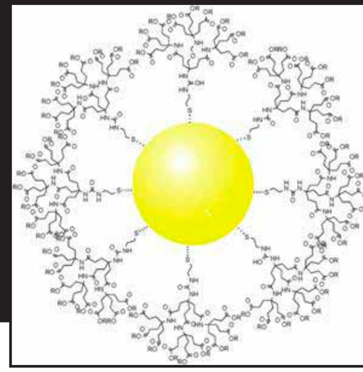
Nanoparticle Measurements and Standards for Biomedical and Health Applications

Objective

Our goal is to develop certified reference materials, standard test methods, measurements, and critical data for the physicochemical characterization of engineered and multifunctional nanoparticles. This body of information will enable widespread acceptance and adoption of nanotechnologies for the diagnosis, treatment, and prevention of human disease, as well as enable evaluation of the environmental, health, and safety (EHS) risks of nanomaterials.



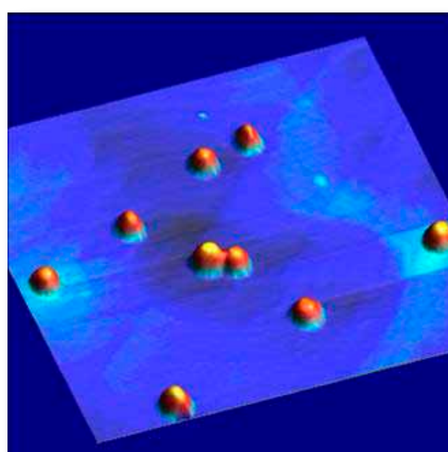
Impact and Customers

- Annual healthcare costs associated with cancer treatment exceed $188 billion, yet the mortality rate for cancer in 2002 was identical to that in 1950. According to the National Cancer Institute (NCI), "nanotechnology will change the very foundations of cancer diagnosis, treatment, and prevention."

- NIST collaboration with NCI and the Food and Drug Administration (FDA) provides a framework for developing a standardized analytical cascade for physical and biological characterization of nanoparticles for imaging, diagnosis and therapy.
- New consensus standards for characterization of biomedical nanoparticles are currently under development within ASTM committee E56 on Nanotechnology.
- NIST interactions with NCI, FDA, the National Institute of Occupational Safety and Health (NIOSH), and the Environmental Protection Agency (EPA) have fostered robust interagency cooperation and enabled us to focus our resources on nanoparticle standards priorities for the biomedical and EHS sectors.

Approach

Taking therapeutic and diagnostic nanoparticle platforms from the laboratory to the clinic requires a well-defined pre-clinical route for FDA approval that must include widely adopted and standardized procedures for assessing the efficacy and toxicity/health risk of new nanomaterials. Certified reference materials underpin the approval procedures and enable interlaboratory comparison and benchmarking. To this end, we are working to develop measurement protocols (assays), consensus standard test methods, critical data and fundamental science related to the physico-chemical properties of different nanoparticle classes under physiologically and environmentally relevant conditions. Particle properties characterized include size and size distribution, surface area, surface charge, zeta potential, crystallinity, aggregation, stability, transport characteristics, chemical composition, purity, and photothermal/plasmonic behavior.



NANOMATERIALS

Accomplishments

Engineered nanoparticles hold great promise for the detection and treatment of disease. Advanced applications in cancer management, for instance, could result in precise in situ imaging and localization of tumors and targeted application of therapeutic agents directly to tumor cells. To bring these technologies to the clinical stage, and enable assessment of the EHS aspects of nanoparticles, we are partnering with FDA, NCI, EPA and NIOSH, and working with international standards organizations, to develop a nanoparticle measurement infrastructure.

Standards

In 2008 NIST issued its first "nano" reference materials targeted for the biomedical research community — literally, "gold standards" for labs studying the biological effects of nanoparticles. This effort involved interagency cooperation between NIST and NCI. The three new reference materials (RMs), citrate-stabilized gold particles nominally 10 nm, 30 nm and 60 nm in diameter, were developed to address needs identified by the cancer research community. Particle dimensions were quantified using six independent methods. Data provided with the RMs include gold content, major ion concentrations, pH, conductivity, and zeta potential. Currently efforts are focused on the development of nanoscale titanium dioxide and silver SRMs for assessing the potential health risks and biological interactions associated with engineered nanomaterials. Also in production is a nanoporous controlled-pore glass for validation of gas sorption instrumentation.

