

What is claimed is:

1. A method for detecting and/or discriminating between post-translational modification variants of an antibody of interest in a sample, comprising:
contacting a sample comprising one or more antibodies of interest with a protease to digest the sample into antibody fragments;
separating the antibody fragments by molecular weight and/or charge in one or more capillaries using microfluidic capillary electrophoresis under native conditions;
eluting the separated antibody fragments from the one or more capillaries; and
determining the mass of the eluted antibody fragments by mass spectrometry analysis, thereby detecting and/or discriminating between post-translational modification variants of the antibody of interest.
2. The method of claim 1, wherein the post-translational modification comprises one or more of deamidation, oxidation, glycation, disulfide formation, N-terminal pyroglutamate formation, C-terminal lysine removal, and high mannose glycosylation.
3. The method of claim 1 or 2, wherein the protease comprises IdeS.
4. The method of any one of claims 1-3, wherein the antibody fragments comprise one or more of an F(ab')₂ or Fc antibody subunit.
5. The method of any one of claims 1-4, wherein the antibody of interest is a monoclonal antibody.
6. The method of any one of claims 1-5, wherein the antibody fragments are separated by charge and the method is a method of detecting and/or discriminating between charge variants of the antibody of interest.
7. The method of any one of claims 1-6, wherein the antibody fragments are separated by molecular weight and the method is a method of detecting and/or discriminating between size variants of the antibody of interest.

8. The method of any one of claims 1-7, further comprising determining a relative or absolute amount of the post-translational modification variants of an antibody of interest in a sample.
9. The method of any one of claims 1-8, wherein the antibody of interest comprises a bispecific antibody.
10. The method of any one of claims 1-9, wherein the sample includes an internal standard.
11. The method of any one of claims 1-9, wherein the one or more capillaries comprise a separation matrix.
12. The method of claim 11, wherein the separation matrix comprises a sieving matrix configured to separate proteins by molecular weight.
13. The method of any one of claims 1-12, wherein eluting separated antibody fragments from the one or more capillaries further comprises separating the antibody fragments into one or more fractions.
14. The method of any one of claims 1-13, further comprising identifying the antibody fragments.
15. The method of any one of claims 1-14, further comprising identifying the post-translational modification present on the antibody fragments.
16. The method of any one of claims 1-14, wherein the antibody of interest is of isotype IgG1, IgG2, IgG3, IgG4, or mixed isotype.
17. The method of any one of claims 1-16, further comprising post-translational modification profiling of the antibody of interest.

18. The method of any one of claims 1-17, further comprising post-translational modification mapping of post-translational modification hotspots by reduced peptide mapping LC-MS/MS analysis.

19. The method of any one of claims 1-18, wherein the sample comprises a mixture of antibodies of interest.

20. The method of any one of claims 1-19, wherein the antibody of interest is an antibody drug conjugate.