Analytical Technique Comparisons using LINK

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Introduction

Characterization and control of protein aggregation requires the use of a wide range of analysis techniques. Transcribing, aggregating and comparing data from multiple measurements with different size ranges, resolutions, and output formats is very labor intensive. Recent advancements in data management and visualization technologies now allow for automated data extraction directly from analytical equipment measurement files, and automated processing of this data for detailed orthogonal and complimentary technique comparisons.

Methods

LINK was used to automatically transcribe measurement data directly from equipment measurement files into a centralized database. Sample information exemplifying a typical stability study, such as storage time point and storage temperature, were parsed from each data file. LINK Analysis templates for the purpose of technology comparisons were constructed, and updated in real-time with each data import.

Sample datasets were made available from Flow Microscopy (MFI), Light Obscuration (HIAC), RMM (Archimedes), NTA (NanoSight), DLS (DynaPro, Zetasizer), and SEC/cIEF (Empower). Analysis templates were developed for the purpose of comparing:

a) Particle Counting Techniques
b) DLS Techniques
b) MFI and HIAC – Stability Study
c) MFI and FlowCAM Sub-Populations
d) Archimedes Sub-Populations
e) Particle Counting and DLS
f) Particle Mass
g) Disparate Techniques
h) High-Throughput EPD Summaries

Dashboard 1: Particle Counting Techniques

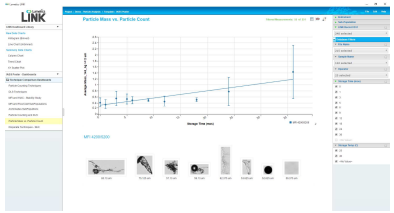
Dashboard 2: DLS Techniques

Dashboard 3: MFI and HIAC – Stability Study

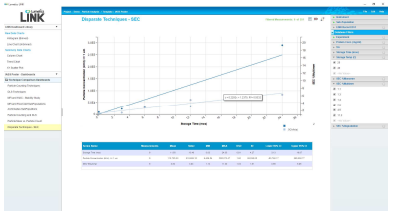
Dashboard 4: MFI and FlowCAM Sub-Populations

Dashboard 5: Archimedes Sub-Populations

Dashboard 6: Particle Counting and DLS



Dashboard 7: Particle/Aggregate Mass



Dashboard 8: Disparate Techniques

Dashboard 9: High-Throughput EPD Summaries

Discussion

Dashboard 1 shows particle counting techniques for user-specified size ranges. Particle images are included, where applicable.

Dashboard 2 compares DLS techniques and provides summary statistics of any parameters measured by equipment software.

Dashboard 3 illustrates particle counting technique comparisons for USP 788/787 size ranges, as a function of stability study parameters (e.g. time, temp), highlighting trends in concentration between different techniques.

Dashboards 4 and 5 permit comparison of multiple user-defined subpopulations (e.g. silicone oil or protein populations) based on particle morphology or particle density/buoyancy assumptions.

Dashboard 6 compares particle counting techniques and DLS using particle volume distributions as a function of size. Particle shape and density assumptions are required to convert count to volume %.

Dashboard 7 highlights the mass of the particle/aggregate population, vs. particle count.

Dashboard 8 compares entirely disparate techniques, such as particle formation detected by counters vs. changes in SEC chromatograms.

Dashboard 9 permits summarization of high-throughput well plate experiments, or specific EPD studies.

Conclusions

It was found that the LINK data management and analysis tool provided direct comparison of orthogonal and complimentary analytical techniques in a fully automated fashion, dramatically improving the speed of analysis and eliminating the possibility of transcription errors. Future work will involve exploring how multi-variate data visualization tools and statistical analysis within the LINK tool might further contribute to the characterization and control of protein formulations.