded materials are particularly valuable for validating system performance, because a single target can generate a stable, broad-range fluorescence output under multiple excitation wavelengths. The company IMT Masken und Teilungen AG, with extensive experience in building sub-micron patterning processes, has developed cost-effective solutions to meet specific users' requirements for photoluminescent patterns on glass. In collaboration with the Swiss Federal Laboratories for Materials Science and Technology (Empa), broadband photo-luminescent coatings have been developed and optimized for use in various application scenarios. These include plasma-deposited inorganic thin-film coatings with high resistance to radiative degradation for high-power illumination, as well as bright photoluminescent organic-based coatings. The susceptibility of the coatings to bleaching has been further reduced by applying additional layers of heat dissipating material. IMT has optimized the processes for depositing photoluminescent layers as well as the nanopatterning processes, to coat arbitrary and large area structures.

A MODULAR APPROACH

Nowadays, imaging modules offer several key advantages, especially in modern, integrated or automated life science and biomedical systems. These modules combine optics, illumination, filters and cameras into a compact unit, reducing footprint and allowing seamless integration into other systems. They can be pre-aligned, pre-calibrated and/or optimized for specific fluorescence applications, which simplifies the design and use processes. And they also allow users to customize them by selecting or upgrading excitation wavelengths, emission filters, detectors or control software to match specific fluorophores or assays.

Within this approach, the German company Opto GmbH is a specialist in advanced imaging and vision systems, offering modular, plug and play digital microscopes, imaging modules, and job-specific vision modules. The company develops optomechatronic components and systems tailored to markets such as biomedical imaging or microfluidics. One interesting example are the Opto's epifluorescence microscopes, which are capable of handling from a single fluorescence channel up to 12 or 16 fluorescence channels in just a few seconds. These fluorescence microscopes are designed for automation and integration into more complex imaging platforms, such as microfluidic screening systems and cell analysis workflows. They include multi-wavelength LED excitation, synchronized to rapid filter switching, and motorized filter wheels for fast spectral channel selection. Some interesting applications are high-throughput screening, DNA/RNA sequencing, microfluidics, and lab-on-chip devices, where fast, multi-color fluorescence imaging is critical.

COST-EFFECTIVE LONG-RANGE IMAGING OCT

Optical Coherence Tomography (OCT) is a powerful, non-invasive imaging technique widely used in biological and biomedical research for capturing high-resolution, cross-sectional images of tissue microstructures. Based on low-coherence interferometry, OCT provides depth-resolved information with micrometer-scale resolution and millimeter-scale penetration, making it ideal for studying layered biological tissues such as skin, retina, cornea, and blood vessels. Unlike traditional histology, OCT allows real-time imaging of living tissues without the need for staining or physical sectioning.

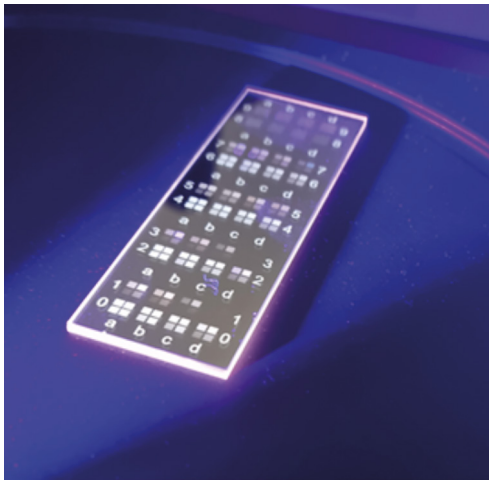
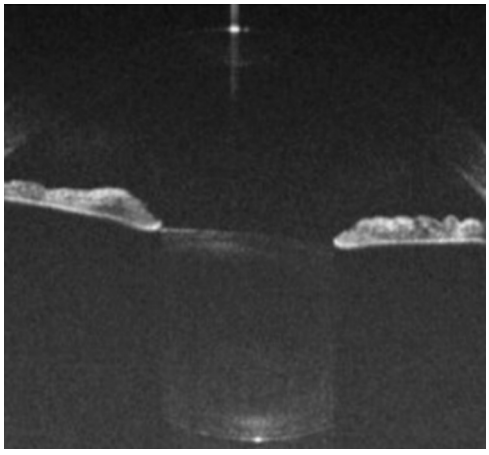


Figure 3: Calibration target for fluorescence microscopy: structured metal coating backlighted with a broadband fluorescent layer (Source: IMT Masken und Teilungen AG,).

