Nanogold Particles Using the Nicomp® System

INTRODUCTION

Gold nanoparticles, also sometimes called colloidal gold, possess unique properties that are beneficial to many applications. They are typically synthesized by controlled reduction of aqueous $HAuCl_4$ solution using a reducing agent such as citrate under varying conditions. There are many types of gold nanoparticles based on the size, shape, and physical properties, Figure 1. Applications for gold nanoparticles include drug delivery,[1] carriers for drugs such as Paclitaxel,[2] tumor detection,[3] biosensors, and many others.

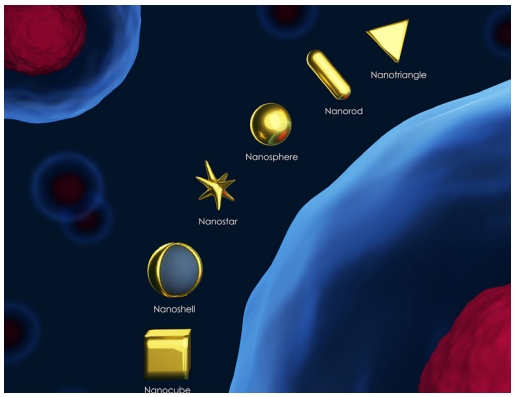

Figure 1. Types of gold nanoparticles (stylized).

The size of gold nanoparticles is a critical physical parameter[4] requiring careful measurement. The particle size affects properties such as absorbance wavelength (increased size = longer wavelength), surface plasmon resonance (SPR) peak, intracellular uptake, blood half-life and biodistribution profile (decreasing size = increased blood half-life). The particle size and width can be used as an indication of suspension stability. Surface charge (zeta potential) measurements are also used as an indication of suspension stability.

The most popular technique for particle size and zeta potential analysis is dynamic light scattering (DLS) and electrophoretic light scattering (ELS). The Nicomp® Z3000 system (Figure 2) is ideally suited for determining size and zeta potential of gold nanoparticles.

Figure 2. Nicomp DLS system.

MATERIALS

The size and zeta potential of several gold nanoparticle samples were analyzed using the Nicomp DLS system. Three different gold nanoparticle samples were purchased from Sigma Aldrich with nominal sizes of 50, 20, and 5 nm. NIST reference material 8012 with a nominal size of 30 nm was also analyzed. The reference physical properties of these samples are shown in Table 1. Sizes analysis results by DLS are given as the intensity mean of the hydrodynamic diameter. Width of the distribution is given as the polydispersity index (PDI). The NIST 8012 Report of Investigation provides mean hydrodynamic diameter at two angles, backscatter at 173° and 90°. The reference zeta potential value for NIST 8012 is also provided, unlike the samples purchased from Sigma Aldrich.

Table 1. Reference physical properties

Sigma Aldrich part number	Polydis-persity Index (PDI)	Core size	Mean hydrodynamic diameter (Z)
742007	≤0.2	47 – 53 nm	58 – 66 nm
741965	≤0.2	18 – 22 nm	28 – 36 nm
741949	≤0.2	4 – 7 nm	14 – 25 nm

NIST RM	Polydis-persity Index (PDI)	DLS, 173°	DLS, 90°	Zeta potential
8012	N/A	28.6 ±0.9 nm	26.5 ±3.6 nm	-33.6 ±6.9 mV

METHOD

All samples were analyzed on a Nicomp Model Z3000 (Figure 2) for particle size and zeta potential. Before these studies began both size and zeta potential standards were analyzed to verify system performance. A concentration study was performed on sample 742007 to investigate if reported particle size varied with concentration. The results from this study indicated the results were insensitive to concentration so all measurements were made at the original sample concentration without dilution. A time of analysis study was performed on sample 741949 to determine an appropriate measurement duration based on achieving stability as shown in the Time History plot seen in Figure 3. This study indicated that an analysis time of five minutes was sufficient.

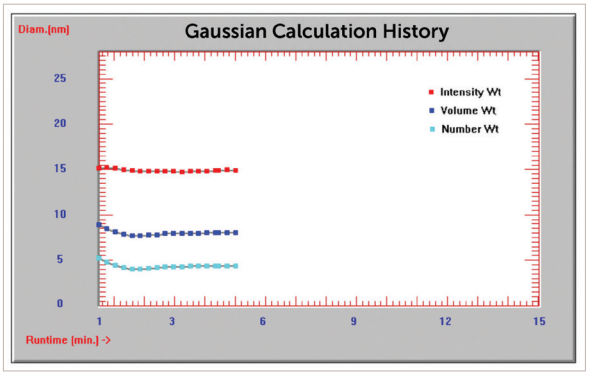

Figure 3. Time history plot diameter (nm) vs. time (min).

