

3D imaging in life sciences

A world of opportunities

The world of decreasing dimensions

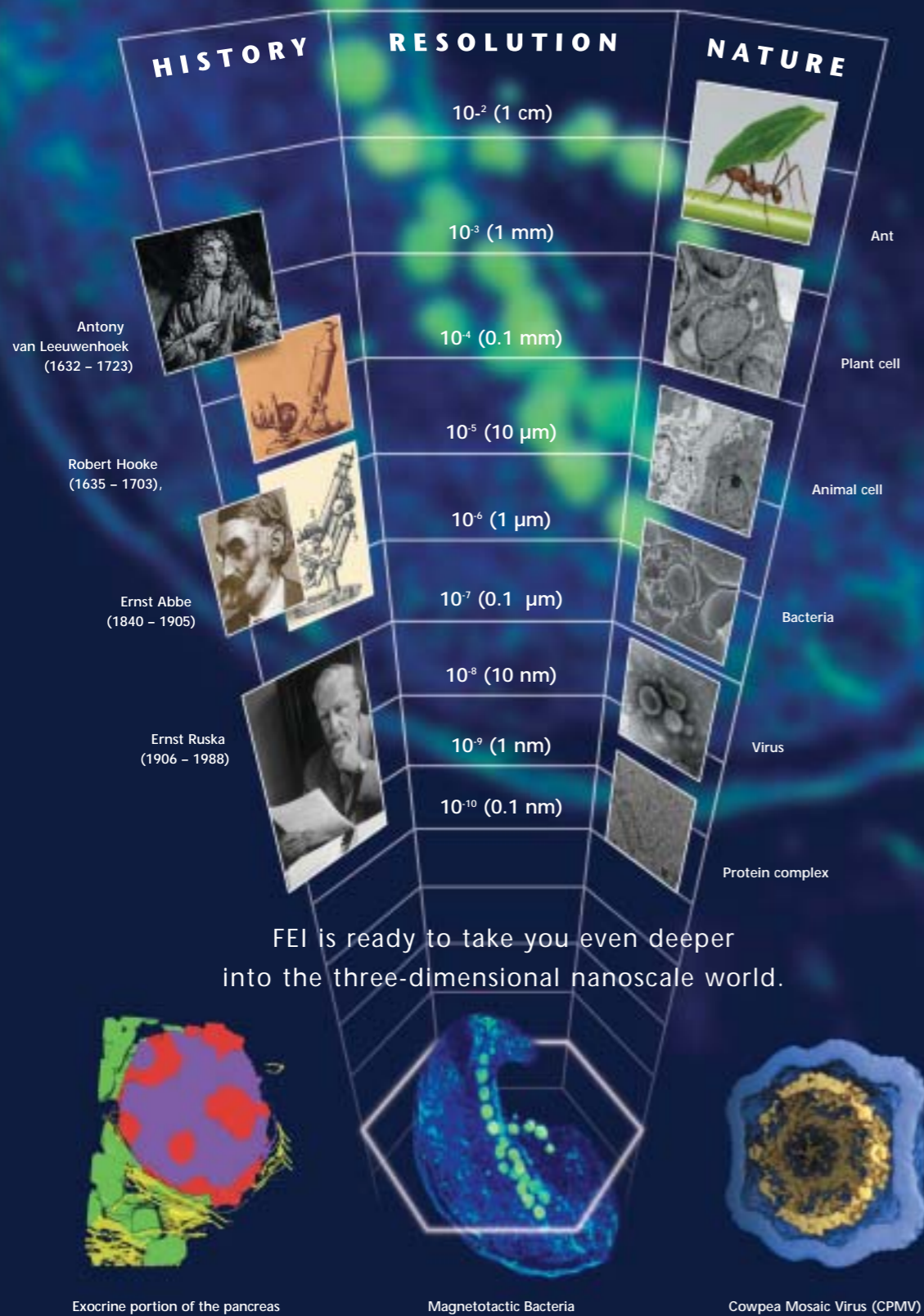
Emerging methods in electron microscopy for life sciences offer new and exciting opportunities to study architectures in 3D at unprecedented resolution, spanning more than 4 orders of magnitude in dimension and detail.

Three-Dimensional Imaging

Looking into and understanding the complex structures of the natural world has always fascinated mankind. Since the seventeenth century, an innovation stream has taken us further and deeper into the micro and nanometer domains. Over the last decade confocal light microscopy, in combination with fluorescent labeling techniques, has helped biologists and life scientists to study the three dimensional structures of biological architectures at tissue and cell level in great detail. The scientific pursuit of higher quality information, greater levels of detail and increased 3D resolution challenged FEI Company to develop a product range enabling investigation of the 3D structure of biological material. As a result, advanced investigations can be carried out with a wide range of dimensions and with the highest resolution possible: from tissue to cell to cell organelle, down to viruses, protein complexes and individual proteins.



