

CLAIMS

1. A method for controlling cell culture medium conditions comprising:
quantifying one or more analytes in the cell culture medium using *in situ* Raman spectroscopy to determine concentrations of the one or more analytes; and
adjusting the concentrations of the one or more analytes in the cell culture medium by the steady-state addition of a dose of nutrients comprising the one or more analytes to match predetermined analyte concentrations that maintain glycation of the protein bioproduct in the cell culture medium to 1.0 to 30 percent,
wherein the one or more analytes comprises glucose, and a shift in the predetermined analyte concentration from a first set point of 3 g/L to a second set point of 5 g/L of glucose decreases glycation of the protein bioproduct in the cell culture medium by more than 50% as compared to standard bolus feed addition .
2. The method of claim 1, wherein the post-translational modification comprises glycation.
3. The method of claim 1, wherein the protein bioproduct comprises an antibody or antigen-binding fragment thereof.
4. The method of claim 1, wherein the protein bioproduct comprises a fusion protein.
5. The method of claim 1, wherein the cell culture medium comprises mammalian cells.
6. The method of claim 5, wherein the mammalian cells comprise Chinese Hamster Ovary cells.
7. The method of claim 1, wherein the glucose concentration is 3.0 g/L.
8. The method of claim 1, wherein the glucose concentration is 5.0 g/L.

9. The method of claim 1, wherein the predetermined analyte concentrations maintain post-translation modifications of proteins in the cell culture medium to 1.0 to 20 percent.
10. The method of claim 1, wherein the predetermined analyte concentrations maintain post-translation modifications of proteins in the cell culture medium to 5.0 to 10 percent.
11. The method of claim 1, wherein the quantifying of one or more analytes is performed continuously.
12. The method of claim 1, wherein the quantifying of one or more analytes is performed intermittently.
13. The method of claim 1, wherein the quantifying of one or more analytes is performed in intervals.
14. The method of claim 1, wherein the quantifying of one or more analytes is performed in 5 minute intervals.
15. The method of claim 1, wherein the quantifying of one or more analytes is performed in 10 minute intervals.
16. The method of claim 1, wherein the quantifying of one or more analytes is performed in 15 minute intervals.
17. The method of claim 1, wherein the quantifying of one or more analytes is performed hourly.
18. The method of claim 1, wherein the quantifying of one or more analytes is performed at least daily.

19. The method of claim 1, wherein the adjusting of one or more analyte concentrations is performed automatically.
20. The method of claim 1, wherein at least two different analytes are quantified.
21. The method of claim 1, wherein at least three different analytes are quantified.
22. The method of claim 1, wherein at least four different analytes are quantified.
23. A method for reducing post-translation modifications of a secreted protein bioproduct comprising:
 - culturing cells secreting the protein bioproduct in a cell culture medium comprising 3.0 g/L to 5.0 g/L glucose;
 - incrementally determining the concentration of glucose in the cell culture medium during culturing of the cells using *in situ* Raman spectroscopy; and
 - adjusting the glucose concentration to maintain the concentration of glucose to 3.0 g/L to 5.0 g/L by automatically delivering multiple doses of glucose per hour to maintain post-translational modifications of the secreted protein bioproduct to 1.0 to 30.0 percent, and
 - wherein a shift in the glucose concentration from a first set point of 3 g/L to a second set point of 5 g/L of glucose decreases glycation of the secreted protein bioproduct in the cell culture medium by more than 50% as compared to standard bolus feed addition.
24. The method of claim 23, wherein the concentration of glucose is 3.0 g/L.
25. The method of claim 23, wherein the concentration of glucose is 5.0 g/L.
26. The method of claim 1 or 23, further comprising quantifying at least one process variable selected from the group consisting of a cell growth rate, a viable cell count, a dead cell count, a concentration of oxygen, a concentration of nitrogen, pH of the cell culture medium, osmolality of the cell culture medium, and combinations thereof in the cell culture medium using *in situ* Raman spectroscopy.