The Nicomp size and zeta potential analysis settings for all measurements are shown in Figures 4 and 5.

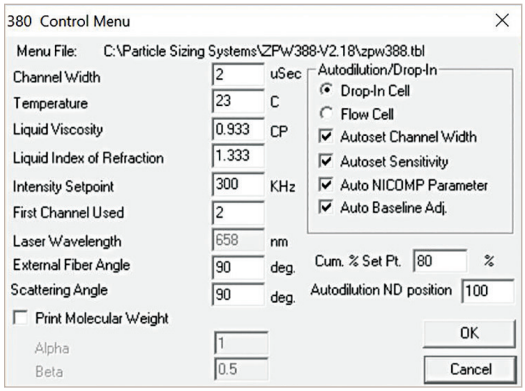

Figure 4. Nicomp size settings.

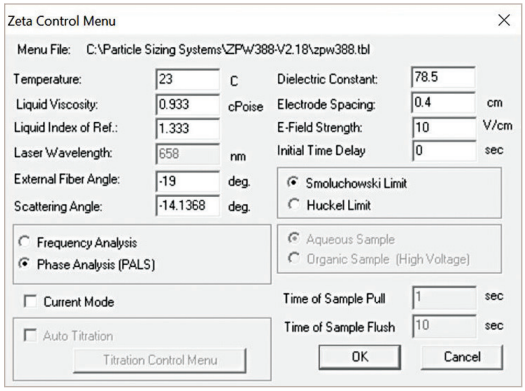

Figure 5. Nicomp zeta potential settings.

RESULTS – PARTICLE SIZE

Typical graphical results for two analyses for each sample are shown in Figures 6 to 10.

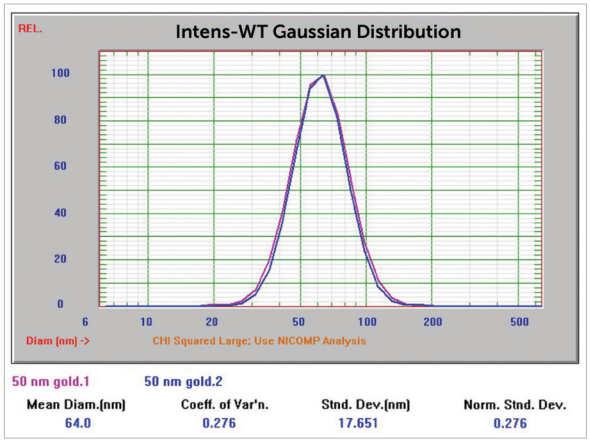

Figure 6. 50 nm Au overlay of two size results.

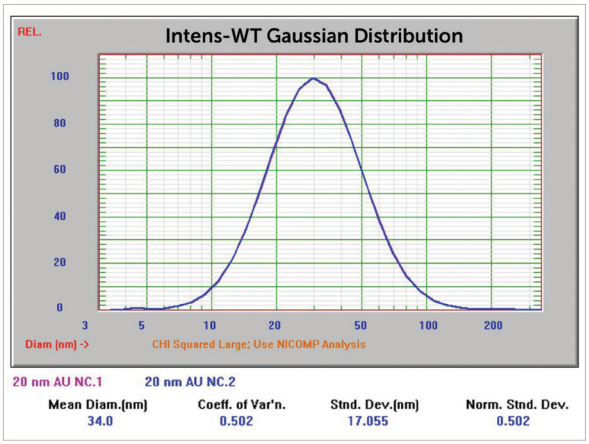

Figure 7. 20 nm Au overlay of two size results.

Sample 741949 (nominal size 5 nm) presented additional challenges to generate results close to the expected values. Figure 8 shows the Gaussian result for the sample when analyzed with no additional sample preparation. Gaussian calculations force the result into one single peak.

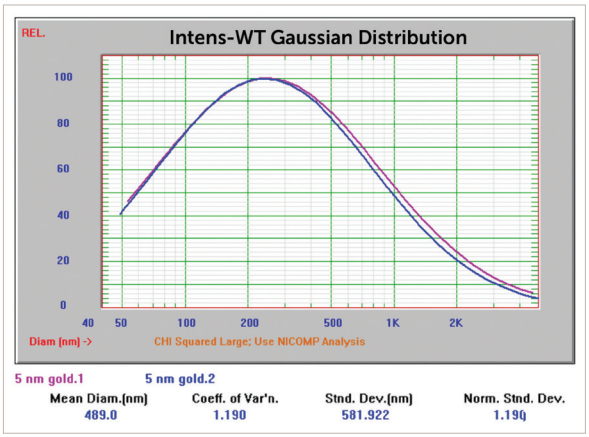

Figure 8. 5 nm Au overlay of two size Gaussian results.

