Claims

1. A computer based method for monitoring and controlling the purification and/or concentration process of a biological product which comprises the use of at least one operation unit, wherein the method comprises the steps of

   a. including at least two independent online sensors in the operation unit,

   b. obtaining a plurality of data values corresponding to the respective output of said online sensors;

   c. importing the data values from said online sensors into a computer database, where they are evaluated by a predictive multivariate statistical analysis model obtained previously from offline data, wherein the offline data were obtained based on samples being removed from the process, and from online data, thereby performing a multivariate statistical analysis for the prediction of concentration, purity and/or potency of the biological product,

   d. diagnosing the actual process data values corresponding to the respective output of the multivariate statistical analysis performed in step c);

   e. monitoring the concentration, purity and/or potency of the biological product in real time.

2. The method according to claim 1, wherein at least one of the online sensors is selected from the group consisting of multi-angle light scattering sensors (MALS), UV-VIS absorption sensors, fluorescence sensors, infrared absorption sensors (IR), attenuated total reflection-fourier transform infrared spectroscopy sensors (ATR FTIR), refractive index (RI) sensors, pH sensors, temperature sensors, conductivity sensors, pressure sensors, small angle x-ray scattering (SAXS) sensors and redox sensors.

3. The method according to claim 1 or 2, wherein at least one of the online sensors is selected from the group consisting of ATR-FTIR, MALS, RI and fluorescence sensors.

4. The method according to any one of claims 1-3, wherein at least one of the online sensors is a non-invasive in situ sensor, wherein the non-invasive in-situ sensor is selected from the group consisting of ATR-FTIR, SAXS, temperature, pH, conductivity and redox sensors.

5. The method according to any one of claims 1-4, wherein the operation unit comprises at least three, at least four, at least five, at least 6, at least 7, at least 8, at least 9, at least 10 or more independent online sensors.

6. The method according to any one of claims 1-5, wherein the operation unit comprises at least one ATR-FTIR sensor, one MALS sensor, one RI sensor and one fluorescence sensor.

7. The method according to any one of claims 1-6, wherein the operation unit additionally comprises at least one temperature sensor, at least one conductivity sensor, at least one pH sensor and at least one pressure sensor.

8. The method according to claim 6 or 7, wherein at least one of the sensors is a non-invasive in-situ sensor selected from the group consisting of ATR-FTIR sensors, temperature sensors, SAXS sensor, conductivity sensors, pH sensors and pressure sensors.

9. The method according to any one of claims 1-8, wherein the operation unit comprises a chromatography unit and/or filtration unit.

10. The method according to claim 9, wherein the chromatography unit is selected from the group consisting of ion exchange chromatography, affinity chromatography, size exclusion chromatography, reversed phase chromatography, hydrophobic interaction chromatography, multi-modal resin chromatography, operated in isocratic, linear, segmented and/ or step gradient elution in bind/elute or flow through mode and the filtration unit is selected from the group consisting of ultrafiltration, microfiltration, nanofiltration, depth filtration, operated in tangential flow filtration, dead end filtration, filtration through absolute pore size membranes.

11. The method according to any one of claims 1-10, further comprising performing process regulation and/or process optimization based on the concentration, purity and/or potency of the biological product obtained in step e).

12. The method according to any one of claims 1-11, further comprising performing parametric or real time release of the biological product based on the concentration, purity and/or potency of the biological product obtained in step e).

13. The method according to claim 11, wherein the process is regulated with regard to any one or a combination of peak collection, correct collection of the biological product after refolding, filtration or precipitation, product quality, and process equipment maintenance.

14. The method according to any one of claims 1-13, wherein said biological product is a biopharmaceutical, a nucleic acid molecule or heterologous protein.

15. The method according to claim 14, wherein said biological product is selected from therapeutic proteins, enzymes and peptides, protein antibiotics, fusion proteins, carbohydrate -protein conjugates, structural proteins, regulatory proteins, vaccines and vaccine like proteins or particles, process enzymes, growth factors, hormones and cytokines, antibodies or a metabolite of said biological product.

16. A method for producing a biological product comprising
purifying a cultured organism or a cultured cell capable of producing the biological product,
wherein purification is monitored and controlled by using at least one operation unit, wherein the operation unit includes at least two independent online sensors and the data values from the online sensors is imported into a computer database where they are evaluated by a predictive multivariate statistical analysis model obtained previously from offline data, wherein the offline data were obtained based on samples being removed from the process, and from online data, thereby performing a multivariate statistical analysis for the prediction of concentration, purity and/or potency of the biological product, wherein the controlling of the purification includes diagnosing the actual process data values corresponding to the respective output of said multivariate statistical analysis and monitoring the concentration, purity and/or potency of the biological product in real time.

17. A device comprising an operation unit for purification and/or concentration of a biological product, wherein the operation unit comprises
a chromatography and/or a filtration unit,
wherein the chromatography or filtration unit comprises at least one online sensor, and
wherein the sensor is configured to be connected to a computer, for the data values
collected by said sensor to be imported into a database for evaluation by a predictive multivariate statistical analysis model obtained previously from offline data, wherein the offline data were obtained based on samples being removed from the process, and from online data, thereby for performance of a multivariate statistical analysis for the prediction of concentration, purity and/or potency of said biological product and for the actual process data values to be then

diagnosed corresponding to the respective output of said multivariate statistical analysis.

18. The device according to claim 17, wherein the at least one online sensor is selected from the group consisting of multi-angle light scattering sensors (MALS), UV-VIS absorption sensors, fluorescence sensors, infrared absorption sensors (IR), attenuated total reflection-fourier transform infrared spectroscopy sensors (ATR-FTIR), light refractive index (RI) sensors, pH sensors, temperature sensors, conductivity sensors, pressure sensors, small angle x-ray scattering (SAXS) sensors and redox sensors.

19. A computer device configured for connection to a device comprising an operation unit for purification and/or concentration of a biological product, wherein the operation unit comprises

a chromatography and/or a filtration unit,

wherein the chromatography or filtration unit comprises at least one online sensor,

wherein the computer device is configured to import data values collected by said sensor into a database for evaluation by a predictive multivariate statistical analysis model obtained previously from offline data, wherein the offline data were obtained based on samples being removed from the process, and from online data, thereby for performance of a multivariate statistical analysis for the prediction of concentration, purity and/or potency of said biological product and for the actual process data values to be then diagnosed corresponding to the respective output of said multivariate statistical analysis.

20. A computer program or computer program product comprising instructions for implementing the method of any one of claims 1 – 16.