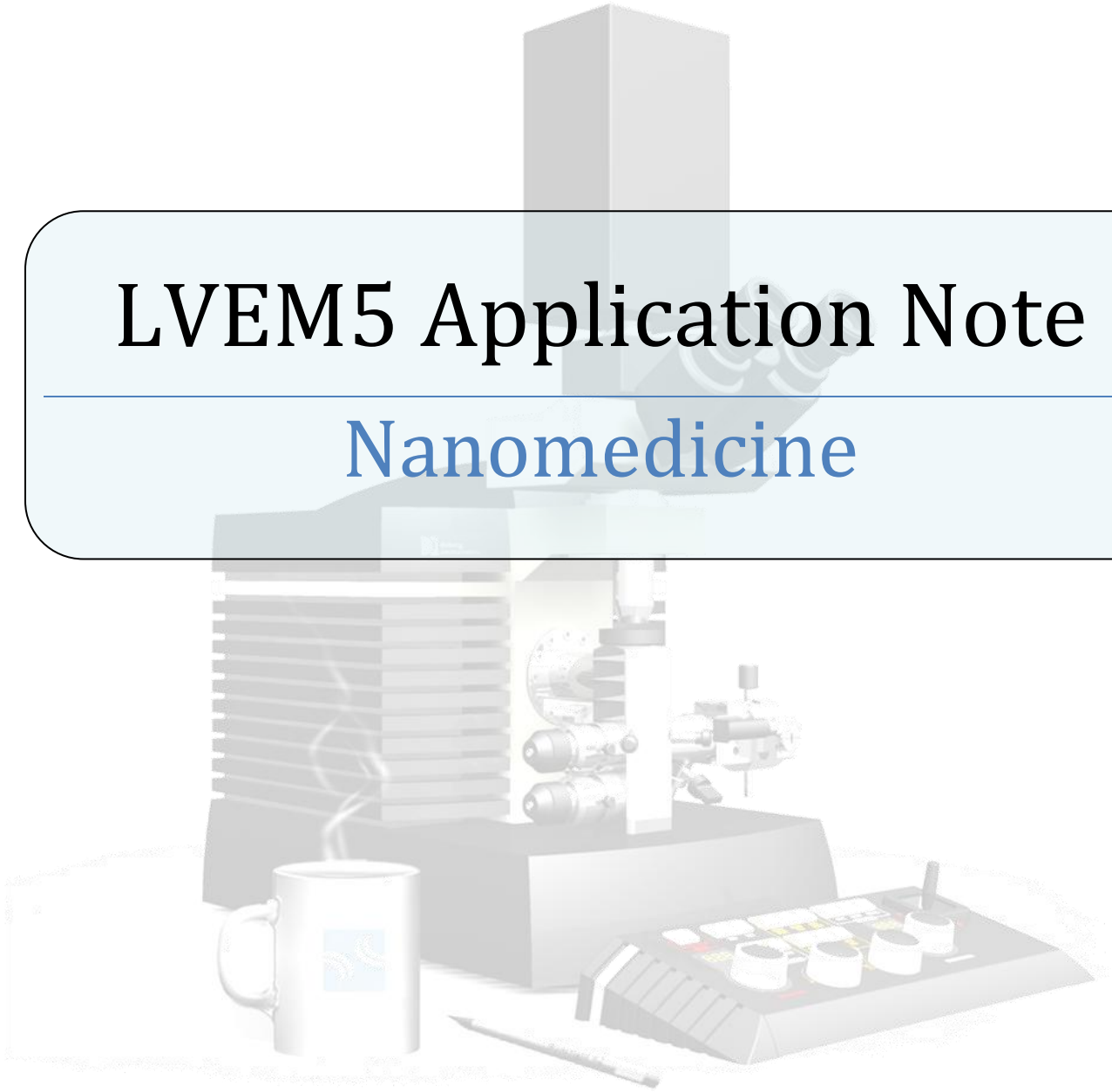
LVEM5 Application Note

Nanomedicine



Delong America
LVEM5 Benchtop TEM
TEM · SEM · STEM · ED

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Nanomedicine

Introduction

Early research on so-called "first-generation" nanomedical materials focused on leveraging small particle size to improve delivery and reduce toxic side effects of existing drugs. The common breast-cancer drug paclitaxel (Taxol, **Bristol-Myers Squibb**) and the ovarian cancer drug doxorubicin HCl (Doxil, **Ortho Biotech**) were both reformulated with nanoparticles to create more effective and less toxic versions.

