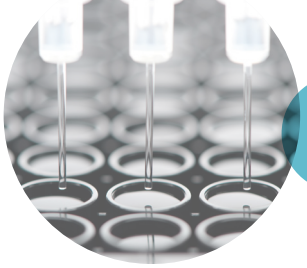
FORTÉBIO



Advancing Upstream Bioprocessing with the Octet Platform

Advances in the optimization of upstream bioprocessing in recent years - primarily, improved cell culturing conditions - have led to higher production of target biologics. This leads to amplified production of process related attributes[1] as well. The selection and optimization of bioprocessing therefore requires the integration of analytical technologies that facilitate both titer determination as well as critical quality attributes assessment of these biologics early on in the discovery and optimization stages. One platform that is increasingly a workhorse for multiple analytical applications in bioprocessing is the Octet® platform. The Octet instrument comes with biosensors and assay kits that offer users both intermediate and high throughput capabilities for titer, host cell protein analysis, residual protein detection and sialic acid content detection. The fluidics-free system allows users to screen for these properties without the need for purification, resulting in significant time and cost savings; it is estimated that with the Octet platform, as much as 12X FTE costs can be saved when compared to ELISA in IgG titer. In addition, the Octet RED384 and HTX systems are automation-ready, allowing for extended walk-away assay times.

- Automation ready platforms suitable for multiple applications (Octet RED384 and Octet HTX systems)
- Real-time label-free data acquisition enabling rapid assay optimization
- Sample plate format allowing for the use of crude and non-purified samples
- Combine titer and sialic acid analysis from the same sample. Analyze 1000 samples in one day on the Octet HTX system
- Complete hands-off, walk-away HCP analysis on the Octet HTX system
- High precision assays with 5–10% CVs
- Detection sensitivity as low as 0.5 ng/mL for HCP assays and 0.1 ng/ml for residual Protein A
- No heating or centrifugation steps required for residual Protein A analysis

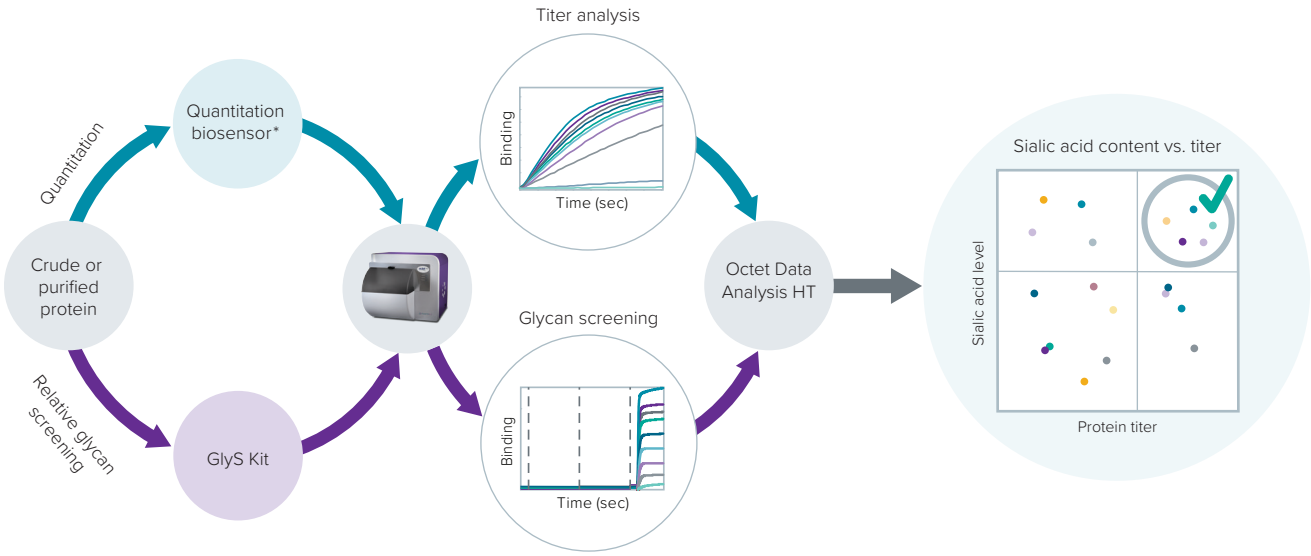


Figure 1: Titer and sialic acid workflow on the Octet system. Sialic acid versus normalized titer can be used to select the best conditions for bioprocessing.