The Nicomp Z3000 system can also generate multi-modal results using the proprietary Nicomp algorithm. The result seen in Figure 8 was recalculated using the Nicomp algorithm the resultant multi-modal size distribution is shown in Figure 9.

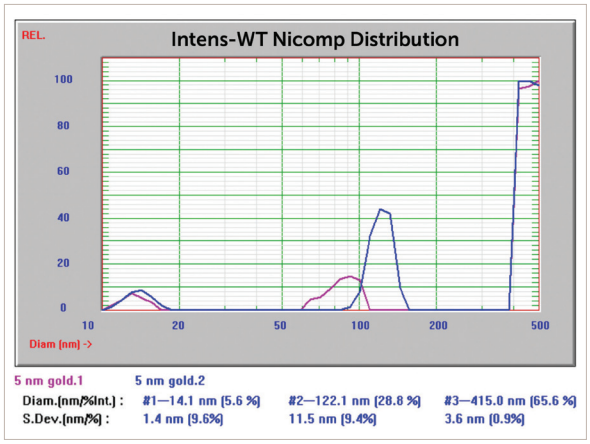

Figure 9. 5 nm Au overlay of two size Nicomp results.

The sample tube was then centrifuged for eight minutes in an attempt to separate the larger particles out of the measurement zone. The same sample tube was analyzed after centrifugation and the result is shown in Figure 10.

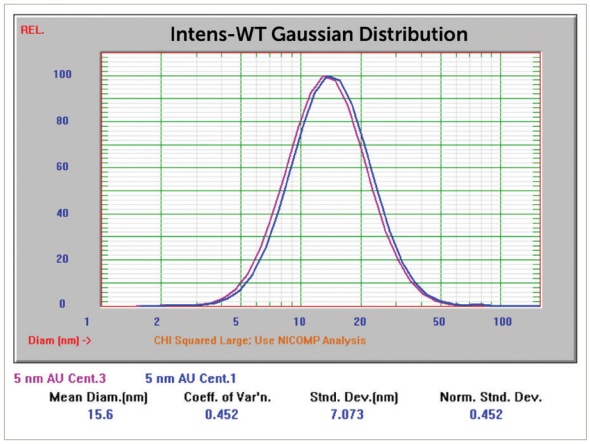

Figure 10. 5 nm Au overlay of two size Nicomp results, centrifuged.

Sample NIST 8012 was analyzed at three angles; backscatter @ 170° (pink), 90° (green), and forward angle at 15° (blue). These three results are shown in Figure 11.

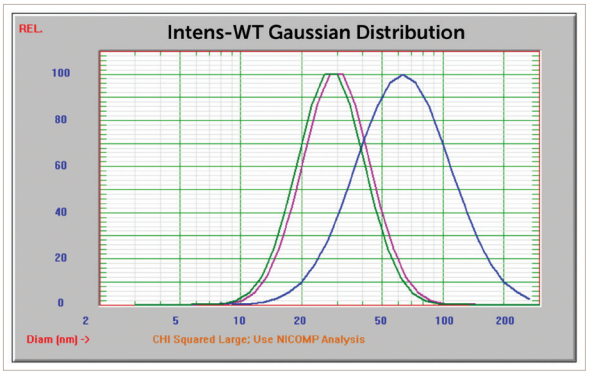

Figure 11. NIST 8012 Au overlay of three size results, 170°, 90°, and 15°.

These results plus zeta potential values are summarized in Table 2.

Table 2. Reported size and zeta potential results

Sample	Expected result	Reported size	Zeta potential
742007	58 – 66 nm	64 nm	-34.58 mV
741965	28 – 36 nm	34 nm	-27.95 mV
741949	14 – 25 nm	15.6 nm	-42.43 mV
8012, 170°	28.6 ±0.9 nm	31.9 nm	—
8012, 90°	26.5 ±3.6 nm	30.8 nm	—
8012, 15°	—	66.6 nm	—
8012 zeta	-33.6 ±6.9 mV	—	-30.49 mV

RESULTS – ZETA POTENTIAL

All samples were also analyzed for zeta potential using the phase analysis electrophoretic light scattering technique (PALS). The zeta potential is a measurement of surface charge used in formulation and suspension stability studies. The zeta potential for these samples is shown in Figures 12 to 15.