FEI provides a total solution for electron tomography. The Tecnai™ G² offers a fully automated data collection, fully embedded detectors and acquisition software for 3D modelling reconstruction. Visualization software is included in the Xplore3D™ package.



3D image of Magnetotactic Bacteria using Xplore3D TEM. Sample Courtesy: National Institute of Advanced Industrial Science and Technology, Osaka, Japan

Antony van Leeuwenhoek (1632 – 1723) was the first to discover the μ m world, seeing bacteria, free-living and parasitic microscopic protists, sperm cells, blood cells, microscopic nematodes and rotifers, and much more.

Robert Hooke (1635 – 1703), of whom no known portrait exists, devised the compound microscope and illumination system, one of the best microscopes of his time.

Ernst Abbe (1840 – 1905) was a brilliant mathematician and physicist who made several of the most important contributions to the design of lenses for optical microscopy. These lenses were the first ever to have been designed based on sound optical theory and the laws of physics.

Ernst Ruska (1906 – 1988) developed the first construction of an electron microscope in 1931. With this instrument, two of the most important processes for image reproduction were introduced: the principles of emission and radiation.

3D imaging using DualBeam™ and Auto *Slice and View*™

One of today's most exciting methods to study the 3D architecture of tissue, whole cells and sub-cellular structures, is the DualBeam™ electron microscope using the *Slice and View* technique.

FEI's DualBeam™ microscope combines a Scanning Electron Microscope (SEM) with a Focused Ion Beam (FIB) in a single, fully-integrated system. The FIB acts as a 'nano-scalpel', enabling high precision cutting and slicing into samples to reveal their 3D internal structures. The SEM provides

high resolution imaging of the freshly cut surfaces. Sequential repetition of cutting and imaging (*Slice and View*) yield a set of data that replicates the 3D reconstruction of the material from tissue level down to cell and cell organelle level. An additional value of DualBeam™ instruments is that the FIB 'nano-scalpel' can be used to swiftly and easily produce Transmission Electron Microscope (TEM) samples from your material without the compression and knife-mark artifacts common to mechanical sample preparation techniques.

3D volume of the exocrine portion of the pancreas generated with Nova Nanolab
Sample Courtesy:
Ingo Gestmann
FEI Company

1 μm



On the right screen in the photo above you can see the 3D Volume reconstruction of parts of an exocrine pancreas cell after automated *Slice and View*.

