Whitepaper for Next Generation Electrophoretic Light Scattering (NG-ELS)

John F. Miller, PhD*
Enlighten Scientific LLC, Hillsborough, NC, USA
November 27, 2023

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SEE ADDENDUM FOR IMPORTANT COMPETITOR UPDATE
One company has finally adopted one of the recommendations I have been pushing for a long time. And they now have a serious competitive advantage!

* email: john@enlightenscientific.com

1. Introduction

In recent years, the field of nanotechnology has seen exponential growth, offering innovative solutions across a wide array of industries ranging from healthcare and pharmaceuticals to environmental science and energy production. Central to these advancements is the ability to understand and manipulate the interactions between nanoparticles in various media, particularly in aqueous solutions with high salt concentrations. The measurement of zeta potentials in nanodispersions has emerged as an indispensable tool for gaining insights into these complex interactions. These measurements are critical for ensuring stability, efficacy, and targeted delivery, among other attributes, across different applications. This whitepaper elucidates the importance of measuring zeta potentials in nanodispersions at high salt concentrations, particularly in the following areas:

Nanomedicines, especially proteins on nanoparticles
In the realm of healthcare, proteins coated on nanoparticles serve as the backbone for next-generation nanomedicines. Accurate zeta potential measurements are critical for understanding the stability and bioavailability of these formulations, directly influencing their therapeutic efficacy.

Lipid Nanoparticles (LNPs) for Vaccines and Gene Therapy
Lipid nanoparticles act as delivery vehicles for a variety of genetic materials in cutting-edge vaccines and gene therapies. The role of zeta potential in predicting the behavior of LNPs in biological systems cannot be overstated, and understanding it becomes even more critical in high-salt environments that mimic physiological conditions.

Industrial Wastewater Treatment
As industries aim for greener solutions, nanoparticle-based techniques for wastewater treatment are becoming increasingly prevalent. Here, the zeta potential of particles at high salt concentrations can greatly affect particle aggregation and, subsequently, the efficiency of contaminant removal.

Enhanced Oil Recovery with Brine
In the energy sector, enhanced oil recovery using brine solutions is becoming popular. The zeta potential of nanoparticles in these brine solutions plays a pivotal role in altering the wettability of rock surfaces, thus affecting oil recovery rates.

Given the rapidly growing importance of these applications, this whitepaper provides an in-depth look into Next Generation Electrophoretic Light Scattering (NG-ELS), a breakthrough invention designed to address the pressing need for accurate, reliable, and efficient zeta potential measurements in high-salt concentration nanodispersions.

2. Problem Statement

2.1. Challenges

As the scope of nanotechnology applications broadens to include increasingly specialized and challenging fields, the limitations of existing instrumentation for measuring zeta potentials in nanodispersions have become glaringly evident. Current-generation instruments, optimized primarily for particle sizing with Electrophoretic Light Scattering (ELS) considered as an unoptimized afterthought, fail to meet the demands of high-salt concentration environments due to several shortcomings:

Electrode Polarization and Electrolysis
Conventional instruments are plagued by electrode polarization and electrolysis, particularly in high-salt solutions, leading to inaccurate measurements.

Interference from Convection Due to Significant Heating
Inadequate thermal management in existing systems causes significant heating during measurements, leading to convection currents that distort zeta potential readings.

Lack of Zeta Potential Distribution to Provide Confidence
These instruments typically provide only average zeta potential values when utilizing original PALS methodology, lacking detailed distribution data that could instill greater confidence in interpretation of results. While conventional ELS can provide a distribution, it is of little value if the fundamental measurement is compromised.

2.2. Solutions

To address these challenges, NG-ELS has been developed with features that set a new standard for zeta potential measurements, particularly in high-salt concentration environments. These include:

Simultaneous Determination of Zeta Potential Using LDE and PALS
NG-ELS allows for the simultaneous determination of zeta potential using both traditional distribution methods (laser-Doppler electrophoresis, LDE) and Phase Analysis Light Scattering (PALS)[1], offering more robust and confident measurements.

Measurements at Higher Field Frequencies
By enabling measurements at higher field frequencies, the system mitigates the effects of electrode polarization and electrolysis, substantially improving the accuracy of the readings.

Electrode Health Monitoring and Polarization Detection/Compensation
Incorporating real-time electrode health monitoring and polarization detection features, the system can compensate for any distortions, ensuring consistently reliable measurements.

Optimized for ELS with Advanced Scattering Techniques
Unlike traditional systems, NG-ELS is explicitly optimized for ELS and maximizes the use of scattered light. It is immune to multiple scattering effects and permits higher turbidity samples, thus broadening the range of academic and industrial applications. Although some commercial DLS/ELS instruments offer backscattering detection for measurement at higher turbidities, the problem of multiple scattering still exists. NG-ELS overcomes this issue.

By solving these critical issues, NG-ELS fulfills the urgent need for more reliable and versatile zeta potential measurement instruments.

3. Objective

The primary objective of NG-ELS aims to deliver:

Reliability
Mitigate the common issues of electrode phenomena and convection interference.

Speed & Accuracy
Facilitate faster and more accurate measurements, even in high salt concentration environments and the media appropriate to the application. i.e., it is not necessary to dilute the sample into lower conductivity media because the existing commercial instruments cannot measure samples dispersed in the original high conductivity media.

User-Friendly Experience
Despite its advanced capabilities, NG-ELS strives to offer users an experience that is familiar, mimicking the user interface and processes of current generation instruments, ensuring a smooth transition and minimal training requirements.

A secondary but equally crucial objective of NG-ELS is its adaptability. In the rapidly evolving landscape of scientific instruments, manufacturers face the dual challenge of constantly innovating while ensuring their existing product lines remain relevant and competitive. Here's where the adaptability of NG-ELS becomes a critical advantage:

Extended Lifecycle for Current Instruments
With some features of the NG-ELS being integrable into older devices, a manufacturer can revitalize and extend the lifecycle of their existing product lines. This not only saves on the costs of developing entirely new devices but also boosts the value proposition of current offerings.

Cost-Efficient Upgrades
Manufacturers can offer upgrades based on NG-ELS's adaptable features, providing existing clients with a cost-effective pathway to improved results. This fosters client loyalty and positions the manufacturer as a forward-thinking, client-centric entity.

Streamlined R&D
Incorporating NG-ELS's innovations into existing instruments can reduce the time and resources spent on research and development, allowing manufacturers to focus on other areas of innovation.

