Vironova

TEM-based analysis system

MiniTEM™

MiniTEM is a semi-automated, compact system for analysis and characterization of nanoparticles, viral vectors and virus-based biotherapeutics.

MiniTEM offers:

- A compact, TEM-based analytical system that can be placed in traditional process development or analytical laboratories—no special infrastructure is required
- Automation that enables non-experts in electron microscopy to rapidly obtain reliable nanoparticle characterization data
- Low acceleration voltage compared to traditional transmission electron microscopes (TEM) allowing for maximum contrast

System overview

The MiniTEM system comprises:

1. The MiniTEM microscope. A 25 kV transmission electron microscope (TEM) with 1 nm resolving power in a compact and vibration tolerant design that is suitable for standard laboratory environments

2. Vironova Imaging and Analysis Software (VIAS) which provides semi-automatic image acquisition as well as subsequent analysis and data presentation. Pattern recognition and machine learning capabilities geared towards viral vectors enable VIAS to perform advanced particle characterization, classification and measurements.

The system enables non-experts in electron microscopy to rapidly obtain nanoparticle characterization data. It automatically images, detects and analyzes particles. Users can quickly generate quantitative data and statistics as well as images of nanoparticles that support understanding and decision making in process development and manufacturing.

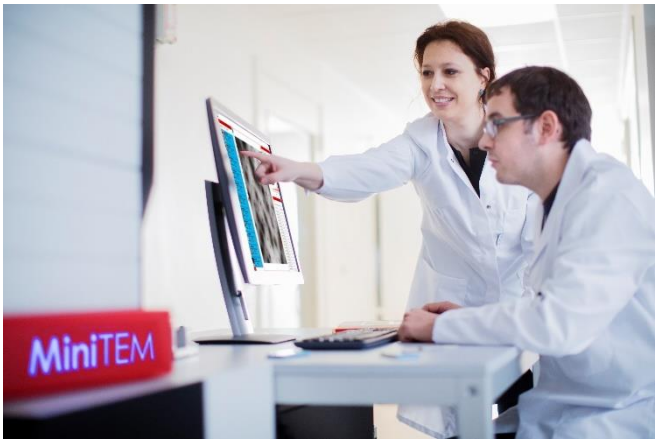

Figure 1 – The MiniTEM system complements existing routine analysis methods in process development and analytical laboratories.

Main applications

MiniTEM in process development

MiniTEM complements existing routine analysis methods in process development. The system can be set up to automatically deliver detailed information about the morphology, integrity and purity of viral vectors, viral vaccines and other nanoparticles.

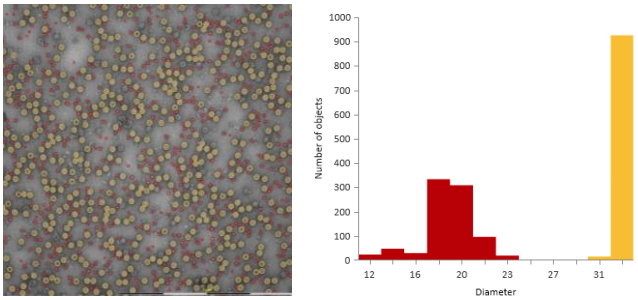

Figure 2 – The image at the left shows viral vectors dispersed among proteasome contaminants. MiniTEM correctly segregates and classifies these species and generates quantitative results as shown on the right.

MiniTEM in product characterization

MiniTEM can rapidly screen and acquire hundreds of images to give an accurate representation of a sample. The acquired images are subsequently analyzed to give meaningful results.

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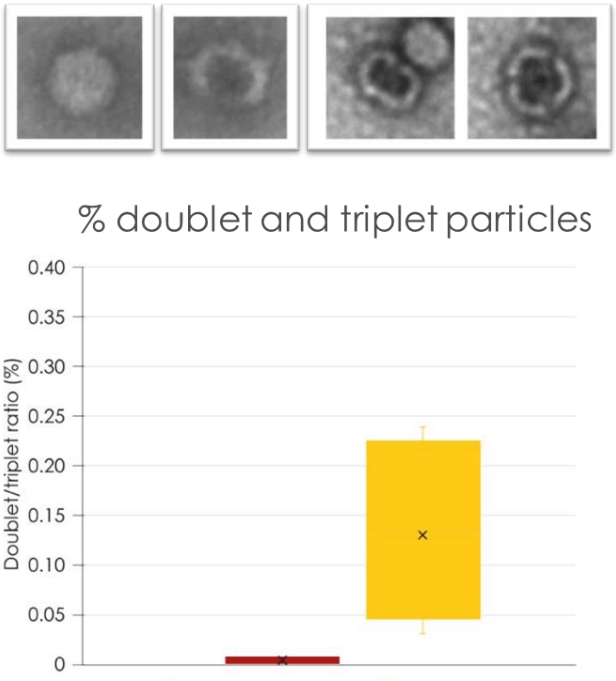

Figure 3 – Adeno-associated viruses (AAV) can form doublets and triplets when they lose integrity, as shown in the images above. In this study, the percentage of doublets/triplets was quantified to compare two batches of the same product. The left (red) bar represents the analysis result from Batch A, while the right (yellow) bar represents the result from Batch B.

MiniTEM in analytical laboratories

Automated analysis of many images and particles can be designed to reach statistical convergence and produce objective results with reduced risk for human error. This makes MiniTEM suitable for product characterization studies.

