

CLAIMS

What is claimed is:

1. A system for controlling a seed train process, comprising:
 - an expansion chamber for receiving an initial cell stock for a cell expansion process into a viable cell culture;
 - a bioreactor in fluid communication with the expansion chamber for receiving the viable cell culture;
 - a pump for effecting transfer of the viable cell culture from the expansion chamber to the bioreactor through a fluid communication path between the expansion chamber and the bioreactor;
 - a Raman spectrometer having at least one probe for monitoring the cell expansion process within the expansion chamber using Raman spectrometry, the Raman spectrometer being adapted to generate Raman spectral data;
 - a multivariate model that provides predictions of one or more process variables based on the Raman spectral data; and
 - a computer system in signal communication with the Raman spectrometer for receiving the Raman spectral data, and in signal communication with the pump for controlling operation of the pump for effecting the transfer of the viable cell culture from the expansion chamber to the bioreactor,wherein the Raman spectrometer is adapted to generate the Raman spectral data, the computer system processes the Raman spectral data received from the Raman spectrometer to generate the multivariate model that provides the predictions of the one or more process variables, and the computer system is adapted to compare one or more process variable measurements to one or more predefined process set points to determine if the one or more process variable measurements have satisfied one of a plurality of stored predefined trigger values,
wherein the computer system is adapted, upon determining that the one or more process variable measurements in the Raman spectral data has satisfied the one of the

plurality of stored predefined trigger values, to control the pump to execute an auto-transfer of a cell culture volume from the expansion chamber to the bioreactor, and wherein the computer system is adapted, when comparing the predictions of one or more process variables from the multivariate model to the one or more predefined process set points, to use the process variable measurements from a plurality of predefined isolated regions of the Raman spectral data in one or more wavelength regions , wherein the one or more wavelength regions are 800-850 cm^{-1} ; 1260-1470 cm^{-1} ; 1650-1840 cm^{-1} ; and 2825- 3080 cm^{-1} .

2. The system according to claim 1, wherein the computer system generates a partial least squares regression model.
3. The system according to claim 1, wherein the plurality of stored predefined trigger values comprise a first predefined trigger value and a second predefined trigger value, and the computer system stores the first predefined trigger value based on a predetermined viable cell density (VCD), and stores the second predefined trigger value based on a predetermined processing variable other than VCD.
4. The system according to claim 3, wherein the second predefined trigger value is a lactate level value.
5. A method of auto-inoculating a bioreactor using the system according to claim 1, comprising: expanding the initial cell stock in the expansion chamber; generating the Raman spectral data, using the Raman spectrometer, to provide data to the multivariate model that provides the predictions of the one or more process variables of the cell expansion process in the expansion chamber; the computer system comparing the predictions of the one or more process variables from the multivariate model with the one or more predefined process set points at the computer system; and

the computer system controlling the pump to auto-inoculate the bioreactor with the viable cell culture from the expansion chamber when the computer system determines that the predictions of the one or more process variables from the multivariate model satisfies the one of the plurality of stored predefined trigger values.

6. The method according to claim 5, wherein the one of the plurality of stored predefined trigger values is a viable cell density (VCD) value.
7. The method according to claim 6, wherein the one of the plurality of stored predefined trigger values is set to a VCD value that is equal to or within a range of -10% of a predetermined target VCD.
8. The method according to claim 5, wherein the one of the plurality of stored predefined trigger values is a lactate level value.
9. The method according to claim 8, wherein the one of the plurality of stored predefined trigger values is set to a lactate level value that is equal to or within a range of +10% of a predetermined minimum lactate level.
10. The method according to claim 5, wherein the one of the plurality of stored predefined trigger values is a model predicted VCD .
11. The method according to claim 10, wherein the one of the plurality of stored predefined trigger values is set to a model predicted VCD value that is equal to or within a range of -10% of a predetermined maximum cell growth rate.
12. The method according to claim 5, wherein the plurality of stored predefined trigger values comprise a first predefined trigger value and a second predefined trigger value,

the computer system stores the first predefined trigger value based on a predetermined VCD, and stores a second predefined trigger value based on a predetermined processing variable other than VCD, and

the computer system is adapted to control the pump to auto-inoculate the bioreactor with the viable cell culture from the expansion chamber when the computer system determines that the predictions of the one or more process variables from the multivariate model satisfies either the first or the second predefined trigger value.

13. The method according to claim 12, wherein the second predefined trigger value is a lactate level value.
14. The method according to claim 12, wherein the first predefined trigger value is a model predicted VCD value.
15. The method according to claim 5, wherein the computer system processes the Raman spectral data received from the Raman spectrometer to generate the multivariate model that provides the predictions of the one or more process variables, and obtains the one or more process variable measurements from the multivariate model for comparison with the plurality of stored predefined trigger values.
16. The method according to claim 15, wherein the computer system generates a partial least squares regression model.