Market Differentiation
By integrating features from a next-generation system like NG-ELS, manufacturers can differentiate their products in a crowded market, gaining a competitive edge.

In essence, NG-ELS isn't just an evolution in zeta potential measurement; it's a bridge between the present and the future. It respects the investments made in current instruments while pointing the way forward, ensuring that manufacturers and users alike benefit from the best of both worlds.

4. Description of the Invention

4.1. Optical design

The NG-ELS design, when contrasted with traditional Electrophoretic Light Scattering (ELS) systems, offers the following advantages:

1. **Crossed-beam Geometry**

   Spatial Coherence

   The crossed-beam setup in NG-ELS tackles the spatial incoherence challenge found in reference beam-based ELS designs. The mixing of scattered light takes place within the sample, obviating the need for maintaining stringent coherence to the detector.

   Elimination of Multiple Scattering

   Traditional ELS can be hampered by multiple scattering events, especially in dense samples. NG-ELS avoids this issue, ensuring undistorted, accurate readings.

   Straightforward Alignment

   The alignment of optical components is simpler in NG-ELS than in traditional ELS with the reference beam approach.

   Enhanced Dynamic Range

   NG-ELS detectors boast a wider dynamic range, negating the need to adjust the intensity of one of the beams, thereby making measurements more straightforward and faster.

2. **Frequency Shifting with AOMs – SEE IMPORTANT ADDENDUM.**

   Precise and Consistent Frequency Shift

   With its dual acousto-optic modulator (AOM) system, NG-ELS delivers a stable and accurate frequency shift, guaranteeing more reliable measurements.

   Cost and Efficiency

   Technological advancements have made AOMs more cost-effective, positioning NG-ELS as not only superior to but economically comparable to traditional ELS systems.

   Durability and Minimized Noise

   NG-ELS, by utilizing AOMs and avoiding moving mirrors, diminishes potential noise sources and wear, yielding consistent readings and prolonging equipment life.

3. **Hybrid Digital and Analog Signal Processing**

   Demodulation

   NG-ELS employs a blend of digital and analog signal processing. This drastically reduces the expense related to data acquisition electronics.

   Higher Frequency Shifts

   The hybrid signal processing technique also enables higher frequency shifts than found in traditional ELS instruments. This capacity allows for better phase resolution, especially crucial for PALS measurements.

4. **Faster and Direct Measurements**

   NG-ELS can commence data collection instantly, without the initial setup or beam intensity adjustments that some traditional ELS systems demand.

5. **Detector Placement Flexibility**

With NG-ELS, detectors can be positioned freely in space, allowing more of the scattered light to be used. This significantly improves signal-to-noise performance from weakly-scattering samples and simplifies optical alignment.

6. **High Phase Resolution and Stability**

   Merging all the technological and design advancements, NG-ELS achieves a remarkable level of phase resolution and stability, surpassing the capabilities of existing commercial instruments.

4.2. Electric field

The Electrolyte Challenge

In the presence of electrolytes, electrical double layers form in solution near the electrode surfaces, leading to polarization. This phenomenon results in a potential drop across each double layer, meaning that the voltage the electrolyte solution perceives is lower than the actual applied voltage (or generated voltage in the case of "constant current drive" designs found in some commercial instruments). Consequently, this causes the estimated zeta potential to be lower than its true value by an unpredictable amount.

Complications at Elevated Salt Concentrations

High salt concentrations introduce three significant complications:

Electrode Polarization - Exacerbated at lower frequencies and lower voltages.

Electrolysis - A chemical reaction between the sample and electrode, intensified at low frequencies and high voltages.

Joule Heating - At high ionic strengths, the reduced electrical resistance of the electrolyte solution will cause increased heating of the sample, introducing turbulence that affects electrophoresis.

Traditional zeta potential measurements are conducted at low, near-DC frequencies (e.g., 1Hz) due to mathematical constraints in computing the distribution from Doppler shift frequencies. However, with NG-ELS's innovative approach, measurements can be extended to frequencies as high as 1kHz without sacrificing the ability to obtain a distribution.

Electrode Monitoring

One of the key features of NG-ELS is its capability to continuously monitor the condition of the electrodes. While many existing instruments overlook the health and status of electrodes, NG-ELS recognizes their crucial role in accurate and repeatable measurements. By actively monitoring the electrodes, NG-ELS ensures consistent measurement quality and can detect – and compensate for – potential issues, such as polarization and electrolysis, in real-time. This feature is particularly invaluable for regulated industries that require validated methods that cannot tolerate undetected changes in instrument performance.

Compensation for Polarization

Figure 1 shows a series of samples with varying concentrations of aqueous potassium chloride (KCl) mixed with Brookhaven Instruments' zeta reference standard ZR5.[2] The concentrations start from 0.5mM on the far left and increase up to 4M on the far right. These samples were left untouched for a week.

The samples containing up to 1M KCl remained stable over the period, the 2M KCl sample showed signs of slight instability, and the 4M KCl sample displayed significant instability. From these visual observations, one can infer the likely trend of zeta potential as KCl concentration increases. The dataset on the left represents this expected trend. The shaded region represents the expected range of zeta potential for ZR5 according to the supplier.

