

What is claimed is:

1. A method of monitoring column chromatography performance, comprising:
acquiring one or more chromatogram ultraviolet (UV) traces generated by a chromatography system during sample purification and/or separation; and
analyzing the one or more acquired chromatogram UV traces with an orthogonal partial least squares (OPLS) model, thereby allowing detection of column deterioration prior to column failure and quantitative analysis of UV signal in the one or more chromatogram UV traces.
2. The method of claim 1, further comprises creating the OPLS model.
3. The method of claim 2, wherein creating the OPLS model comprises:
selecting a process or unit operation of the OPLS model;
collecting raw data for a UV trace of one or more column cycles/lots/runs for the selected process or unit operation;
normalizing and aligning the collected raw data;
optionally generating artificially created curves from normalized raw data;
classifying and formatting data for importation into a multivariate tool;
importing classified and formatted data into the multivariate tool to generate a training set; and
generating the OPLS model.
4. The method of claim 3, further comprising optimizing the generated OPLS model, validating and testing the optimized OPLS model.
5. The method of claim 3 or 4, wherein the process or unit operation is a chromatography unit operation for a single molecule.
6. The method of claim 5, wherein the process or unit operation is a protein affinity chromatography step for the single molecule.
7. The method of any one of claims 3-6, wherein collecting raw data for a UV trace of one or more column cycles/lots/runs for the selected process or unit operation comprises collecting UV absorbance values at corresponding column volumes for the one or more cycles/lots/runs.

8. The method of any one of claims 3-7, wherein normalizing and aligning the collected raw data comprises normalizing and aligning UV absorbance values and aligning column volumes.

9. The method of claim 8, wherein normalizing UV absorbance values comprises removing variation in magnitude differences in UV raw signal.

10. The method of any one of claims 3-9, wherein optionally generating artificially created curves from normalized raw data comprises generating artificially created curves from normalized raw data when one or more unacceptable UV chromatogram traces are not available.

11. The method of any one of claims 1-10, further comprising providing a sample to the chromatography system prior to acquiring the one or more chromatogram ultraviolet (UV) traces generated by a chromatography system during sample purification and/or separation.

12. The method of any one of claims 1-11, wherein the chromatography system is a liquid chromatography system.

13. The method of any one of claims 1-12, wherein the sample comprises a protein.

14. The method of claim 13, wherein the protein is an antibody, a fusion protein, recombinant protein, or a combination thereof.

15. The method of claim 14, wherein the antibody is a monoclonal antibody.

16. The method of claim 15, wherein the monoclonal antibody is of isotype IgG1, IgG2, IgG3, IgG4, or mixed isotype.

17. A method of creating an orthogonal partial least square (OPLS) model for UV monitoring of a chromatography column performance, comprising:
selecting a process or unit operation of the OPLS model;
collecting raw data for a ultraviolet (UV) chromatogram trace of one or more column cycles/lots/runs for the selected process or unit operation;
normalizing and aligning the collected raw data;

optionally generating artificially created curves from normalized raw data;
classifying and formatting data for importation into a multivariate tool;
importing classified and formatted data into the multivariate tool to generate a training set; and
generating the OPLS model.

18. The method of claim 17, further comprising optimizing the generated OPLS model, validating the OPLS model, testing the optimized OPLS model, and applying the optimized OPLS model to future operations to monitor chromatography column performance.

19. The method of claim 17 or 18, wherein the process or unit operation is a chromatography unit operation for a single molecule.

20. The method of claim 19, wherein the process or unit operation is a protein affinity chromatography step for the single molecule.

21. The method of any one of claims 17-20, wherein collecting raw data for a UV chromatogram trace of one or more column cycles/lots/runs for the selected process or unit operation comprises collecting UV absorbance values at corresponding column volumes for the one or more cycles/lots/runs.

22. The method of any one of claims 17-20, wherein normalizing and aligning the collected raw data comprises normalizing and aligning UV absorbance values and aligning column volumes.

23. The method of claim 22, wherein normalizing UV absorbance values comprises removing variation in magnitude differences in UV raw signal.