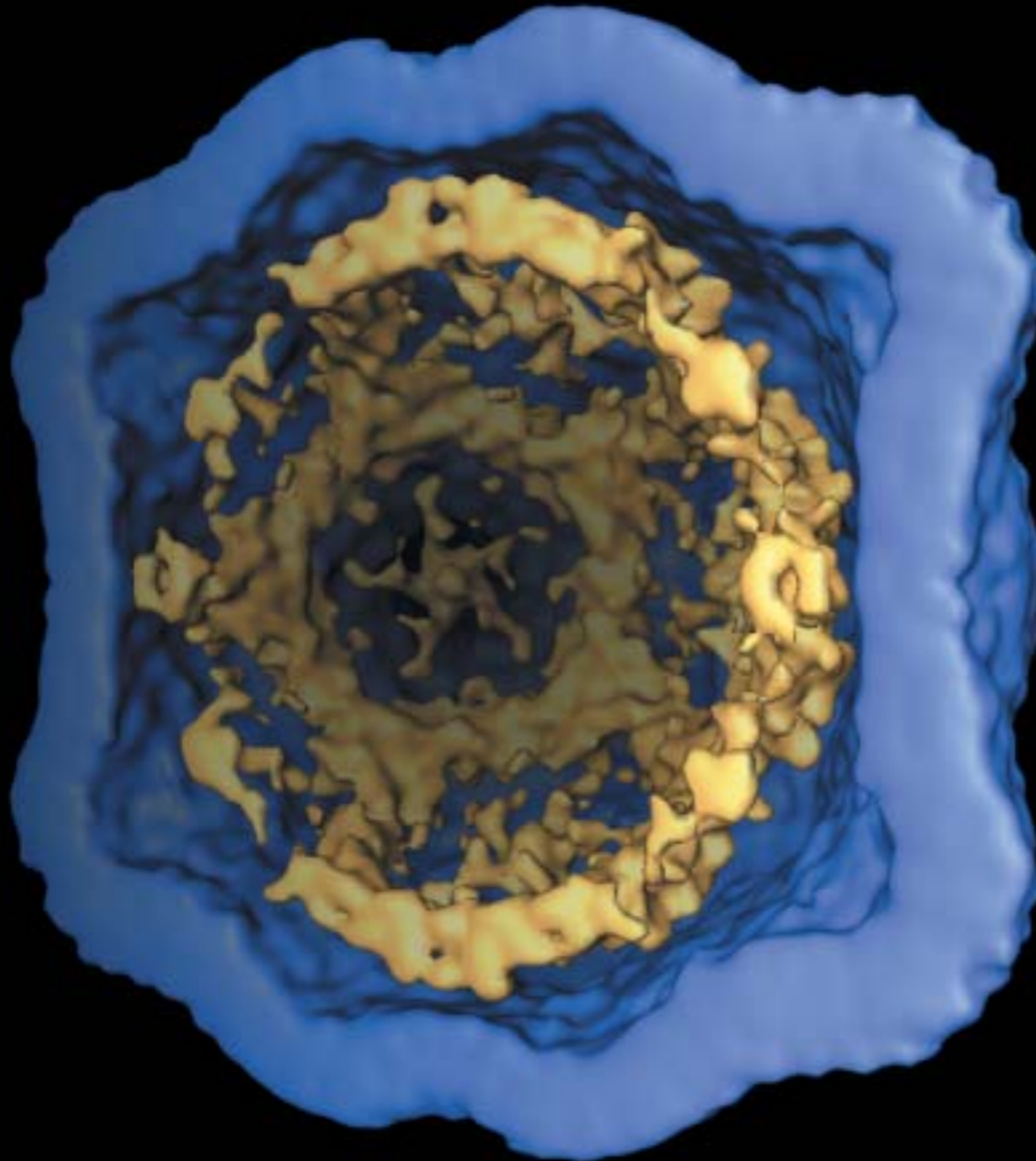
Automated 3D imaging using Electron Tomography and Single Particle Analysis

Further down the 3D resolution scale, Electron Tomography and Single Particle Analysis (SPA) are proven and powerful methods for studying 3D information of sub-cellular structures at the nanoscale. Tomography is a technique whereby images are recorded from a specimen in as many viewing directions as possible. Instead of viewing from only one direction, you are in a sense walking all around the specimen and viewing it from each direction.

Xplore3D™ is FEI's complete 3D imaging solution for FEI Tecnai™ Transmission Electron Microscopes, automating the process of data collection, reconstruction, visualization and analysis. Xplore3D™ enables

you to capture high-quality 3D images to reconstruct the spatial organization of cells (structural maps), to enable ultra thin digital slicing of sections, 3D cytochemistry, and to visualize the 3D spatial organization of cells, organelles, protein complexes and individual proteins.

Another powerful, high resolution technology is Single Particle Analysis (SPA) where a thin layer of a solution containing identical particles (viruses, protein complexes) is frozen and imaged with the TEM. Advanced software is then applied to reconstruct the 3D structure from a large number of these identical particles.



Cowpea Mosaic Virus (CPMV), vitrified and subjected to a single particle reconstruction procedure. The morphological relation between the outer protein shell (blue) and the inner viral genomic material (yellow) is clearly visible.

5 nm



DualBeam technology, Slice and View applications and Xplore3D software enable you to see and understand structures at nanoscale resolution, taking you deeper into the world of decreasing dimensions than ever before.

About FEI: *Tools for Nanotech™*

FEI Company is a leading provider of advanced NanoBiology solutions, bringing our customers tools to support structural cell biology research, and to aid the development of next generation pharmaceuticals and diagnostics. FEI's Tools for Nanotech™ deliver nanoscale 3D characterization, analysis and modification capabilities to a range of customers in research, development and manufacturing in the life sciences, semiconductors, data storage, and materials markets. With R&D centers in North America and Europe, and sales and service operations in more the 40 countries around the world, FEI is bringing the nanoscale within the grasp of leading researchers and manufacturers and helping to turn some of the biggest ideas of this century into reality. Please visit us at www.feicompany.com

3D rendering of a budding yeast cell. Image series was obtained using *Slice and View™* on an FEI DualBeam™ instrument. The results are from an ongoing cooperation between FEI and Sriram Subramaniam and his colleagues at the National Institutes of Health, Bethesda, MD, USA.

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