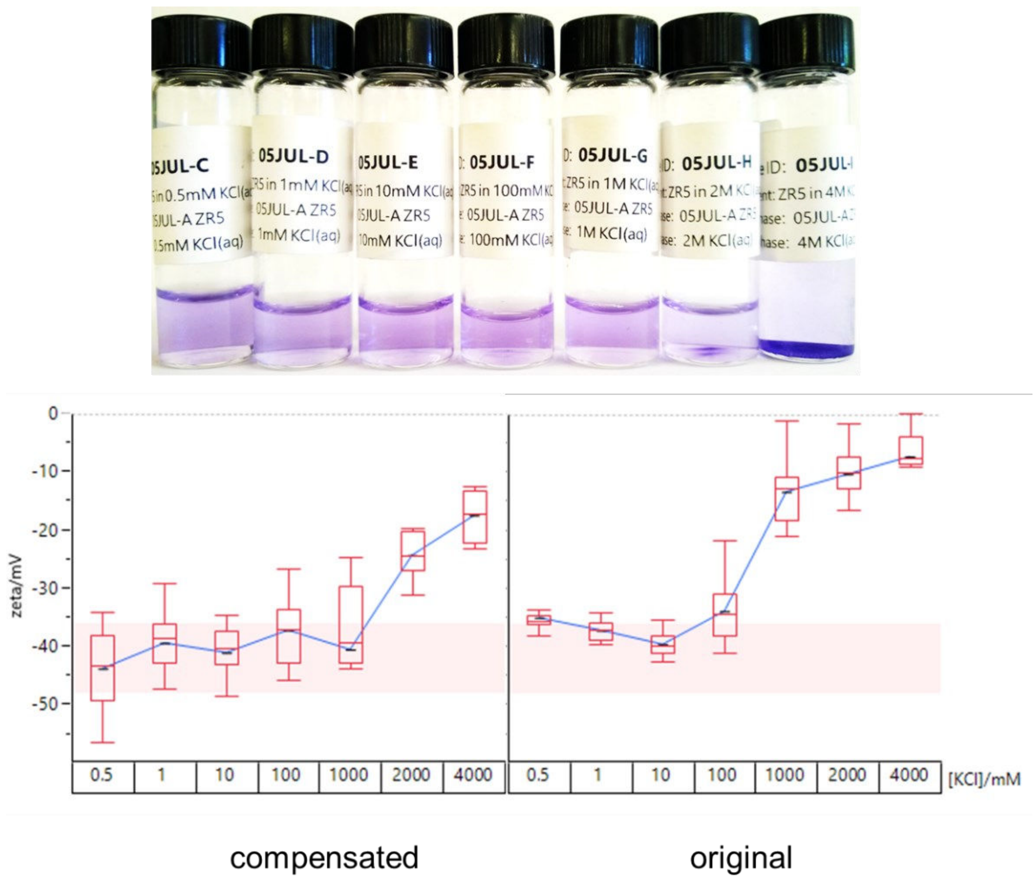


Figure 1 Example of NG-ELS compensation for electrode polarization for ZR5 reference standard dispersed in aqueous KCl solution.

Both the dataset on the left and the one on the right were obtained using the NG-ELS system. Both datasets were derived from a common set of raw light scattering data. NG-ELS can detect and correct for factors that cause the zeta potentials to be measured lower than their actual values. The data on the left have been corrected using this feature, whereas the data on the right haven't been. The experimental parameters, such as electric field strength and frequency, and electrode construction were similar to those typically used in commercial instruments.

4.3. Data processing

Simultaneous distribution and PALS analysis

NG-ELS can concurrently compute both the distribution and phase analysis using the same raw light scattering data. This ensures a more holistic insight, especially vital at high ionic strengths where turbulence can distort measurements.

Hybrid demodulation electronics

By using a combination of analog and digital signal processing techniques, considerable cost savings can be achieved compared to all-digital solutions. Furthermore, by performing the critical demodulation stage (which is simply the numerical multiplication of two signals) using analog multipliers ensures that no quantization noise is introduced that would limit the phase resolution.

5. Examples of published NG-ELS measurements

5.1. Determination of Protein Charge in Aqueous Solution[3]

Studies were reported of the measurement of electrophoretic mobilities of bovine serum albumin (BSA) in aqueous potassium chloride solutions as a function of ionic strength and pH using NG-ELS (see Figure 2).

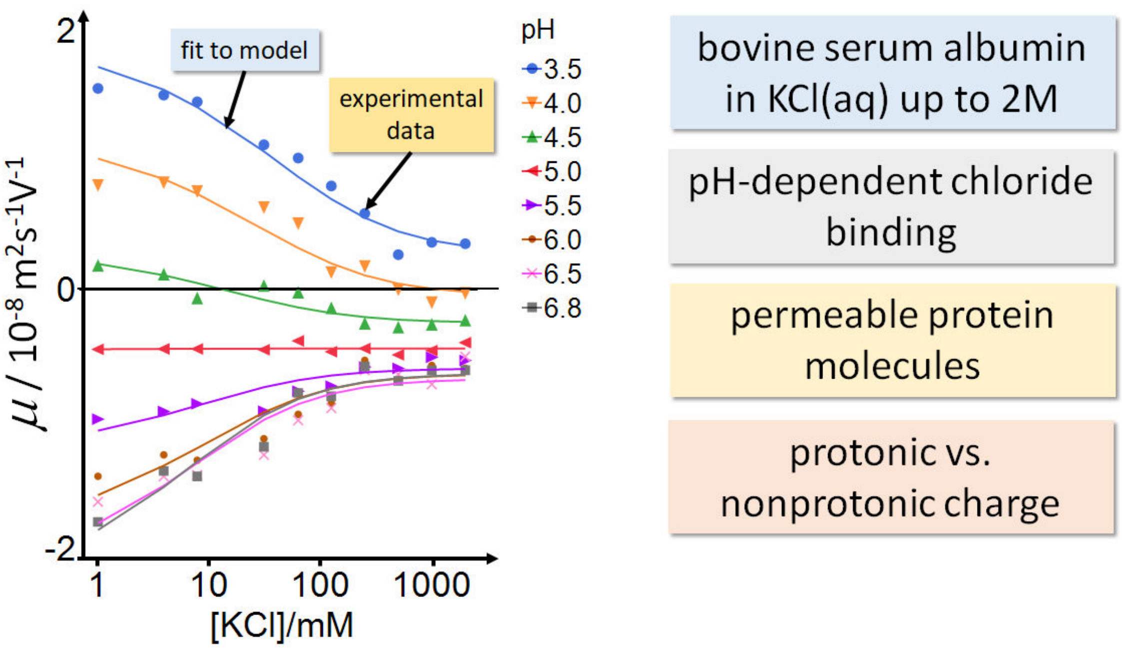


Figure 2 Electrophoretic mobility as a function of [KCl] (grouped by pH). Datum markers are experimental data. Lines show the fit to the Hermans model with compensation for an increased number of counterions bound to each protein molecule at pH ≤ 4.5 compared to that at the iso-ionic point.

Potentiometric acid titration was performed to quantify the amount of protonic charge per protein molecule at the same pH values as the electrophoretic mobility measurements. It was shown that appropriate selection of an electrokinetic model yields excellent agreement between predicted and experimental electrophoretic mobilities across the ranges of pH and ionic strength studied in accordance with the protonic charge values obtained by titration. The experimental results were explained in terms of protonation, chloride counterion binding, and protein molecule permeability. The work highlights specific requirements of using ELS for confident analysis of proteins in aqueous solutions. In particular, accurate and reliable measurement at supermolar ionic strengths is essential for comparing electrokinetic models (e.g., hard impermeable sphere vs. soft permeable spheres) and, thereby, gaining insight into the interfacial characteristics of the dispersed particles. As well as practical benefits, this permits experimental confirmation of advanced electrokinetic theories that have been put forward in recent years but for which no experimental technique has existed to provide verification.

