Cancer Nanotechnology: Characterization of Chemical and Biological Coatings on Gold Nanoparticles by Differential Mobility Analysis

NIST is working closely with the National Cancer Institute/Nanotechnology Characterization Laboratory to develop standards, measurement methods, and protocols for the quantitative and reproducible characterization of nanoparticles. The focus of this project is to develop measurement techniques to characterize the physical size and chemical composition of organic and biological coatings of modified gold nanoparticles. Both the NIH and FDA have stated that an urgent measurement need is the development of novel methods to characterize the chemical or biological coatings on nanoparticle surfaces. These coatings play critical roles in fighting cancers because they frequently are designed as therapeutic or targeting agents.

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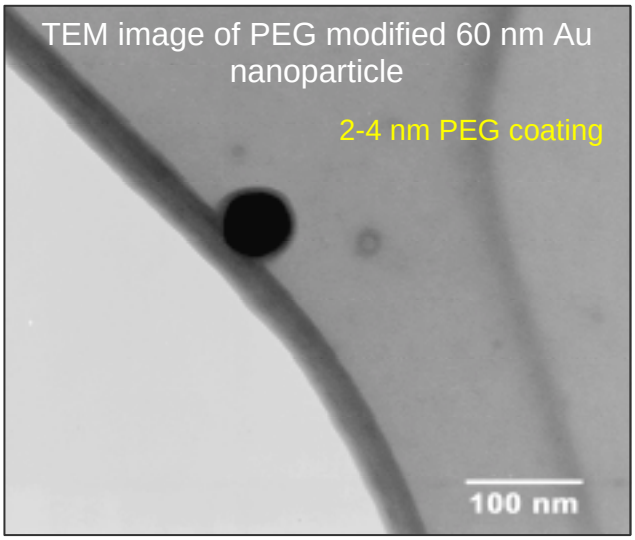
The National Cancer Institute (NCI) of the National Institutes of Health established the Nanotechnology Characterization Laboratory (NCL) to provide the critical infrastructure and characterization services to accelerate the development and application of nanoparticles and nano-devices for the diagnosis and treatment of cancer. Nanotechnology holds huge promise for the design and manufacture of many types of novel medical products—from devices to therapeutics to combination products.

Our approach to characterize the surface coatings is to measure the nanoparticle size before and after surface modification. The difference in particle size provides an estimate of the coating thickness which can be used to deduce the molecular surface coverage of chemical or biological molecules. We use a novel gas phase method to measure nanoparticle size: electrospray ionization - differential mobility analysis (ESI-DMA). The primary advantage of the ESI-DMA is its excellent resolution, being able to discern particle size differences as small as 0.2 nm. To determine the utility of the ESI-DMA method for characterizing nanoparticle coatings we use a model system, Au nanoparticles modified with self-assembled monolayers

(SAMs) of thiolated aliphatic molecules or DNA oligomers. The SAMs produce well-defined chemical coatings on commercially available gold nanoparticles with narrow size distributions. The particle size, d, is characterized based on the difference of electrical mobility, which is inverse proportional to the surface area of a particle. After successful coating process, the electrical mobility of the Au nanoparticle should be reduced due to the increased surface area of the particle due to the molecular coating. The functionalized Au nanoparticles are transferred from solution to the gas phase using electrospray particle generation where Au nanoparticles are carried by a CO_2/air gas flow and then delivered into the analyzer.



Gaining proficiency in quantitative and reproducible characterization of organic and biological coated nanoparticles will aid the NCL in their goal of facilitating nanotechnology as a primary driving force for advances in cancer research.

Gold nanoparticles of 10 nm and 60 nm sizes have been successfully modified with carboxylic acid (negatively charged), tertiary amine (positively charged), and polyethylene glycol (neutral, hydrophilic, bio-compatible) terminated SAMs as characterized using X-ray photoelectron spectroscopy (XPS). After optimizing the DMA operating conditions so that small size differences in coated particle are observable, a shift in particle size of 0.4 – 1.4 nm after coating with polyethylene glycol was observed for a 60 nm Au colloid. We have also successfully coated 20 nm gold particles with thiolated homo-oligonucleotides of thymine

(T_nSH, where n = 10, 20, and 30); DMA results indicate a monotonically increasing trend in the brush length for this series. We expect that an optimized size differentiation of ~0.2 nm can be obtained using our DMA methods. Our current work is directed toward increasing the resolution of this analysis tool.

Future plans: Our future goals include modification and characterization of gold nanoparticles with DNA oligomers followed by DMA analysis, including optimization of DMA running conditions for quantitative and reproducible characterization of gold nanoparticles modified with organic and biological coatings.

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