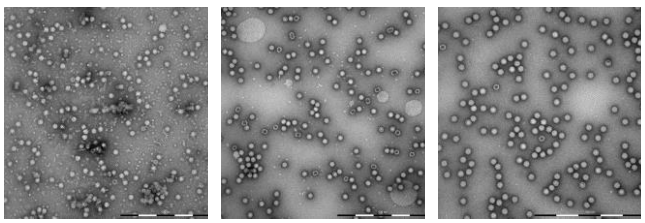

Figure 4 – Product purity is a common analysis performed using MiniTEM in analytical labs. In the above images, the product purity increases from left to right.

Automated imaging and particle analysis

A common workflow for analysis

The automation in MiniTEM goes beyond the settings of the microscope and camera. After the sample (3 µL) is placed on a sample grid, the sample is inserted into the microscope and regions of interest (i.e. waypoints) are easily selected on the grid to be analyzed. Images are automatically acquired at the selected waypoints. The particles in the selected images can automatically be analyzed for morphology, integrity, purity, aggregation or any other characteristic that has been built into the automation workflow by the user. The data can be presented as a list, a bar plot, a scatter plot or a box plot. Images, particle data, statistics and plots can be easily exported for further analysis or archiving.

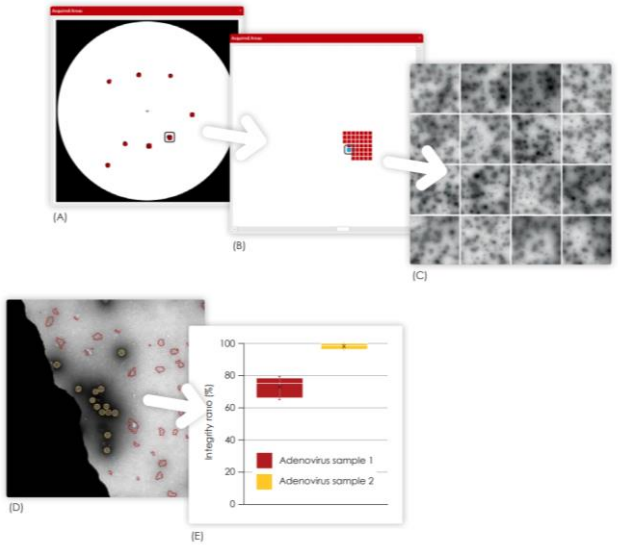

Figure 5 – The MiniTEM analysis workflow. (A) Waypoints are selected (B) Images are automatically acquired at selected waypoints (C) A large number of images are acquired (D) Particles are detected and classified in the images (E) Defined morphological characteristics are transformed into quantitative metrics.

A fast pathway to quantitative data

Translating image data into reliable, quantitative measurements is made possible by MiniTEM's ability to automatically acquire and analyze large subsets of images, while modern computational power dramatically reduces the time from sample acquisition to quantitative result (Figure 6).

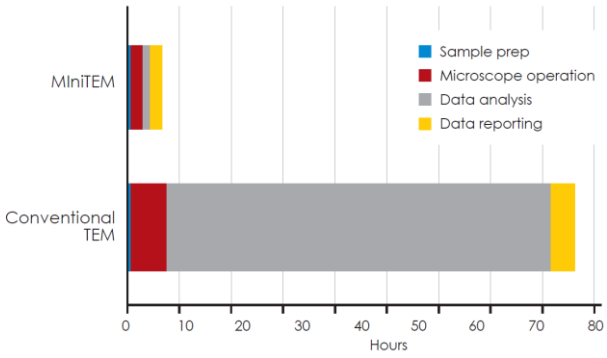

Figure 6 – Software reduces the analysis time dramatically versus traditional methods. Here, the entire analysis of two adenovirus samples, analyzed for relative purity, is reduced from nearly 80 hours to just over 7.

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MiniTEM essential specifications

Technical specifications and characteristics

Specimen size	Standard ø 3.05 mm grids
Sample holder	Single-grid sample holder (2 holders provided)
Resolving power	1.0 nm
Nominal accelerating voltage	25 kV
Field of view	0.35 µm – 32.00 µm
Apertures	Condenser ø 50, 30 µm Objective ø 50, 30 µm
Specimen stage	3-axis piezoelectric stage
Stage traverse	X,Y: total range 2.0 mm, Z: total range 0.7 mm
Electron gun type	SE Cathode ZrO/W[100]
Cathode lifetime	>2000 hours
Vacuum system	Sample and gun chamber: ion getter pumps Airlock system: turbomolecular pump
Digital camera system	ViroCAM (1024x1024 live view, 2048x2048 capture)
Standard features	Beam control, Auto/Manual Illumination, Camera control (Auto/Manual exposure, image capture), 14 preset field of view steps (32 µm – 350 nm), Live Discrete Fourier transform (DFT), Intensity histogram, Focus wobbler, Defocus, Guided sample exchange, Stage controls, Beam alignments, Vacuum and emission monitoring.
Operating environment	18-30°C @ <75% relative humidity
Recommended floor space	Minimum 190 cm (W) x 95 cm (D)
Net weight	220 kg
Mains requirement	Single-phase 100–240 V, 50-60 Hz, earthed mains
Power consumption	Max 550 VA
Cooling water requirement	Not required
Compressed air requirement	Not required
Regulatory compliance	Conforms with the provisions of the following CE directives: 2014/30/EU – EMC (EMC directive) 2014/35/EU – LVD (low voltage directive) 2011/65/EU – RoHS2 (Reduction of Hazardous Substances 2 directive)

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Ordering information

Article number	Description
2001	MiniTEM system

Related products

Article number	Description
4000	ViroTEM™ system
2500	VIAS software license
3000	VAS software license

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