Microscopy at the Core

Presenting the Core Facility for Integrated Microscopy at the University of Copenhagen

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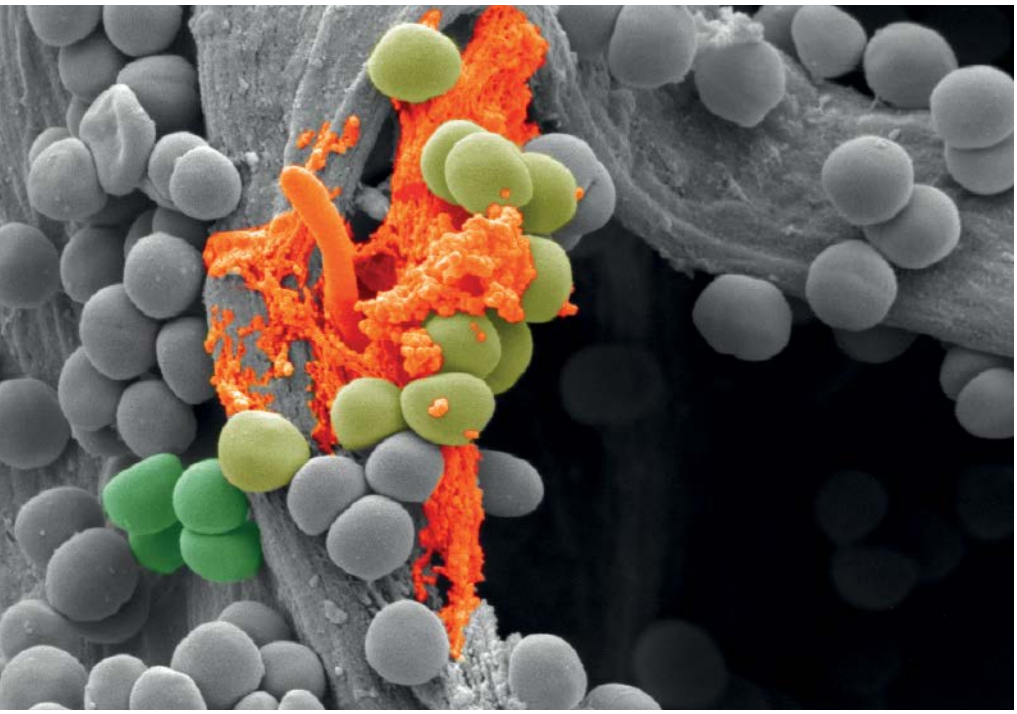

Pseudocoloured scanning electron microscopy image of Staphylococcus aureus killed on biomaterial . Green: intact; Yellow: killed; Red: bacterial exudate. Courtesy of Mathias Mörgelin, Lund university.

In the recent years, microscopy has become an essential tool in life sciences. Technical progress and innovations made microscopes increasingly performant and specialized, however penalizing smaller teams that can neither afford the instrument required, nor have the expertise to perform these experiments. The Core Facility for Integrated Microscopy (CFIM – www.cfim.ku.dk) is a technology platform aiming at democratizing the use of the latest microscopy equipment and techniques within the scientific community.

Electron and Light Microscopy under the Same Roof

As the name indicates, CFIM brings light and electron microscopy together under the same roof, aiming at increasing the interaction and correlation between disciplines. CFIM offers currently access to 15 microscopes (fig. 1), from conventional, yet essential, instruments, such as widefield and confocal light microscopes or transmission and scanning electron microscopes, to specialized, high-end systems including automated slide scanner, laser dissection, super-resolution (fig. 2), live imaging systems, serial block face electron microscopy (fig. 3), cryo-TEM tomography and correlative light and electron microscopes (fig, 4). The diversity of instruments offered allows for a wide range of techniques to be performed and a variety of questions to be tackled [1-4]. This is crucial as CFIM users come not only from the Faculty of Health and Medical Sciences, but also from other local and international academic institutions and commercial companies. Additionally, the range of electron and light microscopes present at the facility prompts CFIM users to experiment and use different microscopy techniques in their research projects [5-8].

In addition to microscopes, the facility offers access to various instruments required for sample preparation, from cryostats to an entire suite of tools required for Cryo-EM, including a high pressure freezer, freeze substitution, and a vitrification robot for example (fig. 1). Two staff members are dedicated to sample preparation for electron microscopy, including advanced techniques like Tokyasu sectioning for immuno-gold labelling, CLEM sample preparation or preparation for dual beam and serial block-face SEM imaging.

CFIM staff takes care of the day-to-day maintenance and calibrations, and keeps close attention to the performance of the microscopes so as to guaranty that microscopes remain in excellent condition.