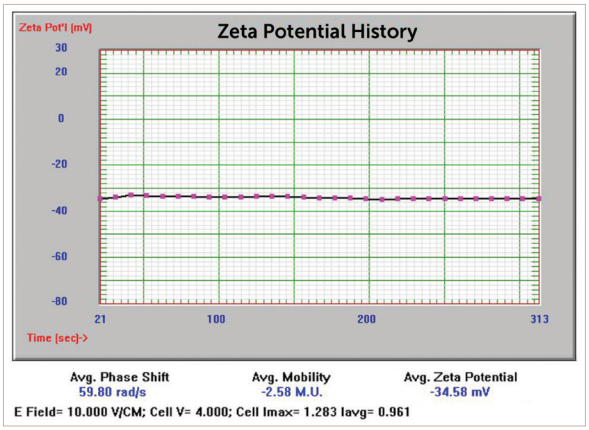

Figure 12. 50 nm Au zeta potential results.

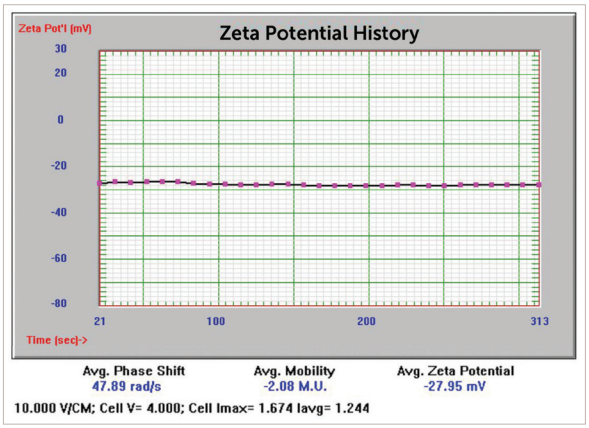

Figure 13. 20 nm Au zeta potential results.

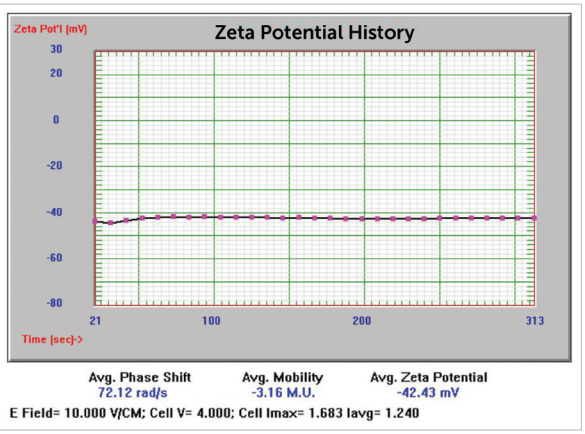

Figure 14. 5 nm Au zeta potential results.

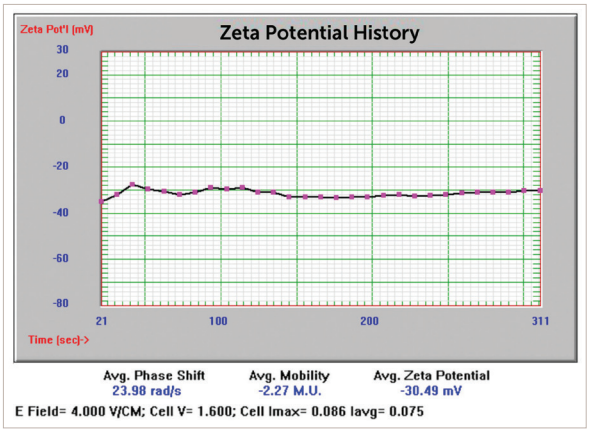

Figure 15. NIST 8012 Au zeta potential results.

The NIST 8012 sample was analyzed at three different angles; 15°, 90°, and 170°. The slightly smaller result at 90° vs. 170° suggests 90° is a better measurement condition vs. backscatter – consistent with other previously reported results.[5] Measurement in the forward angle direction (15°) improved sensitivity to larger particles, as seen in Figure 11. These results suggest that a multi-angle system (a standard and inexpensive Nicomp option) may be superior for some specific applications.

The zeta potential results were all extremely repeatable using the PALS technique. The Nicomp dip cell can measure thousands of samples with a lower cost of ownership than disposable zeta potential cells.