Now, second-generation nanomaterials with inherent nano-properties are in clinical trials. **CytImmune Sciences** (Rockville, Md.) has bound recombinant human tumor necrosis factor alpha (TNF-α) to the surface of PEGylated colloidal gold nanoparticles. Early Phase 1 clinical data indicated that the company's lead drug candidate, Aurimune (CYT-6091), safely and selectively delivered TNF-α to human solid tumors in greater concentrations than previously possible, avoided uptake by the liver and spleen, and was essentially absent from surrounding healthy tissue. Phase 2 studies will combine Aurimune with chemotherapy to treat pancreatic cancer, melanoma, soft tissue sarcoma, ovarian, and breast cancer patients, the company reports.

Taking a different tack, **MagForce Nanotechnologies AG** in Berlin, Germany is conducting three Phase 1 and two Phase 2 trials of nanoparticles made from iron oxide. Liquid-suspended 20-nm nanoparticles are injected into a target tumor and subjected to a 100 kHz magnetic field. The rapidly vibrating particles generate heat, destroying the tumor without affecting surrounding healthy tissue. Released nanoparticles are either reabsorbed by surrounding intact tumor cells, absorbed by macrophages, or stored in the spleen and liver and metabolized for iron. Clinical trials involve glioblastoma, prostate, esophageal, pancreatic, and breast cancers.

Still another approach being developed by Houston-based **Nanospectra Biosciences Inc.** and other companies destroys solid tumors by using photothermal ablation to heat optically active nanoparticles. Nanospectra's particles consist of a thin layer of gold over a silica shell designed to absorb various wavelengths of light, including the near-infrared, which can penetrate tissue.

Introduction
Courtesy of
(Nano-Progress, 2009)

Nanomedicine

How the LVEM5 helps

Versatile

The LVEM5 is the ideal addition to any laboratory doing research in nanomedecine. Its multimodal imaging capabilities makes it a comprehensive imaging tool. The LVEM5 is truly a 3-in-1 electron microscope. Not only is it a Transmission Electron Microscope (TEM), but it can be configured with up to two different scanning modes for use as a Scanning Election Microscope (SEM) and a Scanning Transmission Electron Microscope (STEM). With the LVEM5 you can switch between imaging modes without moving your sample. This way you can capture both surface and transmission images from the same area of interest. With only one tool you can significantly improve the understanding of your nanoparticles.

Miniature Form Factor

The LVEM5 is the only multi-modal electron microscope available in a benchtop configuration. No longer will you need to send batches of samples to a core-imaging facility, wasting time and resources. The LVEM5's miniature size means that it can be installed in your workspace, right where you need it. The LVEM5 does not require a dedicated facility for installation. No special power or cooling requirements are needed and vibration isolation is generally not a concern.

Resolution & Contrast

Don't let the small size of the LVEM5 mislead you. It may be miniature in size but it's a giant advantage in the lab. The LVEM5 is capable of resolving objects as small as 2 nanometers in transmission and scanning modes. Additionally, the LVEM5 is capable of producing higher contrast images than a conventional transmission electron microscope without the need for stain. In no way are you sacrificing imaging quality or obtainable resolution with a benchtop configuration. The LVEM5 easily produces high quality images suitable for presentations or publications.

Accessible

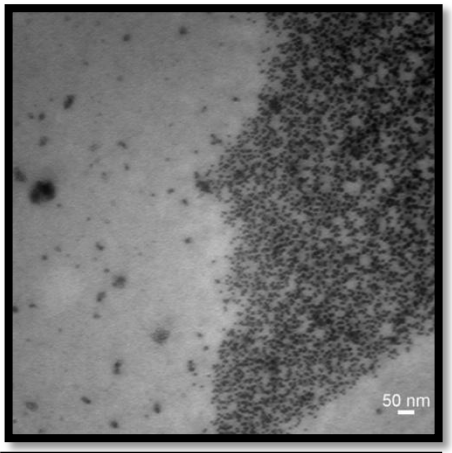
The LVEM5 is so remarkably simple that anyone can use it. No longer will you need highly trained technicians to take electron micrographs. The controls are intuitively configured on an ergonomically designed remote control panel that can be positioned as required. Feedback is provided directly on the control panel as well as through the LVME5's comprehensive software. Every installation of a LVEM5 includes personalized on-site training. By the end of training, users are capturing meaningful images. If support or assistance is ever needed, the LVEM5 technical staff is readily available by phone or email.

