

TEM-based analysis system

ViroTEM™

ViroTEM is an automated and versatile system for analysis and characterization of nanoparticles, viral-based biotherapeutics and other applications in biotherapeutic development and production.

ViroTEM delivers:

- Rapid and efficient specimen searching (full grid overview) and high-resolution image acquisition enabled by a dual-camera system
- High-sample throughput via a “one touch” three specimen holder
- Broad range of applications made possible by the wide accelerating voltage range (20-120 kV)

System overview

The ViroTEM analysis system comprises:

1. A 120 kV transmission electron microscope (TEM) with multiple lens configurations, including a standard lens for unsurpassed high contrast and a class-leading HR lens for high resolution. This innovative design allows for a wide variety of specialized applications.
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 enable VIAS to perform advanced particle characterization, classification and measurements.

The combination of the advanced TEM-system together with VIAS software enables automated 2-level screening which allows the system to determine which grid squares are suitable for imaging and then acquires a series of high-resolution images at a pre-determined number of locations on the grid.



Figure 1 – The ViroTEM system is compact TEM-based analysis tool designed for simple operation but with powerful functionality

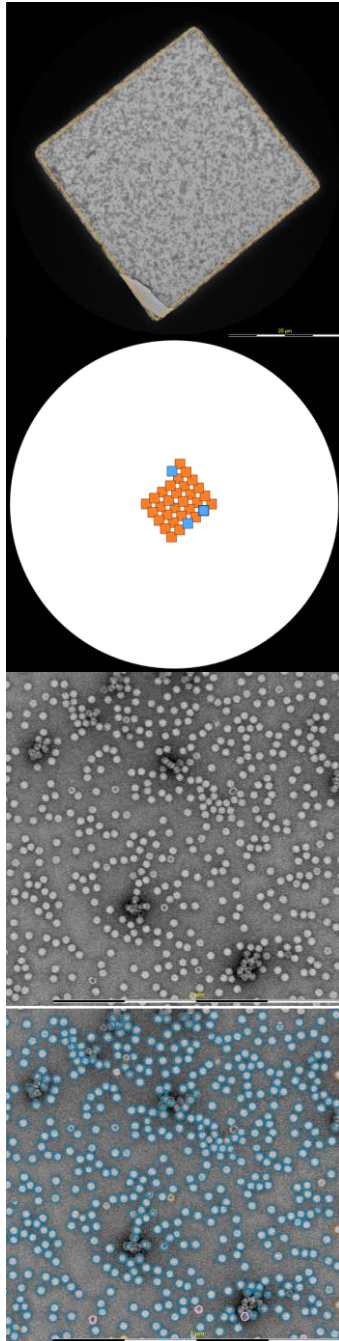
Main applications

The performance and versatility of the ViroTEM system enables a large range of applications.

- Determine particle size distributions of viral vectors and sample components
- Verify sample purity to verify downstream process capabilities and/or batch-to-batch variation
- Assess particle integrity when making changes in process conditions, including formulation buffers
- Visualize sample morphology to extract structural information about the sample
- Identify sample contaminants such as viruses (e.g. in cell bank characterization) or bacteriophage (e.g. in investigations of fermenter contaminations)

Semi-automated multilevel screening

The semi-automated, multilevel screening functionality of ViroTEM involves four main steps:



Step 1

Acquire grid-square images at large field-of-view.

The system automatically adjusts to grid orientation.

Step 2

The system compares each image to reference image(s) to assess suitability for imaging.

Step 3

High-resolution images are obtained from grid squares that have been given a high suitability rating

Step 4

Images are analyzed to identify (i.e. segment) and classify particles.

Figure 2 – The ViroTEM multilevel screening methodology

Reliable data analysis

The ViroTEM system translates TEM image data into quantitative analytics which can be used to make informed decisions in process development and manufacturing. Figure 3 shows an example of an analysis performed on adeno-associated viruses (AAVs).

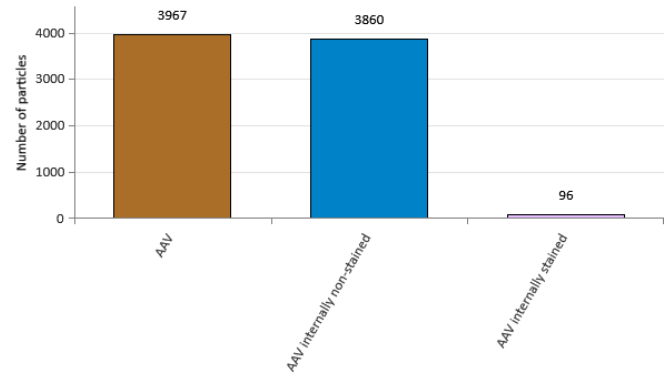


Figure 3 – Analysis of internally-stained versus non-stained AAVs. Internally-stained vectors can be correlated to a loss of vector-integrity.

Secure data storage

The ViroTEM system stores data in a secure SQL database structure. The database can be located locally on the control PC or can be installed in a network environment.

Summary

The ViroTEM system is a powerful tool for biotherapeutic applications, especially those involving viral structures, including:

- Gene therapy
- Cell therapy
- Viral-based vaccines
- Virus and bacteriophage contaminations

ViroTEM essential specifications

Technical specifications and characteristics

Specimen size	Standard \varnothing 3.05 mm grids
Sample holder	One-touch three-specimen holder
Resolving power	0.204 nm
Maximum specimen tilt angle	$\pm 70^\circ$
Accelerating voltage	20-120 kV (in 100V steps)
Magnification zoom	50-1 000X (in LOW MAG mode, 10 steps) 200-200 000X (in HC mode, 30 steps) 4000-600 000X (in HR mode, 20 steps)
Apertures	Movable, four-stage click stop \varnothing 20, 50, 100, 200 μ m
Image rotation	1000-40 000X (HC mode) $\pm 90^\circ$ (15° steps)
Specimen stage	4-axis eucentric goniometer stage
Stage traverse	X,Y: \pm 1 mm, Z \pm 0.3 mm
Filament type	LaB ₆ filament
Cathode lifetime	>500 hours
Digital camera system	<i>Dual camera system</i> Screen camera (1024x1024 display, 1024x1024 record) Main camera (1024x768 display, 4608x3456 record)
Standard features	Autofocus, microtrace, autodriven, autophoto, live FFT display, measurement function (manual/automatic distance measurement), low dose, auto pre-irradiation (API), image navigation, column with mild baking, whole view, drift correction
Operating environment	18-25°C @ 30-60% relative humidity
Recommended floor space	Minimum 360 cm (W) x 480 cm (D)
Net weight	1158 kg
Mains requirement	Single-phase 100VAC \pm 10%, 50-60 Hz, independent grounding with resistance of 100 Ω or less
Power consumption	Max 4.0 kVA
Cooling water requirement	Temperature: 15-20°C (stability \pm 0.1°C/30 min) Flow: 1.8-2.2 L/min, Pressure: Approx. 0.05-0.15 MPa
Compressed air requirement	Air pressure: 0.35-0.50 MPa
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)

Ordering information

Article number	Description
4000	ViroTEM system

Related products

Article number	Description
2001	MiniTEM system
2500	VIAS software license
3000	VAS software license

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