DISCUSSION

The results for Sigma Aldrich 50 and 20 nm nominal size samples were within the range of expected values. The Sigma Aldrich 5 nm nominal size results initially reported particle size significantly higher than expected – indicating aggregation. This was not surprising given the color of this sample as seen in Figure 16, far left. A darker, bluer color typically indicates a much larger particle size distribution. The result before centrifugation (Figure 9) indicates the presence of primary particles near 14 nm and aggregate peaks at 122 and 417 nm. This result displays the power of the Nicomp algorithm to resolve both primary particles and multiple peaks of aggregates. After centrifugation the reported mean size was within expected values.

Figure 16. Left to right; 5, 20, and 50 nm Au sample bottles.

STABILITY STUDY

A stability study was performed on the NIST 8012 sample to investigate the effect of salt concentration on size and appearance. The original size result is shown in Figure 11 with a reported size at 90° of 30.8 nm. First 200 µL of NIST 8102 was pipetted into 200 mL filtered DI water. Next KCl at 3 M was added to the diluted NIST 8012 suspension in increments of 500 µL while observing the color of the sample. A color change was noted after 2 mL of 3 M KCl was added. Figure 17 shows from left to right the NIST 8012 sample after adding the KCL, original sample in cell, and the original sample bottle.

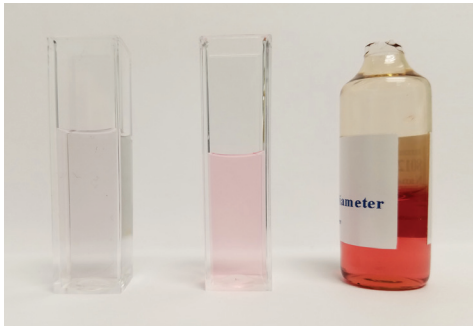

Figure 17. After KCL added, before, original bottle.

The particle size distribution of the NIST 8012 after the addition of KCL is shown in Figure 18. The size increased as a function of time over the fifteen minute analysis time. After twenty four hours the sample had completely aggregated and settled to the bottom of the cuvette as seen in Figure 19.

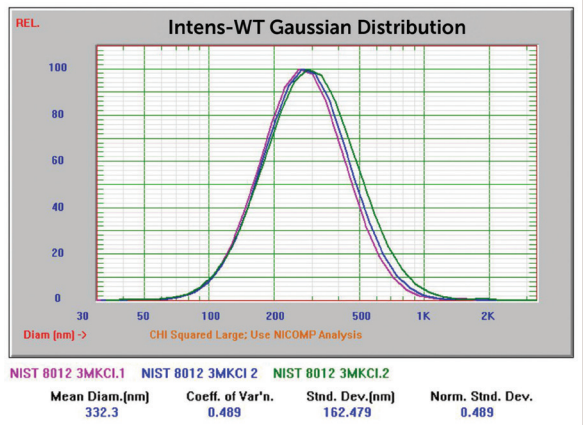

Figure 18. NIST 8012 Au overlay of three size results after KCl addition.

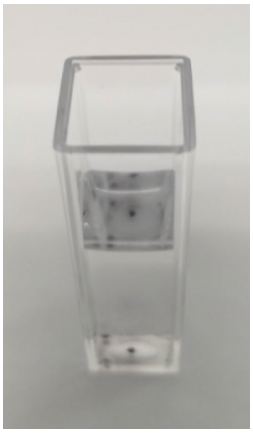

Figure 19. NIST 8012 with settled aggregates.

CONCLUSIONS

Dynamic light scattering is the preferred method for particle size and zeta potential analysis of nanogold particles. The Nicomp Z3000 proved to be an accurate, high-resolution technique generating results close to expected values. The Nicomp algorithm detected the multi-modal mix of primary and aggregated particles for the aggregated samples.

REFERENCES

[1] Han, G., Ghosh, P., and Rotello, V.M., *Functionalized gold nanoparticles for drug delivery,* Nanomedicine, (February 2007), 2 (1): 113–23

[2] Gibson, J.D., Khanal, B.P., and Zubarev, E.R., *Paclitaxel-functionalized gold nanoparticles*, Journal of the American Chemical Society, (September 2007), 129 (37): 11653–61

[3] Sajjadi, A.Y., Suratkar, A.A., Mitra, K.K., and Grace, M.S., *Short-Pulse Laser-Based System for Detection of Tumors: Administration of Gold Nanoparticles Enhances Contrast*, J. Nanotechnol, Eng., (2012), Med. 3 (2): 021002

[4] Dreaden, E.C., Austin, L.A., Mackey, M.A., and El-Sayed, M.A., *Size matters: gold nanoparticles in targeted cancer drug delivery*, Ther Deliv, 2012;3(4):457-78

[5] PSS Technical Note 724 – *Multiangle DLS Measurements*

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