Use of Low Voltage Electron Microscopy For Characterization of Magnetic Nanoparticle Size Distribution

A picture is worth a thousand words. There is simply no substitute for a transmission electron microscope (TEM) image of nanomaterials. This one technique enables identification of morphology, average particle size, and particle size distribution. Low Voltage Electron Microscopy (LVEM) and instruments such as the Delong Instruments LVEM 5 are uniquely suited as a powerful tool with significantly lower initial costs, operating costs, user training requirements, and smaller laboratory footprint (Fig. 1) compared to traditional TEM.

LVEM 5 enables improved size distribution measurements

Magnetoferritin colloids are being explored for controlled heat delivery through magneto-induced hyperthermia. Recently, a Delong Instruments LVEM 5 was used to refine the particle size measurements of magnetoferritin from 5 nm to 4.21 nm. (Balejcikova, 2019) The size measurements are used to determine the loading factor of iron into the magnetoferritin colloids, which in turn provides an important understanding for the structure-property relationship determinations of hyperthermia performance of these materials.

LVEM 5 Enables Core and Shell Imaging of Magnetic Nanoparticles

Magnetic nanomaterials often comprise a core with metal or metal oxide materials, and a shell of organic material that serves primarily as a colloidal stabilizing agent. The shell, which is often referred to as a coating or a capping agent, can also include additional functionalities such as the ability to bind target analytes for biosensor or purification applications. Materials scientists often explore a range of different coating molecules, then characterize the structures of the resulting materials and evaluate their corresponding properties. Good characterization thus underpins successful elucidation of structure-property relationships.

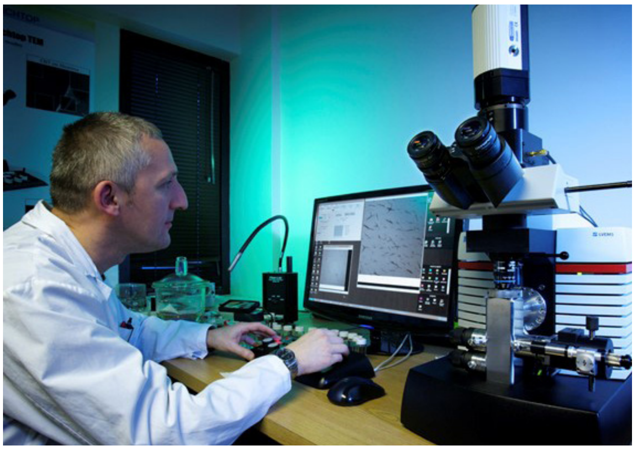
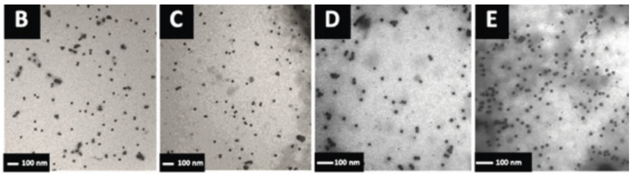


Figure 1. NRC-BRI technical officer Sabahudin Hrapovic uses a LVEM 5 benchtop transmission electron microscope to observe the size and distribution of nanocrystalline cellulose particles.

Traditional TEM provides a good contrast with metal atoms and metal oxide nanomaterials, yet is frequently challenged to achieve good contrast for carbonaceous coatings on these materials. LVEM offers the opportunity to gain good contrast for carbon-based coatings and retain a strong clear contrast for metal and metal oxide core materials in the same image.

LVEM Size Distribution Demonstrates Magnetic Nanoparticle Recovery Applications

A good example of the applications this enables can be found in a paper titled “Magnetic glyconanoparticles for selective lectin separation and purification.” (Oz, 2019) In this work, the authors examine a range of coatings for iron oxide nanoparticles while performing RAFT polymerization on the surface of the formed nanoparticles in techniques described previously and confirmed using LVEM 5. (Arslan, 2014) A range of organic molecule sizes of capping agents are examined, from small molecules such as oleic acid to a RAFT polymerization agent, to the completed polymer polyethylene glycol (PEG).



TEM images of Fe_3O_4@OA (B), Fe_3O_4@CTA (C), Fe_3O_4@PEG (D) and Fe_3O_4@PEG@AD (E) magnetic nanoparticles.

A Delong Instruments LVEM 5 instrument was used to examine the structure of these magnetic nanomaterials. In each case, the organic molecules in the coating become visible as a medium gray contrast surrounding the dark black contrast of the iron oxide core. The increased molecular weight of the coating corresponds to an increased gray area surrounding the black iron oxide particles. Using the traditional approach of TEM diameter being reported on the metal or metal oxide core only, the authors found all samples had an average diameter of 19 nm. Corresponding measurements by Dynamic Light Scattering also confirmed the expected increase total hydrodynamic particle diameter, as the oleic acid coating particles were 20 nm in diameter, the RAFT polymerization agent particles were 17 nm in diameter, and the PEG coated particles were 24 nm in diameter.

LVEM provides a visual confirmation not only of the organic coatings of the particles, but also of the agglomeration state of the particles as they were used to separate and purify the target molecule. As the particles agglomerated in the presence of the target, LVEM revealed the structure of the agglomerates. After using a magnet to recover the agglomerates and a competing molecule to release the target, the now singly dispersed iron oxide nanoparticles were recovered using a magnet, and confirmed by LVEM imaging to have a similar morphology of the iron oxide cores, as well as a similar morphology of the organic coating surrounding the recovered singly dispersed particles.

Straightforward Experimental Procedures

In the articles cited, the authors use a Delong Instruments LVEM 5, operated at nominally 5 kV accelerating voltage. Standard TEM preparation methods are implied in the work. Copper TEM grids of a suitable mesh size, typically between 200 and 400, can be used. A common approach is to evaporate a microliter size droplet of magnetic nanoparticle suspensions onto the grid. With digital images captured by the LVEM 5, sizing can be performed in real time using the Delong software, or can be saved and analyzed with other commonly used software packages such as ImageJ.

Conclusion

The Delong Instruments LVEM 5 is enabling significant advances in magnetic nanoparticle material science, through powerful and efficient characterization of the resulting nanomaterials. Demonstrated applications such as purification of target analytes and refined size measurements of magnetic nanoparticles are enabling improved structure-property relationships and resulting applications to be developed.

References:

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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 through consulting at the business-science interface MacCuspie Innovations is helping companies commercialize and educate on technologies to improve human health.