A Facility is More than Instruments

Besides hosting equipment, CFIM provides expertise, training, and support. Indeed, it takes more than a user manual to produce reliable scientific data with a microscope. Choosing the right imaging technique and microscope to answer a specific scientific question is not trivial as it depends on the sample and the analysis required. Scientists are guided through the process of planning their experiments, and choosing the right techniques to optimally answer their research questions. At CFIM, researchers are trained to perform their own imaging and understand the techniques used. The training is tailored both to the user and the experiment, in one-on-one sessions. The expertise available at CFIM covers a wide range of biological and technical matters as the facility staff members have very diverse backgrounds.

Though knowledge in microscopy is essential to design experiments and develop more advanced techniques, most scientists have little or no training in microscopy. In addition to the personalized training on microscopes, CFIM organizes courses combining theoretical and practical activities. Currently, three PhD courses are organized (light microscopy (twice a year), electron microscopy, and image analysis courses once a year each) as well as one intensive course in light microscopy, open to all (twice a year).

In parallel with training activities, CFIM organizes workshops and conferences to promote new imaging technol-

ogies and foster interactions between microscopists.

Research and Collaborations

CFIM aims at remaining state of the art in offering the latest technologies, and adapting to the researchers needs. The implementation of new techniques relies on collaborations between CFIM staff and research teams requiring technologies not yet available at the facility. Each new microscope and new application requires an expertise which the staff members acquire by attending conferences and courses, visiting other labs, and experimenting. CFIM also works as a partner with microscope and specimen preparation manufacturers, beta-testing new cutting-edge technologies.

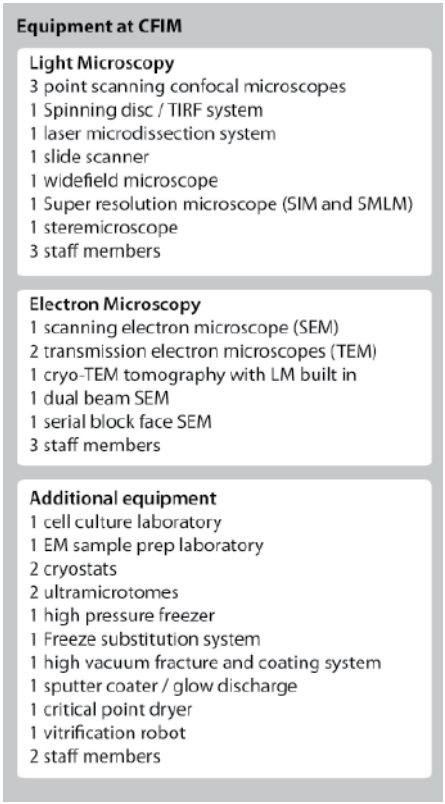

Fig. 1: List of the available equipment at CFIM.

A singularity of CFIM is that it is not only involved in academic research, but also in clinical pathology. Two of the major hospitals in Denmark send biopsies to CFIM for processing and imaging, whilst the diagnosis itself remains the responsibility of the pathologists.

Collaboration is essential for core facilities to promote knowledge exchange, and learn from one another. CFIM is active in various networks and societies related to microscopy, locally and internationally. CFIM is for example involved in the creation of the Danish BioImaging Network, which regroups life sciences researchers interested in microscopy and image analysis in Denmark (dan-

ishbioimaging.dk). In addition to long lasting collaborations with the RMS and Scandem, CFIM is now also a partner in Neubias (www.neubias.org), a European initiative for image analysis, and Bridging Nordic Imaging, a Scandinavian bioimaging network.

Before CFIM was established six years ago, no life sciences microscopy core facility was available in Denmark. With the current activities and 700 users, no one questions the need for such a facility anymore, on the contrary, it is becoming increasingly apparent that core facilities like CFIM need to not only be created but continuously developed to give researchers access to state-of-the art applications and high quality service. One of the current bottlenecks in bioimaging is the extraction of data, especially from large image data sets, thus the establishment of an image analysis infrastructure including hardware, software, and expertise in bioimage analysis is a must, which CFIM is working towards to. A longer term ambition is to establish a CFIM academic superstructure with dedicated academic faculty that uses CFIM microscopes and services for research activities exploring the newest microscopy technologies – in particular CLEM and light sheet microscopy - in close collaboration with CFIM staff. This would give life scientists access to cutting edge applications and would also serve to generate a potential career path for facility staff.