Nanomedicine

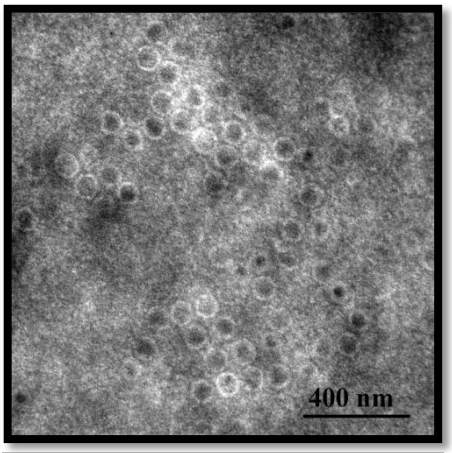
What this all means for you

With the LVEM5 you will be able to resolve the sizes of your nanoparticles with improved contrast to understand the quality of your synthesis on a number of levels. You will be able to discern particle size, quantity and distribution. This can all be easily accomplished in minutes on the LVEM5, right in your own lab. You get all this for a fraction of the price of a conventional electron microscope.

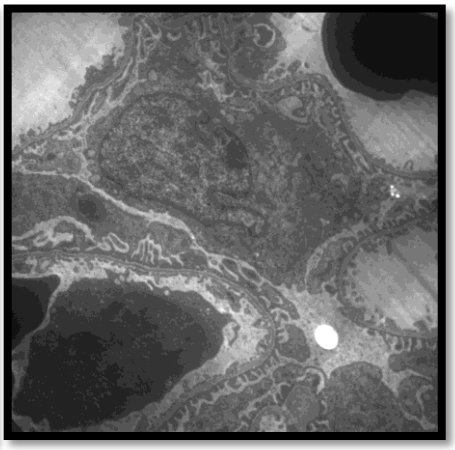
Selected Images



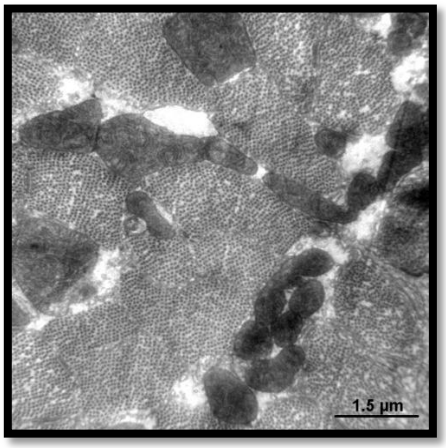
Nanoparticles
TEM



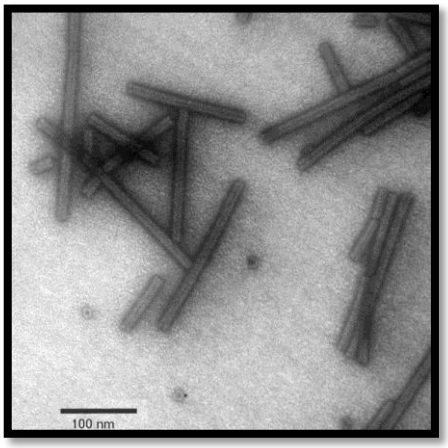
Unstained Adenovirus in Tissue
TEM



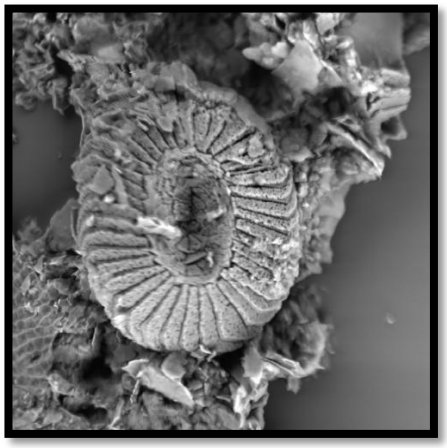
Unstained Kidney Tissue Section
TEM



Grasshopper Muscle
TEM



Negatively Stained TMV
TEM



Fossilized Shell
SEM

Nanomedicine

Specifications

Operation	
Nominal accelerating voltage	5 Kv
Specimen Size	Standard ϕ 3.05 mm grids
Time for sample exchange	Approx 3 min.

