

ZETA POTENTIAL ANALYSIS OF NANOPARTICLES

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Please contact us at info@nanocomposix.com or 858-565-4227 with any questions or suggestions.

Introduction

Zeta Potential analysis is a technique for determining the surface charge of nanoparticles in solution (colloids). Nanoparticles have a surface charge that attracts a thin layer of ions of opposite charge to the nanoparticle surface. This double layer of ions travels with the nanoparticle as it diffuses throughout the solution (**Figure 1**) The electric potential at the boundary of the double layer is known as the Zeta potential of the particles and has values that typically range from +100 mV to -100 mV. The magnitude of the zeta potential is predictive of the colloidal stability. Nanoparticles with Zeta Potential values greater than +25 mV or less than -25 mV typically have high degrees of stability. Dispersions with a low zeta potential value will eventually aggregate due to Van Der Waal inter-particle attractions.

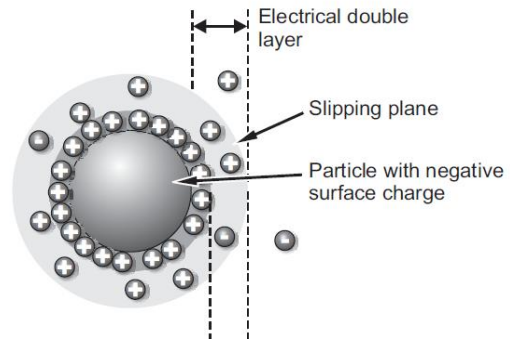


Figure 1: Electric double layer surrounding nanoparticle.

Zeta Potential is an important tool for understanding the state of the nanoparticle surface and predicting the long term stability of the nanoparticle. At nanoComposix we routinely use Zeta Potential analysis to determine if a surface modification to the nanoparticle has been successful or if a processing step has modified the nanoparticle surface. However, the measurement data can be easily mis-interpreted and it is important to understand the strengths and limitations of Zeta potential measurements when interpreting results.

Sample Preparation

Ideal samples from Zeta Potential Analysis are:

- Monodisperse in size
- Are at a high enough concentration to effectively scatter 633 nm light
- Have low salt concentrations (conductivities <1 mS/cm)
- Are suspended in a particulate free, polar dispersant (e.g. high purity water)

Unfortunately, the majority of the samples that we receive do not meet all of the above criteria and may not give high quality Zeta Potential data in the as-prepared solution. Common challenges with received samples are listed below:

1. *High sample conductivity (> 5mS/cm).* In a highly conductive sample, the movement of the conductive ions can lead to electrode polarization and degradation.
2. *Very small particles.* Particles with diameters of <20 nm have a high mobility in solution due to the applied field and Brownian motion. In addition, these particles have very low light scattering properties, as the intensity of light scattered from particles increases as the 6th power of the diameter. Both of these effects lead to a narrow range of sample concentrations that will yield a satisfactory quality result,
3. *Very dilute samples.* Without sufficient light scattering events, the instrument cannot accurately calculate a Zeta Potential value. An attenuator value of 11 (near full-laser power) indicates that the detector is near its detection limit.
4. *Concentrations that are too high.* At very high concentrations, the sample absorbance can diminish the intensity of the scattered light and multiple scattering events can reduce data quality.
5. *Unknown solution properties.* If the temperature dependant viscosity and refractive index of the dispersant are not known, this will affect the calculation that determines Zeta Potential. Dissolved solids (PEG, sugars, polymers) and residual reactants can affect both the viscosity and refractive index of the dispersant.

Interpreting Zeta Potential Data

Unless you have performed Zeta Potential measurements on your sample before, it is difficult to predict the quality of the Zeta Potential data that will be obtained. Our recommendation is to send in a representative sample for a diagnostic analysis. We will provide two reports after analyzing the sample: the first is a summary of your Zeta Potential analysis where the results and parameters from 6 separate measurements will be provided; the second is a Zeta Potential quality report that is the result from an Expert System designed by Malvern to determine if your data meets quality specifications. In order to determine the quality of your results look for these items in your reports:

1. A Data quality field of “Good”. Malvern's expert system will provide advice based upon 6 tests that are performed on a selected record. If the result quality field is “good” then typically there is a uniform zeta potential distribution between runs and a high quality phase plot.
2. Repeatable Results. Your sample will have been run multiple times: 6 separate measurements of 10 runs are included in the attached Excel file. If the data between

each of the 6 runs is reproducible, then there is a high confidence in the obtained number.