Titer and glycan screening

The Octet platform is routinely used for titer determination, especially with monoclonal antibodies in both upstream and downstream bioprocessing. The Octet HTX instrument is capable of analyzing as many as 96-samples in just two minutes in a simple Dip and Read format, where biosensors pre-coated with Protein A or G or other antibody binding proteins are dipped into IgG samples for specific binding response measurement. In addition to titer, the Octet platform is also compatible for use in glycan screening.[2] A common approach for the screening of glycans on the Octet system involves the immobilization of sugar-specific lectins onto the biosensor surface followed by dipping the coated biosensor into the sample under certain buffer conditions. ForteBio has recently released a kit for the screening of sialic acid content in biologics which can be used in combination with titer determination to determine sialic content per mg of IgG Figure 1.

Residual contaminant detection

Contaminants are any molecules that may elute with the target drug product during purification. They can adversely affect the efficacy and immunoreactivity of the drug product and should therefore be cleared from the product through further purifications. The easy to use BLI technology has comparable throughput to manual ELISA but with better precision in contaminant detection. In addition, the platform shows data in real time allowing for a rapid optimization of assays.

TRANSFER YOUR ELISA HOST CELL PROTEIN (HCP) DETECTION ASSAY TO THE OCTET PLATFORM

The clearance of host cell proteins (HCPs) that co-express with biologics is important since high concentrations can adversely affect the safety and efficacy of the biologics. ForteBio's HCP kit comes with all the reagents required to convert a manual HCP ELISA assay into a better controlled automated assay with lower variability (Table 1) and where data can be observed in real time. Unlike ELISA, real-time analysis techniques allow assay developers to monitor every step of the assay enabling the fast detection of areas that need further optimization. The kit comes with biosensors already coated with a Cygnus capture antibody, a purified antigen for the development of the reference curve and the detection reagents. The Octet HTX system can be used to screen > 1000 samples in one day making it highly suitable for screening for these process impurities in a high throughput manner.

Assay performance	Cygnus 3G ELISA Kit	ForteBio-Cygnus Anti-CHO HCP Detection Kit
Time-to-result	210 min	62 min on Octet HTX system
		75 min on Octet RED384 system with Sidekick Station
		90 min on Octet RED96 system with Sidekick Station
Dynamic range	1–100 ng/mL	0.5–200 ng/mL
Precision	15–25%	5–10%

Table 1: Comparison of overall assay performance for HCP analysis on Octet systems and ELISA for 96 samples.

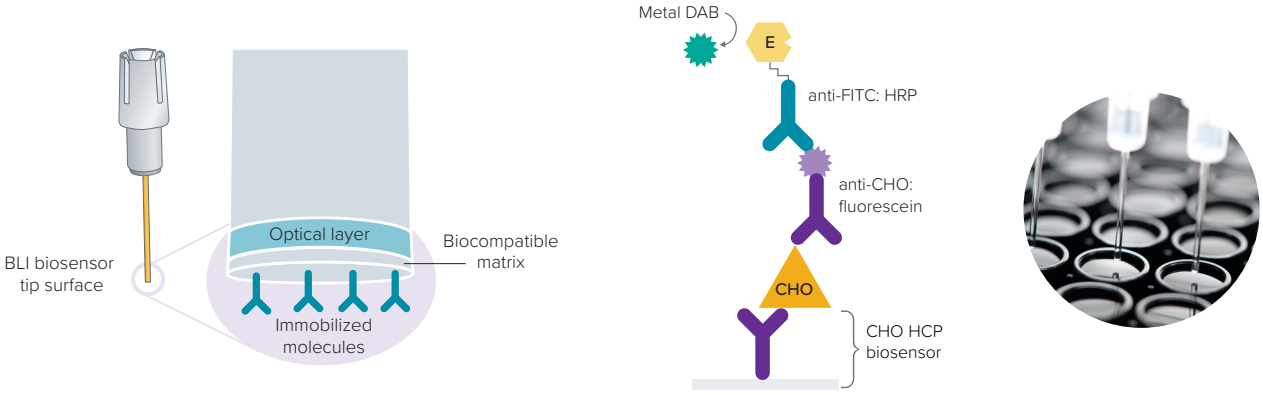


Figure 2: Host cell protein (HCP) detection lay-out on the Octet platform. The biosensors come pre-immobilized with anti-CHO antibody.

