

What is claimed is:

1. —A method for determining the potential of a protein to self-associate, the method comprising:
 - a. combining a protein, 5×10^{11} to 8×10^{11} nanoparticles per mL, and a buffered salt to form a sample;
 - b. exciting the sample with light;
 - c. measuring the light transmitted through the sample at multiple wavelengths ranging from 450 nm to 750 nm;
 - d. calculating the absorbance intensity ratio of the sample, wherein the absorbance intensity ratio is the ratio of absorbance intensity at the maximum absorbance ($\lambda_{\max}$) to the initial absorbance at 450 nm; and
 - e. determining the protein retains 90% or more of its native structure at a high concentration when the absorbance intensity ratio exceeds a threshold value of ≥ 1.7 .
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 $2 \mu\text{g/mL}$ to $512 \mu\text{g/mL}$.
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 20 nm to 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 sample comprises $6\text{--}6.5 \times 10^{11}$ nanoparticles per mL.
10. The method of claim 1, wherein the salt is present in the sample at a concentration of 2 mM to 250 mM.
11. The method of claim 10, wherein the salt is sodium chloride.
12. The method of claim 11, wherein the salt concentration is about 2 mM, about 20 mM, or about 200 mM.

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

14. The method of claim 13, wherein the threshold value of the absorbance intensity ratio is about 1.7.

15. The method of any one of claims 1-14 further comprising repeating steps (a) – (~~de~~) using a different concentration of protein in the sample.

16. The method of any one of claims 1-15 further comprising repeating steps (a) – (~~de~~) using a different concentration of buffered salt in the sample.

17. The method of any one of claims 1-16 further comprising repeating steps (a) – (~~de~~) using a different pH of the sample.

18. The method of any one of claims 1-17 further comprising:

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

19. The method of claim 18, wherein the concentration of the protein is 50 mg/mL to 500 mg/mL.

20. The method of claim 19, wherein the excipient is selected from the group consisting of a tonicifier, a buffer, a surfactant, stabilizer, and a combination thereof.

21. The method of claim 20, wherein the tonicifier is a salt.

22. The method of claim 21, wherein the salt is NaCl.

23. 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 1-8-~~9~~, 10-12, and 13-22;

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 1-8, 10-12, and 13-22 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.

24. The method of claim 23, wherein the viscosity-reducing excipient is para-aminobenzoic acid (PABA).