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Surface Modification of Gold Nanoparticles

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Abstract

We are characterizing different nanoparticles in order to analyze their structure, size, and charge. Nanoparticles are not easy to analyze using traditional methods available for macroscopic-sized particles. The means to which we can accomplish nano-sized characterization includes such tools as Transmission Electron Microscope (TEM), Thin Layer Chromatography (TLC), Dynamic Light Scattering (DLS), and Gel Electrophoresis. We synthesized cationic Au particles, then characterized them to insure that they met the acceptable range of particle size. Following characterization, we attempted to insert the Au particles into DNA packages based on electrostatic and intercalating interactions. Another option is to use another class of artificial sequence-specific polymers known as peptoids, which form a very stable secondary structures. This should allow an unprecedented depth and breadth of control over the geometry, material composition, and assembly of nanomaterials.

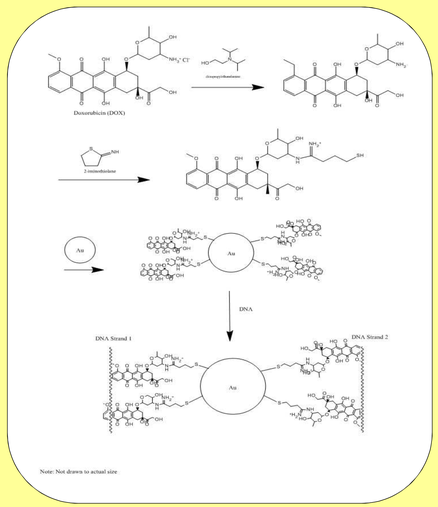
Introduction

Traditional methods of nanoparticle synthesis generally involve trial-and-error combinations of simple surfactants and inorganic precursors. The future of this field, if it is to reach a stage where nanoscale materials can be designed rationally, will require a greater degree of chemical control of the geometry and mechanism of growth. This is very likely to require the use of sequence-specific polymers. Impressive progress over topological control has been made with DNA, and a large body of knowledge exists on polypeptides, and both are candidates for this task. DNA provides a negative framework with in which a cationic Au particle can bind and assemble in a tetrahedron geometry to encapsulate. In addition, by substituting an intercalating functional group such as Tryptophan (Trp), we can supplement the electrostatic DNA/Au interactions. Oligo (N-functional glycines or peptoids, offers more functional diversity than DNA, and is cheaper to synthesize than biopolymers. Phage 112, an analog of peptoids found in bacteriophage viruses has been shown to produce particles of a cylindrical or rod-like geometry. We characterized Phage 112 in its interactions with DNA using TEM and DLS to investigate whether or not a scaffold was created in which the DNA can bind.

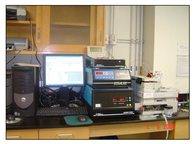
Several tools are necessary to characterize our Au Particles. Gel Electrophoresis is a research technique used to separate molecules (or fragments of a molecule) according to size. Upon electrical stimulation, smaller fragments of a molecule will move faster through the gel than larger fragments. The process is typically done to separate DNA fragments after the DNA has been cut with restriction enzymes. For the purpose of this research, Au particles were examined in the gel as well as the Au with the DNA. The Dynamic Light Scattering (DLS) machine, DAWN EOS by Wyatt Technology, makes absolute particle sizing an accessible alternative to tradition liquid chromatography methods by using a laser. The DLS machine. Finally, the Transmission Electron Microscope (TEM) operates on the same basic principles as the light microscope but uses electrons instead of light. What you can see with a light microscope is limited by the wavelength of light. TEMs use electrons as "light source" and their much lower wavelength makes it possible to get a resolution a thousand times better than with a light microscope. It allows visualization of objects to the order of a few angstrom (10^{-10} m) down to near atomic levels.

Methods

All materials were synthesized in the lab using basic lab methods used in most labs without further purification. Production of molar concentrations of compounds using different thiolated ligands (basic amino acids) were added to Au to create the samples. Volume ratios of Colloid Au and thiolated ligand were generally 10 to 1 with changes in charges of ligands, equivalency, variance of ligands in an effort to stabilize the Au particles. To obtain control over the size of Au materials, we modulate the shape and functionality of the sidegroups to achieve specific ligand interactions with DNA.