If your sample passes both of these cases, "Congratulations!", you've supplied a sample where the Zeta Potential can be accurately measured. The Zeta Potential (mV) under the monomodal analysis section of your report can be reported as the mean value of the Zeta potential of your particles.

If the above is not the case, then the confidence on the Zeta Potential measurement is lower. This does not mean that the obtained data is not correct – it is the nature of some samples that all quality tests cannot be passed. At this point, we can help provide guidance on additional sample processing steps that can be performed to determine if data quality can be improved. The main tool for understanding whether data quality is getting better or worse is the Zeta Potential Phase Plot.

ZETA POTENTIAL PHASE PLOT

A sample cell with two gold electrodes is used to measure the Zeta Potential. Voltages up to 200 V are applied to the cell and the movement of the particles under the influence of the applied electric field is captured by the instrument. The Malvern Zeta Potential instrument measures the phase change in light scattered by particles moving under the influence of an applied electric field, a phenomenon known as electrophoresis. The phase change is proportional to the electrophoretic mobility of the particles, from which the zeta potential can be calculated.

Data from the first (circled) part of the phase plot contains information from the FFR (fast electric field reversal) portion of the measurement where rapidly oscillating lower voltages are used to determine the mean zeta potential value. Data from the secondary part of the phase plot contains information from the SFR (slow field reversal) portion of the measurement over a larger voltage range that is used to determine the zeta

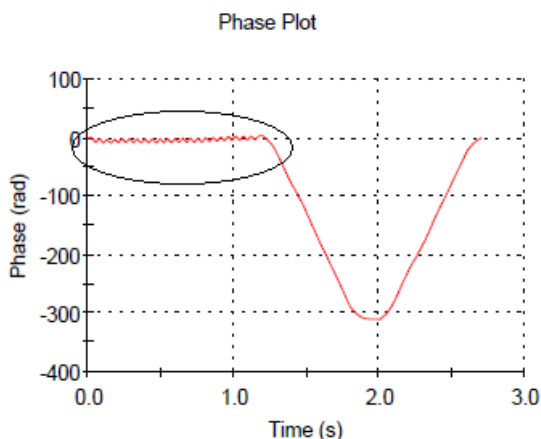


Figure 2: High quality phase data from a Zeta Potential measurement. The circled region is the Fast Electric Field reversal portion of the measurement. The "V" shaped curve is the Slow Field Reversal Region of the measurement.

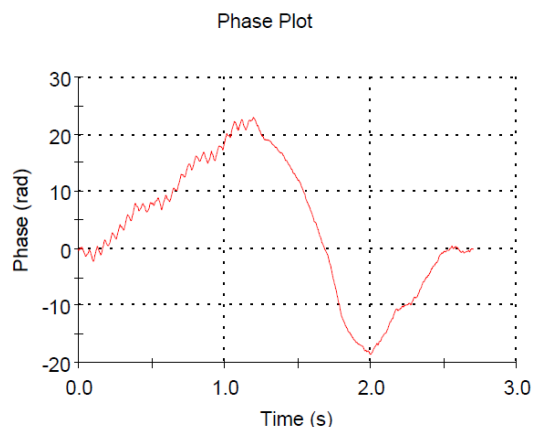


Figure 3: An example of low quality phase data.

potential distribution over a large range. If the sample conductivity is low enough to permit the application of high magnitude voltages both the FFR and SFR are provided.

An example of lower quality phase data is shown in Figure 3. The FFR portion of the measurement is trending and the phase data is noisy. This type of phase data will typically result in a large standard deviation in the reported Zeta Potential values.

