

CLAIMS

What is claimed:

1. A method for predicting or detecting a malfunction in a chromatography process, comprising:
 - (a) generating a reference chromatogram from a chromatography column,
 - (b) generating a process chromatogram from the chromatography column, and
 - (c) detecting an atypical profile in the process chromatogram,wherein the atypical profile indicates a potential or actual malfunction of a chromatography process.
2. The method of claim 1, wherein the method further comprises (d) generating a warning signal.
3. The method of claim 2, wherein the method further comprises (e) repacking the chromatography column.
4. The method of any one of claims 1-3, wherein the chromatography column is suitable for use in ion exchange chromatography.
5. The method of any one of claims 1-3, wherein the chromatography column is suitable for use in affinity chromatography.
6. The method of any one of claims 1-3, wherein the chromatography column is suitable for use in hydrophobic interaction chromatography.
7. The method of any one of claims 1-6, wherein the potential or actual malfunction of the chromatography process is caused by column deterioration.
8. The method of claim 7, wherein the column deterioration comprises column bed fracturing.

9. The method of any one of claims 1-8, wherein the atypical profile comprises an additional peak on the process chromatogram when compared to a comparable position on the reference chromatogram.
10. The method of claim 9, wherein the additional peak occurs during a washing step in the chromatography process.
11. The method of claim 10, wherein the washing step precedes an elution step in the chromatography process.
12. The method of claim 11, wherein the additional peak occurs during the washing step and precedes the elution step in the chromatography process.
13. The method of any one of claims 9-12, wherein the magnitude of the additional peak indicates a degree of severity of the potential or actual malfunction of the chromatography process.
14. The method of claim 13, wherein an increase in the magnitude of the additional peak indicates an increase in the degree of severity of the potential or actual malfunction of the chromatography process.
15. The method of any one of claims 9-14, wherein the malfunction of the chromatography process induces a loss of separation power of the chromatography column.
16. The method of any one of claims 1-8, wherein the atypical profile comprises at least one peak or at least one indentation on the process chromatogram having a decreased sharpness or a decreased magnitude when compared to a peak or an indentation at a comparable position on the reference chromatogram.
17. The method of claim 16, wherein the at least one peak or the at least one indentation on the process chromatogram having a decreased sharpness or a decreased magnitude occurs during the washing step.

18. The method of claim 16 or 17, wherein the at least one peak or the at least one indentation on the process chromatogram having a decreased sharpness or a decreased magnitude follows the elution step.
19. The method of any one of claims 1-8, wherein the atypical profile comprises a first peak or a first indentation having a decreased sharpness or a decreased magnitude on the process chromatogram when compared to a peak or an indentation at a comparable first position on the reference chromatogram and a second peak or a second indentation having a decreased sharpness or a decreased magnitude on the process chromatogram when compared to a peak or indentation at a comparable second position on the reference chromatogram.
20. The method of claim 19, wherein the first peak or the first indentation follows the elution step.
21. The method of claim 20, wherein the first peak or the first indentation corresponds to an indentation occurring at a start of a collecting step.
22. The method of any one of claims 19-21, wherein the second peak or the second indentation follows a collection step.
23. The method of claim 22, wherein the second peak or the second indentation comprises a strip peak.
24. The method of any one of claims 1-23, wherein the process chromatogram comprises a measured absorbance intensity, a maximum absorbance intensity, and an integral volume window.
25. The method of claim 24, wherein the atypical profile comprises a measured absorbance intensity that exceeds a maximum absorbance intensity during an integral volume window.
26. The method of claim 24 or 25, wherein the measured absorbance intensity is determined at a wavelength corresponding to ultraviolet (UV) light.