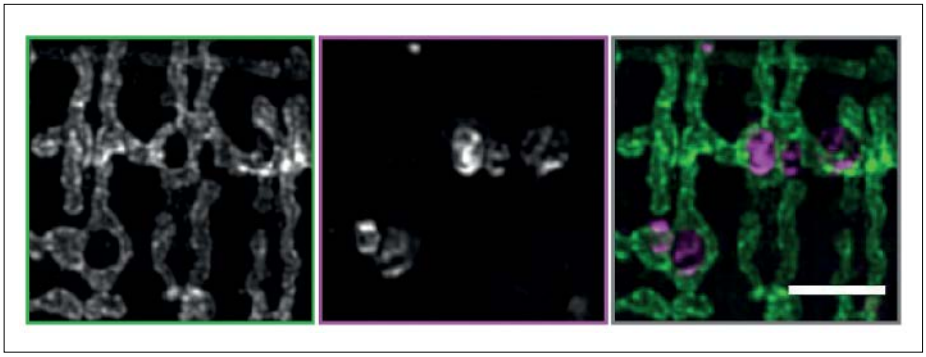

Fig. 2: Structured illumination microscopy of mitochondria (green) and lipid droplets (magenta) in a muscle fibre. Scale bar: 2 µm. Courtesy of Clara Prats, Head of Light Microscopy at CFIM.

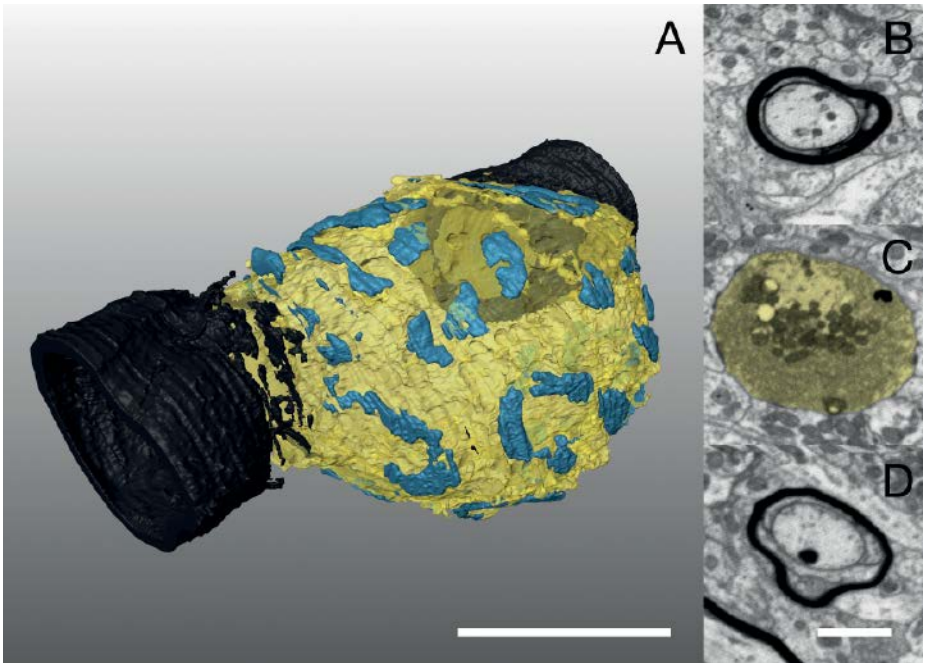

Fig. 3: Rat cerebellum axon (myelin in black) with bouton en passage (yellow) imaged with dual beam SEM. The active zones are shown in blue. Scale bar: 2 µm. Courtesy of Michael Larsen, University of Copenhagen.

References

All references are available online:
hhtp://bit.ly/IM-UniCop

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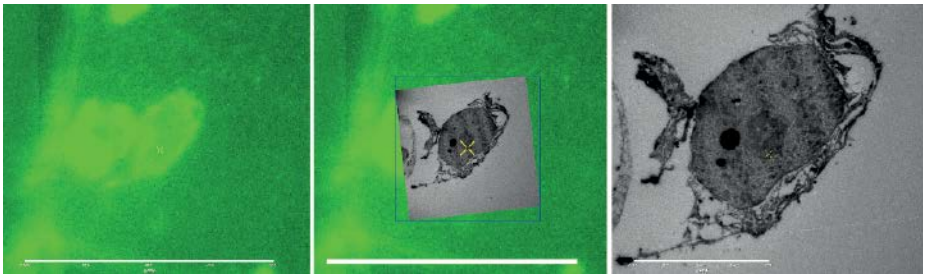

Fig. 4: Correlative light and electron microscopy on GFP expressing endothelial cells. Scale bar 50 µm (left and middle) and 10 µm (right). Courtesy of Anna Mai Jansen, University of Copenhagen.

More information on the CFIM:
http://bit.ly/Mic-CFIM

[1] All references online:
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