5.2. Cationic Sterically Stabilized Diblock Copolymer Nanoparticles[2,4]

Figure 3 shows results from a comparison of measurements with NG-ELS and the state-of-the-art Malvern Panalytical Zetasizer Nano ZS. The particles were approx. 150nm diameter electrosterically-stabilized cationic latex particles dispersed in aqueous KCl solution and supplied as part of a collaboration with the University of Sheffield in the UK.

Samples were measured as a function of ionic strength ranging from 0.5mM to 4M KCl. The graphs clearly show that the Zetasizer significantly underestimates the zeta potential even at physiological ionic strength (150mM). It fails to measure with any confidence at 100mM or higher. The instrument reported that it could not measure a distribution at 100mM or higher. Significant electrolysis, electrode deterioration, sample discoloration were reported by the operator at higher ionic strengths. The quality of the measurements at 1M and 2M – according to the instrument's reports – are very poor and the instrument didn't even attempt to make a measurement at 4M.

In contrast, NG-ELS was able to provide distributions at all of the salt concentrations. There was no electrolysis or electrode deterioration at any of the salt concentrations. There's high confidence in the measurements at all salt concentrations and the instrument was able to make measurements at all of the salt concentrations.

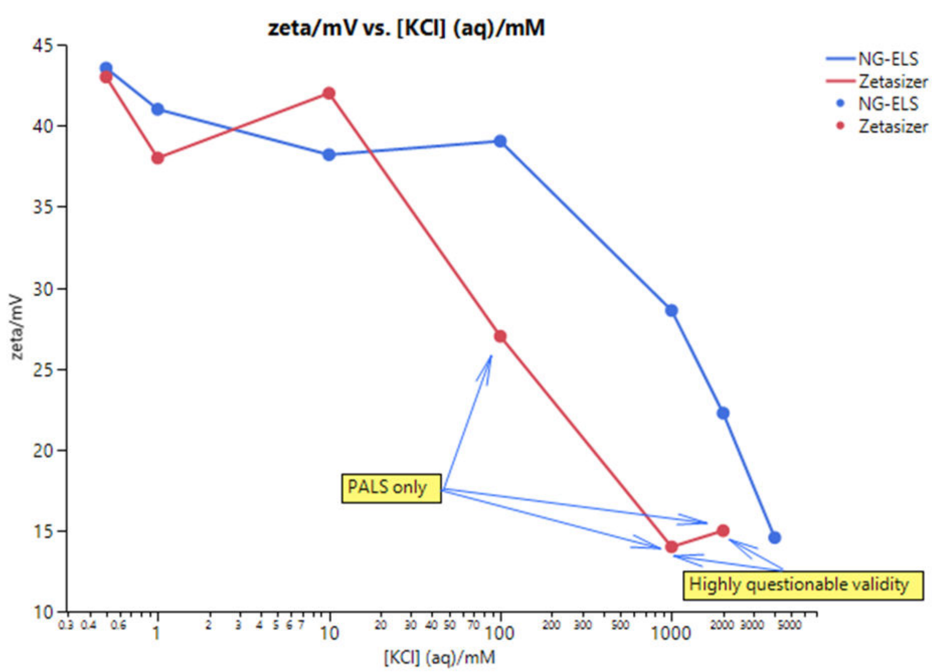


Figure 3 Comparison of zeta potential of cationic sterically-stabilized deblock copolymer nanoparticles measured as a function of KCl(aq) by Malvern Panalytical Zetasizer ZS (red) and NG-ELS (blue).

5.3. RAFT Aqueous Dispersion Polymerization in Highly Salty Media[5]

Sterically-stabilized diblock copolymer particles synthesized at 20% w/w solids via reversible addition–fragmentation chain transfer (RAFT) aqueous dispersion polymerization of N,N′-dimethylacrylamide (DMAC) in highly salty media (2.0 M $(NH_4)_2SO_4$). Traditional zeta potential measurements of such dispersions would require not only optical dilution but dilution of the electrolyte concentration to below 100mM. However, such dilution results in the dissolution of particles. The highly salty environment provides the necessary antisolvent properties to maintain particle integrity. The ionic strength of this system is 6M, neglecting any additional electrolyte due to acid or base. Measurements under these extreme conditions are simply not attainable with any zeta potential instrument currently on the market. Three types of particles were studied with NG-ELS. Based on the chemical structure of the "shell" polymer, it was expected that one type should yield appreciably positive zeta potentials, a second one should be approximately neutral and the third one should be appreciably negative. Figure 4 shows the apparent zeta potentials reported in the study across a wider range of pH. The measurements confirm the anticipated behavior. From these results, important conclusions can be drawn given an appropriate understanding of electrokinetic theory, notably that the surfaces of the particles are not rigid and impermeable but rather "soft" and permeable to the dispersing medium.

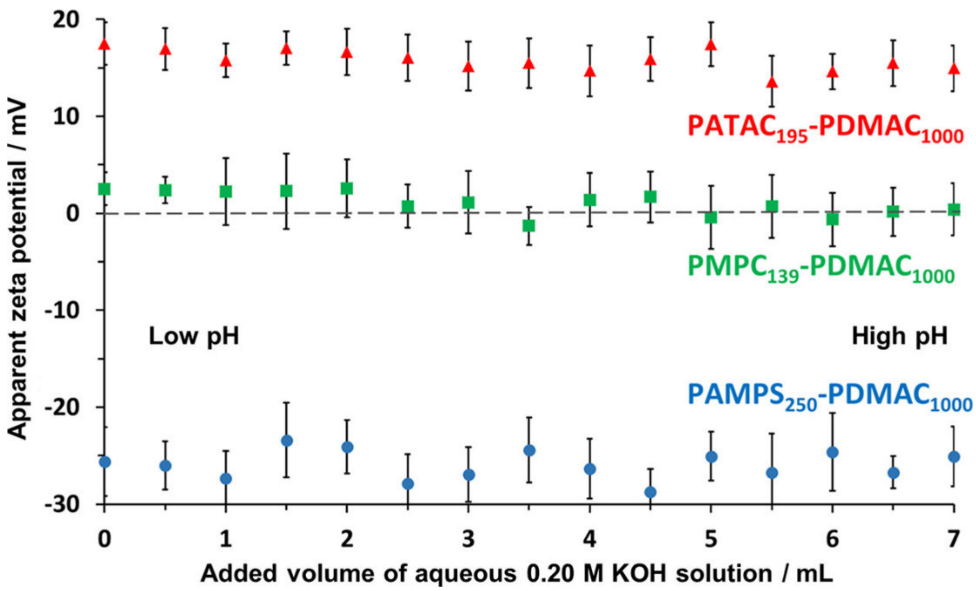


Figure 4 Apparent ζ potentials observed on addition of varying volumes of aqueous 0.2 M KOH solution in the presence of 2.0 M ammonium sulfate(6.1M total ionic strength) for 0.1% w/w aqueous dispersions of $PATAC_{195}$–$PDMAC_{1000}$ (red triangles), $PMPC_{139}$–$PDMAC_{1000}$ (green squares), or $PAMPS_{250}$–$PDMAC_{1000}$ (blue circles) particles.

