WHAT IS CLAIMED IS:

Claim 1. A method for purifying a non-antibody protein (NAP) from a heterogeneous solution, the method comprising:

a) contacting the heterogeneous solution comprising the NAP with an affinity construct comprising a solid support coupled to an affinity ligand that binds the NAP; and

b) isolating the affinity-purified NAP from the heterogeneous solution;

wherein the affinity-purified NAP comprises a critical quality attribute (CQA) that is predictive of the CQA of the NAP produced by a multi-step bioprocess.

Claim 2. A method of predicting a critical quality attribute (CQA) of a non-antibody protein (NAP) produced by a bioprocess unit operation within a multi-step bioprocess, the method comprising

a) purifying the affinity-purified NAP from solution according to the method of claim 1;

a) determining the CQA of the affinity-purified NAP;

b) transforming the CQA of the affinity-purified NAP using a predetermined predictive model,

wherein the predictive model is specific for one or more of the bioprocess unit operations within the multi-step bioprocess; and

c) predicting the CQA of the NAP produced by the bioprocess unit operation within a multi-step bioprocess based on the transformed CQA of the affinity-purified NAP.

Claim 3. A method of monitoring or controlling a bioprocess unit operation within a multi-step bioprocess for producing a NAP, the method comprising:

a) purifying the affinity-purified NAP from solution according to the method of claim 1;

b) determining a critical quality attribute (CQA) of the affinity-purified NAP;

c) comparing the CQA of the affinity-purified NAP to the CQA of the NAP produced by the bioprocess unit operation within a multi-step bioprocess;
d) calculating a difference between the CQA of the affinity-purified NAP and the NAP produced by the bioprocess unit operation within a multi-step bioprocess; and
e) monitoring or controlling the bioprocess unit operation based on the calculated difference in CQAs.

Claim 4. A method of monitoring or controlling a bioprocess unit operation within a multi-step bioprocess for producing a NAP, the method comprising:
a) purifying the affinity-purified NAP from solution according to the method of claim 1;
b) determining a critical quality attribute (CQA) of the affinity-purified NAP;
c) transforming the CQA of the affinity-purified NAP using a predetermined predictive model,
wherein the predictive model is specific for one or more of the bioprocess unit operations within the multi-step bioprocess; and
d) monitoring or controlling the bioprocess unit operation based on the predicted CQAs.

Claim 5. A method of developing a bioprocess for a NAP, the method comprising:
a) processing the NAP using a bioprocess unit operation within the multi-step bioprocess;
b) purifying the affinity-purified NAP from solution according to the method of claim 1;
c) determining a critical quality attribute (CQA) of the NAP produced using the bioprocess unit operation;
d) determining the CQA of the affinity-purified NAP;
e) comparing the CQA of the affinity-purified NAP to the CQA of the NAP produced using the bioprocess unit operation;

f) calculating a difference between the CQA of the affinity-purified NAP and the CQA of the NAP produced using the bioprocess unit operation, and

g) developing the bioprocess by modifying the bioprocess unit operation based on the calculated difference in CQAs.

Claim 6. A method of developing a bioprocess for a NAP, the method comprising:

a) processing the NAP using a bioprocess unit operation within the bioprocess;

b) purifying the affinity-purified NAP from solution according to the method of claim 1;

c) determining the CQA of the affinity-purified NAP;

d) transforming the CQA of the affinity-purified NAP using a predetermined predictive model,

wherein the predictive model is specific for one or more of the bioprocess unit operations within the multi-step bioprocess; and

e) developing the multi-step bioprocess by modifying the bioprocess unit operation based on the predicted CQAs.

Claim 7. The method of claim 2, 4, or 6, wherein the transformed CQA of the affinity-purified NAP is substantially equivalent to the NAP produced by a bioprocess unit operation within the multi-step bioprocess.

