Application Note

PENDOTECH
Leading Process Analytics

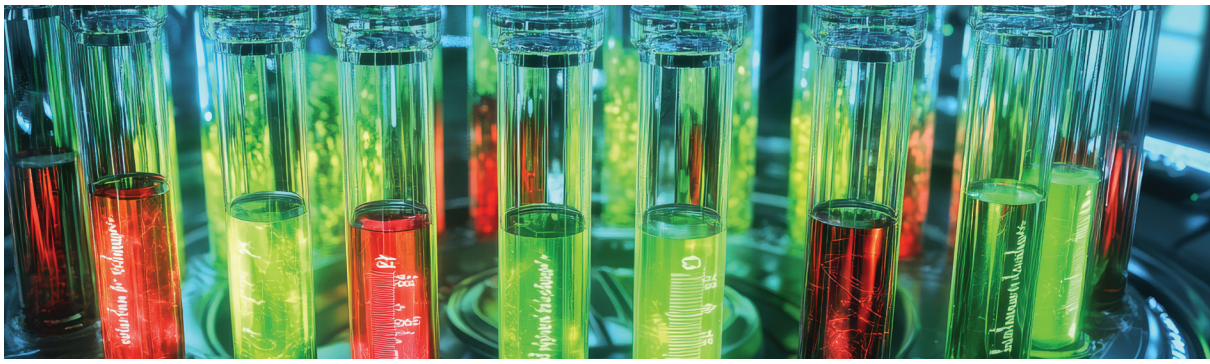
Elevating Bioprocess Efficiency

By Controlled Multicolumn Chromatography

Downstream processes, especially the capture step, are time- and resource-intensive in bioprocessing, particularly for monoclonal antibodies. Traditional single-column chromatography is costly and time-consuming. Multicolumn Chromatography is a more efficient alternative, providing cost savings while maintaining product quality. Effective MCC management allows for real-time adjustments, enhancing operational efficiency by monitoring key parameters such as conductivity, pH, and UV absorbance.

Background

Multicolumn Chromatography (MCC) is an advanced technique designed for the efficient purification of monoclonal antibodies in biopharmaceutical manufacturing. Unlike traditional single-column methods, MCC uses multiple smaller columns in a cyclical fashion, which enhances productivity and throughput. This approach optimizes resin utilization, allowing for quicker binding of monoclonal antibodies while reducing resin requirements. Operating continuously, MCC is ideal for large-scale production, ensuring consistent output. Its adoption in the biopharmaceutical industry is rising due to increased productivity and lower operational costs, all while maintaining high quality standards.



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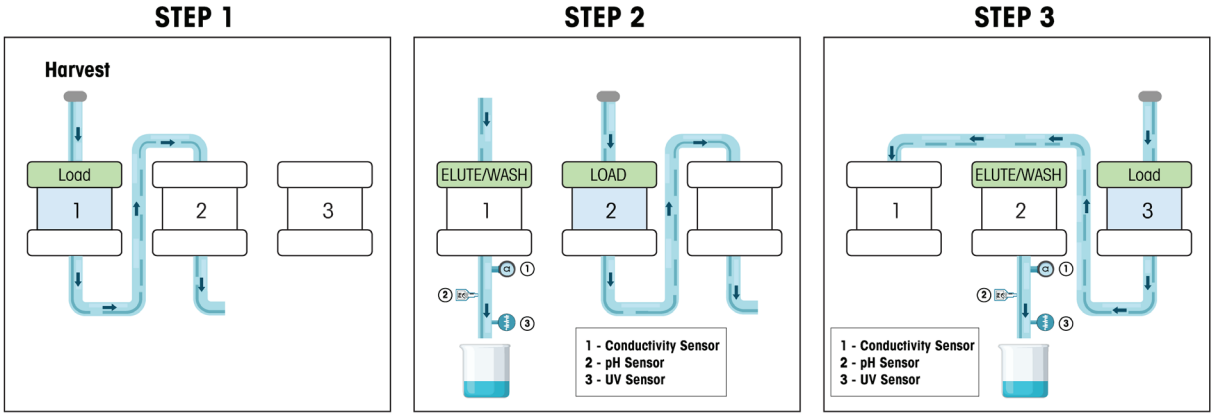

Fig. 1 Schematic diagram of multiple column chromatography

Process

In traditional batch chromatography, the product is loaded into one column, washed, and then eluted for further processing. The resin in this column is typically not used to its full capacity to prevent product loss during breakthrough. To avert unacceptable product loss the dynamic binding capacity (DBC) of a capture resin is determined during development as a mere 5% or 10% of product breakthrough. In manufacturing, the column is then loaded to 80–85% of this DBC, which then corresponds approximately to only 60–70% resin utilization. All operations (loading, washing, elution, etc.) are performed on that single column, with the product flow halting during the non-loading steps like regeneration, washing and elution.