5.4. Microfluidic Systems[6]

As part of a study of a microfluidic system that could estimate the zeta potential of adsorbed CTAB on the glass surface of microchannels via electro-osmosis, the corresponding electrophoretic mobilities of CTAB solutions in 0.1x and 1.0x PBS buffer were measured as a function of CTAB concentration (see Figure 5). Except for the highest concentrations of CTAB, the concentrations correspond to less than the critical micelle concentration. Attempts to measure the sample solutions on a Malvern Panalytical Zetasizer failed due to insufficient scattered light intensity. This was true for particle size, too. These measurements highlight the advantages of the crossed-beam optical geometry recommended for NG-ELS.

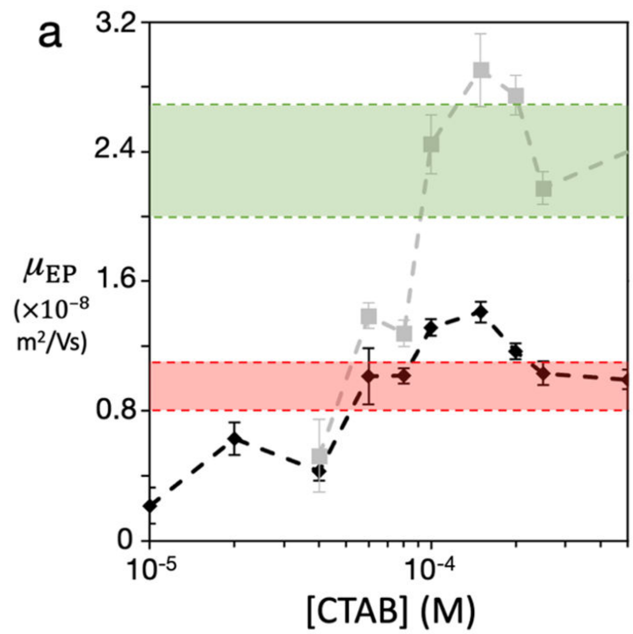


Figure 5 Electrophoretic mobilities of CTAB solutions in 0.1x (grey squares) and 1.0x (black diamonds) PBS buffer solution as a function of CTAB concentration. Discussion of the shaded areas is beyond the scope of this document.

6. Applications with Unmet Needs

In each of the applications mentioned above, zeta potential serves as an essential tool in understanding particle interactions and behavior, which directly impacts the effectiveness, stability, and safety of the products or processes. The increasing number of papers referencing zeta potential underscores its importance in these fields (see Figures Figure 6 to Figure 9)[1]. The following sections demonstrate how zeta potential is becoming increasingly more important in each of the applications. Using NG-ELS will open new marketing opportunities in all these fields.

6.1. Nanomedicines, especially proteins on nanoparticles

Stability

Nanomedicines need to be stable in their formulations to ensure they do not aggregate, sediment, or react in undesirable ways. Zeta potential measurements can provide insights into the colloidal stability of these nanoparticles.

Functionalization

Proteins and other biomolecules attached to nanoparticles might alter their surface charge. Knowing this can be important for predicting nanoparticle behavior, such as interactions with biological systems or other nanoparticles.

Targeting & Cellular Uptake

Zeta potential can impact how nanoparticles interact with cell membranes. Positive or negative charges might affect endocytosis rates or specific targeting to cellular components.

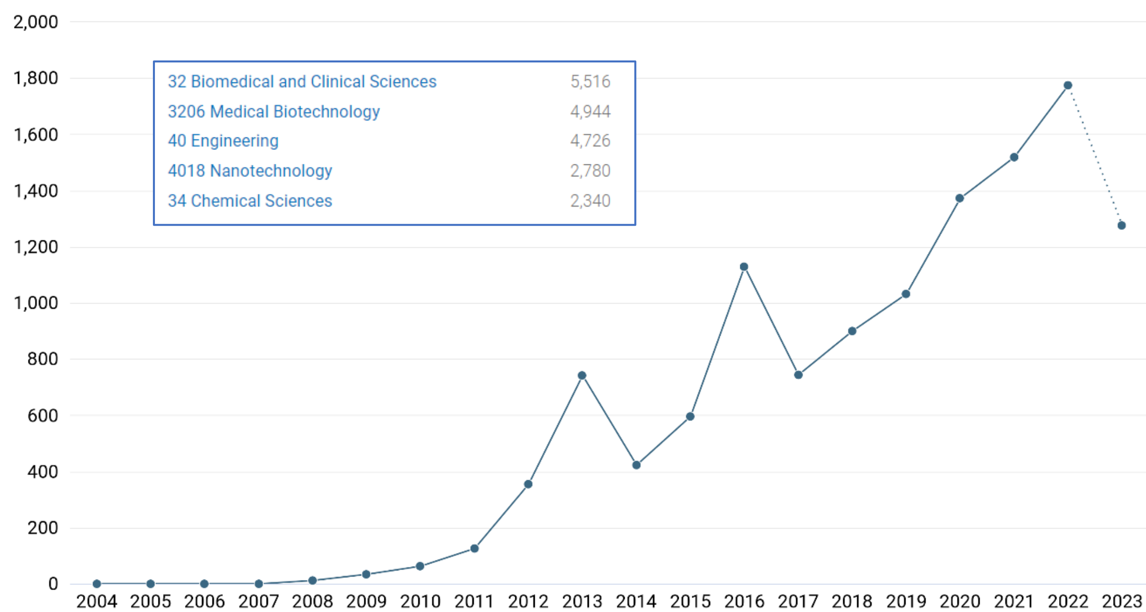


Figure 6 Number of peer-reviewed publications per year for articles related to protein corona and zeta potential. Inset table shows total number of publications by journal classification (Australian and New Zealand Standard Research Classification 2020).

