Optimization of Protein X Fermentation

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In 1930s Arne Tiselius developed electrophoresis into an important tool for separating and characterizing proteins. Then in 1940, Björn Ingelman, at the age of 22, joined Tiselius as a postgraduate researcher. He found out that the non-immunogenic dextran could be a useful plasma substitute, which became very useful during World War II. This led to the first cooperation between the Department of biochemistry and Pharmacia. In the 1950s, Jerker Porath and Per Flodin joined Tiselius's department. They tried to use column chromatography with starch gels to separate proteins, but soon observed that a dextran gel column was superior. This observation resulted in a famous paper published in 1959 "Gel filtration: a method for desalting and group separation". That was the first published example of gel filtration, or SEC, Size Exclusion Chromatography. Nowadays, products based on those old-fashioned separation techniques are still the most profitable parts in today's GE Healthcare Life Sciences.

The protein X that I worked with is for one of those "old-fashioned" media products. The protein has some truncation problems when produced on a large-scale in the factory. So projects were launched to optimize bacterial growth medium for the purpose of increasing the yield and purity of the protein. Here purity refers to the amount of full-length protein excluding truncated fragments and polymers.

The standard concentration of yeast extract in growth media is 3 g/L, hereafter referred to as 1x yeast extract, or 1xYE. Based on previous research made within GE Healthcare R&D, employing a 0.5 liter fermentation scale, it was suggested that increasing the level of yeast extract in the media to 10xYE could result in a yield of 2 mg/mL Protein X with 98% purity, compared with a yield of 1 mg/mL with purity lower than 90% using standard growth media. This project tested this preliminary finding using a 7 liter fermentor with optimization of the yeast extract amount. The hope was that the results of this project would form a bridge to later larger scale fermentations in the production facility. Thus, the project examined Protein X expression levels as a function of different yeast extract levels. It also examined the influence of glucose concentration and prolonged cultivation times on Protein X expression level. The overall aim was to determine cultivation parameters for the 7 liter fermentor that gave the high yield and purity as previously obtained using the 0.5 liter fermentation scale.

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