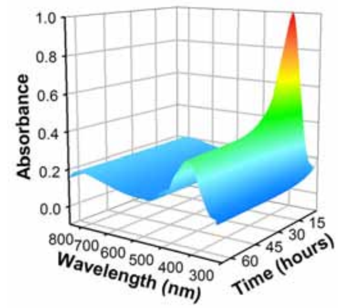
Working with international and other agency partners, we are making progress towards standardizing measurements and protocols that are urgently needed by the nanotechnology research and regulatory communities. Recently, NIST and NCI jointly organized three interlaboratory studies to evaluate physical and biological assays for nanoparticle characterization. As the result of one of these studies, the standards body ASTM International has been able to update its guidelines for a commonly used technique (dynamic light scattering) for measuring the size of nanoparticles in solution. The study enabled updated guidelines that now include statistically evaluated data on the measurement precision achieved by a wide variety of laboratories applying the ASTM standard. Data from the inter-laboratory comparison gathered from 26 participating laboratories will provide a valuable benchmark for those measuring the size and size distribution of nanoparticles suspended in fluids.

Working with partners such as NCI, FDA, NIOSH and the Army Corp of Engineers, we have jointly organized workshops in October 2008 and April 2009, which addressed, respectively, accelerating standards development for nanoparticle characterization, and the unique challenges associated with the study of nanoscale silver in biological and environmental systems.

Measurements and Research

Developing a viable measurement approach for quantifying the dispersion quality of nanoparticles such as carbon nanotubes within a liquid medium or solid matrix remains a challenge due to the variety and complexity of aggregative morphologies that can result. Working with industry and academic partners, we have applied quantitative ultrasmall-angle X-ray scattering (USAXS) methods to a range of single- and multi-wall carbon nanotube (SWCNT and MWCNT) dispersions and composites. A three-component morphology model has been applied to interrogate CNT structures in dispersions. The relative prominence of these components, together with their respective characteristic sizes or persistence lengths, can be related to the observed scattering. When combined with constraints such as the known C mass loading, the model can be used to infer the degree of filling of the tube interiors. The information obtained has implications for the application of CNTs in biomedical and other applications.

Nanoscale silver is the most common engineered nanomaterial incorporated into consumer products today. It is used primarily for its biocidal properties, but nano-silver may present significant risks for human health and the environment according to the EPA, and public awareness of these risks has increased recently. There are substantial challenges associated with the study of nano-silver as a result of its solubility and inherent colloidal instability. We began an effort in 2009 to address these challenges and to provide the research and regulatory communities with critical data on the chemical and colloidal stability of nano-silver under biologically and environmentally relevant conditions. This research also underpins our efforts toward development of nano-silver SRMs.



UV-Vis absorbance of BSA-coated nano-silver

Additional efforts, began in 2009 and 2010, focus on the development of transferable measurement tools to facilitate characterization of molecular species on the surface of nanoparticles, and the development and standardization of protocols for nanoparticle dispersion in biologically and environmentally relevant media. Particle dispersion has proven to be a seminal issue limiting the accurate and reproducible assessment of nanoparticle toxicity. We are collaborating with NCI, the Center for the Environmental Implications of Nanotechnology at Duke University, and others to address these areas.

Learn More

Andrew J. Allen
Tae Joon Cho
Robert I. MacCuspie
Julian S. Taurozzi
De-Hao Tsai

Vincent A. Hackley
(Ceramics Division)
(301) 975-5790
vince.hackley@nist.gov
www.nist.gov/msel/ceramics

Publications

Allen AJ, Hackley VA, Jemian PR, Ilavsky J, Raitano JM and Chan S-W, *In Situ Ultra-Small-Angle X-ray Scattering Study of the Solution-Mediated Formation and Growth of Nanocrystalline Ceria*, J. Appl. Cryst., 41(5), 918-929 (2008).

Hackley VA, Clogston JD, *Measuring the Size of Nanoparticles in Aqueous Media Using Batch-Mode Dynamic Light Scattering*, NIST-NCL Joint Assay Protocol, National Cancer Institute, Nanotechnology Characterization Laboratory, http://ncl.cancer.gov/ (2008).

NIST Reference Materials 'Gold Standard' for Bionanotech Research, Small Times (www.smalltimes.com), January, 2008

Putting to the Test – ILS Program Supports Precision and Bias Statement Development for Nanotechnology Standard, Standardization News, November, 2009.