[1] https://app.dimensions.ai/

6.2. Lipid Nanoparticles (LNPs) for Vaccines and Gene Therapy

Stability

LNPs are used to deliver RNA (e.g., mRNA vaccines) or other therapeutic agents. Their stability in the bloodstream and at storage conditions is crucial for efficacy and shelf life. Zeta potential can indicate potential aggregation or fusion of LNPs.

Cell Interaction

The charge on the LNP might affect how it is taken up by cells, which is critical for delivering the payload (like mRNA) to the cell's interior.

Immune Response Modulation

The surface charge of LNPs might also play a role in modulating immune responses, which can be crucial in vaccine formulations.

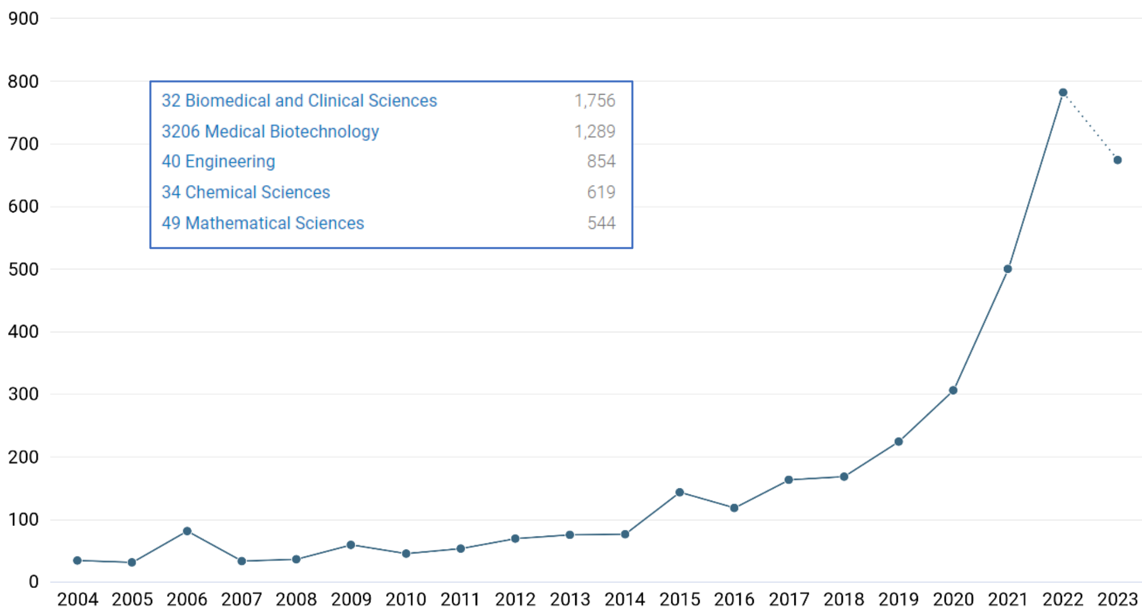


Figure 7 Number of peer-reviewed publications per year for articles related to lipid nanoparticles and zeta potential. Inset table shows total number of publications by journal classification (Australian and New Zealand Standard Research Classification 2020).

6.3. Industrial Wastewater Treatment

Particle Aggregation

Zeta potential helps predict whether particles in wastewater will coagulate or remain dispersed. This impacts the efficiency of solid-liquid separation processes.

Process Optimization

Understanding the zeta potential can help in selecting the right coagulants or flocculants for water treatment.

Contaminant Removal

Many contaminants in wastewater carry charges, and their interaction with charged particles or additives might determine their removal efficiency.

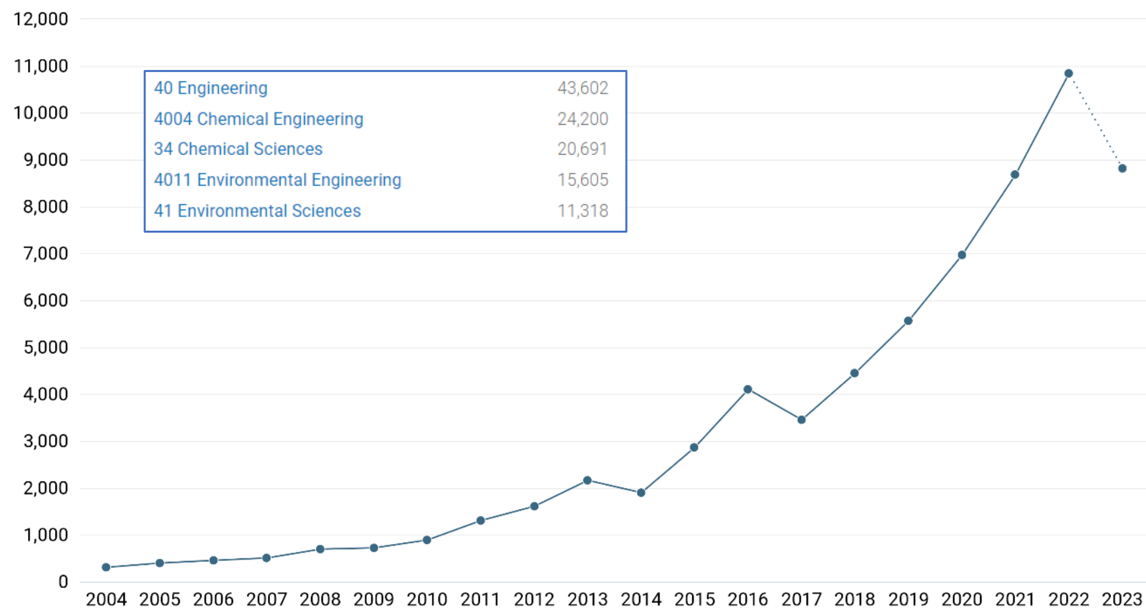


Figure 8 Number of peer-reviewed publications per year for articles related to wastewater and zeta potential. Inset table shows total number of publications by journal classification (Australian and New Zealand Standard Research Classification 2020).

6.4. Enhanced Oil Recovery with Brine

Interactions in the Reservoir

Zeta potential can give insights into how injected brine will interact with reservoir rock and trapped oil droplets. This can affect oil mobilization and displacement.

Scale and Deposit Formation

Understanding the zeta potential can help in predicting the likelihood of scale formation, which can clog equipment and reduce operational efficiency.

Stability of Dispersions

In enhanced oil recovery, stable dispersions of particles (e.g., polymers, surfactants) might be injected. Zeta potential measurements can help determine their stability under reservoir conditions.

