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# Cell Line Development: Accelerating Antibody Discovery by Monitoring Titer and Glycosylation With the Octet<sup>®</sup> Platform

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## Abstract

Cell line development involves multiple processes. Large numbers of clones are screened and selected on the basis of productivity and stability. Octet<sup>®</sup> systems have been an established platform for rapid titer of antibody clones to enable quick selection of high-producing clones. Combined with the Octet<sup>®</sup> Sialic Acid (GlyS) and Octet<sup>®</sup> Mannose (GlyM) kit assays, cell line development scientists can also screen for the relative terminal sialic acid content in crude or purified samples to better select optimal clones that are both high producers and have desirable sialic acid content.

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## Key Features

- Significantly reduce time to develop antibodies by combining titer screening and glycan characterization
- Save FTE costs and perform more projects using the high-throughput Octet® RH16 or RH96 systems respectively.

Cell line development typically includes the screening of thousands of clones in an effort to find the few that are stable, grow as expected, and produce high yields of the bioproduct. The time it takes from engineering an optimal cell line to the production of the target biologic can be prohibitive and may differ from molecule to molecule. While expression level analysis like titer screening is carried out early, other critical quality attributes such as glycan characterization are often assessed only later in the development process due to a lack of appropriate and high-throughput analytical techniques that can be used to perform quick screens (Figure 1).



Figure 1: Automated Octet® platform for enhanced productivity.

Commonly used methods for antibody quantitation require either specialized instrumentation and skilled personnel (HPLC) or are time-consuming (ELISA). In contrast, the Octet® platform (Figure 2) uses Bio-Layer Interferometry (BLI) to detect real-time binding of molecules as a means of

quantification or for kinetic analysis. This technology essentially eliminates any sample preparation beyond an optional dilution step.

BLI measures only what's captured on biosensor chemistries, making it specific when measuring in complex matrices such as crude supernatant. High-throughput Octet® models can process up to 96 samples simultaneously. Enhance your confidence in clone selection during clone screening and process optimization of biotherapeutics by measuring protein titer and sialylation in crude cell culture supernatant using rapid assays on the Octet® RH96 system.

## Titer Measurements

Octet® instruments offer cell line development scientists a platform for the rapid titer of antibody clones that enables a quick selection of optimal clones, allowing for reduced time to drug development. With ready-to-use biosensor surfaces, such as Protein A and G, combined with the automation-ready Octet® RH16 instrument or high-throughput Octet® RH96 instrument, organizations can effect significant FTE cost savings over comparative technologies such as ELISA and HPLC. Moreover, the time to results on the Octet® platform should allow for many more projects run annually than when using either HPLC or ELISA for titer (Table 1).

	ELISA	HPLC	Octet® R8 System <sup>1</sup>
FTE labor costs	15X	3X	X
Time to results (hrs)	625	1040	52
# projects/year	3	2	40

Table 1: Comparison of Octet® R8 system, ELISA and HPLC for mAb screening. The comparison table refers only to the titer segment of the cell line development work-flow. A project in this case is defined as the titer determination of a total of 10,000 mAb clones. The data in the table assumes an analysis labor time of 0.2 hours, 0.5 hours and 3 hours for 96 samples on the Octet®, HPLC and ELISA platforms respectively.<sup>1</sup>

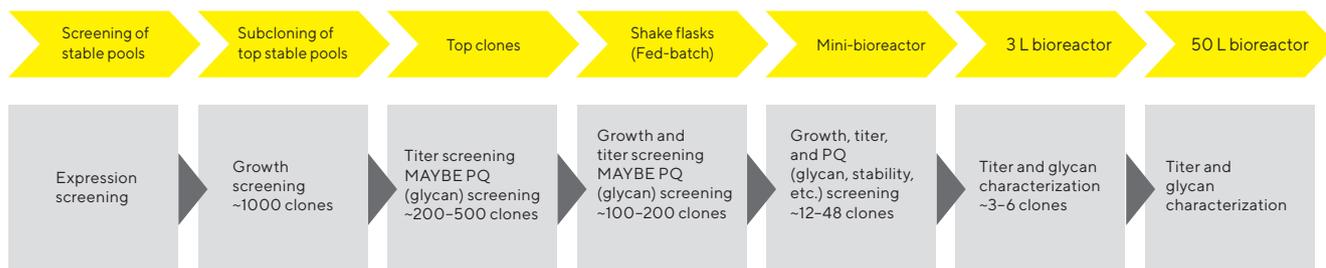


Figure 2: Typical clone selection and optimization workflow with typical screens/tests performed at each stage. Expression and titer are screened earlier in the workflow, while product quality (PQ) attributes are assessed later due to screening limitations.

# Relative Glycan Screening and Titer

Drug product glycosylation is a critical quality attribute (CQA) due to its potential impact on pharmacokinetics properties and stability of the product. The Sartorius Octet® GlyS and GlyM kits enable high-throughput relative screening of sialic acid and manose contents respectively in crude and purified samples (Figure 3). There is no need for sample purification or glycan digestion steps. 1000 clones can be screened in just under 10 hours on the Octet® RH96 system.

