Early detection of protein aggregation in biopharmaceuticals e.g. monoclonal antibodies (mAbs)

Typically monoclonal antibody formulations are made up of monomers. However, during production, filtration and purification steps, the formulation may start to aggregate and form dimers, trimers, fibrils and/or irregular aspherical aggregates. This aggregation has negative consequences for the potency, quality and safety of the end product.

Challenge

Biopharmaceutical companies are interested in tools to help monitor aggregation and detect the onset of aggregation levels as soon as possible so the process can be controlled or even stopped when aggregates begin to form.

Experiment

BRAVE Analytics' nanoparticle analyzer and online particle sensor provide a way to determine when aggregation starts to occur. It monitors the progression of aggregation as it happens via OF2i® and static light scattering signals[1] and delivers results in real-time, eliminating the delay inherent in waiting for offline measurements.

Application highlights

The BRAVE B-Aware module of the BRAVE B-Curious nanoparticle analyzer determines scattering from a very defined scanning volume (Fig 1.). This scattering signal is used to calculate aggregation thresholds and determine larger objects (e.g. fibrils) on a single-particle-based resolution (counting-based method). At known concentrations, OF2i® physical models are able to give absolute aggregation values and/or provide critical quality attributes (CQA) continously and in real time.

OF2i® SINGLE PARTICLE LIGHT SCATTERING MODEL

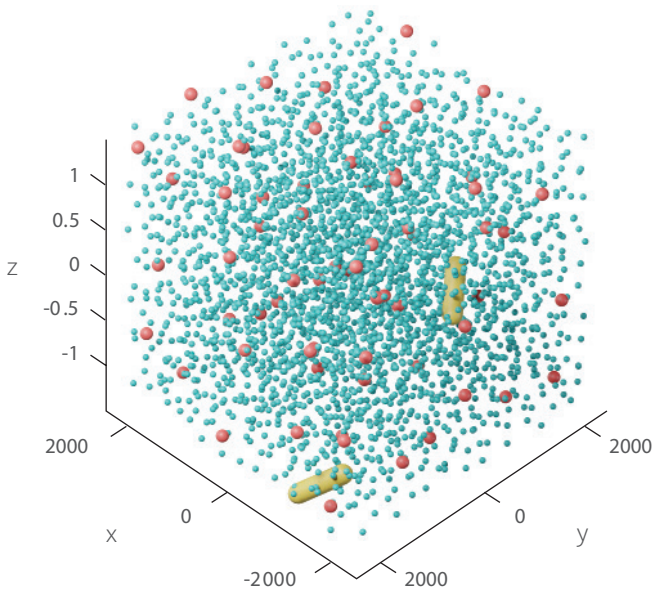
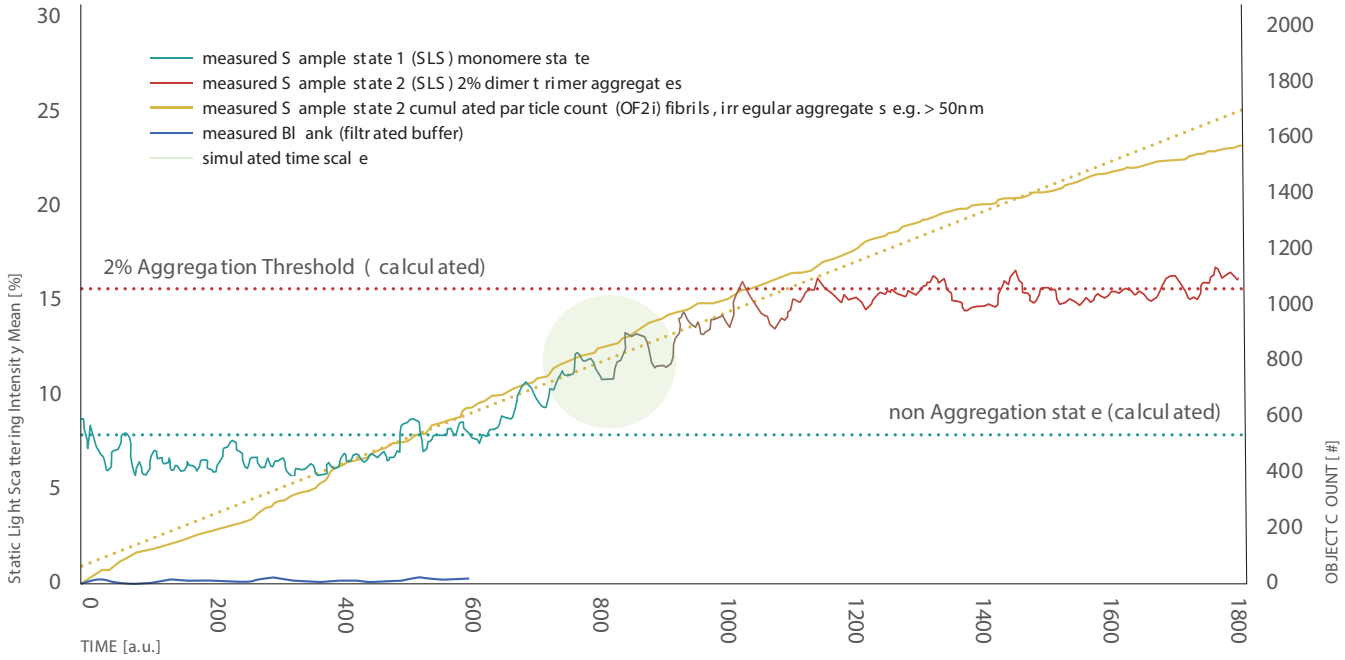


Fig. 1: OF2i®-based calculation of aggregation states to determine aggregation thresholds

OF2i® Comparison of Protein Aggregation
Static Light Scattering Intensity Mean and Object Count over time



[1] Imaging the scattered light of a nanoparticle through a cylindrical capillary. Ulrich Hohenester, Christian Neuper, Marko Šimić, and Christian Hill. *Nanophotonics*, 13(4):457–463, 2024.