We claim:

1 A method for assessing the stoichiometry and size distribution of heterogeneous protein complexes in a sample to identify a protein that forms fewer large heterogeneous protein:ligand complexes, the method comprising:

fractionating the sample by asymmetrical flow field flow fractionation (A4F) using a perpendicularly-opposed cross flow separation field; and

determining the molar mass, stoichiometry, and size distribution of the heterogeneous protein complexes in the sample using Multi-Angle Laser Light Scattering (MALLS), wherein the heterogeneous protein complexes comprise heterogeneous protein:ligand complexes comprising more than one protein bound to the ligand; and

identifying the stoichiometry and size distribution of the heterogeneous protein:ligand complexes.

2. The method of claim 1, wherein the ligand is a soluble ligand.

3. The method of claim 1 or 2, wherein the protein in the heterogeneous protein:ligand complexes is a monoclonal antibody or an antigen binding fragment thereof.

4. The method of claim 3, wherein the monoclonal antibody is a bispecific antibody or an antigen binding fragment thereof.

5. The method of claim 3, wherein the antibody in the heterogeneous protein:ligand complexes is the same type of antibody.

6. The method of claim 1, wherein the heterogeneous protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of 2:1.

7. The method of claim 1, wherein the heterogeneous–protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of 3:2.

8. The method of claim 1, wherein the heterogeneous–protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of 2:3.

9. The method of claim 1, wherein the heterogeneous–protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of 3:3.

10. The method of claim 1, wherein the heterogeneous–protein:ligand–complex is an antibody:ligand complex having an antibody to ligand molar ratio of 3:4.

11. The method of claim 1, wherein the heterogeneous–protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of 4:4.

12. The method of claim 1, wherein the heterogeneous–protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of 6:6.

13. The method of claim 1, wherein the heterogeneous–protein:ligand complex is an antibody:ligand complex having an antibody to ligand molar ratio of $[2:2]_n$.

14. The method of claim 3, wherein the heterogeneous antibody:ligand complex has a molecular weight of 700 kDa to 8000 kDa.

15. The method of claim 3, wherein the heterogeneous antibody:ligand complex has a molecular weight of 500 kDa to 4000 kDa.

16. The method of claim 3, wherein the A4F is performed with a channel with a W350 spacer foil having a thickness of 350 µm and a width of 2.2 cm.

17. The method of claim 3, wherein the A4F is performed with a channel with a W490 spacer foil having a thickness of 490 µm and a width of 2.2 cm.

18. The method according to claim 1, wherein the fractionating step comprises (i) injection of the sample into the sample inlet port of the A4F channel and (ii) then focus of the sample by allowing the carrier fluid to flow into the channel from an inlet port and an outlet port.

19. The method according to claim 18, wherein smaller protein:ligand complexes will elute before larger protein:ligand complexes.

20. The method according to claim 3, wherein the fractionating step comprises (i) injection of the sample into the sample inlet port of the A4F channel and (ii) then focus of the sample by allowing the carrier fluid to flow into the channel from an inlet port and an outlet port.

21. The method according to claim 20, wherein smaller protein:ligand complexes will elute before larger antibody:ligand complexes.

22. A method for assessing the ability of a protein to form heterogeneous protein:ligand complexes, wherein the method is capable of separating the complexes in the sample over a course of 60 minutes, wherein the method comprises the steps of:

fractionating a heterogeneous protein complex sample by asymmetrical flow field flow fractionation (A4F) using a channel flow and a perpendicularly-opposed cross-flow separation field that has a linear gradient flow, wherein the samples are separated using the linear gradient; and

assessing size distribution of heterogeneous protein complexes in the sample using Multi-Angle Laser Light Scattering (MALLS), wherein the heterogeneous protein complexes comprise heterogeneous protein:ligand complexes.

23. The method according to claim 22, wherein the protein is a monoclonal antibody or an antigen binding fragment thereof.

24. The method according to claim 22, wherein the protein is a bispecific antibody or an antigen binding fragment thereof.

25. The method according to claim 22, wherein the protein is an Fc fusion protein.

26. The method according to claim 22, wherein the protein is a receptor Fc fusion protein.

27. The method according to claim 22, wherein the linear gradient flow is from 3.0 ml/min to 0 ml/min.

28. The method according to claim 22, wherein the linear gradient flow is from 2 ml/min to 0 ml/min.

29. The method according to claim 22, wherein the linear gradient flow is from 1.2 ml/min to 0 ml/min.

30. The method according to claim 22, wherein the stoichiometry of the heterogeneous protein complexes is assessed.