24. The method of any one of claims 17-23, wherein optionally generating artificially created curves from normalized raw data comprises generating artificially created curves from normalized raw data when one or more unacceptable UV chromatogram traces are not available.

25. The method of any one of 17-24, wherein the one or more UV chromatogram traces is one or more UV chromatogram traces generated by a chromatography system during sample purification and/or separation.

26. The method of claim 25, wherein the chromatography system is a liquid chromatography system.
27. The method of claim 25 or claim 26, wherein the sample comprises a protein.
28. The method of claim 27, wherein the protein is an antibody, a fusion protein, recombinant protein, or a combination thereof.
29. The method of claim 28, wherein the antibody is a monoclonal antibody.
30. The method of claim 15, wherein the monoclonal antibody is of isotype IgG1, IgG2, IgG3, IgG4, or mixed isotype.
31. A non-transitory computer-readable storage medium with an executable program stored thereon for monitoring column chromatography performance, wherein the program instructs a microprocessor to perform the steps of:
- acquiring one or more chromatogram ultraviolet (UV) traces generated by a chromatography system during sample purification and/or separation; and
 - analyzing the one or more acquired chromatogram UV traces with an orthogonal partial least squares (OPLS) model, thereby allowing detection of column deterioration prior to column failure and quantitative analysis of UV signal in the one or more chromatogram UV traces.
32. The non-transitory computer-readable storage medium of claim 31, further comprises instructions for creating the OPLS model.
33. The non-transitory computer-readable storage medium of claim 32, wherein creating the OPLS model comprises:
- selecting a process or unit operation of the OPLS model;
 - collecting raw data for a UV trace of one or more column cycles/lots/runs for the selected process or unit operation;
 - normalizing and aligning the collected raw data;
 - optionally generating artificially created curves from normalized raw data;
 - classifying and formatting data for importation into a multivariate tool;

importing classified and formatted data into the multivariate tool to generate a training set; and
generating the OPLS model.

34. The non-transitory computer-readable storage medium of claim 33, further comprising optimizing the generated OPLS model, validating and testing the optimized OPLS model.

35. The non-transitory computer-readable storage medium of claim 33 or 34, wherein the process or unit operation is a chromatography unit operation for a single molecule.

36. The non-transitory computer-readable storage medium of claim 35, wherein the process or unit operation is a protein affinity chromatography step for the single molecule.

37. The non-transitory computer-readable storage medium of any one of claims 33-36, wherein collecting raw data for a UV trace of one or more column cycles/lots/runs for the selected process or unit operation comprises collecting UV absorbance values at corresponding column volumes for the one or more cycles/lots/runs.

38. The non-transitory computer-readable storage medium of any one of claims 33-37, wherein normalizing and aligning the collected raw data comprises normalizing and aligning UV absorbance values and aligning column volumes.

39. The non-transitory computer-readable storage medium of claim 38, wherein normalizing UV absorbance values comprises removing variation in magnitude differences in UV raw signal.

40. The non-transitory computer-readable storage medium of any one of claims 33-39, wherein optionally generating artificially created curves from normalized raw data comprises generating artificially created curves from normalized raw data when one or more unacceptable UV chromatogram traces are not available.

41. The non-transitory computer-readable storage medium of any one of claims 31-40, further comprising providing a sample to the chromatography system prior to acquiring the one

or more chromatogram ultraviolet (UV) traces generated by a chromatography system during sample purification and/or separation.

42. The non-transitory computer-readable storage medium of any one of claims 31-41, wherein the chromatography system is a liquid chromatography system.

43. The non-transitory computer-readable storage medium of any one of claims 31-42, wherein the sample comprises a protein.

44. The non-transitory computer-readable storage medium of claim 43, wherein the protein is an antibody, a fusion protein, recombinant protein, or a combination thereof.

45. The non-transitory computer-readable storage medium of claim 44, wherein the antibody is a monoclonal antibody.

46. The non-transitory computer-readable storage medium of claim 45, wherein the monoclonal antibody is of isotype IgG1, IgG2, IgG3, IgG4, or mixed isotype.