A combination of the Octet® GlyS and GlyM kits and Octet® ProA Biosensors, or any of the Sartorius quantitation biosensors can be used to perform titer and sialic acid content screening on the same samples using Octet® systems. Octet® Analysis Studio Software allows titer data to be combined with sialic acid and mannose content data (Figure 4). The ability to view and choose from desired titer and sialylation and mannose content levels at the same time provides more in-depth knowledge that facilitates more informed decisions. The software produces data and reports with these combined CQAs that can be used directly for further reporting.

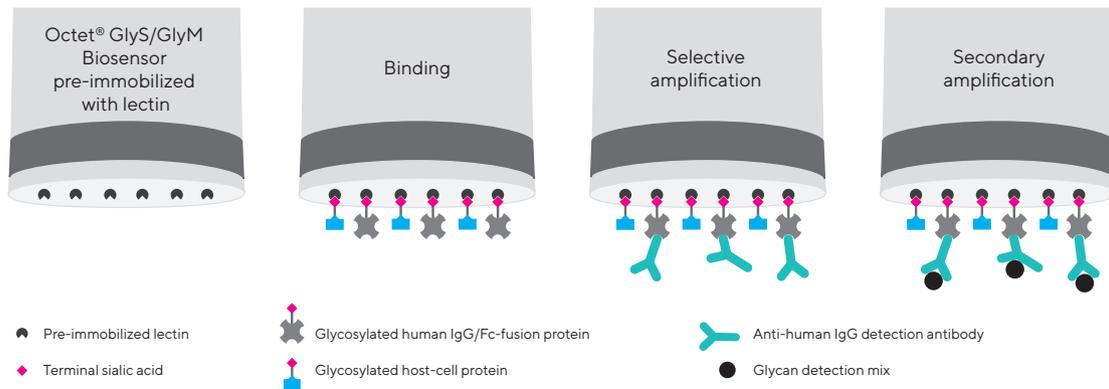


Figure 3: Example assay workflow for human IgG or human Fc-fusion proteins. Selective amplification of signal is from the protein of interest and not from host-cell proteins (HCP). Refer to the Octet® GlyS and GlyM user guides for additional protocols and assay guidelines.

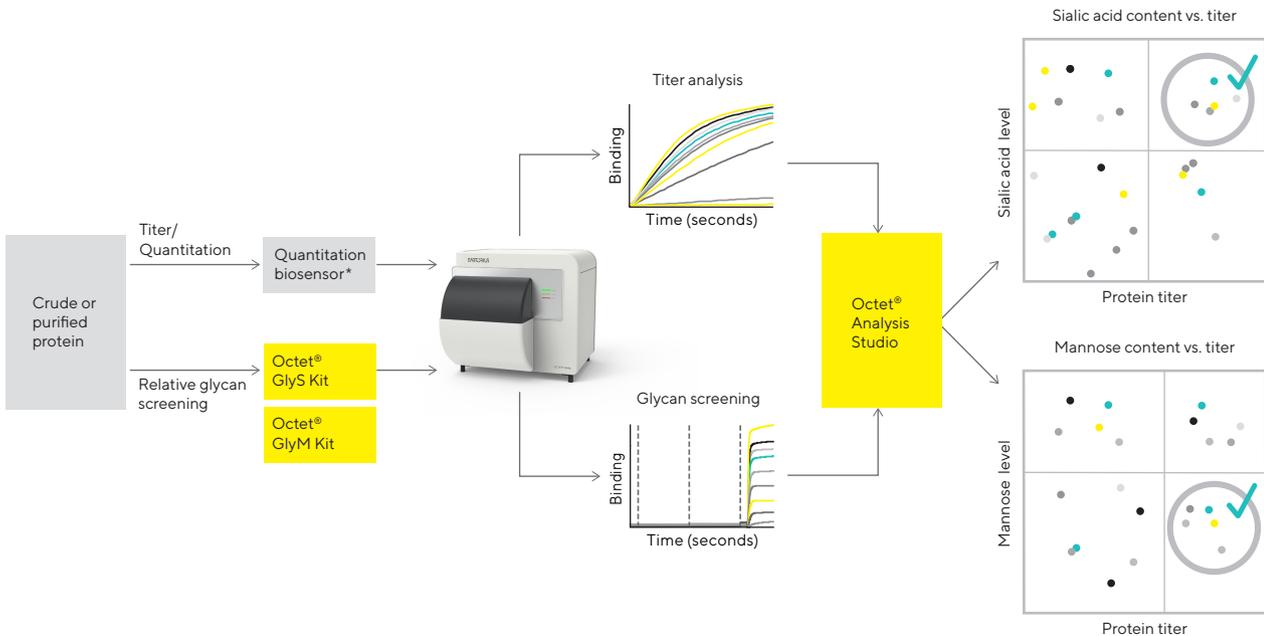


Figure 4: Workflow of titer analysis and glycan screening on the Octet® platform.

## Reference

1. Biolayer Interferometry as an Alternative to HPLC for Measuring Product Concentration in Fermentation Broth, Anurag S. et al., LCGC, Volume 35, Issue 12, 870-877.

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