Claim 8. The method of any of the preceding claims, wherein the CQA of the NAP is determined at the following stages within the multi-step bioprocess:

a) immediately upstream of a particular bioprocess unit operation;

b) immediately downstream of the particular bioprocess unit operation;

c) both upstream and downstream of a particular bioprocess unit operation, and/or

d) within a particular bioprocess unit operation at one or more timepoints.

Claim 9. The method of any of the preceding claims, wherein the CQA of the NAP is determined at one or more timepoints within the multi-step bioprocess.

Claim 10. The method of any of the preceding claims, wherein the bioprocess is selected from the group consisting of continuous, semi-continuous, and batch.

Claim 11. The method of any of the preceding claims, wherein the NAP is a biotherapeutic drug substance or a commercial biologic.

Claim 12. The method of any of the preceding claims, wherein the multi-step bioprocess for the NAP is a commercial and/or manufacturing process.

Claim 13. The method of any of the preceding claims, wherein the CQA is product purity, potency, charged isoform profile, post-translational modifications, oxidation, reductions, deamidation, adduct formation, clipped forms, enzymatic cleavage, specific activity, peptide map, dimer content, product aggregation, site specific glycosylation, total glycans, and/or glycosylation profile.

Claim 14. The method of claim 10, wherein the CQA is measured using a high-throughput and/or rapid analytical technique.

Claim 15. The method of claim 11, wherein the analytical technique is high-performance liquid chromatography (HPLC), differential refractometry, fluorescence, ultra-performance liquid chromatography (UPLC), multi-angle laser light scattering analysis (MALLS), mass spectroscopy, tandem mass spectroscopy, isoelectric focusing, and/or differential scanning calorimetry.

Claim 16. The method of any of the preceding claims, wherein one or more purification steps are performed by a robot.

Claim 17. The method of any of the preceding claims, wherein the ligand of the affinity ligand-coupled based solid support is an antibody.

Claim 18. The method of any of the preceding claims, wherein the bioprocess unit operation is selected from the group consisting of a bioreactor process, seed train, capture chromatography, intermediate chromatography, filtration, centrifugation, precipitation, flocculation, UV irradiation, and viral inactivation.

Claim 19. The method of any of the preceding claims, wherein the affinity construct is integrated with the bioprocess in a manner selected from the group consisting of at-line mode, offline mode, and in-line mode.

Claim 20. The method of any of the preceding claims, wherein the affinity construct comprises a parameter that is optimized to maximize the quality and/or purity of the affinity-purified NAP.

WHAT IS CLAIMED IS:

Claim 1. A method for purifying a non-antibody protein (NAP) from a heterogeneous solution, the method comprising:

a) contacting a heterogeneous solution comprising a NAP with an affinity construct comprising a solid support coupled to an affinity ligand that binds the NAP; and

b) isolating the affinity-purified NAP from the heterogeneous solution; and

c) determining a critical quality attribute (CQA) of the NAP,

wherein the CQA comprises at least one of charged isoform profile, post-translational modifications, oxidation, reduction, deamidation, adduct formation, clipped forms, enzymatic cleavage, specific activity, peptide map, dimer content, product aggregation, site specific glycosylation, total glycans, and/or glycosylation profile, and

wherein the determined CQA is predictive of a CQA of the NAP produced by a multi-step bioprocess.

Claim 2. A method of predicting a critical quality attribute (CQA) of a non-antibody protein (NAP) produced by a bioprocess unit operation within a multi-step bioprocess, the method comprising:

a) purifying an affinity-purified NAP from solution according to the method of claim 1; and

b) transforming the determined CQA of the affinity-purified NAP using a predetermined predictive model,

wherein the predictive model is specific for one or more of the bioprocess unit operations within the multi-step bioprocess; and

c) predicting a CQA of the NAP produced by the bioprocess unit operation within a multi-step bioprocess based on the transformed CQA of the affinity-purified NAP.

