Comparison of LVEM and classical TEM for Nanoparticle Sizing

Background

Nanoparticles are intrinsically defined by their measured size. Thus, the ability to quickly, easily and accurately measure their size is of critical importance to the research community and manufacturers making or utilizing nanomaterials.

This report will study a recent peer-reviewed literature article comparing low voltage electron microscopy (LVEM) with classical transmission electron microscopy (TEM) for nanoparticle size measurements (Dazon, 2019). Highlights of the strengths of each instrumentation technique and the best approaches for sample preparation methods will be presented.

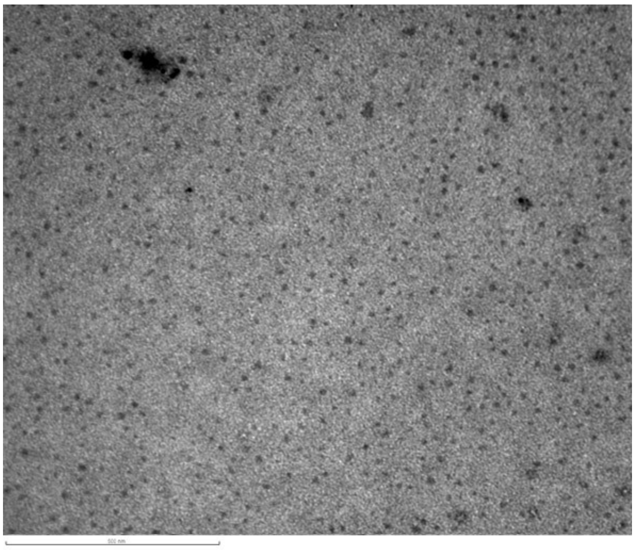

Figure 1. Dendrimer polymer nanoparticles imaged on an LVEM 5.

LVEM Characterization of Nanoparticles

LVEM has been utilized to measure a variety of nanoparticle materials in studies ranging from copper oxide's impact on seed germination (Das, 2020), to single molecule dendrimers (Drummy, 2004), to complex structures made from a combination cellulose nanocrystals, gold nanoparticles, and iron oxide nanoparticles (Mahmoud, 2013).

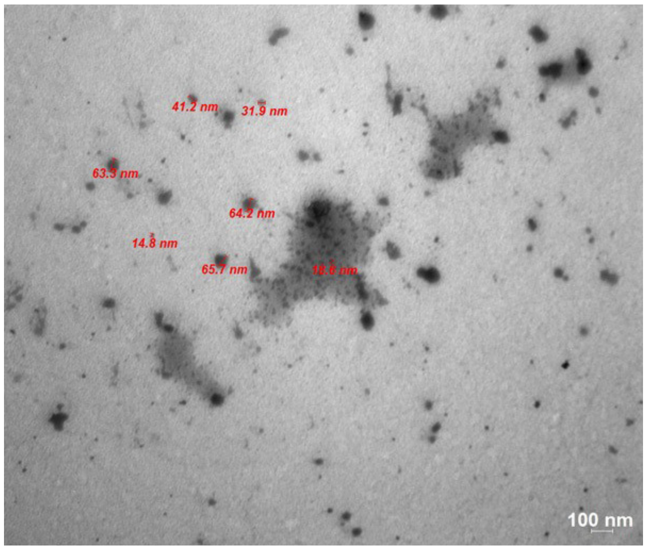

Figure 2. Silver nanoparticles imaged on an LVEM 5.

The lower accelerating voltage provides a darker contrast with lower atomic number (Z) elements. This is a strong advantage for carbon-based polymer nanoparticles such as dendrimers (Figure 1), and provides sharper images even for SiO_2 and TiO_2 nanoparticles. While this contrast difference becomes less noticeable for metals such as silver nanoparticles (Figure 2) and gold nanoparticles (Figure 3), when thick organic surface coatings are applied to the metal nanoparticle core, it allows for easier imaging of these more complex nanostructures.

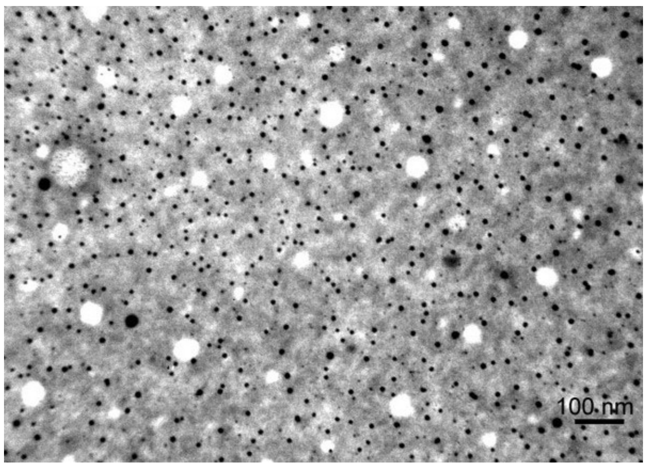

Figure 3. Gold nanoparticles imaged on an LVEM 5.

Nanoparticle Coatings

The outer surface, or shell, or capping agents, or coating molecules are all important when evaluating "what the cell sees" when a nanoparticle encounters the cell surface (Walczyk, 2010). The implications of the biological fate, cellular uptake, and transport mechanisms are influenced by this shell, with applications in nanomedicine, environmental health and safety studies. Observing the organic molecules coating gold nanoparticles also have profound impact developing diagnostics such as antibody-based colorimetric aggregation assays or lateral flow assays. In materials science applications, having polymer coatings on the metal nanoparticles allows for easier incorporation into other material matrices, by tuning the interfacial properties of the nanomaterial surface presented to the matrix.