Electron Optics	
Condenser lens	**Permanent magnet**
Focal length*	4.30 nm
The smallest illuminated area	100 nm
Condenser aperture	Φ 50, 30 µm
**calculated for 5 Kv*	
Objective lens	**Permanent magnet**
Focal length*	1.26 mm
C_s (spherical aberration coefficient)	0.64 mm
C_c (chromatic aberration coefficient)	0.89 mm
δ_{theor} (theoretical resolution)	1.12 nm
α_{theor} (theoretical aperture angle)	10^{-2} rad
Objective aperture	Φ 50, 30 µm
**calculated for 5 Kv*	
Projection Lens	**electrostatic**
Electron Gun	**SE Cathode ZrO/W[100]**
Current density	0.2mA sr^{-1}
Lifetime	> 2,000 hours

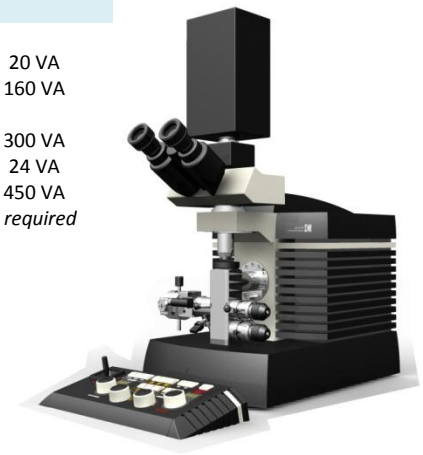
Light Optics	
Objective Olympus M 40x	NA 0.90
Objective Olympus M 4x	NA 0.13
Binocular M 10x	
Olympus U-TR30-2 widefield trinocular observation tube	
TEM image capture	
Camera	Retiga 400R CCD
Pixel size	2048 x 2048 pixels
Digitalization	12 bits
Pixel size	7.4 x 7.4 µm
Cooling	Peltier cooling
Scan image capture	
monitor	512 x 512 pixels
Saving image	Up to 2048 x 2048 pixels
digitalization	8 bits

Imaging Modes	
TEM	
Resolving power	
TEM BOOST	1.2 nm
Basic System	2.0 nm
Total magnification	
TEM BOOST	1,400 – 700,0000x
Basic System	5,000 – 202,0000x
ED	
Minimum probe size	100 nm
Diffraction lens	Magnification 3.5
STEM	
Resolving power	2.0 nm
Minimum magnification	(25 x 25 µm) 6,000x
SEM (BSE detector)	
Resolving power	3 nm
Minimum magnification	(200 x 200 µm) 640x

Vacuum	
Airlock System	
Diaphragm and turbomolecular pump	10^{-5} mbar
Object space	
Ion getter pump (10 l sec^{-1})	10^{-8} mbar
Electron Gun	
Ion getter pump (7 l sec^{-1})	10^{-9} mbar

Consumption	
Control electronics in standby (ion getter pumps only)	20 VA
Control electronics	160 VA
Including airlock pumping system	300 VA
Camera	24 VA
PC and monitor	450 VA
No cooling water for the microscope is required	

Weights and Dimensions	
Electron and light optics	
Weight	25 kg
Dimensions (w/o camera)	29 x 45 x 43 cm
Airlock pumping system	
Weight	15 kg
Dimensions	30 x 30 x 34 cm
Control Electronics	
Weight	19 kg
Dimensions	47 x 27 x 27 cm



Works Cited

Agres, T. (2009, September 01). *Nano-Progress.* Retrieved 09 23, 2009, from Drug Discovery and Development: http://www.dddmag.com/article-nano-progress-090409.aspx

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