Au particle Reaction



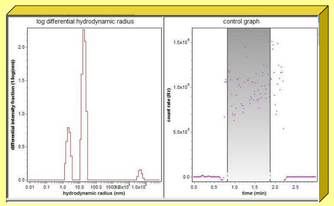
Light Scattering Machine

After Au samples were made, the order at which characterization was performed varied due to time, material, availability, and personnel constraints. With respect to Light Scattering, the Au samples were diluted with H2O and were then injected into quartz microcuvettes and placed in the machine. Program ran the experiment using water for initial baseline in 3 minute cycles. The baselines and peaks were outlined and the radius of the particles were analyzed. Results summary were noted followed by computer regularization.

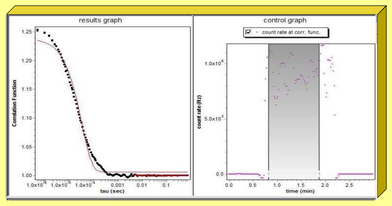
Thiolated Au samples were then combined with both single and double stranded (ladder) DNA and then run through gel electrophoresis along with the samples that did not have DNA. Both fresh (.6 MOF) and pre-made gels (E-gel 0.8% double comb) were used with Au Control, DNA ladder marker, and a Au + ladder mix control. 20uL samples were loaded into the wells and run for 13 minutes cycles. Light, to measure Au marker and fluorescent to measure DNA marker scans were done to record results.

Results

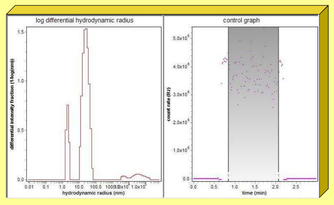
Characterization of Au nanoparticles was met with intense trial and error as several different thiolated ligands (Glycinate, Asparagine, Serine, Tryptophan, Argentine, Cysteine, Methionine, and TRIS) were used in conjunction with single stranded DNA, DNA Ladder, and Doxorubicin, used to treat cancer. The results varied with initial particle size being in excess of 100 nanometers followed by average sizes as small as 6.5 nanometers once the reactions were stabilized. It was discovered that both Ammonium Glycinate and Sodium Glycinate brought the best results.



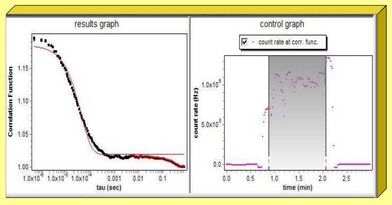
Regularization of Light Scattering for DOX (A)



Light Scattering Rh Qels for DOX (A)

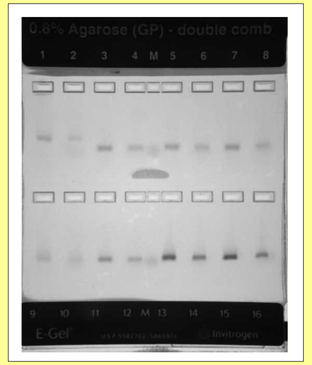


Regularization of Light Scattering for DOX (B)



Light Scattering Rh Qels for DOX (B)

Electrophoretic mobility of DNA bound Au/DOX samples differed from a control of DNA and Au samples. DNA migration slowed in the presence of Au/DOX relative to the DNA control, and its final position in the gel overlapped with Au's.



Light Gels of DOX A, B, C, and DNA Ladder

Fluorescent Gels of DOX A, B, C, and DNA Ladder

Discussion

Both DNA and Au samples were negatively charged and expected to move toward the cathode during electrophoresis. Parallel movement makes distinguishing between electrophoretic mobility and DNA/Au interaction a difficult task. LS can help by demonstrating that Au particles bound to DNA via DOX show a slight increase in hydrodynamic radius. LS regularizations results show such an increase, and while they may not be conclusive because of the quenching interaction between DNA and Au, DNA/Au interaction can be further supported by decreased DNA migration in an electric field relative to a control. Electrophoresis demonstrated such a shift, in addition to confirming the particulate sizes derived from LS. Gels with an average pore size of 5 to 15 nm would occlude any particles above the upper limit, and/or show streaking in a solution of non-homogenous particulate size. Glycinate demonstrate uniform particulate size in LS on the order of 7 nm and a very narrow band within a prefabricated gel. Thus, Glycinate was a desirable target for thiolation with 2-iminothiolane. Future work will involved using DNA intercalators with stronger DNA affinity and internal thiol functional groups to avoid the need of using 2-iminothiolane. In addition, due to DNA's structural flexibility and ease of modification, we will investigate additional DNA motifs to serve as scaffolds for unique organic/inorganic interactions.

Acknowledgements

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