

PEMBROKE INSTRUMENTS, LLC

U.S. Product Information & Quotations

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Asuryan

CHAUVIN ARNOUX INDATECH

Pharma Biotech



In-line detection of protein aggregation

In a constantly-expanding pharmaceutical industry, we are witnessing a significant increase in bioproduction, which continues to grow as a portion of global drug production.

As protein aggregation is an indicator of their improper folding, it constitutes one of the most important criteria for assessing the quality of biopharmaceuticals.

To guarantee the quality and the therapeutic potential of the end-product, proteins must be perfectly stable in their native form. During the development of the manufacturing process, it is therefore essential to identify with in-line measurement the conditions which are liable to favor aggregation.

Goals

Indatech offers a range of optical accessories to perform UV-VIS measurements in different configurations, particularly in bioreactors (with a probe), on a flow (with a flow cell) or in the laboratory during the exploratory phase (with a multi-angle cuvette holder system). In the context of a proof of concept, Indatech's scientific team focused on studying the aggregation of specific proteins, a frequent biological process characterized by incorrect folding due to various external and/or internal factors. These factors may be diverse, such as mutations, synthesis defects, protein aging or environmental stress.

By using Indatech's optical accessories, you can measure protein aggregation and identify the factors contributing to the phenomenon. This information is essential for the development, production and physiological monitoring of biomolecules with high therapeutic potential.



Experimentation for in-line measurement

A qualitative study of immunoglobulin G (IgG) in solution was carried out by submitting the solutions to thermal stress. To limit the use of large volumes, the measurements were performed using a transflective probe and the Asuryan UV-VIS multi-channel spectrometer which offers a high acquisition rate.

The Indatech ASR Ready software was used to perform the measurements and univariate modelling of the aggregation factor. This software is certified according to the CFR Part 11 regulations and can communicate with production PLCs via OPC UA. This functionality facilitates integration of the quality measurements in the production process and ensures traceability of the data.

Example:
Qualification of the level of immunoglobulin G aggregation

An IgG solution with a concentration of 0.5 mg/mL was monitored for nearly 4 hours while increasing the temperature by 5 °C every 15 minutes up to 75 °C.

The spectra were acquired with a Transflection probe equipped with a 2 mm optical path length and their absorbance was recorded, using distilled water as the blank reference (I_0).

The aggregation index (AI) was then calculated using

$$AI = \left(\frac{A_{350}}{A_{280} - A_{350}} \right) \times 100$$

This index is a semi-quantitative indicator of the protein aggregation rate.

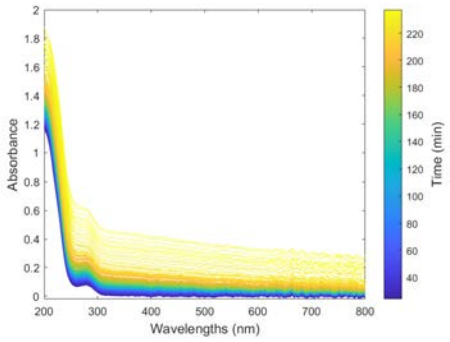

Figure 1
Evolution of the absorbance spectra, colored according to the heating time

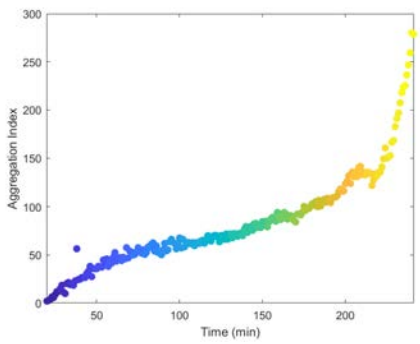

Figure 2
Monitoring of the protein aggregation index according to the heating time

Figure 1 shows the increase in absorbance as a function of the temperature. An increase of the baseline of the entire UV/Vis spectrum is seen at 280 nm.

Figure 2 shows the calculation of the protein aggregation index. An aggregation index below 10, as at the beginning of the experiment, corresponds to solutions with an insignificant number of soluble aggregates. In function of the thermal stress induced, an increase in the aggregation index can then be observed, indicating the formation of aggregates.

Advantages of Asuryan

Asuryan offers a means of in-line and/or at-line measurement and inspection suitable for biopharmaceutical production:

- Sensitivity and measurement accuracy as soon as the first temperature variations occur (ambient temperature + 10 °C)
- Stability over time thanks to an internal reference measurement
- Possibility of measurements at several points using different optical path lengths and scattering angles

This system offers a variety of probes suitable for precise measurement to assess the aggregation of therapeutic proteins, making it possible to monitor the quality of the finished product (validation of bioproduction, filling, conservation, etc.)

The teams at INDATECH will be delighted to answer your questions by telephone: +33 4 80 78 01 40



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