

WHAT IS CLAIMED IS:

1. A method for determining the potential of a protein to self-associate, the method comprising:

- a. combining a protein, a nanoparticle, and a buffered salt to form a sample;
- b. exciting the sample with light;
- c. measuring the light transmitted through the sample;
- d. calculating the absorbance intensity ratio of the sample,

wherein the protein is stable at high concentration when the absorbance intensity ratio exceeds a threshold value.

2. The method of claim 1, wherein the protein is an antigen-binding protein.
3. The method of claim 2, wherein the antigen-binding protein is an antibody, an antibody fragment, or a receptor-Fc-fusion protein.
4. The method of claim 3, wherein the antigen-binding protein is a human monoclonal antibody.
5. The method of claim 1, wherein the protein is in the sample at a concentration of about 2 $\mu\text{g/mL}$ to about 512 $\mu\text{g/mL}$.
6. The method of claim 1, wherein the nanoparticle is a gold nanoparticle.
7. The method of claim 6, wherein the gold nanoparticle has a diameter of about 20 nm to about 100 nm.
8. The method of claim 7, wherein the diameter of the gold nanoparticle is about 20 nm.
9. The method of claim 1, wherein the sample comprises about 5×10^{11} to about 8×10^{11} nanoparticles per mL.
10. The method of claim 9, wherein sample comprises about $6\text{--}6.5 \times 10^{11}$ nanoparticles per mL.
11. The method of claim 1, wherein the salt is present in the sample at a concentration of about 2 mM to about 250 mM.
12. The method of claim 11, wherein the salt is sodium chloride.
13. The method of claim 12, wherein the salt concentration is about 2 mM, about 20 mM, or about 200 mM.

14. The method of claim 1, wherein the transmitted light is measured at multiple wavelengths ranging from about 450 nm to about 750 nm.

15. The method of claim 1, wherein the absorbance intensity ratio is the ratio of the absorbance maximum to the initial absorbance.

16. The method of claim 15, wherein the threshold value of the absorbance intensity ratio is about 1.7.

17. The method of any one of claims 1-17 further comprising repeating steps (a) – (d) using a different concentration of protein in the sample.

18. The method of any one of claims 1-18 further comprising repeating steps (a) – (d) using a different concentration of salt in the sample.

19. The method of any one of claims 1-18 further comprising repeating steps (a) – (d) using a different pH of the sample.

20. The method of any one of claims 1-19 further comprising:

- e. combining the highly soluble protein at a high concentration with an excipient to form a formulated drug substance.

21. The method of claim 20, wherein the concentration of the protein is about 50 mg/mL to about 500 mg/mL.

22. The method of claim 21, wherein the excipient is selected from the group consisting of a tonicifier, a buffer, a surfactant, stabilizer, and a combination thereof.

23. The method of claim 22, wherein the tonicifier is a salt.

24. The method of claim 23, wherein the salt is NaCl.

26. A bioanalytical mixture comprising:

- a. at least two nanoparticles;
- b. a protein in at least two phases; and
- c. a salt or a buffer.

27. The bioanalytical mixture of claim 36, wherein the first of the at least two phases of the protein is a soluble phase.

28. The bioanalytical mixture of claim 37, wherein the second of the at least two phases of the protein is an adherent phase, wherein the protein is adhered to the surface of each of the at least two nanoparticles.

29. The bioanalytical mixture of claim 38, wherein the third of the at least two phases of the protein is an aggregated phase, wherein the protein is self-associated to form an aggregate.
30. The bioanalytical mixture of claim 39, wherein one or more of the aggregated protein is also adhered to the surface of a nanoparticle.
31. The bioanalytical mixture of claim 36, wherein each of the at least two nanoparticles comprises gold.
32. The bioanalytical mixture of claim 41, wherein each of the at least two nanoparticles comprises a diameter of about 20 nm to about 100 nm.
33. The bioanalytical mixture of claim 42, wherein the diameter is about 20 nm.
34. The bioanalytical mixture of claim 36, wherein each of the at least two nanoparticles is saturated with the protein.
35. The bioanalytical mixture of claim 36, wherein the nanoparticles are present at a density of about 6×10^{11} to about 7×10^{11} microparticles per milliliter of mixture.
36. The bioanalytical mixture of claim 36, wherein the protein is present at a concentration of about 2 $\mu\text{g/mL}$ to about 512 $\mu\text{g/mL}$.
37. The bioanalytical mixture of claim 36, wherein the protein is an antigen-binding protein.
38. The bioanalytical mixture of claim 47, wherein the antigen-binding protein is selected from the group consisting of antibody, antibody fragment, aptamer and receptor-Fc-fusion protein.
39. The bioanalytical mixture of claim 48, wherein the antigen-binding protein is an antibody.
40. The bioanalytical mixture of claim 49, wherein the antibody is a human monoclonal antibody.
41. The bioanalytical mixture of claim 36, wherein the salt is present at a concentration of about 2 mM to about 300 mM.
42. The bioanalytical mixture of claim 51, wherein the salt is present at a concentration of about 2 mM, about 20 mM, or about 200 mM.
43. The bioanalytical mixture of claim 36, wherein the salt comprises NaCl.
44. A method of making a low viscosity pharmaceutical formulation containing a protein, the method comprising:

- a. determining the potential of the protein to self-associate according to the method of any one of claims 1-24;
 - b. combining a viscosity-reducing excipient with the protein;
 - c. determining the potential of the protein to self-associate according to the method of any one of claims 1-24 in the presence of the viscosity-reducing excipient; and
 - d. formulating the protein with the viscosity-reducing excipient at a level that reduces the viscosity of the protein solution by at least 50% than without the viscosity-reducing excipient.
45. The method of claim 44, wherein the viscosity-reducing excipient is para-aminobenzoic acid (PABA).