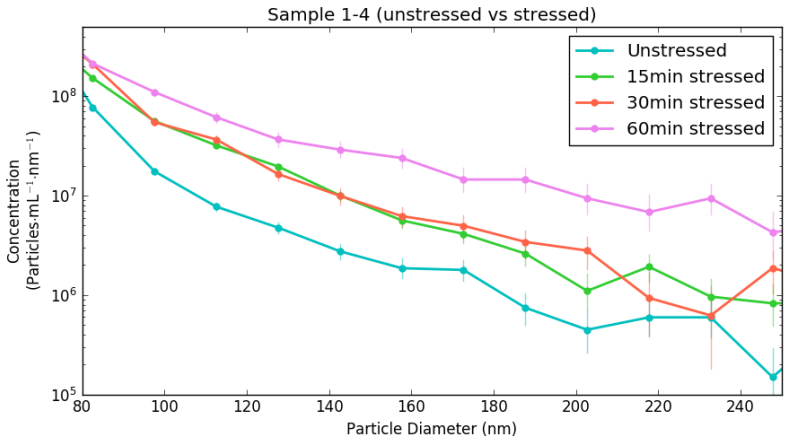
Earlier Detection of Aggregates in Protein Formulations

Early detection of protein aggregation in drug formulations is critical for the assessment of drug safety and efficacy. Aggregation is a continuous process, with small aggregates forming much sooner than larger ones, and significant time savings can be achieved if particles can be detected earlier. However, the most common techniques for characterizing protein aggregation use light scattering, and are not sufficiently sensitive to reliably detect particles smaller than 100-200nm in diameter.

Spectradyne's nCS1™ employs a novel implementation of resistive pulse sensing (RPS) to accurately measure the size and concentration of particles as small as 50 nm in diameter. Leveraging microfluidic technology, the measurement platform delivers practical results quickly and easily and requires only 3 microliters of sample for analysis. For independent validation of the nCS1 in protein aggregation applications, please see reference (1).

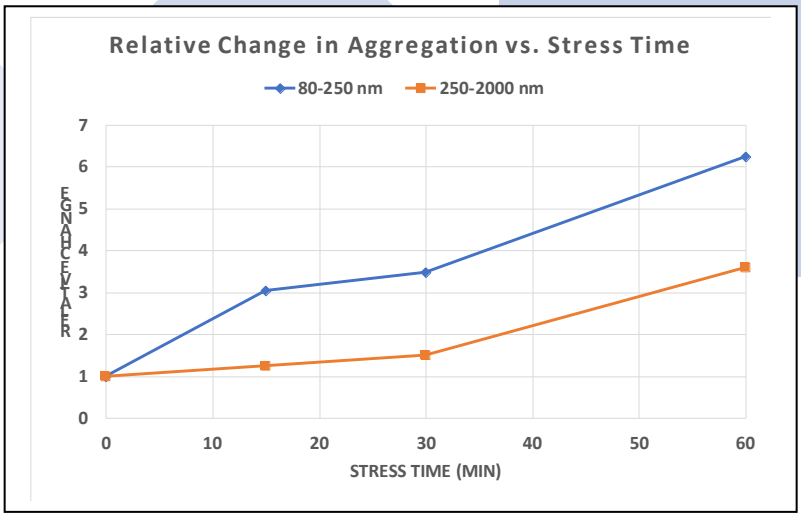
We demonstrated the nCS1's ability to detect aggregation early by evaluating several protein drug formulations that had been stressed to varying degrees (0, 15, 30, 60 minutes).

The formulations were provided to Spectradyne by the manufacturer and measured over a broad size range, from 80 nm to 2 µm. The results show significant differences in particle concentration due to stress. Small aggregates 80-250 nm in diameter were readily detected after as little as 15 mins of stress (right).



Particle size distribution of protein samples stressed to varying degrees. The y-axis is particle concentration in logarithm scale. Aggregates can be readily detected after just 15 mins of stress time.

A clear trend of increasing particle concentration with increasing stress time was observed over the full range of measured diameters, although the relative change for small diameters increased significantly more than for large diameters (see below).



Identifying failing formulations earlier in the drug development process allows resources to be redirected to successful formulations sooner, saving significant time and cost. The nCS1 is the only practical technology available that can accurately characterize small aggregates early, providing direct savings to its users.

[1]Barnett, G.V., Perhacs, J.M., Das, T.K. et al. Submicron Protein Particle Characterization using Resistive Pulse Sensing and Conventional Light Scattering Based Approaches. Pharm Res. 2018 Feb 8;35(3):58.

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