Long-range imaging Optical Coherence Tomography is an advanced form of this technology designed to capture high-resolution, depth-resolved images over extended axial ranges. It is very beneficial in different biomedical fields. In ophthalmology, for example, long-range imaging is beneficial for examination of the full anterior chamber, from cornea to crystalline lens, as it permits a more complete image of the eye to be acquired in less time for assessment of eye health. It also facilitates wide-field imaging of the retina, the curvature of which requires a greater range of imaging depth, particularly in clinical settings where the patient is unlikely to remain static. In general medicine, long-range OCT can be of great benefit for lumen imaging in intravascular and gastrointestinal applications. In such scenarios the structures of interest may be more than a few millimeters from the imaging catheter and therefore fall outside the typical OCT imaging window. A long imaging depth can account for such variability in distance between the imaging probe and area of interest, facilitating better imaging outcomes.

Figure 4: Image of the eye, anterior chamber, and lens taken by the new Cobra-S long-range imaging spectrometer, CS800-831/28 (Source: Wasatch Photonics).



Imaging range in SD-OCT depends on both the center wavelength and on the bandwidth of the light source. So, longer wavelengths have been traditionally required in order to probe depths greater than a few millimeters in a single scan. 1300 nm has been the preferred wavelength when imaging depths of >5 mm are needed. But the use of this wavelength requires InGaAs cameras, which are significantly more expensive than the detectors used in other regions of the spectra. In order to offer a cost-effective solution which can extend the use of long-range imaging OCT, the company Wasatch Photonics has developed an

ultra-high resolution optical spectrometer that can achieve imaging depths of up to 14 mm using an 800 nm OCT. With this new design, they have translated the benefits of long-range imaging to 800 nm SD-OCT. The model CS800-841/28 is capable of 0.015 nm resolution over a 28 nm bandwidth centered at 841 nm. It has been designed to minimize roll-off with diffraction-limited optics and a low-crosstalk detector. Roll-off at 10 mm imaging depth is <12 dB, ensuring high clarity images even at extended depths. Due to the shorter center wavelength of the Cobra-S long-range imaging model, scatter in tissue will be higher, though absorption in water will be lower. This may change the contrast of structures slightly, and in some cases offer improvements in differentiation, *i.e.*, for some inner retinal structures such as ganglion cells.

QUANTUM DOTS FOR THE FUTURE OF BIOSENSING

Quantum dot–based NIR semiconductor sensors are an exciting and rapidly advancing technology for biological and biomedical applications. These sensors exploit the size-tunable bandgap of quantum dots to detect or emit light in the NIR/SWIR region, roughly from 700 nm up to 1700 nm or beyond, which is highly attractive for bioimaging and sensing due to reduced tissue absorption, lower autofluorescence, and deeper penetration. Recent research has explored NIR quantum dots as fluorescent probes in vivo, as contrast agents for imaging, and in biosensing modalities.

In sensor form, quantum dot–based detectors can be engineered for spectroscopic readout, photodetection, and multiplexed sensing of biological analytes. The company Serino, spinoff from the LMU University Munich, is focused on making near infrared spectroscopy more accessible through quantum dot–based NIR semiconductor sensors. Their platform aims to reduce the cost of spectroscopy by up to 90% while increasing pixel density to deliver higher precision and sharper imaging. Serino offers customized multi-pixel detectors tailored to match the unique infrared fingerprint of a target material, thereby optimizing sensitivity and specificity. With higher pixel densities and advanced quantum NIR materials, their goal is offering a spectral system with great performance and a much lower cost point, opening spectroscopy to broader adoption in precision agriculture, recycling, pharma...

CONCLUSION

Photonics continues to revolutionize the fields of bioimaging and spectroscopy, providing researchers and clinicians with powerful tools for noninvasive, high-resolution analysis of biological systems. The transition from traditional light sources to advanced LEDs for fluorescence microscopy has significantly enhanced stability, energy efficiency, and spectral control. In parallel, photo-luminescent coatings used as calibration targets ensure consistent performance across fluorescence systems, supporting standardization and quantitative imaging workflows. Emerging quantum dot–based sensors offer a new generation of compact, wavelength-selective detectors for spectroscopy, combining high sensitivity with customizable spectral response tailored to specific analytes or biological signatures. Additionally, the developments of spectrometers for long-range imaging Optical Coherence Tomography (OCT) at lower wavelengths will allow the manufacturing of cost-effective systems to obtain deeper tissue imaging at high speed and resolution. They will expand the range of applications of this technology. Finally, modular imaging modules are increasingly adopted in biomedical instrumentation, offering plug-and-play solutions that integrate optics, detectors, and illumination into compact units. OEMs and embedded bioanalysis platforms will benefit for the new developments in this field. Together, these photonic technologies are converging to form highly integrated, precise, and scalable solutions that will shape the future of biomedical diagnostics, monitoring, and research.