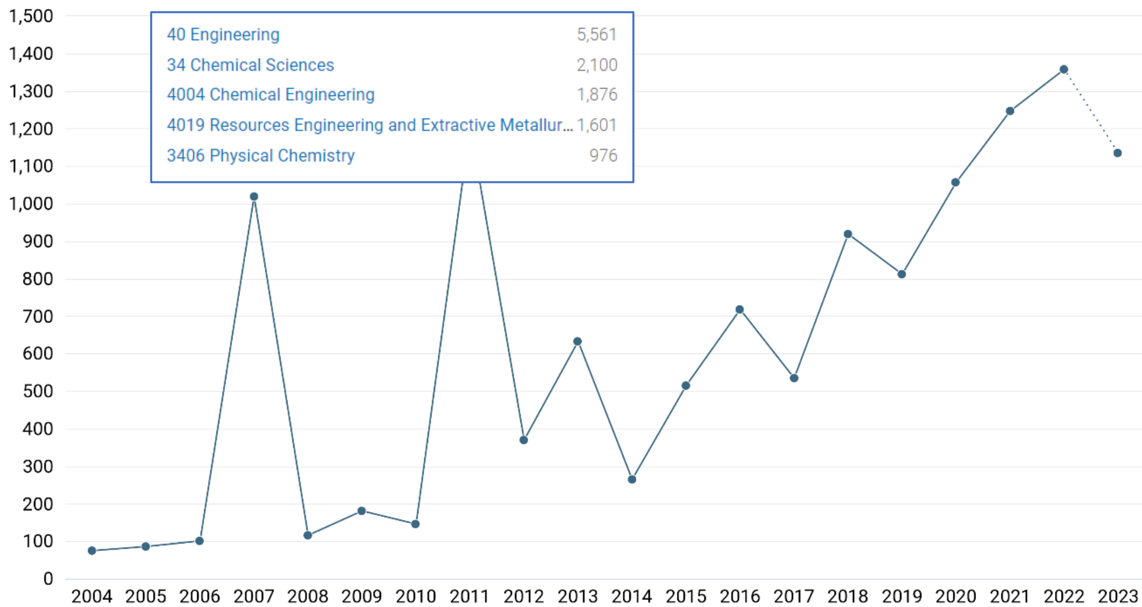


Figure 9 Number of peer-reviewed publications per year for articles related to crude oil and zeta potential. Inset table shows total number of publications by journal classification (Australian and New Zealand Standard Research Classification 2020).

7. Intellectual Property

Many of the key features of NG-ELS are protected by strong intellectual property rights that have been rigorously examined and granted by both the United States Patent and Trademark Office (USPTO) and the United Kingdom Intellectual Property Office (UKIPO). Below are the details of the patents that protect NG-ELS:

Jurisdiction	Patent Number	Granted Date	Anticipated Expiry
United States	US10690625B2[7]	23 June 2020	2038
United Kingdom	GB2578193 (B)[8]	25 August 2021	2038
United Kingdom	GB2590883 (B)[9]	06 October 2021	2039

The patented technology encapsulates several features as described in previous sections, setting a new standard for zeta potential measurements in high ionic strength environments. These patents grant exclusive rights to the use, development, and licensing of NG-ELS through the year 2038.

Given the significant market demand for more accurate and reliable zeta potential measurement instruments, especially in emerging fields like nanomedicines, gene therapies, industrial wastewater treatment, and enhanced oil recovery, these patents provide a powerful competitive advantage. They offer the opportunity for exclusive collaborations, licensing agreements, and other business ventures that can fully leverage the unique capabilities of NG-ELS. The adaptable nature of some features in NG-ELS allows for integration into existing commercial instruments. This extends the range of applications of current instruments, offering vendors a pathway for improvements with only minor modifications.

By securing these patents, Enlighten Scientific has laid a strong foundation for commercializing NG-ELS, inviting collaborations, and driving innovations in various applications that require precise and reliable zeta potential measurements.

8. Conclusion

The field of nanotechnology, with its myriad applications from nanomedicines and gene therapies to industrial wastewater treatment and enhanced oil recovery, has long suffered from the limitations of existing zeta potential measurement instruments. These traditional systems are plagued by various shortcomings, such as electrode polarization, thermal convection interference, and a reliance of PALS-only measurements at moderate ionic strengths and higher.

Next Generation Electrophoretic Light Scattering mitigates these challenges through simultaneous determination methods, higher field frequency measurements, real-time electrode health monitoring, and explicit optimization for Electrophoretic Light Scattering (ELS). With its advanced measurement techniques, the system accommodates a wider range of research conditions and sample turbidity, serving as a catalyst for advancements in multiple disciplines.

Certain features of NG-ELS can be readily integrated into existing commercial instruments, allowing vendors to significantly extend the range of applications for their current offerings with only minor modifications. This offers an immediate pathway for enhancing the capabilities of established systems, thereby amplifying the impact of this invention across the industry.

In summary, NG-ELS not only promises to push the boundaries of current scientific understanding and technological capability but also offers an immediate avenue for improvement in existing systems. It opens the door for more effective nanomedicines, more efficient industrial processes, and more sustainable environmental solutions, making it a cornerstone for future advancements in these and other fields. Using NG-ELS will open new marketing opportunities in all these fields.

9. References

(1) Miller, J. F. The Determination of Very Small Electrophoretic Mobilities in Polar and Nonpolar Colloidal Dispersions Using Phase Analysis Light Scattering. PhD, University of Bristol, 1990.

(2) Miller, J. F. Determination of Zeta Potential in High Ionic Strength Aqueous Colloidal Dispersions Using next Generation Electrophoretic Light Scattering (NG-ELS), 2018. http://colloidssurfaces.sites.acs.org/256%20COLL%20Abstracts.pdf (accessed 2019-09-06).

(3) Miller, J. F. Determination of Protein Charge in Aqueous Solution Using Electrophoretic Light Scattering: A Critical Investigation of the Theoretical Fundamentals and Experimental Methodologies. *Langmuir* **2020**, *36* (29), 8641–8654. https://doi.org/10.1021/acs.langmuir.0c01694 .

(4) Byard, S. J.; Adam Blanazs; Miller, J.; Armes, S. P. Cationic Sterically-Stabilized Diblock Copolymer Nanoparticles Exhibit Exceptional Tolerance towards Added Salt. *Langmuir* **2019**. https://doi.org/10.1021/acs.langmuir.9b02789 .