Claim 3. A method of monitoring or controlling a bioprocess unit operation within a multi-step bioprocess for producing a NAP, the method comprising:

a) purifying an affinity-purified NAP from solution according to the method of claim 1;

b) comparing the determined CQA of the affinity-purified NAP to a CQA of the NAP produced by the bioprocess unit operation within a multi-step bioprocess;

c) calculating a difference between the determined CQA of the affinity-purified NAP and the CQA of the NAP produced by the bioprocess unit operation within a multi-step bioprocess; and

d) monitoring or controlling the bioprocess unit operation based on the calculated difference in CQAs.

Claim 4. A method of monitoring or controlling a bioprocess unit operation within a multi-step bioprocess for producing a NAP, the method comprising:

a) purifying an affinity-purified NAP from solution according to the method of claim 1;

b) transforming the determined CQA of the affinity-purified NAP using a predetermined predictive model to render a predicted CQA,

wherein the predictive model is specific for one or more of the bioprocess unit operations within the multi-step bioprocess; and

c) monitoring or controlling the bioprocess unit operation based on the predicted CQAs.

Claim 5. A method of developing a bioprocess for a NAP, the method comprising:

a) processing a NAP using a bioprocess unit operation within the multi-step bioprocess;

b) purifying an affinity-purified NAP from solution according to the method of claim 1;

c) determining a critical quality attribute (CQA) of the NAP produced using the bioprocess unit operation;

d) comparing the determined CQA of the affinity-purified NAP to the CQA of the NAP produced using the bioprocess unit operation;

e) calculating a difference between the determined CQA of the affinity-purified NAP and the CQA of the NAP produced using the bioprocess unit operation, and

f) developing the bioprocess by modifying the bioprocess unit operation based on the calculated difference in CQAs.

Claim 6. A method of developing a bioprocess for a NAP, the method comprising:

a) processing a NAP using a bioprocess unit operation within the bioprocess;

b) purifying an affinity-purified NAP from solution according to the method of claim 1;

c) transforming the determined CQA of the affinity-purified NAP using a predetermined predictive model,

wherein the predictive model is specific for one or more of the bioprocess unit operations within the multi-step bioprocess; and

d) developing the multi-step bioprocess by modifying the bioprocess unit operation based on the predicted CQAs.

Claim 7. The method of any of the preceding claims, wherein the CQA of the NAP is

determined at the following stages within the multi-step bioprocess:

a) immediately upstream of a particular bioprocess unit operation;

b) immediately downstream of the particular bioprocess unit operation;

c) both upstream and downstream of a particular bioprocess unit operation, and/or

d) within a particular bioprocess unit operation at one or more timepoints.

Claim 8. The method of any of the preceding claims, wherein the bioprocess is selected from the group consisting of continuous, semi-continuous, and batch.

Claim 9. The method of any of the preceding claims, wherein the NAP is a biotherapeutic drug substance or a commercial biologic.

Claim 10. The method of any of the preceding claims, wherein the multi-step bioprocess for the NAP is a commercial and/or manufacturing process.

Claim 11. The method of claim 1, wherein the CQA is measured using a high-throughput and/or rapid analytical technique.

Claim 12. The method of claim 11, wherein the analytical technique is high-performance liquid chromatography (HPLC), differential refractometry, fluorescence, ultra-performance liquid chromatography (UPLC), multi-angle laser light scattering analysis (MALLS), mass spectroscopy, tandem mass spectroscopy, isoelectric focusing, and/or differential scanning calorimetry.

Claim 13. The method of any of the preceding claims, wherein one or more purification steps are performed by a robot.

Claim 14. The method of any of the preceding claims, wherein the ligand of the affinity ligand- coupled based solid support is an antibody.

Claim 15. The method of any of the preceding claims, wherein the bioprocess unit operation is selected from the group consisting of a bioreactor process, seed train, capture chromatography, intermediate chromatography, filtration, centrifugation, precipitation, flocculation, UV irradiation, and viral inactivation.

Claim 16. The method of any of the preceding claims, wherein the affinity construct is integrated with the bioprocess in a manner selected from the group consisting of at-line

mode, offline mode, and in-line mode, and wherein the affinity construct comprises a parameter that is optimized to maximize the quality and/or purity of the affinity-purified NAP.