For high conductivity samples only the FFR is provided. Sharp responses to the applied voltage are clearly visible. An example of good FFR data is shown in Figure 4. Figure 5 shows an example of lower quality FFR data. Malvern’s algorithms for determining the electrophoretic mobility (and the corresponding Zeta Potential) will produce low quality and reproducibility from such a phase plot.

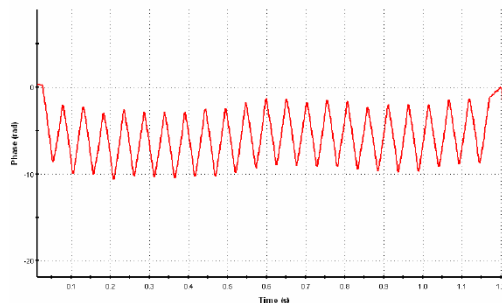


Figure 4: High quality phase FFR data.

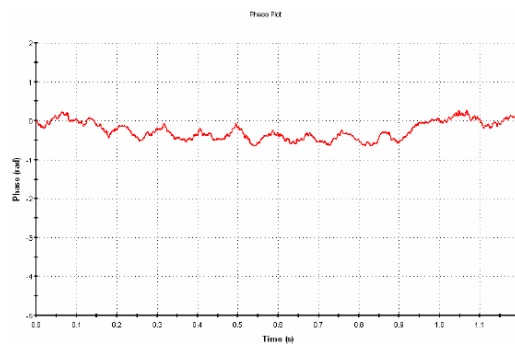


Figure 5: Low quality phase FFR data.

NEXT STEPS

After analyzing your Zeta Potential data and Quality report, if necessary, a nanoComposix analytical specialist will make a recommendation on further processing that could be done to improve data quality. Listed below are some sample preparation techniques that commonly improve the accuracy and reproducibility of Zeta samples submitted to nanoComposix:

1. Filter your sample: If there are any visible particulates in your sample, these large contaminants can interfere with the measurement. Filtration that removes these larger particles while retaining the nanoparticles can improve your measurements.
2. Concentrate: The table in Figure 6 provides recommended minimum and maximum concentrations for Zeta Potential measurements. In practice, we’ve found that the optimal concentrations depend on the specific sample and much narrower concentration ranges are required for high quality data.

<i>Particle size</i>	<i>Min. Concentration (Recommended)</i>	<i>Max. Concentration (Recommended)</i>
< 10nm	0.5g/l	<i>Only limited by the sample material interaction, aggregation, gelation etc.</i>
10nm to 100nm	0.1mg/l	5% mass (assuming a density of 1g/cm ³)
100nm to 1µm	0.01g/l (10 ⁻³ % mass)	1% mass (assuming a density of 1g/cm ³)
> 1µm	0.1g/l (10 ⁻² % mass)	1% mass (assuming a density of 1g/cm ³)

Figure 6: Malvern's recommendations for Zeta Potential concentrations.

3. Dilute: Dilution of a concentrated sample can reduce issues associated with absorption and multiple scattering events. If the solution is being diluted with water, it will also reduce the conductivity of the sample which typically improves data quality. It is important to re-measure the pH after dilution.
4. Centrifuge and reconstitute: Residual reactants, large non-analyte organic molecules and dissolved ions can interfere with obtaining a reliable, repeatable result. This is especially the case if the sample has a high conductivity (>5 mS/cm). Spinning the sample in a centrifuge and reconstituting in clean media is a method of “washing” the particles. When performing this wash step, it is important to make sure that the centrifugation did not aggregate the particles and that the new pH of the reconstituted solution is measured.

If your data quality is questionable, some of the above sample preparation techniques may help improve the quality. Additional samples can be sent in or, if requested, an analytical specialist at nanoComposix can perform sample optimizations and re-measure Zeta Potential.

MALVERN TECH NOTE BIBLIOGRAPHY:

- (1) [Malvern Zeta potential - An introduction in 30 minutes MRK654-01.pdf](#)
- (2) [Malvern Zeta potential quality report for the Zetasizer Nano MRK751-01.pdf](#)