MCC is an advanced purification technique that employs a series of smaller columns arranged in a sequential manner to achieve continuous processing of biological samples containing target molecules. The process begins with preparing the sample, which is loaded onto the first column, where the target molecule selectively binds to the resin while unbound components flow through to the second column. As the first column approaches saturation, the feed is redirected to the second column, allowing the breakthrough from the first to continue to the second column. This innovative setup ensures that while the second column is loading with additional feed, the first column is simultaneously undergoing washing and elution processes to remove impurities and release the captured target molecule. After elution, the first column is regenerated, restoring it to its original state for the next cycle. This cyclical and overlapping operation allows MCC to maintain continuous purification, significantly enhancing productivity and efficiency. By leveraging multiple columns, MCC optimizes the purification process, making it a powerful and effective method for bioprocessing applications.

In MCC, monitoring critical process parameters like conductivity, pH and UV absorption, help ensure effective separation and process control. Conductivity sensors in MCC measure the ionic strength of the mobile phase, which is vital for optimal separation conditions. Continuous monitoring allows the system to adjust buffer flows, ensuring consistent separation performance and enhancing overall process control. UV detection identifies when target molecules break through the first column, triggering a switch to maximize resin utilization, and helps precise collection of target molecule fractions during elution while minimizing impurities. Continuous UV monitoring ensures consistency, quality, and effectiveness, quickly identifying any process deviations. Managing pH in MCC is vital for optimizing separation and achieving reproducibility. The mobile phase's pH has a considerable impact on the retention time and selectivity of ionizable compounds. By adjusting the buffer composition and pH, the elution of target molecules is enhanced, ensuring optimal conditions throughout the process.

METTLER TOLEDO Pendotech Solutions

Conductivity Sensor

METTLER TOLEDO Pendotech Single-Use Conductivity Sensors™ and Conductivity Monitor provide an ideal solution for precise measurement of conductivity and temperature without the hassle of sensor calibration. These sensors feature automatic temperature compensation, ensuring conductivity readings are normalized to 25°C. The conductivity monitor provides 4-20mA outputs for both conductivity and temperature, allowing for seamless integration with higher-level control systems such as a PLC or DCS. Additionally, an RS-232 output facilitates data collection on a PC. Designed to measure conductivity within a range of 0.1 to 100mS/cm and temperatures from 2°C to 50°C, these sensors enhance the efficiency and productivity of your bioprocess operations.

UV Absorbance Sensor

METTLER TOLEDO Pendotech photometer is a versatile instrument for both laboratory and process environments, available in benchtop and panel mount versions. It features pre-configured options with seven wavelength combinations, facilitating seamless integration with data acquisition systems. With two 4-20mA output signals and an onboard display, it ensures straightforward monitoring. The device is compatible with multiple data acquisition setups and supports digital communication protocols. Its non-invasive, real-time UV absorbance measurement accurately detects target molecules, concentration changes, and absorbance peaks. Moreover, it offers a cost-effective option for single-use applications, featuring gamma-irradiatable flow cells designed for one-time use. The Single-Use UV Flow Cells, paired with a compact PM2 photometer and fiber optic cable, enable the measurement of UV absorbance in chromatography processes without the need for sampling product. The photometer supports various flow cell sizes and path lengths to meet diverse application requirements and process scales.

pH Sensor

METTLER TOLEDO Pendotech Single-Use In-line pH Sensors utilize advanced InSUS 307 pH probe technology, ensuring precise and reliable pH measurements in downstream bioprocessing applications. These sensors perform exceptionally well in the pH range of 3 to 10, achieving an accuracy of ± 0.10 pH when operating within ± 1.50 pH units of the single-point process calibration. With a quick response time of under 20 seconds between pH 4 and 7, they can effectively capture rapid pH changes due to process variations. The InSUS 307 pH sensors are also rated for temperatures from 5 to 60°C and pressures of 4 bar at 25°C, 2 bar at 40°C, and 1 bar at 60°C, making them a highly adaptable and efficient choice for bioprocessing operations.

Conclusion

Multicolumn Chromatography stands out as an excellent alternative to single-column chromatography, providing substantial cost savings while maintaining high product quality. By facilitating continuous purification and optimal resin usage, MCC boosts productivity and operational efficiency. To sustain process control and product quality, it is crucial to closely monitor key parameters such as conductivity, pH, and UV absorbance. These parameters enable real-time adjustments, making the purification process both effective and adaptable to varying conditions. METTLER TOLEDO Pendotech offers advanced solutions for the real-time monitoring of these essential parameters, equipping bioprocessing operations to meet their objectives with accuracy and dependability. As the bioprocessing sector continues to advance, embracing technologies like MCC, along with robust monitoring systems, will be essential for enhancing efficiency, lowering costs, and ensuring the successful purification of biological targets.

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