(5) McBride, R. J.; Miller, J. F.; Blanazs, A.; Hähnle, H.-J.; Armes, S. P. Synthesis of High Molecular Weight Water-Soluble Polymers as Low-Viscosity Latex Particles by RAFT Aqueous Dispersion Polymerization in Highly Salty Media. *Macromolecules* **2022**, acs.macromol.2c01071. https://doi.org/10.1021/acs.macromol.2c01071 .

(6) Abrams, A. Transport and Reaction Mechanisms of Dynamic Coatings in Microfluidic Systems, UC Santa Barbara, 2022. https://escholarship.org/uc/item/49x8h8nh (accessed 2023-10-31).

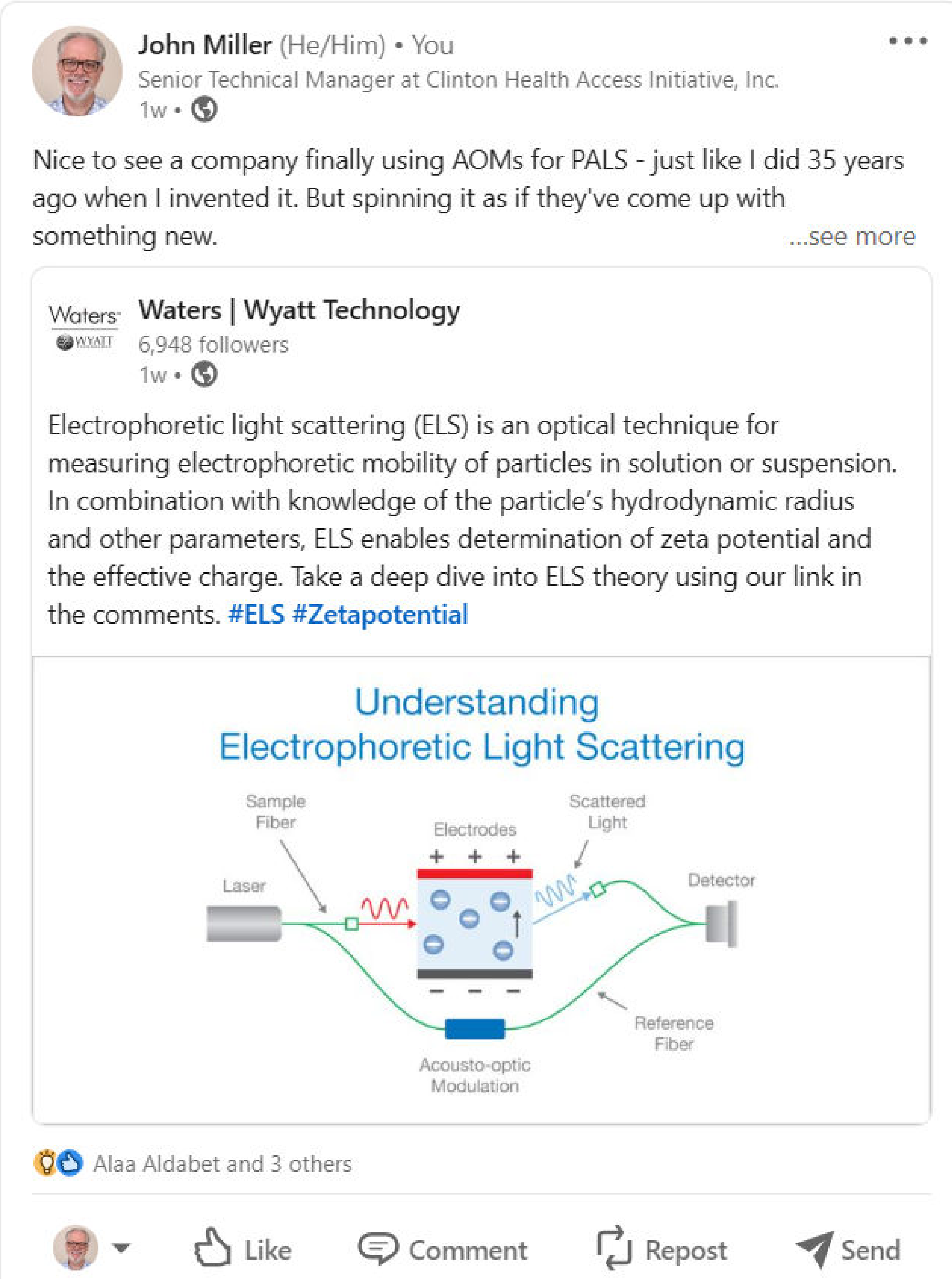
(7) Miller, J. F. Measuring Electrophoretic Mobility. U.S. Patent 10,690,625, June 23, 2020. https://patents.google.com/patent/US10690625B2/ .

(8) Miller, J. Measuring Electrophoretic Mobility. U.K. Patent GB 2578193 (B), August 25, 2021. https://patents.google.com/patent/GB2578193B/ .

(9) Miller, J. Measuring Electrophoretic Mobility. U.K. Patent GB 2590883 (B), October 6, 2021. https://patents.google.com/patent/GB2590883B/ .

IMPORTANT COMPETITOR UPDATE

A few hours after I published this whitepaper, I saw [an announcement on LinkedIn]() from Waters | Wyatt Technology:


John Miller (He/Him) • You
Senior Technical Manager at Clinton Health Access Initiative, Inc.
1w •

Nice to see a company finally using AOMs for PALS - just like I did 35 years ago when I invented it. But spinning it as if they've come up with something new. ...see more

Waters | Wyatt Technology
6,948 followers
1w •

Electrophoretic light scattering (ELS) is an optical technique for measuring electrophoretic mobility of particles in solution or suspension. In combination with knowledge of the particle's hydrodynamic radius and other parameters, ELS enables determination of zeta potential and the effective charge. Take a deep dive into ELS theory using our link in the comments. #ELS #Zetapotential

Alaa Aldabet and 3 others

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They've adopted acousto-optic modulation (AOM), a method I suggested to Wyatt seven years back and included in my patent two years ago for enhancing reference beam configurations (the only claim that the USPTO denied!)

While Wyatt deserves recognition for this integration, it's important to note that there's still much room for improvement. Their current approach doesn't even begin to overcome the limitations that prevent both their instruments and those of their competitors to analyzing high salt concentration samples.

This shift towards AOM use in ELS instruments also significantly impacts the landscape of competitive technologies, leveling the playing field with Anton-Paar's previously unique cmPALS technology in their LiteSizer 500. It's clear that the industry is evolving, and it's exciting to see these advancements unfold. I am uniquely positioned to help YOU to be the true pioneer.