Residual Protein A (RPA) detection

A common challenge in bioprocessing is the copurification of antibody-based biologics with the Protein A leaching off purification columns. Similar to HCPs, these proteins can affect the efficacy of the drug molecule and need to be detected and cleared. ForteBio's residual Protein A detection kit has a highly simplified workflow compared to traditional methods. The commonly used heat denaturation and sample centrifugation steps which can result into high process variability have been removed resulting into a significantly reduced assay time. This combined with the throughput and the automation capabilities of the Octet instruments especially the HTX and the RED384, results into a rapid assay; 96-samples can be analyzed in under 2 hours on the Octet HTX system. The ForteBio kit can be adopted for the detection of leached Protein A from a resin that utilizes either recombinant Protein A or MabSelect Sure.

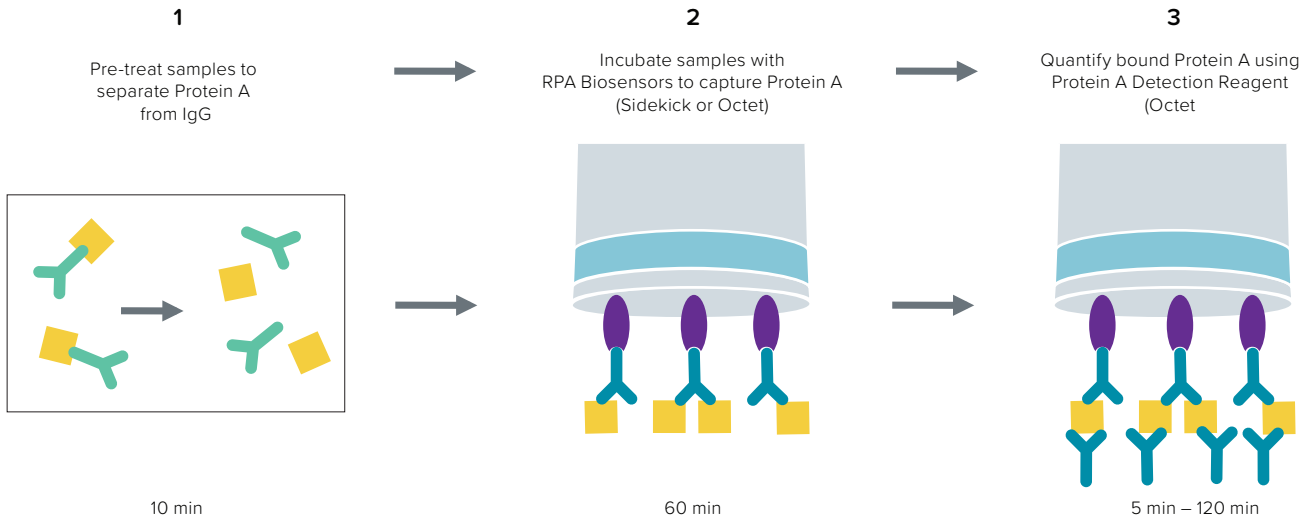


Figure 3: Residual Protein A workflow on the Octet platform, no heating step is required.

References

1 Trends in Upstream and Downstream Process Development for Antibody Manufacturing, *Bioengineering* 2014, 1(4), 188-212; Petra Gronemeyer, Reinhard Ditz and Jochen Strube.

2 High-throughput sialylation measurement using lectins on an Octet platform for clone screening; *Analytical Methods*. 2016, Issue 39; Kanvasri N. Jonnalagadda, Lam Raga A. Markely, Bing Guan, Christina Alves and Shashi Prajapati.

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