CLAIMS

What is claimed is:

1. A method for preparing a target polypeptide from a mixture including the target polypeptide, the method comprising:

passing the mixture including the target polypeptide to a first column of a plurality of chromatographic columns in a hydrophobic interaction chromatography (HIC) apparatus, wherein each of the plurality of columns comprises an outlet connectable to another column of the plurality of columns;

passing an effluent including the target polypeptide from the first column to a second column of the plurality of columns;

passing one or more mobile phases to a third column of the plurality of columns; and

passing the target polypeptide through the outlets of each of the plurality of columns, wherein a sum of residence times for the mixture including the target polypeptide in the first column and second column is approximately the same as the sum of the residence times of the one or more mobile phases in the third column.

2. The method of claim 1, further comprising passing one or more mobile phases to each of the plurality of columns.

3. The method of claim 1, wherein passing one or more mobile phases to a column includes:

passing a wash buffer to the column; and

after passing a wash buffer to the column, regenerating the column, wherein regenerating the column comprises passing water, an alkaline solution, an alcohol solution, or an equilibration buffer to the column.

4. The method of claim 3, wherein the step of passing a target polypeptide through the outlet of a column occurs after a wash buffer has been passed to the column.

5. The method of claim 1, wherein one or more of an ultraviolet absorption, electrical conductivity, or pH of a resident solution are measured at the outlet of either the first column or second column.

6. The method of claim 3, wherein the HIC apparatus includes four columns and the sum of the residence times for the mixture including the target polypeptide in the first column and the second column is approximately the same as the sum of the regeneration times of the third column and the fourth columns.

7. The method of claim 1, wherein the target polypeptide is a monoclonal antibody.

8. The method of claim 1, wherein the one or more mobile phases comprises an equilibration buffer and a wash buffer.

9. The method of claim 1, wherein one or more of an ultraviolet absorption, electrical conductivity, or pH of a resident solution are measured at the outlets of each of the plurality of columns.

10. The method of claim 1, wherein the target polypeptide is prepared at a productivity greater than or equal to 50 g/L·hr.

11. The method of claim 10, wherein a percentage of high molecular weight species in the mixture is reduced by a HMW CF of at least approximately 1.3.