

What is claimed is:

1. A method for quantifying an impurity in a sample, said method comprising:

contacting said sample to a chromatographic system having a mixed-mode size exclusion chromatography resin with an additional functionality;

washing said mixed-mode size exclusion chromatography resin using a mobile phase to provide an eluent including the impurity; and

quantifying an amount of the impurity in said eluent using a mass spectrometer.
2. The method of claim 1, wherein the mobile phase used to elute the impurity has ammonium acetate, ammonium bicarbonate, or ammonium formate, or combinations thereof.
3. The method of claim 1, wherein the mobile phase used to elute the impurity has a total concentration of less than about 600 mM of ammonium acetate and ammonium bicarbonate.
4. The method of claim 1, wherein the mobile phase used to elute the impurity has a flow rate of ~~about~~ 0.2 ml/min – ~~about~~ 0.4 ml/min.
5. The method of claim 1, wherein the amount of the sample loaded onto the mixed-mode size exclusion chromatography resin is ~~about~~ 10 µg to ~~about~~ 100 µg.
6. The method of claim 1, wherein the impurity is a product-related impurity.
7. The method of claim 1, wherein the impurity is a homodimer.
8. The method of claim 1, wherein the sample includes the impurity and at least one target protein that are separated when eluted.
9. The method of claim 8, wherein the target protein is an antibody.
10. The method of claim 9, wherein the antibody is a bispecific antibody.
11. The method of claim 8, wherein the target protein is a therapeutic antibody.

12. The method of claim 1, wherein the mass spectrometer is coupled to the chromatographic system.
13. The method of claim 1, wherein the additional functionality is a hydrophobic interaction functionality.
14. The method of claim 1, wherein the additional functionality is a charge-charge interaction functionality.
15. The method of claim 1, wherein the mass spectrometer is a native mass spectrometer.
16. A method for detecting an impurity in a sample, said method comprising:

contacting said sample to a chromatographic system having a mixed-mode size exclusion chromatography resin with an additional functionality;

washing said mixed-mode size exclusion chromatography resin using a mobile phase to provide an eluent including the impurity; and

detecting the impurity in said eluent using a mass spectrometer.
17. A method for quantifying a target protein in a sample, said method comprising:

contacting said sample to a chromatographic system having a mixed-mode size exclusion chromatography resin with an additional functionality;

washing the mixed-mode size exclusion chromatography resin using a mobile phase to provide an eluent including the target protein; and

quantifying the target protein in said eluent using a mass spectrometer.
18. A method for detecting a target protein in a sample, said method comprising:

contacting said sample to a chromatographic system having a mixed-mode size exclusion chromatography resin with an additional functionality;

washing the mixed-mode size exclusion chromatography resin using a mobile phase to provide an eluent including the target protein; and

detecting the target protein in said eluent using a mass spectrometer.

19. A mixed-mode chromatography system comprising:

a chromatographic column having a mixed-mode size exclusion chromatography resin with an additional functionality, wherein the column is capable of receiving a mobile phase and a sample having a target protein, and

a mass spectrometer coupled to said chromatographic column for detecting the target protein.