27. The method of claim 26, wherein the measured absorbance intensity is determined at a wavelength of between 260 nanometers (nm) and 280 nm, inclusive of the endpoints.
28. The method of claim 26, wherein the measured absorbance intensity is determined at a wavelength of 260 nm, providing an A_{260} value.
29. The method of claim 26, wherein the measured absorbance intensity is determined at a wavelength of 280 nm, providing an A_{280} value.
30. The method of claim 28 or 29, wherein the atypical profile comprises a measured absorbance intensity that exceeds a maximum absorbance intensity during an integral volume window and wherein the maximum absorbance intensity has an A_{260} value or an A_{280} value of at least 0.05.
31. The method of any one of claims 1-30, wherein a typical profile comprises a measured absorbance intensity that does not exceed a maximum absorbance intensity during an integral volume window and wherein the maximum absorbance intensity has an A_{260} value or an A_{280} value of 0.05 or less.
32. The method of any one of claims 1-31, wherein the integral volume window occurs between 1000 L and 2500 L, inclusive of the endpoints.
33. The method of claim 32, wherein the integral volume window occurs between 1250 L and 2250 L, inclusive of the endpoints.
34. The method of claim 32, wherein the integral volume window occurs between 1600 L and 1800 L, inclusive of the endpoints.
35. The method of any one of claims 1-34, wherein the chromatography column comprises a Q Sepharose anion exchange resin.
36. The method of any one of claims 1-35, wherein the step of (a) generating the reference chromatogram comprises

(1) contacting a starting composition comprising a plurality of pre-determined analytes and a separation composition comprising a matrix, under conditions sufficient for at least one analyte of the starting composition to reversibly bind to the matrix, wherein the chromatography column comprises the separation composition, to produce an analyte-bound column and a first waste composition;

(2) contacting the analyte-bound column of (1) and a washing composition, wherein only the at least one analyte of the starting composition remains bound to the matrix to produce a purified analyte-bound column and a second waste composition;

(3) contacting the purified analyte-bound column of (2) and an elution composition, wherein the at least one analyte of the starting composition is released from the matrix into the elution composition to produce an eluted analyte composition;

(4) collecting the eluted analyte composition;

(5) simultaneously with each of steps (1)-(4), contacting each of the first waste composition, the second waste composition, and the eluted analyte composition with ultraviolet (UV) light,

(6) measuring an absorbance of the UV light of each of the first waste composition, the second waste composition, and the eluted analyte composition to produce an absorbance value for each of the first waste composition, the second waste composition, and the eluted analyte composition; and

(7) generating a chromatogram by plotting the absorbance value of each of the first waste composition, the second waste composition, and the eluted analyte composition as a function of volume of liquid that traverses the chromatography column.

37. The method of any one of claims 1-35, wherein the step of (b) generating the process chromatogram comprises

(1) contacting a starting composition comprising a plurality of test analytes and a separation composition comprising a matrix, under conditions sufficient for at least one analyte of the starting composition to reversibly bind to the matrix, wherein the chromatography column comprises the separation composition, to produce an analyte-bound column and a first waste composition;

(2) contacting the analyte-bound column of (1) and a washing composition, wherein only the at least one analyte of the starting composition remains bound to the matrix to produce a purified analyte-bound column and a second waste composition;

(3) contacting the purified analyte-bound column of (2) and an elution composition, wherein the at least one analyte of the starting composition is released from the matrix into the elution composition to produce an eluted analyte composition;

(4) collecting the eluted analyte composition;

(5) simultaneously with each of steps (1)-(4), contacting each of the first waste composition, the second waste composition, and the eluted analyte composition with ultraviolet (UV) light,

(6) measuring an absorbance of the UV light of each of the first waste composition, the second waste composition, and the eluted analyte composition to produce an absorbance value for each of the first waste composition, the second waste composition, and the eluted analyte composition; and

(7) generating a chromatogram by plotting the absorbance value of each of the first waste composition, the second waste composition, and the eluted analyte composition as a function of volume of liquid that traverses the chromatography column.

38. The method of claim 36 or 37, wherein the contacting step (5) and measuring step (6) are continuous.

39. The method of any one of claims 36-38, wherein the matrix comprises a resin.

40. The method of any one of claims 36-38, wherein the test analyte is a biologic composition.

41. The method of claim 40, wherein the biologic composition is a therapeutic composition for use in a method of treatment of a human subject.

42. The method of any one of claims 2-41, wherein the warning signal is communicated electronically to a processor and wherein the processor is operably linked to the chromatography column.

43. The method of claim 42, wherein the processor receives the warning signal and interrupts the chromatography process or prevents the initiation of a further chromatography process until the potential or actual malfunction of the chromatography column is resolved.