Electron microscopy imaging of the shell around the nanoparticle core provides important context when comparing traditional TEM results with other techniques. For example, Dynamic Light Scattering results include the metal core, the surface coating molecules, and a sphere of hydration around the nanoparticles, compared to typically just the metal core being reported by traditional TEM size measurements (MacCuspie, 2011). LVEM offers the potential capability to bridge this gap between techniques by distinguishing metal core and organic shell with better contrast resolution.

LVEM Instruments

There are two models of LVEM offered by Delong Instruments, offering a much smaller footprint than traditional TEM (Figure 4). The original model, the LVEM 5, offers a small benchtop footprint and easy operation. The LVEM 25 provides a compact footprint and imaging of thicker samples. The LVEM 5 is a versatile tool for characterizing nanomaterials. By being able to operate in either SEM, TEM or STEM modes, and with the smallest footprint available for this suite of capabilities, the LVEM 5 is powerfully positioned to improve research efficiency. The LVEM 5 is operated at an accelerating voltage of 5 kV from a field emission gun (FEG). Typical sample thickness is 20–50 nm, when nanoparticles are embedded in other material matrices. Feature resolutions of 2 nm and down to 1.2 nm in boost mode are possible.

The LVEM 25 offers 10, 15, and 25kV accelerating voltages. This enables up to 200 nm sample thickness, and feature resolution down to 1 nm. The instrument is mounted on a mobile cart, making for easier laboratory cleaning and maintenance operations. With straightforward and intuitive operation, operators with a broad range of technical training and backgrounds are able to quickly learn the instrument and obtain high quality images.

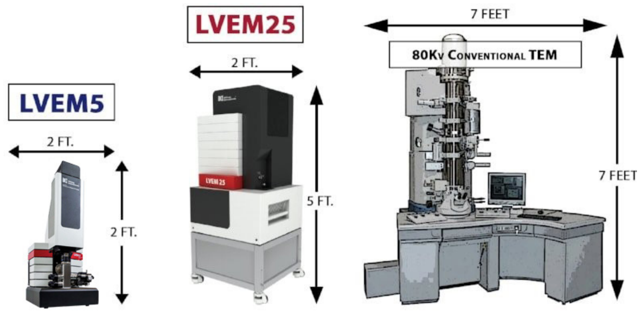

Figure 4. The LVEM 5 fits on a 2 ft wide benchtop, and the LVEM 25 footprint is about 2 ft by 3 ft, compared to 7 ft by 8 ft for conventional TEM.

TEM Characterization of Nanoparticles

TEM as a technique has been around for nearly a century. The widespread availability and powerful magnification capability of this instrumentation has led to TEM being considered the 'gold standard' technique for nanoparticle size measurements. When considering the numerous choices that exist, TEM has been shown to reduce some of the challenges of silver nanoparticle size characterization across laboratories, especially when nanoparticle manufacturers use TEM to verify the size of their products (MacCuspie, 2011).

Comparison of results

Recently, a side by side comparison of data was obtained on a LVEM 5 and a Philips CM200, with four samples of nanoparticle reference materials of different types, including TiO_2, SiO_2 and Ag (Dazon, 2019). The study reported the difference between the number size distribution and the median diameters D50 obtained by two techniques was as small as ± 2.5 % for the TiO_2, with a maximum of ± 15 % across all samples. The authors concluded this consistency "is relatively good taking into account the standard deviations obtained."

Table 1. Agreement of nanoparticle standard size measurements between LVEM and TEM :

MEASUREMENT AGREEMENT	MIN	MAX
LVEM 5 vs. Philips CM200 (Ref: Dazon, 2019)	± 2.5 %	± 15 %

delong instruments

It is worth pointing out that careful calibration of TEM instruments is an important aspect of ensuring the accuracy of results. Frequent performance verification of an instrument's operational capabilities by the use of traceable standards ensures the highest quality results.

LVEM Advantages

There are several well-established advantages to LVEM compared to traditional TEM instruments.

- Lower initial cost
- Lower operating cost
- Easier operation
- Easier maintenance
- Smaller laboratory footprint
- No specialized site prep required

The significantly lower initial cost of a new LVEM instrument compared to even a used TEM is a tremendous advantage, allowing routine access to electron microscopy images when otherwise unobtainable and freeing up larger budgets for other critical tasks.

Additionally, placement of an LVEM is possible in many laboratories, making for much more efficient collection of routine characterization data. Much as low-cost instruments are ubiquitous in synthesis labs for initial screening characterization, LVEM enables electron microscopy to now become a rapid, affordable and easy screening tool for nanoparticle size characterization, eliminating the need for costly core user facilities.

Conclusion

Low voltage transmission electron microscopy is a powerful tool for characterizing the size of nanoparticles with great accuracy and fidelity compared to traditional high voltage TEM. Added benefits of LVEM include lower costs, easier operation, and rapid results. The 2019 study by Dazon concludes "that benchtop LVTEM is a suitable device for generating quality micrographs with a resolution comparable to its TEM equivalent."

The world's best benchtop electron microscope, the Delong LVEM 5, continues to contribute to important areas of nanotechnology, biology, and materials science research.

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About the author:

Robert I. MacCuspie, Ph.D., has over twenty years of experience in nanotechnology and materials characterization. Career highlights include leading the team that developed the silver nanoparticle reference materials at the National Institute of Standards and Technology, the first faculty and Director of Nanotechnology and Multifunctional Materials Program at Florida Polytechnic University, and over five years of consulting at the business-science interface from MacCuspie Innovations, helping companies commercialize and educate on technologies to improve human health.