number of diseases and conditions, the large-scale production of these proteins remains a challenge.

[0006] Regarding recombinant Factor VIII, particularly, this protein is expensive to produce due to the relatively low yields obtained in processes known in the art. The yield per cell tends to be low compared to the yield that might be obtained for other recombinant proteins. Generally, secreted FVIII is separated from source CHO cells, debris and DNA using depth filtration that employs charged CUNO filters. The charged depth filter binds to the FVIII product thereby reducing the final recovery of the protein.

[0007] Based on the foregoing, new techniques that enhance production and recovery of recombinantly-produced therapeutic proteins are needed.

SUMMARY OF THE DISCLOSURE

[0008] The present disclosure provides systems and methods that increase protein yield from recombinant manufacturing processes. In particular embodiments, the systems and methods treat used depth filters with bound proteins of interest as a stationary phase exchange resin to recapture bound protein of interest using a high salt elution buffer. By increasing protein yield from recombinant manufacturing process, these systems and methods improve the efficiency and cost of manufacturing therapeutic proteins.

[0008a] In an aspect, there is provided a method of increasing the amount of a protein of interest available for recovery from a sample containing other components and following a first purification step of the sample comprising: passing the sample through a depth filter with a positive charge; exposing the depth filter to a salt elution buffer wherein exposure to the salt elution buffer releases the protein of interest from the filter for subsequent recovery.

[0008b] In another aspect, there is provided a method of manufacturing and recovering a protein of interest comprising: recombinantly producing a protein of interest using a host cell within a medium; filtering the medium using depth filtration; exposing a depth filter with a positive charge to a salt elution buffer to release protein of interest from the depth filter; recovering released protein of interest from the salt elution buffer; recovering further protein of interest from the sample passed through the depth filter.

[0008c] In yet another aspect, there is provided a method of manufacturing a pharmaceutical composition comprising: recombinantly producing a therapeutic protein of interest using a host cell within a medium; filtering the medium using a depth filter with a positive charge; exposing the

depth filter to a salt elution buffer with a conductivity of at least 20 mS/cm to release protein of interest from the depth filter; recovering released protein of interest from the salt elution buffer; recovering further protein of interest form the sample passed through the depth filter; combining recovered protein of interest with pharmaceutically acceptable carriers thereby forming the pharmaceutical composition.

[0009] Particularly, one embodiment includes a method of increasing the amount of a protein of interest available for recovery from a sample containing other components and following a first purification step of the sample comprising: exposing a filter through which the sample has been passed to an elution buffer wherein exposure to the elution buffer releases the protein of interest from the filter for subsequent recovery.

[0010] Another embodiment further includes recovering the released protein of interest from the elution buffer.

[0011] In another embodiment, the elution buffer is a salt elution buffer.

[0012] In another embodiment, the elution buffer has a conductivity of at least 20 mS/cm.

[0013] In another embodiment, the filter is positively-charged.

[0014] In another embodiment, the filter is a depth filter.