

CLAIMS

1. A method for screening monoclonal antibodies (mAb) comprising,
 - a. Adding Fluorescent dye to mAb samples in solution,
 - b. Inducing mAb aggregation by applying stress, to mimic the formation of mAb aggregates during cell culture, bioprocessing, shipment or storage, or combinations of the foregoing, wherein the added dye increases in fluorescence in linear proportion to the mAb's aggregation content as measured by size-exclusion chromatography,
 - c. Measuring the fluorescence, and
 - d. Elucidating the linear relationship between fluorescence signal and mAb aggregation content in calibration experiments, and using said relationship to rapidly estimate aggregation in subsequent experiments.
2. The method of claim 1, wherein the fluorescent dye is a tetraphenylethylene derivative.
3. The method of claim 2, wherein the dye is disodium 3,3'-{[(E)-1,2-diphenyl-1,2-ethenediyl]bis(4,1-phenyleneoxy)}di(1-propanesulfonate).
4. The method of claim 3, wherein the analysis of each sample takes ≤ 10 seconds.
5. The method of claim 4, wherein the analysis is performed using a fluorimeter in a multi-well plate format.
6. The method of claim 5, wherein the analysis is performed in 96-well plates on a Cary Eclipse with multi-well plate attachment.
7. The method of claim 1, wherein the stress is selected from the group including low pH and high temperature.
8. The method of claim 1, wherein the analysis of each sample takes ≤ 30 seconds.
9. The method of claim 1, wherein the analysis of each sample takes ≤ 60 seconds.
10. The method of claim 1, wherein the analysis of each sample takes ≤ 120 seconds.
11. A method for determining monoclonal antibody aggregation comprising
 - a. Adding Fluorescent dye to mAb samples in solution,
 - b. Inducing mAb aggregation by applying stress, to mimic the formation of mAb aggregates during cell culture, bioprocessing, and/or shipment and storage, wherein the added dye increases in fluorescence in linear proportion to the mAb's aggregation content as measured by size-exclusion chromatography,
 - c. Measuring the fluorescence in multi-well plate format using a fluorimeter,

- d. Elucidating the linear relationship between fluorescence signal and mAb aggregation content in calibration experiments, and using said relationship to rapidly estimate aggregation in subsequent experiments.
12. A method for determining monoclonal antibody (mAb) aggregation comprising
- a. Adding a fluorescent dye to an mAb sample to be tested in solution, wherein aggregated mAb in the sample reacts with the fluorescent dye,
 - b. Detecting fluorescence in the sample to be tested,
 - c. Adding the fluorescent dye to a reference aggregated mAb in solution,
 - d. Detecting fluorescence of the reference aggregated mAb; wherein a standard curve of aggregation is constructed according to the fluorescence intensity of a reference aggregated mAb and the concentration of a reference aggregated mAb, the standard curve having a horizontal coordinate of concentration and vertical coordinate of fluorescence intensity; and
 - e. comparing the fluorescence of the mAb sample to be tested with the standard curve to quantify the concentration of aggregated mAb in the sample to be tested.
13. A method for determining monoclonal antibody aggregation (mAb) comprising
- a. Adding a fluorescent dye to an mAb sample to be tested in solution, wherein aggregated mAb in the sample reacts with the fluorescent dye,
 - b. Detecting fluorescence in the sample to be tested,
 - c. Comparing the fluorescence to a standard curve of aggregation derived from fluorescence of an aggregation reference standard to quantify the aggregation content of the sample to be tested.
14. The method of claim 13, wherein the standard curve of aggregation is constructed according to the fluorescence intensity of the reference aggregated mAb and a concentration of the reference aggregated mAb, the standard curve having a horizontal coordinate of concentration and vertical coordinate of fluorescence intensity.
15. The method of claim 14, wherein the aggregation content of the reference aggregated mAb is measured by size-exclusion chromatography.
16. The method of claim 13, wherein the standard curve is linear, or wherein a linear trendline is fitted to the standard curve.

17. The method of claim 12 or 13, wherein the fluorescent dye is a tetraphenylethylene derivative.
18. The method of claim 17, wherein the dye is disodium 3,3'-{[(E)-1,2-diphenyl-1,2-ethenediyl]bis(4,1-phenyleneoxy)}di(1-propanesulfonate).
19. The method of claim 18, wherein the analysis of each sample takes ≤ 10 seconds.
20. The method of claim 19, wherein the analysis is performed using a fluorimeter in a multi-well plate format.
21. The method of claim 20, wherein the analysis is performed in 96-well plates on a Cary Eclipse with multi-well plate attachment.
22. The method of claim 12 or 13, wherein the stress is selected from the group including low pH and high temperature.
23. The method of claim 12 or 13, wherein the analysis of each sample takes ≤ 30 seconds.
24. The method of claim 12 or 13, wherein the analysis of each sample takes ≤ 60 seconds.
25. The method of claim 12 or 13, wherein the analysis of each sample takes ≤ 120 seconds.